frontiers | Research Topics

Innovative value-based medicine: lessons from China's healthcare evolution

Edited by
Kevin Lu, Gang Lv and Jing Yuan

Published in
Frontiers in Public Health
Frontiers in Health Services

FRONTIERS EBOOK COPYRIGHT STATEMENT

The copyright in the text of individual articles in this ebook is the property of their respective authors or their respective institutions or funders. The copyright in graphics and images within each article may be subject to copyright of other parties. In both cases this is subject to a license granted to Frontiers.

The compilation of articles constituting this ebook is the property of Frontiers.

Each article within this ebook, and the ebook itself, are published under the most recent version of the Creative Commons CC-BY licence. The version current at the date of publication of this ebook is CC-BY 4.0. If the CC-BY licence is updated, the licence granted by Frontiers is automatically updated to the new version.

When exercising any right under the CC-BY licence, Frontiers must be attributed as the original publisher of the article or ebook, as applicable.

Authors have the responsibility of ensuring that any graphics or other materials which are the property of others may be included in the CC-BY licence, but this should be checked before relying on the CC-BY licence to reproduce those materials. Any copyright notices relating to those materials must be complied with.

Copyright and source acknowledgement notices may not be removed and must be displayed in any copy, derivative work or partial copy which includes the elements in question.

All copyright, and all rights therein, are protected by national and international copyright laws. The above represents a summary only. For further information please read Frontiers' Conditions for Website Use and Copyright Statement, and the applicable CC-BY licence.

ISSN 1664-8714
ISBN 978-2-8325-7479-9
DOI 10.3389/978-2-8325-7479-9

Generative AI statement
Any alternative text (Alt text) provided alongside figures in the articles in this ebook has been generated by Frontiers with the support of artificial intelligence and reasonable efforts have been made to ensure accuracy, including review by the authors wherever possible. If you identify any issues, please contact us.

About Frontiers

Frontiers is more than just an open access publisher of scholarly articles: it is a pioneering approach to the world of academia, radically improving the way scholarly research is managed. The grand vision of Frontiers is a world where all people have an equal opportunity to seek, share and generate knowledge. Frontiers provides immediate and permanent online open access to all its publications, but this alone is not enough to realize our grand goals.

Frontiers journal series

The Frontiers journal series is a multi-tier and interdisciplinary set of open-access, online journals, promising a paradigm shift from the current review, selection and dissemination processes in academic publishing. All Frontiers journals are driven by researchers for researchers; therefore, they constitute a service to the scholarly community. At the same time, the *Frontiers journal series* operates on a revolutionary invention, the tiered publishing system, initially addressing specific communities of scholars, and gradually climbing up to broader public understanding, thus serving the interests of the lay society, too.

Dedication to quality

Each Frontiers article is a landmark of the highest quality, thanks to genuinely collaborative interactions between authors and review editors, who include some of the world's best academicians. Research must be certified by peers before entering a stream of knowledge that may eventually reach the public - and shape society; therefore, Frontiers only applies the most rigorous and unbiased reviews. Frontiers revolutionizes research publishing by freely delivering the most outstanding research, evaluated with no bias from both the academic and social point of view. By applying the most advanced information technologies, Frontiers is catapulting scholarly publishing into a new generation.

What are Frontiers Research Topics?

Frontiers Research Topics are very popular trademarks of the *Frontiers journals series*: they are collections of at least ten articles, all centered on a particular subject. With their unique mix of varied contributions from Original Research to Review Articles, Frontiers Research Topics unify the most influential researchers, the latest key findings and historical advances in a hot research area.

Find out more on how to host your own Frontiers Research Topic or contribute to one as an author by contacting the Frontiers editorial office: frontiersin.org/about/contact

Innovative value-based medicine: lessons from China's healthcare evolution

Topic editors

Kevin Lu — University of South Carolina, United States

Gang Lv — People's Liberation Army General Hospital, China

Jing Yuan — Fudan University, China

Citation

Lu, K., Lv, G., Yuan, J., eds. (2026). *Innovative value-based medicine: lessons from China's healthcare evolution*. Lausanne: Frontiers Media SA.

doi: 10.3389/978-2-8325-7479-9

Table of contents

frontiers | Frontiers in Public Health

TYPE Editorial
PUBLISHED 26 January 2026
DOI 10.3389/fpubh.2026.1783125

Check for updates

OPEN ACCESS

EDITED AND REVIEWED BY
Xiaozhen Lai,
Peking University, China

*CORRESPONDENCE
Jing Yuan
jingyuan@um.edu.mo
Z. Kevin Lu
lu32@email.sc.edu

RECEIVED 07 January 2026
ACCEPTED 12 January 2026
PUBLISHED 26 January 2026

CITATION
Lv G, Jiang X, Yuan J and Lu ZK (2026) Editorial: Innovative value-based medicine: lessons from China's healthcare evolution. *Front. Public Health* 14:1783125. doi: 10.3389/fpubh.2026.1783125

COPYRIGHT
© 2026 Lv, Jiang, Yuan and Lu. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

Editorial: Innovative value-based medicine: lessons from China's healthcare evolution

Gang Lv[1], Xiangxiang Jiang[2], Jing Yuan[3]* and Z. Kevin Lu[2]*

[1]Department of General Surgery, The First Medical Center of Chinese PLA General Hospital, Beijing, China, [2]Department of Clinical Pharmacy and Outcomes Sciences, College of Pharmacy, University of South Carolina, Columbia, SC, United States, [3]Institute of Chinese Medical Sciences, University of Macau, Taipa, Macau, China

KEYWORDS

China, cost-effectiveness, health policy, health system reform, value-based medicine

Editorial on the Research Topic
Innovative value-based medicine: lessons from China's healthcare evolution

Healthcare systems face a dual challenge of ensuring access to innovations while preserving financial sustainability, giving rise to value-based medicine (VBM), which balances clinical benefit and cost to optimize population health outcomes (1). Additionally, VBM aligns incentives among payers, providers, and patients by emphasizing outcomes, efficiency, and sustainability (1).

China offers a compelling case study in the global evolution of VBM (Table 1). Over the past decade, China has piloted strategies to balance innovation with sustainable financing, including reforms in hospital governance (2), introduction of novel drug payment mechanisms (2), and broader adoption of big data and artificial intelligence (AI) for monitoring costs and clinical outcomes. (3) These reforms highlight how large health systems apply VBM under demographic change, chronic disease growth, and equity demands.

A central element of China's VBM is transparent drug pricing and reimbursement negotiations. Through the National Reimbursement Drug List (NRDL) (4), bulk purchasing has made high-cost drugs more accessible. Simultaneously, payment reforms such as the Diagnosis-Intervention Packet (DIP) system (5) bundle payments to limit unnecessary use and improve efficiency. These reforms reflect a shift away from volume-based incentives and toward structures that prioritize clinical effectiveness and sustainability.

Another frontier of innovation in VBM is the incorporation of technology-driven insights. China's experience with electronic health records, big data, and AI illustrates the potential of digital infrastructure to support outcome measurement, identify inefficiencies, and forecast future healthcare needs. These tools enable more precise, equitable, and sustainable care. For instance, AI-powered models can stratify patients by risk and guide resource allocation, ensuring that interventions generate the greatest health return per unit cost (3).

China's experience reflects global debates on sustainable healthcare financing: high-income countries face the rising costs of biologics and gene therapies, while low- and middle-income nations struggle to expand access without straining budgets. Value-based approaches offer a common framework by linking innovation, outcomes, and affordability.

TABLE 1 Summary of studies on value-based medicine (VBM) in China.

Study	Focus	Study design	Main findings	VBM implications
Zuo et al.	Hospitalization patterns and costs in cross-border medical tourism for knee replacement	Retrospective cohort study using inpatient record data (2023–2024)	Cross-border patients had shorter length of stay and lower hospitalization costs; length of stay fully mediated cost differences, indicating higher care efficiency	Cross-border care integration may enhance value-based care by improving efficiency, reducing unnecessary resource use, and optimizing costs without compromising outcomes
Guanyi et al.	Relationship between buyer market power, spatial spillover effects, and pharmaceutical industry profitability in China	Empirical analysis using a spatial Durbin model on industry data (2001–2021)	Local buyer market power reduces local pharmaceutical firm profitability and exerts weak negative spillover effects on neighboring regions; supplier counter-power and firm size mitigate some impacts	The VBM policies should align purchasing power with performance-based pricing to sustain efficiency, competition, and long-term value creation
Zhao et al.	Determinants of primary care physicians' intention to provide breast cancer screening services for rural women	Cross-sectional survey of 1,101 primary care physicians using an extended theory of planned behavior model	Subjective norms most strongly predicted intention to provide screening, followed by attitudes and perceived behavioral control; screening knowledge and past behavior also influenced intentions indirectly	Supporting primary care physicians through training, social norms, and enabling resources can increase preventive screening uptake and improve value-based outcomes in underserved populations
Zhang H. et al.	Cost-effectiveness of durvalumab consolidation therapy after chemoradiation for stage III small-cell lung cancer in China	Markov model cost-utility analysis using data from the Phase III trial	Durvalumab improved survival but was not cost-effective at current prices in China, with ICER far above WTP thresholds; sensitivity emphasized drug price as key driver of economics	Balancing clinical benefit with price and reimbursement strategies is crucial to deliver high-value cancer care and ensure innovative therapies provide both health and economic value
Chen et al.	DRG payment reform and costs of lumbar disc herniation	Quasi-experimental (pre-post comparison) design using hospital inpatient records (2017–2022)	The DRG reform is associated with lower hospitalization costs and reduced costs for both Chinese medicine and Western medicine	True VBM in TCM hospitals requires linking payments to outcomes and tailoring reimbursement models to TCM's unique treatment characteristics
Zhang X. et al.	The optimal strategies for supplementing MAs with Internet-based healthcare	A two-stage queuing game-theoretic model	Supplementing MAs with internet hospitals can increase downward referral volume and provider effort under favorable cost, arrival rate, and revenue-sharing conditions, especially within tightly integrated alliances	Integrating digital health platforms into alliance networks can enhance value-based care by improving flow efficiency and resource allocation
Jiang et al.	The effect of China's NVBP policy exclusively for insulin	An interrupted time series analysis using procurement data (2020–2024)	NVBP policy significantly reduced insulin expenditure while improving treatment accessibility and affordability for insulin	NVBP advances VBM by reducing insulin costs and improving access while encouraging the use of cost-effective, higher-value therapies
Wang et al.	Cost-effectiveness of Xianling Gubao Capsules compared to Jintiange Capsules and non-treatment for postmenopausal osteoporosis	Markov model-based cost-effectiveness analysis using data from a network meta-analysis	The ICERs for the Jintiange capsule compared to the Xianling Gubao capsule ranged from $11,955 per QALY at age 55 to $9,711 per QALY at age 74	Integrating Chinese patent medicines supports VBM by emphasizing cost-effective treatments that improve patient outcomes and optimize healthcare resource use
Xu Y. et al.	Developing a standardized MCDA framework tailored for implantable medical devices in China	A mixed-methods design combining a discrete choice experiment and MCDA	Clinical safety (35.45%) and cost (27.94%) are the top-ranked criteria for implantable medical devices	Using MCDA framework can help guide implantable medical device evaluations toward transparent, evidence-driven, and outcome-oriented resource allocation decisions
Wu et al.	Service capacity of secondary hospitals in Guangzhou	Multi-method empirical design	Capacity improved overall, but disparities widened; shift to bimodal distribution	Governance and resource allocation must address efficiency and equity across tiers
Li	MAH system and ESG of pharmaceutical firms	Difference-in-differences using panel data (2012–2019)	MAH enhanced ESG via R&D, pay equity, supply chain; strongest in non-SOEs	Institutional innovation can align corporate behavior with sustainable health goals
Tao et al.	DIP reform and coronary heart disease costs	Interrupted time series analysis using claims data (2020–2023)	Costs and LOS declined, but divergent OOP effects by insurance type	Payment reforms improve efficiency but must be tailored to protect equity

(Continued)

TABLE 1 (Continued)

Study	Focus	Study design	Main findings	VBM implications
Chang et al.	Barriers/facilitators in DIP reform implementation	Qualitative case study using the CFIR framework, based on semi-structured interviews	Leadership and guidelines facilitated reform; staff resistance and resource strain hindered	Organizational readiness and adaptive capacity are essential for reform success
Hong et al.	Cost-effectiveness of rezvilutamide in prostate cancer	Markov model-based cost-effectiveness analysis using data from the CHART phase III clinical trial	Rezvilutamide added QALYs but not cost-effective at current pricing; would be cost-effective if priced below ~$705	Pricing strategies must align innovation with affordability
Liu et al.	Digital economy and cross-border supply chain resilience	Observational provincial panel analysis (2013–2022)	Digitalization strengthened resilience via diversification and reduced concentration; strongest in west	Digital infrastructure supports resilience and sustainable access
Yang et al.	Cost-effectiveness of toripalimab in ES-SCLC	Partitioned survival model using data from the phase III EXTENTORCH trial	Cost-effective in China ($29k/QALY) but not in US ($916k/QALY)	Cost-effectiveness is context-specific, requiring alignment with local thresholds
Xu H. et al.	DIP reform and cancer costs (hematologic vs solid tumors)	Retrospective, single-center observational study	Costs declined post-reform, but hematology care exceeded reimbursement, causing deficits	Payment standards must reflect clinical complexity to ensure sustainability

VBM, value-based medicine; ICER, incremental cost-effectiveness ratio; WTP, willingness-to-pay; DRG, Diagnosis-Related Groups; TCM, Traditional Chinese Medicine; MAs: medical alliances; NVBP, National Volume-Based Procurement; QALY, quality-adjusted life year; MCDA: multicriteria decision analysis; DIP, diagnosis-intervention packet; CHD, coronary heart disease; CFIR, Consolidated Framework for Implementation Research; MAH, Marketing Authorisation Holder; ESG, environmental, social, and governance; SOE, state-owned enterprise; LOS, length of stay; ES-SCLC, extensive-stage small-cell lung cancer.

This Research Topic adds valuable evidence from China, spanning hospital governance, drug pricing, supply chains, and oncology cost-effectiveness, highlighting both the promise and complexity of implementing VBM. Collectively, these studies provide a roadmap for policymakers and clinicians to balance innovation and sustainability in China and beyond.

Zhao et al. examined determinants of physicians' willingness to provide preventive services and found that intentions are shaped by norms and capacity, implying that supportive environments and digital technologies can strengthen sustainable, value-based health systems.

Chen et al. analyzed Diagnosis-Related Groups (DRG) reform effects on lumbar disc herniation patients, and found reduced hospitalization and drug costs. This study suggests that to advance VBM, payment reforms must better align with Traditional Chinese Medicine (TCM) treatment characteristics and outcome-based incentives.

Jiang et al. used interrupted time series analysis of Guangdong's insulin procurement data and found that China's National Volume-Based Procurement (NVBP) policy significantly increased insulin use while reducing total spending and unit costs. These results suggest that centralized procurement can enhance VBM by improving affordability and access without compromising treatment availability.

Xu Y. et al. established a multicriteria decision analysis framework for evaluating implantable medical devices in China, and they found that clinical safety and cost were the most influential criteria, highlighting the framework's potential to promote transparent, VBM allocation.

Wu et al. assessed the service capacity of public hospitals and found that while overall service capacity improved, disparities between hospitals widened, mainly due to inter-group differences. The authors suggest strengthening coordination, optimizing resource allocation, and improving performance evaluation to promote more balanced, value-based hospital development.

Li found that China's Marketing Authorization Holder system significantly improved pharmaceutical firms' environmental, social, and corporate governance performance by boosting investment and reducing internal inequality, supporting more sustainable, value-based industry development.

Tao et al. analyzed data from 264 hospitals and found that China's DIP reform significantly reduced hospitalization costs and length of stay for coronary heart disease patients. However, differences in out-of-pocket ratios between insurance types highlight the need to balance efficiency gains with equity in value-based payment reforms.

Chang et al. conducted qualitative interviews and found leadership support and clear guidelines that facilitated DIP reform, while resource constraints and staff resistance hindered their adoption. The study recommends strengthening internal management, communication, and staff training, underscoring that successful VBM reform requires organizational readiness and adaptive capacity alongside policy design.

Liu et al. assessed the digital economy's impact on resilience and found that digitalization strengthens resilience by reducing trade dependence, increasing export complexity, and lowering concentration. The study illustrates how digital infrastructure supports continuity of care and economic stability, extending VBM to the domain of global supply chain sustainability.

Xu H. et al. evaluated DIP reform's impact on costs for hematologic malignancies (HM). While overall costs decreased, HM treatments remained above reimbursement standards. This underscores the need to refine payment standards to reflect clinical

complexity and resource intensity, ensuring departments remain financially viable.

Additionally, Zhang H. et al., Wang et al., Hong et al., and Yang et al. conducted cost-effectiveness analyses of oncology, immunotherapy, and pharmaceutical interventions, showing that clinical benefits often depend on price levels and reimbursement thresholds, underscoring the importance of price negotiation for realizing value. Zuo et al. demonstrated that cross-border knee replacement care achieved lower costs through shorter length of stay, highlighting efficiency gains from system integration. Guanyi et al. found that excessive buyer market power may suppress pharmaceutical profitability, suggesting the need to balance affordability with innovation incentives. Zhang X. et al. showed that integrating internet hospitals into medical alliances can improve referral efficiency and stakeholder value under appropriate cost-sharing arrangements, supporting value-based care by optimizing resource allocation and access across healthcare tiers.

Conclusion

These studies show how China's healthcare reforms serve as laboratories for value-based models and illustrate the diverse domains where VBM principles apply. Key lessons include the need for equity-sensitive design, the role of technology in resilience, and the importance of aligning pricing and reimbursement with clinical and economic realities.

As health systems worldwide face rising costs and unequal access, these findings stress that value-based medicine is not monolithic but a flexible, context-sensitive paradigm. Integrating lessons from China with global best practices can help build systems that are innovative, equitable, and sustainable.

Author contributions

GL: Writing – original draft, Writing – review & editing, Conceptualization, Validation. XJ: Writing – original draft, Writing – review & editing. JY: Writing – original draft, Writing – review & editing, Conceptualization, Investigation, Supervision, Validation. ZL: Investigation, Supervision, Writing – original draft, Writing – review & editing, Methodology, Resources.

Conflict of interest

The author(s) declared that this work was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The author(s) declared that generative AI was not used in the creation of this manuscript.

Any alternative text (alt text) provided alongside figures in this article has been generated by Frontiers with the support of artificial intelligence and reasonable efforts have been made to ensure accuracy, including review by the authors wherever possible. If you identify any issues, please contact us.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

References

1. Teisberg E, Wallace S, O'Hara S. Defining and implementing value-based health care: a strategic framework. *Acad Med May.* (2020) 95:682–5. doi: 10.1097/ACM.0000000000003122

2. Jakovljevic M, Chang H, Pan J, Guo C, Hui J, Hu H, et al. Successes and challenges of China's health care reform: a four-decade perspective spanning 1985-2023. *Cost Eff Resour Alloc Aug 30.* (2023) 21:59. doi: 10.1186/s12962-023-00461-9

3. Qi Y, Mohamad E, Azlan AA, Zhang C. Utilization of artificial intelligence in clinical practice: a systematic review of China's experiences. *Digit Health Jan-Dec.* (2025) 11:20552076251343752. doi: 10.1177/20552076251343752

4. Zhu Z, Zhang J, Xu Z, Wang Q, Qi W, Yang L. Impacts of National Reimbursement Drug Price Negotiation on drug accessibility, utilization, and cost in China: a systematic review. *Int J Equity Health.* (2025) 24:36. doi: 10.1186/s12939-025-02390-w

5. Ding Y, Yin J, Zheng C, Dixon S, Sun Q. The impacts of diagnosis-intervention packet payment on the providers' behavior of inpatient care-evidence from a national pilot city in China. *Front Public Health.* (2023) 11:1069131. doi: 10.3389/fpubh.2023.1069131

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 07 May 2025
DOI 10.3389/fpubh.2025.1453367

Check for updates

OPEN ACCESS

EDITED BY
Xiaozhen Lai,
Peking University, China

REVIEWED BY
Karolina Sobczyk,
Medical University of Silesia, Poland
Valentin Marian Antohi,
Dunarea de Jos University, Romania
Xinyi Xu,
Guangxi Medical University, China

*CORRESPONDENCE
Linjun Xie
xielj18@gmail.com
Shaogui Zhang
zsg2005048@163.com

†These authors have contributed equally to this work and share first authorship

RECEIVED 23 June 2024
ACCEPTED 25 April 2025
PUBLISHED 07 May 2025

CITATION
Xu H, She Q, Zhang B, Zhang S and Xie L (2025) The impacts of diagnosis-intervention packet payment on inpatient medical costs for hematologic malignancies and solid tumors: evidence from a retrospective study in China. *Front. Public Health* 13:1453367. doi: 10.3389/fpubh.2025.1453367

COPYRIGHT
© 2025 Xu, She, Zhang, Zhang and Xie. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

The impacts of diagnosis-intervention packet payment on inpatient medical costs for hematologic malignancies and solid tumors: evidence from a retrospective study in China

Huiping Xu[1†], Qunqing She[1†], Beibei Zhang[1], Shaogui Zhang[1*] and Linjun Xie[1,2*]

[1]The First Hospital of Putian City, Putian, China, [2]The School of Clinical Medicine, Fujian Medical University, Fuzhou, China

Background: This study aims to analyze and compare the impact of the diagnosis-intervention packet (DIP) payment on inpatient medical costs for hematologic malignancies (HM) and solid tumors (ST) patients, and to explore its implications for hospital financial sustainability and payment reform.

Methods: Using a retrospective research design, this study focused on HM and ST patients treated before and after the implementation of the DIP payment at a large tertiary general hospital in A city, located in the eastern coastal area of China. Data were collected, organized, and analyzed to compare differences in inpatient medical costs between HM and ST patients and to examine their impact on the income of the department of hematology.

Results: The study included 5,115 cases from both before and after the DIP payment implementation. Post-implementation, the median inpatient medical costs per case decreased from 5,544.45 CNY to 5,169.66 CNY, with costs for both HM and ST hospitalizations showing a decline. Specifically, the inpatient medical costs per case for HM were 5,722.46 (4,471.08, 11,508.78) CNY, higher than those for ST at 4,779.28 (3,056.70, 7,152.64) CNY, and exceeding the DIP payment standard. Wilcoxon signed-rank test and regression analysis indicated that HM inpatient medical costs surpass the standard payments, resulting in financial losses. All findings were statistically significant ($p < 0.05$). These results suggest a structural mismatch between DIP reimbursement rates and the resource intensity of hematologic malignancy treatment, which may jeopardize the financial viability of hematology departments.

Conclusion: Despite a reduction in median inpatient medical costs following the implementation of the DIP payment, departments treating HM patients continue to experience financial losses due to costs exceeding the payment standard. These findings highlight the need to refine DIP payment standards to better account for clinical complexity and technological advancements. Future reforms should aim to improve alignment between payments and actual care needs to ensure financial sustainability and equity. However, this study is limited by its single-center design and lack of control for potential confounders.

Broader multi-center studies with more detailed clinical data are needed to validate and extend these findings.

KEYWORDS

diagnosis-intervention packet, hematologic malignancies, solid tumors, inpatient medical costs, China

1 Introduction

In recent years, as healthcare costs have risen and resource allocation has become more complex, diagnosis-related group (DRG) payment systems have gained increasing attention and widespread use globally (1). Initially proposed in the United States and subsequently implemented in many European and American countries, DRG systems have demonstrated significant effectiveness in controlling hospital costs, optimizing health insurance payments, and improving the efficiency of healthcare services (2, 3). To curb the rapid growth of healthcare expenditures, China introduced the diagnosis-intervention packet (DIP) payment system in 2020 (4). The DIP payment system, while similar to DRG system, distinguishes itself by emphasizing the integration of primary diagnoses and treatment methods through big data analysis. By establishing case combinations and payment standards, a unified standard system and resource allocation model were created to enhance the efficiency of health insurance fund utilization, rationally guide the allocation of healthcare resources, and ensure the basic medical needs of insured individuals. This innovative case-based payment method aims to replace the traditional fee-for-service model and address issues related to the DRG system's coverage and demand behavior (5, 6).

After the implementation of the DIP payment system in China, research has shown that it effectively curbed the growth of healthcare expenditures, promoted the rational allocation of healthcare resources, and reduced unreasonable practices such as overtreatment and induced demand (7–9). However, the majority of these studies have concentrated on the system's overall economic impact and operational feasibility, with limited attention paid to patient subgroups with rare or high-cost diseases. For instance, hematologic malignancies (HM) are a minority within the category of malignant tumors and are grouped together with the entire oncology population under the DIP payment system. The policy sets a standardized payment amount for patients with previously diagnosed malignant tumors undergoing maintenance chemotherapy, without differentiating between HM and solid tumors (ST) despite significant disparities in their pathophysiology, treatment regimens, and inpatient medical costs (10, 11). This raises important concerns about fairness in health financing under the DIP payment system. The existing literature has not adequately explored whether the "averaging effect" inherent in big-data-driven payment systems may unintentionally disadvantage vulnerable populations such as HM patients.

In this context, this study selects a large tertiary general hospital (referred to as Hospital A) in A City, a pilot city for DIP payment reform in the eastern coastal area of China, as a case study. The aim is to investigate the trends and differences in inpatient medical costs for HM and ST patients under the DIP payment system and to analyze its impact on the revenue of the department of hematology. The findings intend to inform more equitable payment reforms that better align reimbursement standards with clinical realities and patient needs.

2 Methods

2.1 Study design

This study adopted a retrospective design based on inpatient data from Hospital A. Hospital A is a Class A tertiary hospital with over 1,500 beds and comprehensive clinical departments, including a well-established hematology unit with a high volume of HM cases. As one of the early pilot institutions for the DIP payment reform, Hospital A was selected due to its policy representativeness and the availability of complete and continuous DIP payment data both before and after the policy implementation, which allowed for a longitudinal assessment of its impact. Leveraging this dataset, the study focused on comparing inpatient medical costs between patients with HM and those with ST under the DIP payment system, and further explored the financial implications for the hematology department.

2.2 Data sources

This study utilized hospital admission records from Hospital A for HM and ST patients treated between 2021 and 2023, encompassing patient characteristics, hospitalization duration, diagnoses, and inpatient costs. 2022 marked the DIP implementation transition; 2021 and 2023 data served as pre- and post-implementation samples, respectively (note: some HM cases originated from departments outside hematology). The study also analyzed 2023 revenue details of Hospital A's hematology department under the DIP payment system.

2.3 Sample selection

Inclusion criteria for this study were as follows: (1) Patients diagnosed with HM or ST, with HM types including acute leukemia (AL), lymphoma, and multiple myeloma (MM); (2) Primary diagnosis on the first page of the medical record indicating maintenance chemotherapy for malignant tumors (Z51.103), tumor chemotherapy course (Z51.100), malignant tumor immunotherapy (Z51.800), or targeted therapy for malignant tumors (Z51.801); (3) Availability of complete clinical records and treatment documentation. Exclusion criteria included: (1) Discharge within 24 h without complete clinical data; (2) Presence of severe chronic diseases or complications resulting in hospital stays exceeding 45 days; (3) Single hospitalization costs exceeding CNY 180,000; (4) Cases requiring intensive care or multidisciplinary treatment.

2.4 Statistical analysis

Data processing utilized Python version 3.12 with pandas and SciPy libraries. Categorical data were summarized with counts and percentages, analyzed using chi-square tests. Normally distributed continuous data were presented as mean ± standard deviation and compared using independent or paired t-tests. Non-normally distributed continuous data were expressed as median (Q1, Q3) and analyzed with Mann–Whitney U or Wilcoxon signed-rank tests. Matplotlib and seaborn libraries facilitated data visualization. Statistical significance was defined as $p < 0.05$.

2.5 Ethical considerations

Patient privacy and confidentiality were paramount throughout this study. All patient information was de-identified and securely managed. Access to data was restricted to authorized personnel only, and electronic medical records were stored on a password-protected secure server. Data analysis was conducted in aggregate form to prevent the identification of individual patients.

3 Results

3.1 Overall trends in hospitalization days and costs pre- and post-DIP payment implementation

This study included 2,247 cases before and 2,868 cases after the implementation of DIP payment in the city A. There were no significant differences in gender and age between the two groups, with a median hospitalization duration of 5 days for both groups. The median inpatient medical costs per case decreased from 5,544.45 (3,449.39, 8,960.18) CNY in 2021 to 5,169.66 (3,184.57, 7,657.74) CNY in 2023, representing a statistically significant 6.76% reduction ($p < 0.001$). Regarding the cost structure, medical service and consumables costs increased, while treatment, western medicine, and other costs decreased ($p < 0.001$). Detailed breakdown and changes in cost structure for both groups are shown in Table 1.

3.2 Subgroup comparison between HM and ST groups

The two groups of patients were divided into HM and ST groups, with 246 cases in the HM group and 2,001 cases in the ST group before the implementation of DIP payment. After implementation, there were 606 cases in the HM group and 2,262 cases in the ST group. Implementation of DIP payment led to statistically significant reductions in both inpatient medical and western medicine costs for both the HM and ST groups compared to pre-implementation levels ($p < 0.05$). Additionally, it can be observed that the cost distribution in the HM group exhibits a distinct bimodal pattern compared to the ST group (Figures 1A–D).

Before and after the implementation of the DIP payment system, there were no significant differences in gender and age characteristics between HM and ST patients. In 2021, patients in the HM group had a median hospitalization duration of 7 days and median inpatient medical costs of 8,459.62 CNY, both significantly higher than those in the ST group ($p < 0.001$). The median western medicine cost per case for HM patients was also notably higher, at 4,951.32 CNY ($p < 0.001$). By 2023, the median hospitalization duration for the HM group had decreased to 3 days, shorter than that of the ST group. Median inpatient medical costs per case declined to 5,722.46 CNY, while western medicine costs slightly increased to 4,966.32 CNY. Despite the overall reductions in hospitalization duration and total inpatient costs, western medicine costs for HM patients remained significantly higher than those in the ST group ($p < 0.001$). Detailed data are presented in Table 2.

3.3 Subgroup comparison within the HM group

Before and after the implementation of the DIP payment system, both the inpatient medical costs and western medicine costs per case

TABLE 1 Trend analysis of inpatient medical costs per case and structural changes pre- and post-DIP payment implementation (costs in CNY).

Characteristics	Pre-DIP payment (2021)	Post-DIP payment (2023)	Difference	*p*
Female (%)	1,018 (45.30%)	1,311 (45.71%)	–	0.794
Age (years)	62.30 ± 11.38	62.53 ± 11.19	–	0.455
Hospitalization days	5.00 (3.00, 8.00)	5.00 (2.00, 8.00)	–	–
Medical service costs	340.00 (166.75, 525.50)	447.50 (199.38, 865.08)	31.62%	<0.001
Diagnostic costs	893.00 (549.50, 1800.50)	900.75 (508.00, 1840.38)	0.87%	0.366
Treatment costs	186.10 (89.20, 320.35)	0.00 (0.00, 123.78)	−100.00%	<0.001
Western medicine costs	3082.57 (1504.26, 6189.44)	2591.12 (1218.99, 5176.36)	−15.94%	<0.001
Traditional Chinese medicine costs	0.00 (0.00, 55.50)	0.00 (0.00, 0.00)	–	–
Blood products costs	0.00 (0.00, 0.00)	0.00 (0.00, 0.00)	–	–
Consumables costs	40.76 (0.00, 260.66)	68.12 (29.01, 123.14)	67.14%	<0.001
Other costs	126.00 (72.00, 227.13)	0.00 (0.00, 72.00)	−100.00%	<0.001
Inpatient medical costs (Total costs)	5544.45 (3449.39, 8960.18)	5169.66 (3184.57, 7657.74)	−6.76%	<0.001

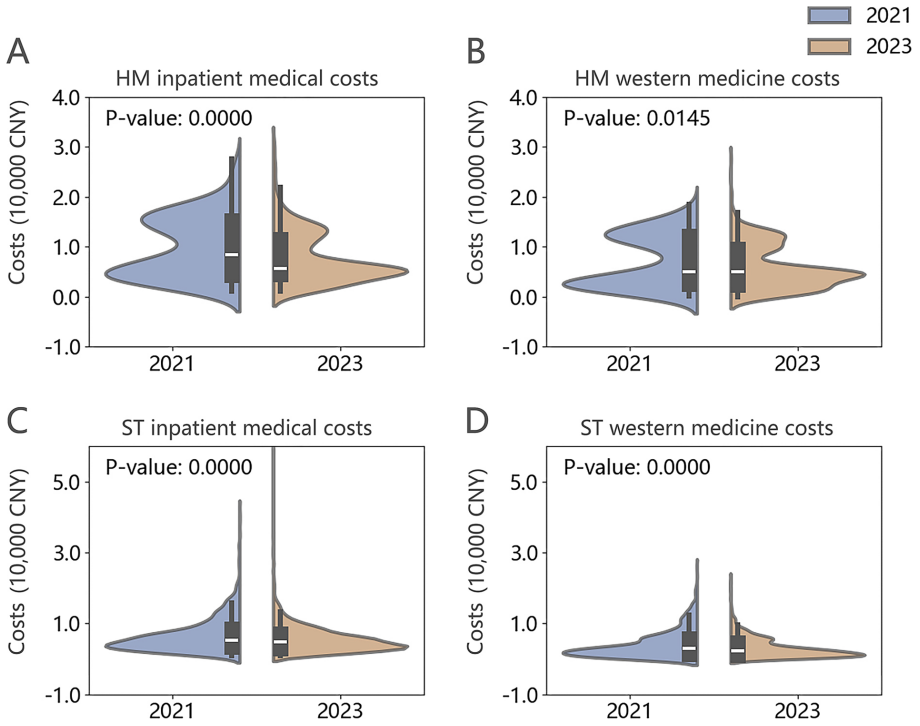


FIGURE 1
(A–D) Violin plots of inpatient medical and western medicine costs per case for HM and ST groups in 2021 and 2023.

TABLE 2 **Comparison of hospitalization days and inpatient medical costs per case between HM and ST groups pre- and post-DIP payment implementation (costs in CNY).**

	Pre-DIP payment (2021)			Post-DIP payment (2023)		
	HM	ST	*p*	HM	ST	*p*
Female (%)	105 (42.68%)	913 (45.63%)	0.419	285 (47.03%)	1,026 (45.36%)	0.492
Age (years)	61.28 ± 13.27	62.42 ± 11.12	0.136	63.06 ± 11.62	62.39 ± 11.07	0.191
Hospitalization days	7.00 (4.00, 9.00)	5.00 (3.00, 8.00)	<0.001	3.00 (1.00, 7.00)	5.00 (2.00, 8.00)	<0.001
Inpatient medical costs	8459.62 (4291.66, 15211.18)	5379.33 (3350.56, 8379.23)	<0.001	5722.46 (4471.08, 11508.78)	4779.28 (3056.70, 7152.64)	<0.001
Western medicine costs	4951.32 (2515.50, 12091.61)	2899.93 (1403.14, 5836.70)	<0.001	4966.32 (2383.89, 9490.56)	2278.44 (1044.07, 4496.58)	<0.001

for the HM group decreased, with Mann–Whitney U test analysis indicating statistically significant differences. Analysis of case composition within the HM group in 2023 revealed a notable increase in MM cases, accompanied by a rise in both median inpatient medical and western medicine costs. However, these differences were not statistically significant. Conversely, lymphoma cases showed a decrease in both inpatient medical and western medicine costs ($p < 0.05$). Detailed data can be found in Table 3.

3.4 Analysis of the relationship between costs, hospitalization days, and age in the HM group, and intra-group differences

Analysis of scatter plots and fitted lines for inpatient medical and western medicine costs within the HM group in 2021 and 2023 (Figures 2A–D) revealed a positive correlation with hospitalization days, although the slopes differed between years. Notably, there was an increase in MM cases in 2023, concentrated among individuals aged 40–60. While no overall age trend was observed, specifically, lymphoma costs in 2021 showed a positive correlation with age, while MM costs in 2023 exhibited a negative correlation with age (Figures 2C,D, $p < 0.05$). Further analysis within the HM group demonstrated statistically significant differences in inpatient medical and western medicine costs across different subtypes of HM (Figures 2E,F).

3.5 Analysis of the 2023 financial balance in the department of hematology under the DIP payment system

In 2023, a total of 1,429 cases from the Department of Hematology were included in the analysis, with total inpatient medical costs reaching 8,935,167.84 CNY and corresponding DIP standard

TABLE 3 General information of cases in HM group (costs in CNY).

		Pre-DIP payment (2021)	Post-DIP payment (2023)	*p*
AL	Cases	39 (15.85%)	46 (7.59%)	–
	Inpatient medical costs	6034.18 (3251.88, 8154.86)	6015.36 (4876.62, 8164.05)	0.182
	Western medicine costs	4164.89 (1967.29, 4994.85)	4007.58 (2893.49, 5188.91)	0.390
Lymphoma	Cases	170 (69.11%)	220 (36.30%)	–
	Inpatient medical costs	13264.41 (5949.89, 16462.09)	11319.76 (5974.81, 13834.43)	0.002
	Western medicine costs	11146.55 (2657.63, 13105.66)	9632.50 (3844.62, 12003.49)	0.046
MM	Cases	37 (15.04%)	340 (56.11%)	–
	Inpatient medical costs	4016.11 (3430.16, 6281.97)	5215.74 (3012.97, 5957.96)	0.107
	Western medicine costs	3217.52 (2343.36, 4553.01)	4201.37 (1609.64, 5154.28)	0.061
Total	Inpatient medical costs	8459.62 (4291.66, 15211.18)	5722.46 (4471.08, 11508.78)	<0.001
	Western medicine costs	4951.32 (2515.50, 12091.61)	4966.32 (2383.89, 9490.56)	0.015

payments amounting to 8,398,670.79 CNY. This resulted in an overall departmental deficit of 536,497.05 CNY, among which 529 cases were attributed to the HM group (Figure 3A). For the HM group, total inpatient medical costs were 3,827,303.52 CNY, while DIP standard payments amounted to 3,363,359.22 CNY, leading to a deficit of 463,944.30 CNY—accounting for 86.48% of the department's total loss.

At the case level, the median inpatient medical cost per HM case was 5,540.46 CNY (4,350.89, 10,198.37), compared to a median DIP standard payment of 6,300.00 CNY (3,560.37, 8,250.00). Although the median standard payment was marginally higher, the wider interquartile range suggests that actual inpatient costs often exceeded reimbursement. The Shapiro–Wilk test indicated a non-normal distribution of cost differences, which was further supported by a statistically significant result from the Wilcoxon signed-rank test (Figure 3B).

A scatter plot illustrating inpatient medical costs versus standard payments revealed a negatively sloped fitted line, suggesting that higher inpatient expenditures were associated with greater financial deficits (Figure 3C, $p < 0.05$). Notably, the bimodal distribution observed in the HM group's cost structure may be a contributing factor to this imbalance.

4 Discussion

President Xi Jinping has pointed out, "The principal contradiction in Chinese society has evolved into the contradiction between the people's ever-growing needs for a better life and unbalanced and inadequate development (12)." This perspective is also reflected in medical diagnosis and treatment. The increasing demand for novel and efficient treatment methods by patients has resulted in a significant gap between the allocation of medical resources and the pace of technological advancements (13, 14). In "Contradiction Theory," Comrade Mao Zedong emphasized that contradictions are ubiquitous and serve as the fundamental driving force for development. In recent years, China has significantly increased healthcare expenditure, expanded healthcare coverage, and established special funds to pay for high-value drugs and innovative medicines (15). Additionally, national centralized drug procurement and price negotiations have substantially reduced drug prices, gradually alleviating the financial burden on patients during treatment (16). Moreover, DIP payments have leveraged the characteristics of China's medical resources. Through big data analysis and intelligent algorithms, DIP payments achieve precise classification of diseases and optimized allocation of resources, showing great potential in promoting the rational use of medical resources and enhancing service levels (17).

City A was chosen as a pilot city for the total budget model, utilizing regional point methods and DIP payments, beginning trial implementation in 2022. Our research demonstrates that after the implementation of the policy, both the inpatient medical and western medicine costs at Hospital A have decreased, while medical service fees have increased, consistent with reports from other studies in China (7, 8). Zhang et al. (18) also examined the impact of the DIP payment policy on hospitalization costs for cancer patients, reporting a significant reduction in total inpatient expenses, particularly in drug-related costs. At the same time, expenditures on technical medical services increased, suggesting a gradual shift toward value-based healthcare. These findings align with our results, indicating that the DIP model may effectively curb irrational drug use and incentivize hospitals to reallocate resources toward professional service provision. Similarly, Liu et al. (19) found that the DRG-based payment reform in China contributed to shorter average lengths of stay and lower hospitalization costs, demonstrating comparable cost-containment outcomes under different payment models. However, the emergence of similar results across diverse regions and reform types raises concerns about potential unintended consequences, such as cost-shifting behaviors or selective admission practices (20, 21). This highlights the importance of enhancing the dynamic adjustment of point-value standards and reinforcing supervision mechanisms to ensure that payment reforms lead to sustainable and equitable improvements in healthcare delivery.

Unlike most existing studies that primarily assess the overall impact of DIP reform at the hospital or regional level, this study innovatively focuses on disease-specific cost disparities, particularly between HM and ST patients, which have received limited attention in prior research. Our analysis found that while inpatient medical and Western medicine costs for the HM group have decreased compared to previous periods, they remain significantly higher than those for

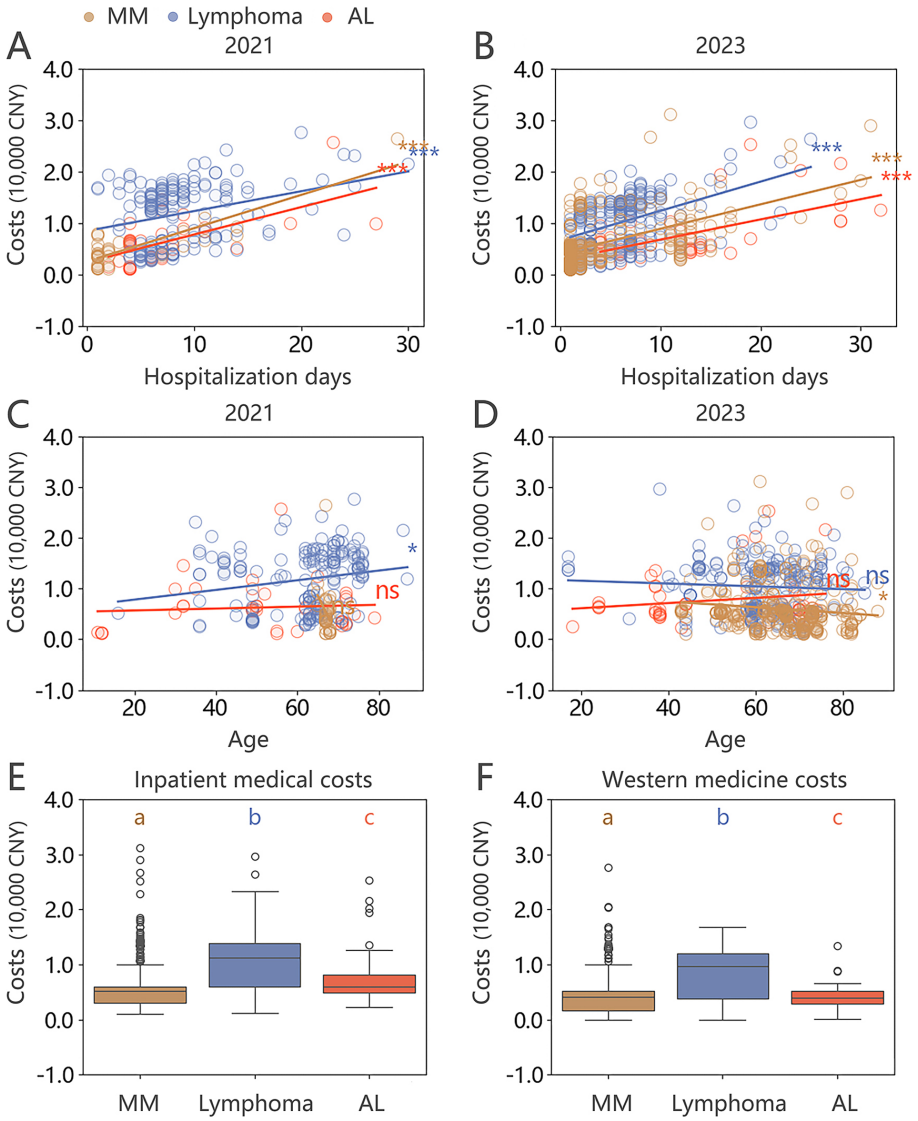


FIGURE 2
(A–D) Scatter plots and fitted lines for hospitalization days, age, and inpatient medical costs per case in the HM group for 2021 and 2023 (Mann–Whitney U test: ns no statistical significance; * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$). **(E,F)** Box plots of inpatient medical costs and western medicine costs for different types of HM in 2023, with Mann–Whitney U test indicating significant differences between each subgroup (denoted by abc, $p < 0.05$).

the ST group. The treatment methods for ST are relatively mature, leading to more stable cost growth, whereas the diagnosis and treatment of HM have progressed rapidly (11). The swift advancement in targeted and immunotherapeutic strategies has markedly augmented personalized treatments for HM, leading to impressive improvements. Innovations such as CAR-T cell therapy and cutting-edge targeted medications, including Bruton's tyrosine kinase inhibitors, Bcl-2 inhibitors, and CD38 monoclonal antibodies, have the potential to significantly boost survival rates and the quality of life for patients (22–25). Nonetheless, these pioneering treatments tend to be costly, precipitating a sharp increase in the expenses associated with HM treatment. It is noteworthy that, despite a reduction in expenses for other cancer types such as AL and lymphoma, there has been a notable escalation in the number of MM instances, along with the median costs. This trend could be attributed to an increased prevalence of MM, updates in treatment regimens, and the introduction of new pharmaceuticals (26, 27). While the advent of these novel therapeutic options and drugs enhances treatment efficacy, it concurrently escalates the treatment expenditure.

The DIP payment system utilizes a total budget model, assigning a point value to each medical institution based on annual medical insurance payments, insurance payment ratios, and overall case scores. This system establishes standardized payments per case. Currently, this policy determines scores and makes DIP standard payments for the maintenance treatment of various types of malignant tumors based solely on different treatment methods. However, payment standards based solely on historical costs may not adequately account for the rapid advancements in HM treatments, potentially resulting in underpayments (28). Our study corroborated this concern. In 2023, after the implementation of the

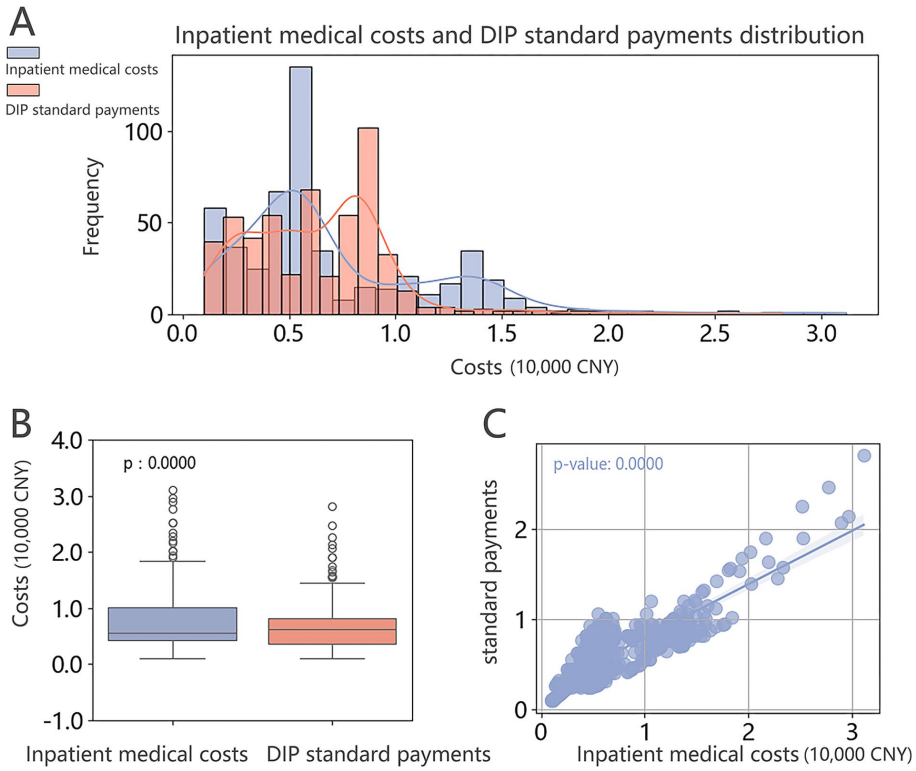


FIGURE 3
Comparison of inpatient medical costs and DIP standard payments per case in the HM group. **(A)** Distribution plot; **(B)** Box plot showing the median and interquartile range, with the Wilcoxon signed-rank test indicating statistically significant differences between groups. **(C)** Scatter plot with fitted line showing the trend.

DIP payment system, the hematology department of Hospital A experienced a loss of 463,944.3 yuan in the HM group, accounting for 86.48% of the total loss. If this situation persists, the actual costs of medical services cannot be effectively compensated, which may demotivate frontline medical staff and affect the quality of medical services, as well as the sustainable development of the deficit department. Ensuring fair reimbursement for these two types of tumors within the DIP payment framework has become a pressing issue that needs to be addressed.

Contradictions exhibit both universality and particularity. The unique clinical and economic challenges associated with the treatment of HM, in contrast to ST, are clearly reflected in the substantial financial losses faced by hematology departments under the current DIP system. To address this specific issue, it is essential to adjust medical insurance payment standards accordingly. In this regard, international DRG-based payment systems offer valuable lessons. For example, Germany's G-DRG system incorporates patient clinical complexity levels that account for comorbidities and complications, allowing for differentiated reimbursement even within the same diagnosis group (29). For advanced therapies like CAR-T and allo-HSCT, DRG-based reimbursement varies considerably, and the use of comorbidity indices such as the Charlson Comorbidity Index improves the assessment of clinical complexity, length of stay, and total treatment costs (30). These mature systems demonstrate that incorporating severity and treatment complexity indicators is critical to achieving both payment fairness and efficiency. In contrast, China's DIP system still lacks sufficient risk adjustment mechanisms, which may result in undercompensation for resource-intensive subgroups like HM patients.

Therefore, future reforms should focus on refining DIP grouping and scoring rules by integrating indicators of clinical severity, treatment intensity, drug specificity, and supplementary scores based on tumor characteristics (e.g., secondary diagnoses). This would improve the alignment between reimbursement levels and actual resource consumption. Such reforms would help capture evolving clinical practices more accurately, promote rational resource allocation, and better support the delivery of high-quality care.

This study relied solely on data from a single tertiary hospital due to limitations in data access. This single-center design presents several challenges, including limited sample representativeness, a restricted study period, potential concerns about data integrity and quality, and an insufficient exploration of diverse treatment approaches. In addition, the study lacked control for potential confounding factors, such as variations in disease severity, treatment regimens, or patient socioeconomic status, which may have influenced cost outcomes. These limitations may affect the generalizability and reliability of the findings. Future research should address these issues by incorporating data from multiple centers, extending the study duration, applying multivariable analytical approaches to control for confounders, and enhancing data quality.

Such improvements will provide a more robust foundation for evidence-based medical decision-making.

5 Conclusion

This study offers a comprehensive analysis of the effects of DIP payments on inpatient medical costs across different tumor types and the financial outcomes within the hematology department at Hospital A. Our findings reveal that although DIP payments have successfully lowered the overall inpatient medical costs and expenses related to western medicine, the treatment expenses for the HM group remain substantially higher compared to those for the ST group, resulting in financial losses for the department. The study highlights the financial losses incurred by minority groups due to the averaging effect of big data, emphasizing the need for policy adjustments. Future initiatives should concentrate on refining precision payment methods for various tumors, alongside broadening health care reforms and optimizing policy measures, to guarantee the fair and sustainable distribution of medical resources. This approach aims to fulfill the patients' demands for high-quality medical services. However, this study has several limitations, including the reliance on data and sample size from a single hospital and the lack of control for potential confounding factors. Future investigations need to expand the scope of samples, apply multivariable methods, and delve into the diversity of treatment protocols to enhance the generalizability and credibility of these findings.

Data availability statement

The data analyzed in this study is subject to the following licenses/restrictions: the data that support the findings of this study are available from the hospital quality control department but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Requests to access these datasets should be directed to the corresponding author. Requests to access these datasets should be directed to LX, xielj18@gmail.com.

Author contributions

HX: Data curation, Formal analysis, Writing – original draft. QS: Data curation, Formal analysis, Writing – original draft. BZ: Data curation, Formal analysis, Writing – review & editing. SZ: Supervision, Writing – review & editing. LX: Conceptualization, Visualization, Writing – review & editing.

Funding

The author(s) declare that no financial support was received for the research and/or publication of this article.

Acknowledgments

The authors sincerely thank the staff involved in data collection and management. Special thanks to Gang Lv (the People's Liberation Army General Hospital) and Xiaozhen Lai (Peking University) for their editorial support. The authors also appreciate the dedication and professionalism of the entire editorial team, and they thank the peer reviewers for their insightful feedback that greatly improved this work.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

References

1. Kone I, Maria ZB, Nordstrom K, Simone EB, Wangmo T. A scoping review of empirical evidence on the impacts of the DRG introduction in Germany and Switzerland. *Int J Health Plan Manag*. (2019) 34:56–70. doi: 10.1002/hpm.2669

2. Barouni M, Ahmadian L, Anari HS, Mohsenbeigi E. Investigation of the impact of DRG based reimbursement mechanisms on quality of care, capacity utilization, and efficiency-a systematic review. *Int J Healthc Manag*. (2021) 14:1463–74. doi: 10.1080/20479700.2020.1782663

3. Kim S, Jung C, Yon J, Park H, Yang H, Kang H, et al. A review of the complexity adjustment in the Korean diagnosis-related group (KDRG). *Health Inf Manag J*. (2020) 49:62–8. doi: 10.1177/1833358318795804

4. National Healthcare Security Administration. Notification about publishing the pilot implementation scheme of the regional points of global budget and the case-based payment methods (in Chinese). (2020). Available online at: https://www.gov.cn/zhengce/zhengceku/2020-11/05/content_5557627.htm (Accessed April 28, 2025).

5. Yu L, Lang J. Diagnosis-related groups (DRG) pricing and payment policy in China: where are we? *Hepatobil Surg Nutr*. (2020) 9:771–3. doi: 10.21037/hbsn-2020-8

6. Zhao C, Wang C, Shen C, Wang Q. Diagnosis-related group (DRG)-based case-mix funding system, a promising alternative for fee for service payment in China. *Biosci Trends*. (2018) 12:109–15. doi: 10.5582/bst.2017.01289

7. Ding Y, Yin J, Zheng C, Dixon S, Sun Q. The impacts of diagnosis-intervention packet payment on the providers' behavior of inpatient care—evidence from a national pilot city in China. *Front Public Health*. (2023) 11:1069131. doi: 10.3389/fpubh.2023.1069131

8. Chen J, Yang J, Gan L, Yang W, Zeng Y, Xiong M, et al. Evaluate the effectiveness of diagnosis-intervention packet (DIP) reform among inpatients diagnosed with cancer in Guangzhou, China: interrupted time-series analyses based on a 5-year research period. *Authorea Preprints*. (2023). doi: 10.22541/au.167819115.59006907/v1

9. Wang S, Wu N, Wang H, Zhang X, Li F, Wang X, et al. Impacts of a new diagnosis-related group point payment system on children's medical services in China: length of stay and costs. *Int J Health Plann Manag*. (2024) 39:432–46. doi: 10.1002/hpm.3739

10. Su CT, Veenstra CM, Patel MR. Divergent patterns in care utilization and financial distress between patients with blood cancers and solid tumors: a National Health Interview Survey Study, 2014–2020. *Cancers*. (2022) 14:1605. doi: 10.3390/cancers14071605

11. Yang S, Lee E. Healthcare utilization and cost at the end of life of hematological malignancies and solid tumors in South Korea. *Value Health*. (2018) 21:S20. doi: 10.1016/j.jval.2018.07.154

12. Xi J. Secure a decisive victory in building a moderately prosperous Society in all Respects and Strive for the great success of socialism with Chinese characteristics for a new era. People's Daily (2017). Available online at: http://paper.people.com.cn/rmrbhwb/html/2017-10/19/content_1811529.htm (Accessed April 28, 2025).

13. Wan S, Chen Y, Xiao Y, Zhao Q, Li M, Wu S. Spatial analysis and evaluation of medical resource allocation in China based on geographic big data. *BMC Health Serv Res*. (2021) 21:1084–18. doi: 10.1186/s12913-021-07119-3

14. Xi Y, Ding Y, Cheng Y, Zhao J, Zhou M, Qin S. Evaluation of the medical resource allocation: evidence from China. *Healthcare*. (2023) 11:829. doi: 10.3390/healthcare11060829

15. Liu GG, Wu J, He X, Jiang Y. Policy updates on access to and affordability of innovative medicines in China. *Value Health Reg Issues*. (2022) 30:59–66. doi: 10.1016/j.vhri.2021.12.003

16. Lu J, Long H, Shen Y, Wang J, Geng X, Yang Y, et al. The change of drug utilization in China's public healthcare institutions under the "4+ 7" centralized drug procurement policy: evidence from a natural experiment in China. *Front Pharmacol*. (2022) 13:923209. doi: 10.3389/fphar.2022.923209

17. Zhou T, Zhang F, Wang Y, Niu B, Wang H. Visualized analyses of the research on DRG and DIP in China. Proceedings of the 2023 8th international conference on intelligent information processing. (2023) 106–113.

18. Zhang M, Wang G, Liu H, Wen Y, Chen L. Impact of China's diagnosis-intervention packet policy on hospitalization costs for patients with malignant tumors: a 2019–2022 interrupted time series analysis. *Risk Manag Healthc Policy*. (2025) 18:655–65. doi: 10.2147/RMHP.S502474

19. Liu Y, Du S, Cao J, Niu H, Jiang F, Gong L. Effects of a diagnosis-related group payment reform on length and costs of hospitalization in Sichuan, China: a synthetic control study. *Risk Manag Healthc Policy*. (2024) 17:1623–37. doi: 10.2147/RMHP.S463276

20. Tan H, Zhang X, Guo D, Bi S, Chen Y, Peng X, et al. Cost shifting in lung Cancer inpatient care under diagnosis-intervention packet reform: a pilot study in China. *Risk Manag Healthc Policy*. (2025) 18:759–73. doi: 10.2147/RMHP.S498634

21. Zhang X, Tang S, Wang R, Qian M, Ying X, Maciejewski ML. Hospital response to a new case-based payment system in China: the patient selection effect. *Health Policy Plan*. (2024) 39:519–27. doi: 10.1093/heapol/czae022

22. Brown JR, Eichhorst B, Hillmen P, Jurczak W, Kaźmierczak M, Lamanna N, et al. Zanubrutinib or ibrutinib in relapsed or refractory chronic lymphocytic leukemia. *N Engl J Med*. (2023) 388:319–32. doi: 10.1056/NEJMoa2211582

23. Tam CS, Opat S, D'Sa S, Jurczak W, Lee HP, Cull G, et al. A randomized phase 3 trial of zanubrutinib vs ibrutinib in symptomatic Waldenström macroglobulinemia: the ASPEN study. *Blood*. (2020) 136:2038–50. doi: 10.1182/blood.2020006844

24. DiNardo CD, Jonas BA, Pullarkat V, Thirman MJ, Garcia JS, Wei AH, et al. Azacitidine and venetoclax in previously untreated acute myeloid leukemia. *N Engl J Med*. (2020) 383:617–29. doi: 10.1056/NEJMoa2012971

25. Sonneveld P, Dimopoulos MA, Boccadoro M, Quach H, Ho PJ, Beksac M, et al. Daratumumab, bortezomib, lenalidomide, and dexamethasone for multiple myeloma. *N Engl J Med*. (2024) 390:301–13. doi: 10.1056/NEJMoa2312054

26. Cowan AJ, Allen C, Barac A, Basaleem H, Bensenor I, Curado MP, et al. Global burden of multiple myeloma: a systematic analysis for the global burden of disease study 2016. *JAMA Oncol*. (2018) 4:1221–7. doi: 10.1001/jamaoncol.2018.2128

27. Seefat MR, Cucchi DG, Dirven S, Groen K, Zweegman S, Blommestein HM. A systematic review of cost-effectiveness analyses of novel agents in the treatment of multiple myeloma. *Cancers*. (2021) 13:5606. doi: 10.3390/cancers13225606

28. Busse R, Geissler A, Aaviksoo A, Cots F, Häkkinen U, Kobel C, et al. Diagnosis related groups in Europe: moving towards transparency, efficiency, and quality in hospitals? *BMJ*. (2013) 346:346. doi: 10.1136/bmj.f3197

29. Stocker H, Kron F, Hartmann P, Kron F, Hartmann P, Hartmann P, et al. Caseload, clinical spectrum and economic burden of infectious diseases in patients discharged from hospitals in Germany. *Infection*. (2025):1–11. doi: 10.1007/s15010-025-02507-x

30. Ahmadi P, Ghandili S, Jakobs F, Konnopka C, Morgner-Miehlke A, Kröger N, et al. Cost analysis of patients undergoing allogeneic stem cell transplantation or chimeric antigen receptor T-cell therapy in relapsed or refractory diffuse large B-cell lymphoma from a German healthcare payer perspective. *Bone Marrow Transplant*. (2024) 59:572–4. doi: 10.1038/s41409-024-02228-z

frontiers | Frontiers in Immunology

TYPE Original Research
PUBLISHED 16 May 2025
DOI 10.3389/fimmu.2025.1556100

Check for updates

OPEN ACCESS

EDITED BY
Kevin Lu,
University of South Carolina, United States

REVIEWED BY
George Gourzoulidis,
Health Through Evidence, Greece
Guanming Chen,
University of North America, United States

*CORRESPONDENCE
Hao Wang
halsey_glyy@163.com
Yunchun Long
chrrich9854@163.com

†These authors have contributed equally to this work and share first authorship

RECEIVED 06 January 2025
ACCEPTED 28 April 2025
PUBLISHED 16 May 2025

CITATION
Yang J, Chen F, Li J, Zhou Y, Wang H and Long Y (2025) Cost-effectiveness analysis of Toripalimab regimen for extensive-stage small-cell lung cancer in China and America. *Front. Immunol.* 16:1556100. doi: 10.3389/fimmu.2025.1556100

COPYRIGHT
© 2025 Yang, Chen, Li, Zhou, Wang and Long. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

Cost-effectiveness analysis of Toripalimab regimen for extensive-stage small-cell lung cancer in China and America

Jing Yang[1†], Fang Chen[2†], Junlin Li[3†], Yujie Zhou[4], Hao Wang[5*] and Yunchun Long[6*]

[1]Department of Pharmacy, Chengdu Second People's Hospital, Chengdu, Sichuan, China, [2]Department of Pharmacy, The First Affiliated Hospital of Xiamen University, Xiamen, Fujian, China, [3]Department of Pharmacy, Nanan People's Hospital of Chongqing, Chongqing, China, [4]Department of Respiratory and Critical Care Medicine, Nanjing Drum Tower Hospital, Nanjing, Jiangsu, China, [5]Department of Pharmacy, Nanjing Drum Tower Hospital, Nanjing, Jiangsu, China, [6]School of Basic Medicine and Clinical Pharmacy, China Pharmaceutical University, Nanjing, Jiangsu, China

Objectives: Toripalimab combined with chemotherapy is a clinically valuable and important regimen in the treatment of extensive–stage small–cell lung cancer (ES-SCLC). However, there are no studies on the cost-effectiveness of this regimen, so this study was designed to evaluate the cost-effectiveness of Toripalimab regimen for the treatment of ES-SCLC from the perspectives of the Chinese health system and the U.S. health system, respectively.

Methods: A partitioned survival model was developed to simulate the clinical progression and cost consumption of ES-SCLC using the results of the EXTENTORCH study as a source of survival data and incorporating direct medical costs. Model output metrics included incremental cost-effectiveness ratio (ICER), quality-adjusted life-years (QALYs), incremental QALYs, total costs, and incremental costs. The cost-effectiveness of the Toripalimab scheme was judged by comparing the ICER with the willingness to pay (WTP). The robustness of the model was verified by sensitivity analysis and scenario analysis.

Results: The results of the basic analysis showed that from the perspective of the Chinese health system, the Toripalimab group gained 0.18 QALYs more at a cost of $5,204, with an ICER of $29,139/QALY (<WTP). From the standpoint of the U.S. health system, the Toripalimab group spent $156,923 more and also gained 0.17 QALYs more, but the ICER ($915,965/QALY) was much higher than the WTP. Sensitivity and scenario analyses showed the model to be generally stable.

Conclusions: Compared with chemotherapy, the Toripalimab regimen for the treatment of ES-SCLC is cost-effective from the perspective of the Chinese health system, but not from the perspective of the US health system.

KEYWORDS

cost-effectiveness analysis, extensive-stage small-cell lung cancer, Toripalimab, chemotherapy, EXTENTORCH study

1 Introduction

Global cancer statistics show that in 2022, there were 2.48 million new cases of lung cancer, accounting for 12.4% of the total number of new cancer cases, and 1.8 million new lung cancer deaths, accounting for 18.7% of the total cancer deaths, which makes lung cancer the malignant tumor with the highest morbidity and mortality rate in the world (1). In China, lung cancer is also the top malignant tumor in terms of incidence and mortality (1, 2). In the US, lung cancer is the third most common cancer and the first in terms of mortality (1). Small-cell lung cancer (SCLC) is a highly aggressive subtype of lung cancer, accounting for 15%-17% of the total incidence of lung cancer (3, 4). SCLC exhibits rapid growth, a high degree of malignancy, and a propensity for metastasis. Nearly 70% of patients are in extensive stage when diagnosed, and are identified as having extensive-stage small-cell lung cancer (ES-SCLC), with a 5-year survival rate of less than 7% (5–7).

Before 2019, platinum-based DNA cross-linking agents (such as cisplatin or carboplatin) in combination with topoisomerase inhibitors (such as etoposide or irinotecan) is the preferred chemotherapy regimens for ES-SCLC (5). Although the short-term efficacy of this combination therapy is remarkable, due to the biological characteristics of SCLC, patients are highly susceptible to drug resistance leading to tumor recurrence, with a median overall survival (mOS) of 9–11 months (6, 8, 9). In recent years, the role of immunotherapy in the treatment of ES-SCLC has become increasingly prominent. Several studies have shown that immunotherapy represented by programmed death-1 (PD-1) inhibitor and programmed death- ligand 1 (PD-L1) inhibitors significantly prolonged the mOS and median progression-free survival (mPFS) of ES-SCLC patients (10–13). Toripalimab is a PD-1 inhibitor developed in China and approved for marketing in China in December 2018 and in the US in October 2023. The EXTENTORCH study compared the efficacy and safety of Toripalimab combined with chemotherapy (Etoposide + Carboplatin/Cisplatin, EC) versus chemotherapy in the treatment of ES-SCLC (14). The results showed that compared with chemotherapy, Toripalimab plus chemotherapy prolonged the mOS (14.6 vs 13.3 months, hazard ratio [HR] = 0.8, 95% confidence interval [CI] 0.65-0.98) and mPFS (5.8 vs 5.6 months, HR = 0.67, 95%CI: 0.54-0.82), and the security is controllable.

Although Toripalimab combination chemotherapy extended the survival time of ES-SCLC patients compared with conventional chemotherapy, there is a lack of economic evidence to support its use. Choosing a safe, effective and relatively inexpensive drug not only reduces the economic burden on patients but also facilitates the rational allocation of healthcare resources. Therefore, this study is aims to evaluate the cost-effectiveness of Toripalimab in combination with chemotherapy in the field of first-line treatment of ES-SCLC based on the perspective of the health system in China and the US.

2 Methods

2.1 Study design

The study was designed and conducted in accordance with the Consolidated Health Economic Evaluation Report Standards (CHEERS) checklist (Supplementary Table S1) (15). Study data were obtained from the EXTENTORCH study (ClinicalTrials.gov Identifier: NCT04012606), the Menet (https://www.menet.com.cn/), the Drug. price guide (https://www.drugs.com/price-guide/) and published literature.

The target patients included in this study were consistent with the EXTENTORCH study, that is, age ≥ 18 years and diagnosis of ES-SCLC confirmed by pathology or histology, and more detailed clinical characteristics of the patients are shown in Supplementary Table S2 (14). The target patients received drug therapy in two groups (1). Toripalimab group:first received 4 cycles (1 cycle = 3 weeks = 21 days) of Toripalimab (240mg, day1) + Etoposide (100mg/m^2, day1-day3) + Carboplatin (AUC=5mg/mL/min, day1)/Cisplatin (75mg/m^2, day1), followed by Toripalimab (240mg, day1) until disease progression (2); EC group: first received 4 cycles of Placebo (day1) + Etoposide (100mg/m^2, day1-day3) + Carboplatin (AUC=5mg/mL/min, day1)/Cisplatin (75mg/m^2, day1), followed by Placebo (day1) until disease progression. The treatment plan after disease progression provided by the EXTENTORCH study was not detailed, so Topotecan (1.25 mg/m^2/day, day1-day5) was chosen as the second-line treatment according to the NCCN guideline and the CSCO guideline (16, 17). And best supportive care (BSC) was given to patients not receiving Topotecan. All drugs were given by intravenous route.

2.2 Model overview

A partitioned survival model was developed to simulate the progression of ES-SCLC by TreeAge Pro software (Version:2022). The model starts from the progression-free survival (PFS) state, and patients in the PFS state can transfer to the PFS state, progressive disease (PD) or the death state, and patients in the PD state can also transfer to the PD state or the death state. The model structure is shown in Figure 1. Considering the survival of ES-SCLC patients and the treatment cycle of the EXTENTORCH study, a time horizon (TH) of 10 years with a 21-day modeling cycle was set in this study. The model output metrics included incremental cost-effectiveness ratio (ICER), quality-adjusted life-years (QALYs), incremental QALYs, total cost, and incremental cost.

2.3 Survival estimate

The EXTENTORCH study provided survival-related data (14). Firstly, survival information from PFS curves and OS curves in the EXTENTORCH study was digitally extracted using Engauge

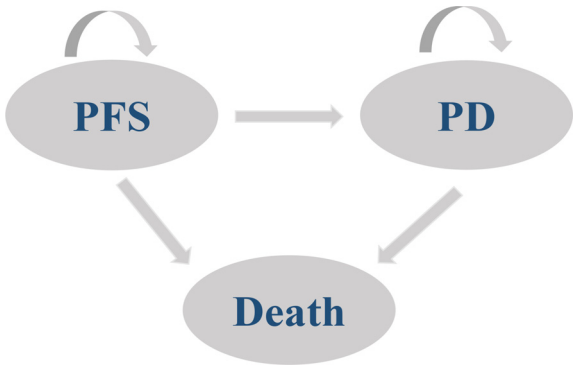


FIGURE 1
Schematic of the model structure. PFS, Progression-free survival; PD, Progressive disease.

Digitizer software. The individual data were then reconstructed according to the method by Guyot P et al. (18). The survHE package in R software (4.3.1) (https://www.r-project.org/) was then invoked to fit the parameter distributions of the survival curves. The optimal fitting model was selected by combining the visual inspection with Akaike information criterion (AIC) and Bayesian information criterion (BIC). Smaller values of AIC and BIC indicate better fitting. Supplementary Table S3 shows the AIC and BIC values of each model, and it can be seen that Log-logistic distribution is the optimal fitting model for all curves. The relevant fitting parameters are shown in Supplementary Table S4, and the fitting curve graphs are shown in Supplementary Figure S1.

2.4 Cost and utility estimate

The perspective was the health system, so only direct healthcare costs were considered, including drug costs, BSC costs, adverse reactions (ADRs) handling costs, hospitalization costs and follow-up costs. Drug cost information was obtained from the Menet and Drug. price guide, and all other costs were obtained from the relevant literature. ADRs treatment costs were only considered for grade 3–4 ADRs with an incidence rate greater than 5%, and it was assumed that ADRs treatment costs were one-time costs. To calculate the drug cycle cost, it was assumed that the body weight of the Chinese patient was 65Kg, the body surface area (BSA) was 1.72m^2, and the creatinine clearance (CCR) was 70ml/min (19, 20); American patients had a body weight of 70Kg, a BSA of 1.82m^2, and a CCR of 70ml/min (21, 22). Tables 1, 2 provide detailed cost information.

The utility value information was extracted from an international study, which showed that Chinese patients had a utility value of 0.804 in the PFS stage and 0.321 in the PD stage, whereas American patients had a utility value of 0.84 in the PFS stage and 0.166 in the PD stage (23). The reduction in the utility value due to ADRs was also obtained from the published literature, and the specific information on the utility value is shown in Tables 1, 2.

When the TH is more than 1 year, the costs and health outputs occurring in the future need to be discounted. The TH of this study is 10 years, so an annual discount rate of 5% was taken for China and 3% for the United States based on relevant guidelines and literature recommendations (24, 25).

2.5 Basic analysis

The economy of Toripalimab regimen was judged by comparing the ICER with the willingness to pay (WTP), if the ICER is greater than the WTP, it is considered that Toripalimab regimen does not have cost-effective advantage, and conversely, it is cost-effective. According to the literature and guideline recommendations, the WTP for China was set to be 3 times the gross domestic product (GDP) per capita in 2023 (WTP = 3*GDP = 3*$12,291 = $36,874/QALY) for the basic analysis, whereas that for the US was set to be $150,000/QALY (24, 26)

2.6 Sensitivity analysis

One-way sensitivity analysis (OWSA) was performed to investigate the effect of single parameter changes on the model, and the results was presented as a tornado plot. The Menet provides a range of values for the cost parameter, published literature provides a range of values for the utility value, the discount rate is recommended to be set at 0-8% according to the guideline, and the ranges of the other parameters are set at± 20% of their base values (24, 26).

The effects of simultaneous changes in multiple parameters on the model were examined by probabilistic sensitivity analysis (PSA), and the results were presented as a cost-effectiveness scatterplot and a cost-effectiveness acceptability curve (CEAC). Second-order Monte Carlo simulations were used to perform PSA for 1,000 random repeated samples of parameters conforming to different probability distributions. In this study, the costs obeyed the Gamma distribution, and the utility values, the incidence of ADRs, and the discount rate obeyed the Beta distribution.

2.7 Scenario analysis

Scenario Analysis 1:In order to explore the effect of different TH on the results, the TH was set to 5 and 8 years for the scenario analysis, respectively.

Scenario Analysis 2:Health utility values are often one of the most important causes of variation in the results of pharmacoeconomic evaluations (27). To assess the impact of utility values on outcomes, Scenario Analysis 2 used the results of

10.3389/fimmu.2025.1556100

TABLE 1 Model parameters in China.

Variable	Baseline value	Range	Distribution	Source
Cost (US$)				
Toripalimab per 240mg	261.2	208.96~313.44	Gamma	*
Durvalumab per 500mg	2,488.03	1,990.43~2,985.64	Gamma	*
Atezolizumab per 1,200mg	4,511.69	3,609.35~5,414.03	Gamma	*
Etoposide per 100mg	19.55	1.07~61.9	Gamma	*
Carboplatin per 100mg	7.59	7.1~12.63	Gamma	*
Cisplatin per 30mg	2.78	2.63~3.85	Gamma	*
Topotecan per 2mg	14.12	11.29~16.94	Gamma	*
BSC per cycle	345.6	276.48~414.72	Gamma	(26)
Follow-up per cycle	164.73	131.79~197.68	Gamma	(39)
Hospitalization per cycle	61.57	49.25~73.88	Gamma	(39)
Decreased platelet count	1,505.92	1,204.74~1,807.1	Gamma	(40)
Decreased WBC count	115.01	92.01~138.01	Gamma	(40)
Anemia	138.75	111~166.5	Gamma	(40)
Decreased neutrophil count	115.01	92.01~138.01	Gamma	(40)
Hyponatremia	0.29	0.232~0.348	Gamma	(41)
Febrile neutropenia	115.01	92.01~138.01	Gamma	(40)
Incidence of ADRs in Toripalimab group				
Decreased platelet count	24.8%	19.84%~29.76%	Beta	(14)
Decreased WBC count	38.7%	30.96%~46.44%	Beta	(14)
Anemia	30.6%	24.48%~36.72%	Beta	(14)
Decreased neutrophil count	74.3%	59.44%~89.16%	Beta	(14)
Hyponatremia	6.3%	5.04%~7.56%	Beta	(14)
Incidence of ADRs in EC group				
Decreased platelet count	34.3%	27.44%~41.16%	Beta	(14)
Decreased WBC count	44.9%	35.92%~53.88%	Beta	(14)
Anemia	34.7%	27.76%~41.64%	Beta	(14)
Decreased neutrophil count	75%	60%~90%	Beta	(14)
Hyponatremia	6.5%	5.2%~7.8%	Beta	(14)
Incidence of ADRs in DEC group				
Decreased platelet count	6%	4.8%~7.2%	Beta	(13)
Febrile neutropenia	6%	4.8%~7.2%	Beta	(13)
Anemia	9%	7.2%~10.8%	Beta	(13)
Decreased neutrophil count	24%	19.2%~28.8%	Beta	(13)
Incidence of ADRs in AEC group				
Decreased platelet count	10%	8%~12%	Beta	(29)
Decreased WBC count	5%	4%~6%	Beta	(29)
Anemia	14%	11.2%~16.8%	Beta	(29)

(Continued)

TABLE 1 Continued

Variable	Baseline value	Range	Distribution	Source
Incidence of ADRs in AEC group				
Decreased neutrophil count	23%	18.4%~27.6%	Beta	(29)
Utility value				
PFS	0.804	0.536~0.84	Beta	(23)
PD	0.321	0.05~0.473	Beta	(23)
Disutility value				
Decreased platelet count	0.05	0.04~0.06	Beta	(40)
Decreased WBC count	0.2	0.16~0.24	Beta	(23)
Anemia	0.073	0.059~0.089	Beta	(23)
Decreased neutrophil count	0.2	0.16~0.24	Beta	(23)
Hyponatremia	0.09	0.072~0.108	Beta	(41)
Febrile neutropenia	0.2	0.16~0.24	Beta	(23)
Proportion of patients receiving second-line treatment				
Toripalimab group	55.2%	44.16%~66.24%	Beta	(14)
EC group	69.4%	55.52%~83.28%	Beta	(14)
Others				
Discount rate	5%	0~8%	Beta	(24)
Weight	65	52~78	Normal	(19, 20)
Body surface area	1.72	1.376~2.064	Normal	(19, 20)
Creatinine clearance	70	56~84	Normal	(19, 20)

* refers to The Menet (https://www.menet.com.cn/).
BSC, Best supportive care; WBC, White blood cell; ADRs, Adverse reactions; PFS, Progression-free survival; PD, Progressive disease.

TABLE 2 Model parameters in the US.

Variable	Baseline value	Range	Distribution	Source
Cost (US$)				
Toripalimab per 240mg	9,711.6	7,769.28~11,653.92	Gamma	*
Durvalumab per 500mg	4,404.96	3,523.97~5,285.95	Gamma	*
Atezolizumab per 1,200mg	11,756.14	9,404.91~14,107.37	Gamma	*
Etoposide per 100mg	13.68	10.94~16.42	Gamma	*
Carboplatin per 50mg	13.79	11.03~16.55	Gamma	*
Cisplatin per 50mg	15.8	12.64~18.96	Gamma	*
Topotecan per 4mg	80.17	64.14~96.2	Gamma	*
BSC per cycle	1,447.79	1,158.23~1,737.35	Gamma	(26)
Follow-up per cycle	241	192.8~289.2	Gamma	(26)
Hospitalization per cycle	61.57	49.25~73.88	Gamma	(39)
Decreased platelet count	13,105	10,484~15,726	Gamma	(26)
Decreased WBC count	13,105	10,484~15,726	Gamma	(26)

(Continued)

10.3389/fimmu.2025.1556100

TABLE 2 Continued

Variable	Baseline value	Range	Distribution	Source
Cost (US$)				
Anemia	7,941	6,352.8~9,529.2	Gamma	(26)
Decreased neutrophil count	13,656	10,924.8~16,387.2	Gamma	(26)
Hyponatremia	0.29	0.232~0.348	Gamma	(41)
Febrile neutropenia	13,656	10,924.8~16,387.2	Gamma	(26)
Incidence of ADRs in Toripalimab group				
Decreased platelet count	24.8%	19.84%~29.76%	Beta	(14)
Decreased WBC count	38.7%	30.96%~46.44%	Beta	(14)
Anemia	30.6%	24.48%~36.72%	Beta	(14)
Decreased neutrophil count	74.3%	59.44%~89.16%	Beta	(14)
Hyponatremia	6.3%	5.04%~7.56%	Beta	(14)
Incidence of ADRs in EC group				
Decreased platelet count	34.3%	27.44%~41.16%	Beta	(14)
Decreased WBC count	44.9%	35.92%~53.88%	Beta	(14)
Anemia	34.7%	27.76%~41.64%	Beta	(14)
Decreased neutrophil count	75%	60%~90%	Beta	(14)
Hyponatremia	6.5%	5.2%~7.8%	Beta	(14)
Incidence of ADRs in DEC group				
Decreased platelet count	6%	4.8%~7.2%	Beta	(13)
Febrile neutropenia	6%	4.8%~7.2%	Beta	(13)
Anemia	9%	7.2%~10.8%	Beta	(13)
Decreased neutrophil count	24%	19.2%~28.8%	Beta	(13)
Incidence of ADRs in AEC group				
Decreased platelet count	10%	8%~12%	Beta	(29)
Decreased WBC count	5%	4%~6%	Beta	(29)
Anemia	14%	11.2%~16.8%	Beta	(29)
Decreased neutrophil count	23%	18.4%~27.6%	Beta	(29)
Utility value				
PFS	0.84	0.536~0.84	Beta	(23)
PD	0.166	0.05~0.473	Beta	(23)
Disutility value				
Decreased platelet count	0.05	0.04~0.06	Beta	(40)
Decreased WBC count	0.2	0.16~0.24	Beta	(23)
Anemia	0.073	0.059~0.089	Beta	(23)
Decreased neutrophil count	0.2	0.16~0.24	Beta	(23)
Hyponatremia	0.09	0.072~0.108	Beta	(41)
Febrile neutropenia	0.2	0.16~0.24	Beta	(23)
Proportion of patients receiving second-line treatment				

(Continued)

TABLE 2 Continued

Variable	Baseline value	Range	Distribution	Source
Proportion of patients receiving second-line treatment				
Toripalimab group	55.2%	44.16%~66.24%	Beta	(14)
EC group	69.4%	55.52%~83.28%	Beta	(14)
Others				
Discount rate	3%	0~8%	Beta	(25)
Weight	65	52~78	Normal	(21, 22)
Body surface area	1.72	1.376~2.064	Normal	(21, 22)
Creatinine clearance	70	56~84	Normal	(21, 22)

* refers to The Drug. price guide (https://www.drugs.com/price-guide/).
BSC, Best supportive care; WBC, White blood cell; ADRs, Adverse reactions; PFS, Progression-free survival; PD, Progressive disease.

a real-world study for a cost-effectiveness analysis with utility values of 0.7 for the PFS stage and 0.6 for the PD stage (28).

2.8 Exploratory analysis

The two internationally recognized first-line immunotherapy regimens for ES-SCLC are Durvalumab plus EC (DEC) and Atezolizumab plus EC (AEC). This exploratory analysis aims to compare the cost-effectiveness of DEC/AEC vs Toripalimab combined with EC (TEC) in the treatment of ES-SCLC. The CASPIAN and IMpower133 trials provided therapeutic and survival information for ES-SCLC patients (13, 29). Firstly, given the absence of head-to-head clinical trials of DEC/AEC vs TEC, this study designated TEC as the control group and employed network meta-analysis (NMA) to construct a comparative framework. This approach enabled the estimation of hazard ratios (HRs) of PFS and OS for DEC/AEC vs TEC, and the detailed results are presented in Supplementary Table S5. Subsequently, referencing the methodology proposed by Hoyle et al. in the pharmacoeconomic evaluation of advanced renal cancer, the following parametric transformation formula was applied to adjust and calibrate the survival data of DEC group and AEC group (30).

$$\gamma_{comparator\ drug} = \gamma_{control\ drug},\ \lambda_{comparison\ drug} = \lambda_{control\ drug} * HR$$

Finally, the costs of DEC group and AEC group were calculated in accordance with the methodology outlined in Section 2.4 ("Cost and Utility Estimate"). By integrating costs and survival information, models can be established to perform a comprehensive cost-effectiveness of TEC vs DEC/AEC in the treatment of ES-SCLC.

3 Results

3.1 Results of basic analysis

The results of the basic analysis showed that not only were the total costs higher in the Toripalimab group than in the EC group, both in China and in the US ($16,714 vs $11,510, $57,561 vs $ 214,484), but the health outputs were also more than in the EC group (0.93 QALYs vs 0.75 QALYs, 0.79 QALYs vs 0.62 QALYs). Toripalimab regimen was cost-effective in China (ICER: $29,139/QALY< WTP: $36,874/QALY) but not in the US (ICER: $915,965/QALY > WTP: $150,000/QALY). See Table 3 for details of the results.

3.2 Results of sensitivity analysis

The results of OWSA are shown in Figure 2. As can be seen from the tornado plot, in China, the utility value of the PFS stage

TABLE 3 Results of basic analysis.

Variable	Cost ($)	Incremental cost ($)	QALYs	Incremental QALYs	ICER ($/QALY)
China					
EC group	11,510		0.75		
Toripalimab group	16,714	5,204	0.93	0.18	29,139
US					
EC group	57,561		0.62		
Toripalimab group	214,484	156,923	0.79	0.17	915,965

QALYs, Quality-adjusted life years; ICER, Incremental cost-effectiveness ratio.

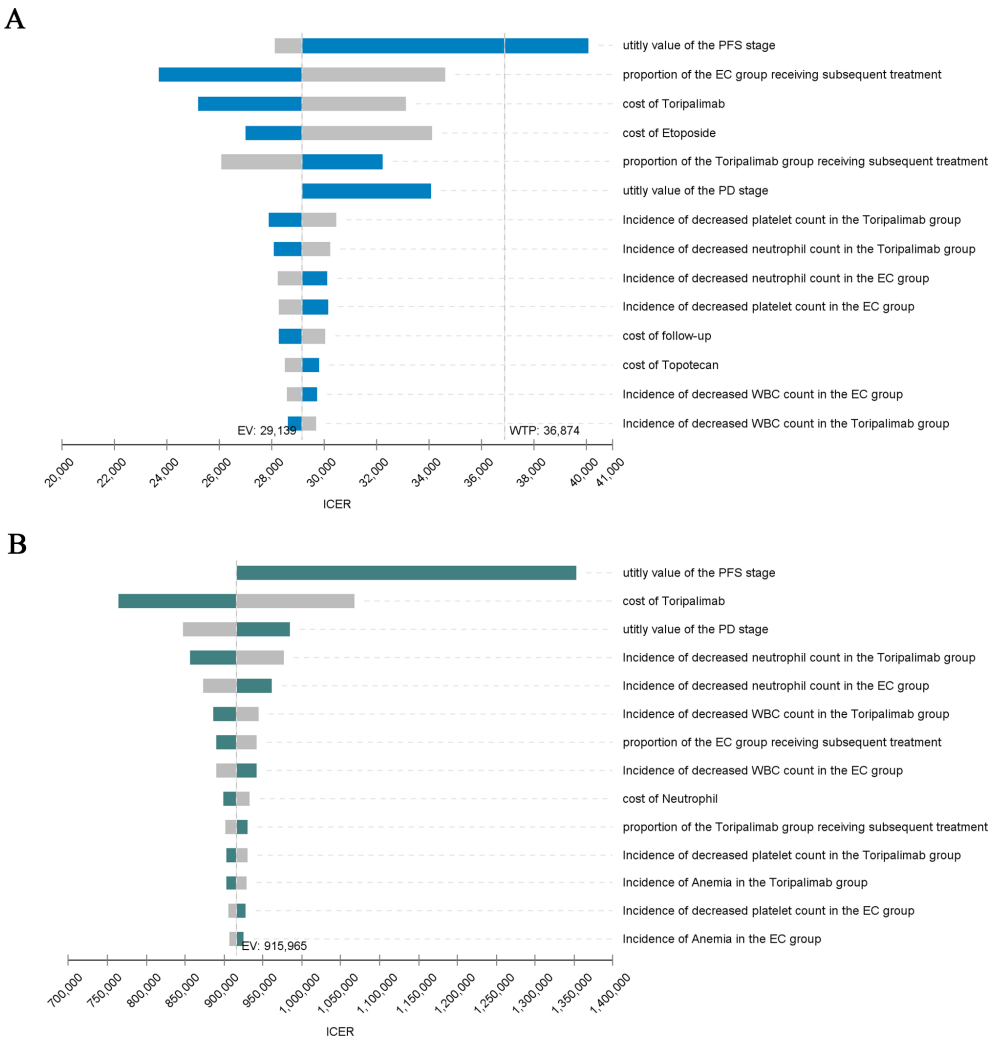


FIGURE 2
Tornado Diagram. **(A)** China: Tornado Diagram. **(B)** America: Tornado Diagram. PFS, Progression-free survival; PD, Progressive disease; ICER, Incremental cost-effectiveness ratio; EV, Expected value; WTP, Willingness to pay; WBC, White blood cell.

had the greatest impact on ICER, and the proportion of patients in the EC group receiving second-line therapy, the cost of Toripalimab and Etoposide, and the utility value of the PD stage also had a moderate impact on ICER. In the US, the parameters that had the greatest impact on ICER included the utility value of the PFS stage and the cost of Toripalimab, and the other parameters had a small impact on ICER.

The results of PSA are shown in Figures 2, 3, respectively. The cost-effectiveness scatter plot for China shows that when WTP is set to 1*GDP, 2*GDP and 3*GDP, the economic probabilities of Toripalimab scheme are 0.7%, 29.7% and 77.1%, respectively. However, the cost-effectiveness scatter plot for America shows that Toripalimab is unlikely to be economical even if WTP is set at the current high value ($150,000/QALY). The CEAC chart demonstrates that the Toripalimab regimen begins to demonstrate potential economic advantage (probability = 0.1%) at a WTP threshold of $6,667/QALY in the Chinese healthcare context. Conversely, in the U.S. healthcare system, a significantly higher WTP threshold of $540,000/QALY is required for the Toripalimab regimen to demonstrate comparable economic viability. In China, the Toripalimab regimen attains a 50.5% probability of cost-effectiveness at a WTP threshold of $28,400/QALY, thereby surpassing conventional chemotherapy in economic efficiency. By contrast, within the US healthcare paradigm, the Toripalimab regimen necessitates an exceptionally high WTP threshold ($867,000/QALY) to achieve equivalent cost-effectiveness probability (50%) relative to conventional chemotherapy approaches.

3.3 Results of scenario analysis

Table 4 provides the results of the detailed scenario analysis. Scenario analysis 1 shows that the Toripalimab regimen is economical in China, but not in the US, regardless of whether the

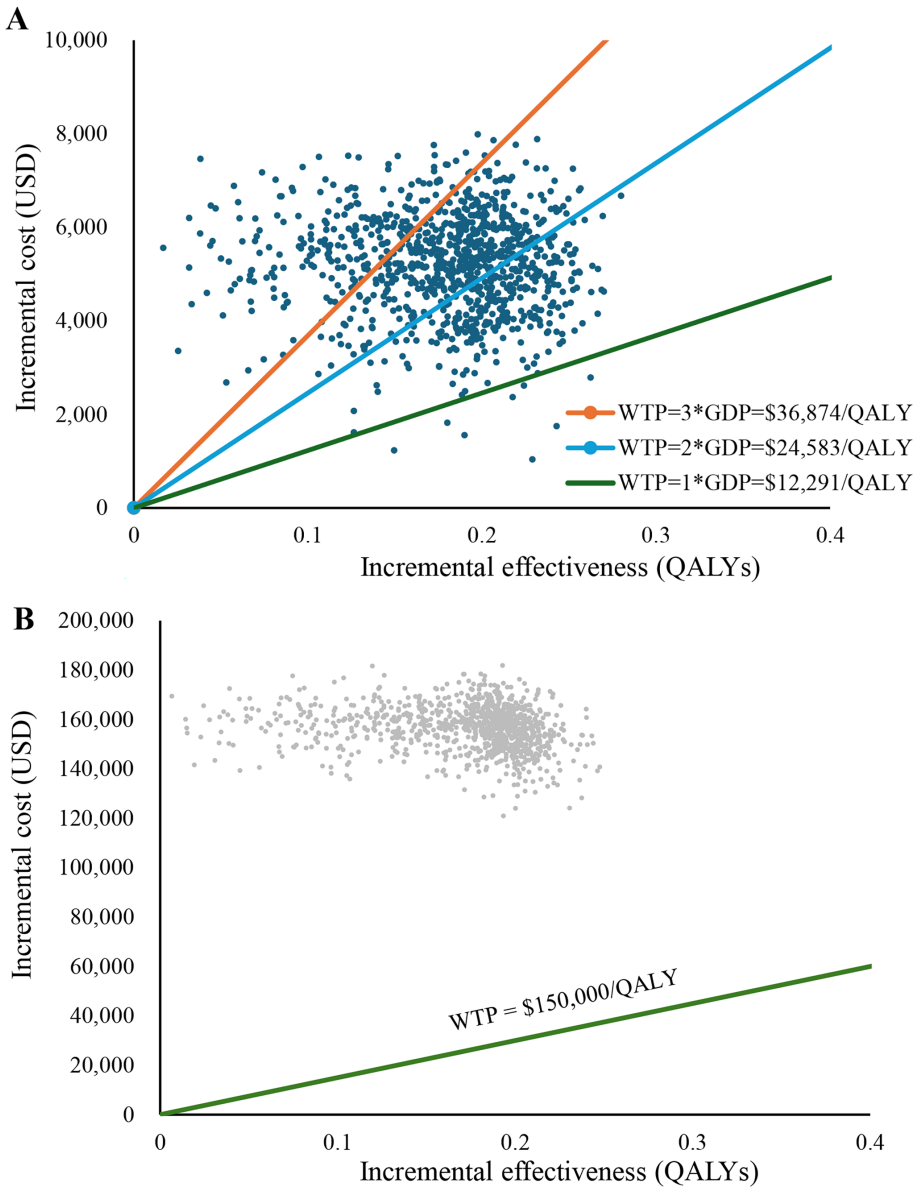


FIGURE 3
Cost-effectiveness scatter plot. **(A)** China: Cost-effectiveness scatter plot. **(B)** America: Cost-effectiveness scatter plot. WTP, Willingness to pay; GDP, gross domestic product; QALY, Quality-adjusted life year.

TH is 5 or 8 years. Scenario analysis 2 shows that after changing the utility value, the ICER decreases to $28,199/QALY (<WTP) in China and to $850,350/QALY (> WTP) in the US.

3.4 Results of exploratory analysis

The exploratory analysis (Table 2) indicates that TEC demonstrates cost-effectiveness for ES-SCLC treatment compared with DEC/AEC within the Chinese healthcare system ($ICER_{DEC\ vs\ TEC}$: $1,368,881/QALY, $ICER_{AEC\ vs\ TEC}$: $1,808,957/QALY), whereas it fails to demonstrate economic viability in the US context ($ICER_{DEC\ vs\ TEC}$: $$12,928/QALY, $ICER_{AEC\ vs\ TEC}$: $125,496/QALY).

4 Discussion

Recent years have witnessed significant advancements in the clinical application of immunotherapy for ES-SCLC. Currently, DEC and AEC regimens have been established as internationally recognized first-line immunotherapy standards for ES-SCLC. On the one hand, comparative pricing analysis reveals that Toripalimab demonstrates cost advantages over both Durvalumab and Atezolizumab in pharmaceutical markets across China and the US. T The cost of Toripalimab ($261.20/cycle) was significantly lower than that of Atezolizumab ($4,511.69/cycle) and Durvalumab ($7,464.10/cycle) in the Chinese market. Similarly, Toripalimab ($9,711.60/cycle) also offers a price advantage over Atezolizumab ($11,756.14/cycle) and Durvalumab ($13,214.88/cycle) in the U.S.

10.3389/fimmu.2025.1556100

TABLE 4 Results of scenario analysis and exploratory analysis.

Variable	Cost ($)	Incremental cost ($)	QALYs	Incremental QALYs	ICER($/QALY)
Scenario Analysis 1: TH = 5 years					
China					
EC group	11,186		0.73		
Toripalimab group	16,018	4,831	0.89	0.16	30,341
US					
EC group	56,802		0.61		
Toripalimab group	211,082	154,281	0.77	0.16	983,320
Scenario Analysis 1: TH = 8 years					
China					
EC group	11,439		0.75		
Toripalimab group	16,552	5,113	0.92	0.17	29,403
US					
EC group	57,395		0.62		
Toripalimab group	213,703	156,308	0.79	0.17	931,041
Scenario Analysis 2					
China					
EC group	11,510		0.96		
Toripalimab group	16,714	5,204	1.14	0.18	28,199
US					
EC group	57,561		0.96		
Toripalimab group	214,484	156,923	1.14	0.18	850,350
Exploratory Analysis					
China:DEC VS TEC					
TEC group	16,714		0.93		
DEC group	111,159	94,445	1.00	0.07	1,368,881
China:AEC VS TEC					
TEC group	16,714		0.93		
AEC group	82,674	65,960	0.96	0.04	1,808,957
US:DEC VS TEC					
TEC group	214,484		0.79		
DEC group	215,910	1,426	0.90	0.11	12,928
US:AEC VS TEC					
TEC group	214,484		0.79		
AEC group	226,134	11,650	0.88	0.09	125,496

QALYs, Quality-adjusted life years; ICER, Incremental cost-effectiveness ratio.

market. On the other hand, the EXTENTORCH trial demonstrated survival benefits with Toripalimab regimen compared to chemotherapy alone. This combination of clinical efficacy and price advantage strongly suggests that Toripalimab regimen may have a unique cost-effectiveness advantage. Existing studies have consistently demonstrated the AEC and DEC regimens are not cost-effective in the treatment of ES-SCLC in China and the US (31–34). However, no study has evaluated the cost-effectiveness of TEC regimen in the treatment of ES-SCLC. Considering the price advantage and clinical benefits of Toripalimab, a systematic

pharmacoeconomic assessment of Toripalimab regimen carries important clinical and policy implications. Therefore, this study evaluated the cost-effectiveness of TEC regimen for ES-SCLC from the perspective of health systems in China and the US. The results showed that Toripalimab regimen was economical in China and uneconomical in the US when compared with either chemotherapy or AEC/DEC regimen.

OWSA showed that the health utility value at the PFS stage was the parameter that had the greatest impact on ICER in both the Chinese and American perspectives. The utility value directly affects the calculation of QALY, which is a key indicator for assessing the effectiveness of medical interventions. The utility value expresses the quality of life between full health and death, and the QALY allows the conversion of life years of different interventions into equivalent years of health status, thus facilitating the comparison of costs and effects between different treatment options. In the cost-effectiveness analysis, too high utility value leads to a relatively low ICER. Conversely, if the utility value is underestimated, the ICER will be higher. Therefore, choosing an appropriate utility value is crucial for calculating ICER. Unfortunately, the EXTENTORCH study did not report the utility value data, and there is a lack of research on the quality of life (i.e., utility value) of patients with SCLC. For the basic analysis, this study referred to published studies and chose to use the results of a large international study on the utility value in non-small cell lung cancer as an alternative to the utility value for SCLC (31, 32). But in scenario analysis 2, this study also changed the health utility values for PFS stage and PD stage based on the results of a study on the quality of life of SCLC patients (28). Considering the small sample size included in that real-world study, the results may not be representative enough to be analyzed as a special scenario only. Fortunately, scenario analysis 2 was consistent with the findings of the basic analysis.

PSA not only elucidated the economic disparities of the Toripalimab regimen across different geographical contexts, but also provided a quantifiable comparison basis for cross-regional investigations through specific WTP thresholds and corresponding economic probabilities. The China Guidelines for Pharmacoeconomic Evaluation (2020) recommend using 1~3 times the national GDP per capita as the WTP (24). When performing PSA, this study sets WTP to 1*GDP, 2*GDP, and 3*GDP respectively. The analytical outcomes revealed that across 1,000 simulations, he Toripalimab regimen demonstrated cost-effectiveness probabilities of 0.7%, 29.7%, and 77.1%, respectively, under these progressive WTP thresholds, thereby indicating substantial sensitivity of the regimen's economic viability to WTP parameters within the Chinese healthcare context. From the perspective of the US healthcare system, where cost-effectiveness evaluations for oncological interventions typically employ WTP thresholds ranging from $100,000 to $150,000/QALY (35). In this study, the Toripalimab regimen failed to demonstrate economic viability even at a high WTP of $150,000/QALY gained. This observation potentially reflects an incongruity between the pricing structure of Toripalimab and its corresponding clinical benefit profile within the US healthcare framework.

Given that TH also has a significant impact on ICER, scenario analysis 1 calculated ICER under different TH (36). Typically, the TH for pharmacoeconomic evaluation should be sufficiently long to obtain the full impact of the intervention measures on the costs and health outcomes of the subjects (24, 37). When fitting and extrapolating the survival curves, we found that the mortality rate in the Toripalimab group reached 99% when the TH was set to 10 years, so a TH of 10 years was chosen for the basic analysis. We also found that the mortality rate in the EC group had reached 99% when the TH = 8 years, so the ICER at TH = 8 years was also calculated in scenario analysis 1. Considering that the ES-SCLC is extremely malignant and the 5-year survival rate of patients receiving EC therapy is also low, so a TH of 5 years was also set. Previously Kim et al. found that the ICER decreases with increasing TH in most of the pharmacoeconomically evaluated studies (36). Scenario analysis 1 also showed that incremental costs and incremental QALYs increase with increasing TH, but the advantage of increasing incremental QALYs is sufficient to compensate for the disadvantage of increasing incremental costs, so it leads to smaller ICER, which confirms the findings of Kim et al. The costs of immunotherapy are mostly incurred in the short term, but because of the "delayed effect" of immunosuppressants, it takes a relatively long time for their health benefits to be realized (36, 38). Therefore, the longer the TH, the more QALYs are captured, leading to a reduction in ICER.

There are also some limitations of this study (1). There are some inevitable biases when survival curves fitting and extrapolation methods are used to obtain survival information beyond the observation period (2). Due to the lack of studies on health utility values in ES-SCLC patients, the use of alternative utility values may have slightly affected the results (3). Given the limited treatment pathway details reported in the EXTENTORCH trial, this study unified subsequent anticancer therapy, which may be different from clinical practice (4). The data utilized for this exploratory analysis were not derived from "head-to-head" clinical trials. Despite the implementation of methodologically rigorous NMA to adjust and calibrate survival data, the indirect nature of these comparisons introduces inherent methodological uncertainties (5). The enrollment population of the EXTENTORCH study did not include U.S. ES-SCLC patients, which may be somewhat different from the actual survival rate of U.S. ES-SCLC. Despite these limitations, this study also verified the stability of the model through sensitivity and scenario analyses, so the results of the study can still provide economic references for policy makers, clinicians and patients.

5 Conclusions

This study conducted a comprehensive cost-effectiveness analysis comparing Toripalimab plus chemotherapy versus chemotherapy alone as first-line treatment for ES-SCLC from the dual perspectives of Chinese and US healthcare systems through a modeling approach using data from a phase III clinical trial, and validated the stability of the model through a sensitivity analysis with

a series of scenario analyses. The findings demonstrated Toripalimab combination chemotherapy was economic in China when compared to chemotherapy alone, while was uneconomic in the US.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material. Further inquiries can be directed to the corresponding authors.

Author contributions

JY: Conceptualization, Data curation, Formal Analysis, Methodology, Project administration, Software, Validation, Visualization, Writing – original draft, Writing – review & editing. FC: Conceptualization, Data curation, Formal Analysis, Funding acquisition, Methodology, Software, Validation, Visualization, Writing – original draft, Writing – review & editing. JL: Formal Analysis, Methodology, Validation, Visualization, Software, Writing – review & editing. YZ: Formal Analysis, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. HW: Conceptualization, Methodology, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. YL: Conceptualization, Formal Analysis, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

Funding

The author(s) declare that financial support was received for the research and/or publication of this article. This research is supported by the Natural Science Foundation of Fujian Province (number: 2024J011357).

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The author(s) declare that no Generative AI was used in the creation of this manuscript.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fimmu.2025.1556100/full#supplementary-material

References

1. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. (2024) 74:229–63. doi: 10.3322/caac.21834

2. Han B, Zheng R, Zeng H, Wang S, Sun K, Chen R, et al. Cancer incidence and mortality in China, 2022. *J Natl Cancer Cent*. (2024) 4:47–53. doi: 10.1016/j.jncc.2024.01.006

3. Oronsky B, Reid TR, Oronsky A, Carter CA. What's new in SCLC? A review. *Neoplasia*. (2017) 19:842–47. doi: 10.1016/j.neo.2017.07.007

4. Wang S, Tang J, Sun T, Zheng X, Li J, Sun H, et al. Survival changes in patients with small cell lung cancer and disparities between different sexes, socioeconomic statuses and ages. *Sci Rep*. (2017) 7:1339. doi: 10.1038/s41598-017-01571-0

5. Megyesfalvi Z, Gay CM, Popper H, Pirker R, Ostoros G, Heeke S, et al. Clinical insights into small cell lung cancer: Tumor heterogeneity, diagnosis, therapy, and future directions. *CA Cancer J Clin*. (2023) 73:620–52. doi: 10.3322/caac.21785

6. Semenova EA, Nagel R, Berns A. Origins, genetic landscape, and emerging therapies of small cell lung cancer. *Genes Dev*. (2015) 29:1447–62. doi: 10.1101/gad.263145.115

7. Byers LA, Rudin CM. Small cell lung cancer: where do we go from here? *Cancer*. (2015) 121:664–72. doi: 10.1002/cncr.29098

8. Farago AF, Keane FK. Current standards for clinical management of small cell lung cancer. *Transl Lung Cancer Res*. (2018) 7:69–79. doi: 10.21037/tlcr.2018.01.16

9. Demedts IK, Vermaelen KY, van Meerbeeck JP. Treatment of extensive-stage small cell lung carcinoma: current status and future prospects. *Eur Respir J*. (2010) 35:202–15. doi: 10.1183/09031936.00105009

10. Cheng Y, Han L, Wu L, Chen J, Sun H, Wen G, et al. Effect of first-line serplulimab vs placebo added to chemotherapy on survival in patients with extensive-stage small cell lung cancer: the ASTRUM-005 randomized clinical trial. *Jama*. (2022) 328:1223–32. doi: 10.1001/jama.2022.16464

11. Cheng Y, Chen J, Zhang W, Xie C, Hu Q, Zhou N, et al. Benmelstobart, anlotinib and chemotherapy in extensive-stage small-cell lung cancer: a randomized phase 3 trial. *Nat Med*. (2024) 30:2967–76. doi: 10.1038/s41591-024-03132-1

12. Wang J, Zhou C, Yao W, Wang Q, Min X, Chen G, et al. Adebrelimab or placebo plus carboplatin and etoposide as first-line treatment for extensive-stage small-cell lung cancer (CAPSTONE-1): a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Oncol*. (2022) 23:739–47. doi: 10.1016/s1470-2045(22)00224-8

13. Paz-Ares L, Chen Y, Reinmuth N, Hotta K, Trukhin D, Statsenko G, et al. Durvalumab, with or without tremelimumab, plus platinum-etoposide in first-line treatment of extensive-stage small-cell lung cancer: 3-year overall survival update from CASPIAN. *ESMO Open*. (2022) 7:100408. doi: 10.1016/j.esmoop.2022.100408

14. Cheng Y, Zhang W, Wu L, Zhou C, Wang D, Xia B, et al. Toripalimab plus chemotherapy as a first-line therapy for extensive-stage small cell lung cancer: the phase 3 EXTENTORCH randomized clinical trial. *JAMA Oncol*. (2024) 11:16–25. doi: 10.1001/jamaoncol.2024.5019

15. Husereau D, Drummond M, Augustovski F, de Bekker-Grob E, Briggs AH, Carswell C, et al. Consolidated health economic evaluation reporting standards 2022 (CHEERS 2022) statement: updated reporting guidance for health economic evaluations. *Value Health*. (2022) 25:3–9. doi: 10.1016/j.jval.2021.11.1351

16. Ganti AKP, Loo BW, Bassetti M, Blakely C, Chiang A, D'Amico TA, et al. Small cell lung cancer, version 2.2022, NCCN clinical practice guidelines in oncology. *J Natl Compr Canc Netw*. (2021) 19:1441–64. doi: 10.6004/jnccn.2021.0058

17. Health Commission Of The People's Republic Of China N. National guidelines for diagnosis and treatment of lung cancer 2022 in China (English version). *Chin J Cancer Res*. (2022) 34:176–206. doi: 10.21147/j.issn.1000-9604.2022.03.03

18. Guyot P, Ades AE, Ouwens MJ, Welton NJ. Enhanced secondary analysis of survival data: reconstructing the data from published Kaplan-Meier survival curves. *BMC Med Res Methodol*. (2012) 12:9. doi: 10.1186/1471-2288-12-9

19. Qiao L, Zhou Z, Zeng X, Tan C. Cost-effectiveness of domestic PD-1 inhibitor camrelizumab combined with chemotherapy in the first-line treatment of advanced nonsquamous non-small-cell lung cancer in China. *Front Pharmacol*. (2021) 12:728440. doi: 10.3389/fphar.2021.728440

20. Luo X, Zhou Z, Zeng X, Liu Q. The cost-effectiveness of tislelizumab plus chemotherapy for locally advanced or metastatic nonsquamous non-small cell lung cancer. *Front Pharmacol*. (2022) 13:935581. doi: 10.3389/fphar.2022.935581

21. Lin S, Luo S, Gu D, Li M, Rao X, Wang C, et al. First-line durvalumab in addition to etoposide and platinum for extensive-stage small cell lung cancer: A U.S.-based cost-effectiveness analysis. *Oncologist*. (2021) 26:e2013–e20. doi: 10.1002/onco.13954

22. Wan X, Luo X, Tan C, Zeng X, Zhang Y, Peng L. First-line atezolizumab in addition to bevacizumab plus chemotherapy for metastatic, nonsquamous non-small cell lung cancer: A United States-based cost-effectiveness analysis. *Cancer*. (2019) 125:3526–34. doi: 10.1002/cncr.32368

23. Nafees B, Lloyd AJ, Dewilde S, Rajan N, Lorenzo M. Health state utilities in non-small cell lung cancer: An international study. *Asia Pac J Clin Oncol*. (2017) 13:e195–203. doi: 10.1111/ajco.12477

24. Association CP. *China guidelines for pharmacoeconomic evaluations* (2020). Available online at: https://www.cpa.org.cn/cpadmn/attached/file/20201203/1606977380634185.pdf (Accessed December 31, 2025).

25. Su D, Wu B, Shi L. Cost-effectiveness of atezolizumab plus bevacizumab vs sorafenib as first-line treatment of unresectable hepatocellular carcinoma. *JAMA Netw Open*. (2021) 4:e210037. doi: 10.1001/jamanetworkopen.2021.0037

26. Shao T, Zhao M, Liang L, Tang W. Serplulimab plus chemotherapy vs chemotherapy for treatment of US and chinese patients with extensive-stage small-cell lung cancer: A cost-effectiveness analysis to inform drug pricing. *BioDrugs*. (2023) 37:421–32. doi: 10.1007/s40259-023-00586-6

27. Hatswell AJ, Bullement A, Schlichting M, Bharmal M. What is the impact of the analysis method used for health state utility values on QALYs in oncology? A simulation study comparing progression-based and time-to-death approaches. *Appl Health Econ Health Policy*. (2021) 19:389–401. doi: 10.1007/s40258-020-00620-6

28. Vedadi A, Shakik S, Brown MC, Lok BH, Shepherd FA, Leighl NB, et al. The impact of symptoms and comorbidity on health utility scores and health-related quality of life in small cell lung cancer using real world data. *Qual Life Res*. (2021) 30:445–54. doi: 10.1007/s11136-020-02615-1

29. Horn L, Mansfield AS, Szczęsna A, Havel L, Krzakowski M, Hochmair MJ, et al. First-line atezolizumab plus chemotherapy in extensive-stage small-cell lung cancer. *N Engl J Med*. (2018) 379:2220–29. doi: 10.1056/NEJMoa1809064

30. Hoyle M, Green C, Thompson-Coon J, Liu Z, Welch K, Moxham T, et al. Cost-effectiveness of temsirolimus for first line treatment of advanced renal cell carcinoma. *Value Health*. (2010) 13:61–8. doi: 10.1111/j.1524-4733.2009.00617.x

31. Ding D, Hu H, Li S, Zhu Y, Shi Y, Liao M, et al. Cost-effectiveness analysis of durvalumab plus chemotherapy in the first-line treatment of extensive-stage small cell lung cancer. *J Natl Compr Canc Netw*. (2021) 19:1141–47. doi: 10.6004/jnccn.2020.7796

32. Zhou K, Zhou J, Huang J, Zhang N, Bai L, Yang Y, et al. Cost-effectiveness analysis of atezolizumab plus chemotherapy in the first-line treatment of extensive-stage small-cell lung cancer. *Lung Cancer*. (2019) 130:1–4. doi: 10.1016/j.lungcan.2019.01.019

33. Li LY, Wang H, Chen X, Li WQ, Cui JW. First-line atezolizumab plus chemotherapy in treatment of extensive small cell lung cancer: a cost-effectiveness analysis from China. *Chin Med J (Engl)*. (2019) 132:2790–94. doi: 10.1097/cm9.0000000000000053

34. Liu G, Kang S. Cost-effectiveness of adding durvalumab to first-line chemotherapy for extensive-stage small-cell lung cancer in China. *Expert Rev Pharmacoecon Outcomes Res*. (2022) 22:85–91. doi: 10.1080/14737167.2021.1888717

35. Bae YH, Mullins CD. Do value thresholds for oncology drugs differ from nononcology drugs? *J Manag Care Spec Pharm*. (2014) 20:1086–92. doi: 10.18553/jmcp.2014.20.11.1086

36. Kim DD, Wilkinson CL, Pope EF, Chambers JD, Cohen JT, Neumann PJ. The influence of time horizon on results of cost-effectiveness analyses. *Expert Rev Pharmacoecon Outcomes Res*. (2017) 17:615–23. doi: 10.1080/14737167.2017.1331432

37. Ramsey SD, Willke RJ, Glick H, Reed SD, Augustovski F, Jonsson B, et al. Cost-effectiveness analysis alongside clinical trials II-An ISPOR Good Research Practices Task Force report. *Value Health*. (2015) 18:161–72. doi: 10.1016/j.jval.2015.02.001

38. Adunlin G, Ferreri SP, Dong J, Freeman MK. Immuno-oncology medicines: policy implications and economic considerations. *Innov Pharm*. (2019) 10(3):10.24926/iip.v10i3.1799. doi: 10.24926/iip.v10i3.1799

39. Long Y, Wang H, Xie X, Li J, Xu Y, Zhou Y. Updated cost-effectiveness analysis of adebrelimab plus chemotherapy for extensive-stage small cell lung cancer in China. *BMJ Open*. (2024) 14:e077090. doi: 10.1136/bmjopen-2023-077090

40. Rui M, Fei Z, Wang Y, Zhang X, Ma A, Sun H, et al. Cost-effectiveness analysis of sintilimab + chemotherapy versus camrelizumab + chemotherapy for the treatment of first-line locally advanced or metastatic nonsquamous NSCLC in China. *J Med Econ*. (2022) 25:618–29. doi: 10.1080/13696998.2022.2071066

41. Yi L, Zhou Z, Zeng X, Tan C, Liu Q. First-line treatments for extensive-stage small-cell lung cancer with immune checkpoint inhibitors plus chemotherapy: a China-based cost-effectiveness analysis. *Front Immunol*. (2024) 15:1408928. doi: 10.3389/fimmu.2024.1408928

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 23 May 2025
DOI 10.3389/fpubh.2025.1570338

Check for updates

OPEN ACCESS

EDITED BY
Jing Yuan,
Fudan University, China

REVIEWED BY
Wei Zhang,
Honghe University, China
Wenhao Qi,
Jilin Agriculture University, China

*CORRESPONDENCE
Siyi Mao
maosiyi0223@163.com
Lin Lu
lulin355@163.com
Yuan Jing
2637104729@qq.com

†These authors share first authorship

RECEIVED 03 February 2025
ACCEPTED 06 May 2025
PUBLISHED 23 May 2025

CITATION
Liu J, Mao S, Lu L, Jing Y, Yang X, Xu H and Ren Y (2025) The impact of digital economy on the supply chain resilience of cross-border healthcare e-commerce.
Front. Public Health 13:1570338.
doi: 10.3389/fpubh.2025.1570338

COPYRIGHT
© 2025 Liu, Mao, Lu, Jing, Yang, Xu and Ren. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

The impact of digital economy on the supply chain resilience of cross-border healthcare e-commerce

Jianyu Liu[1,2†], Siyi Mao[1*†], Lin Lu[1,3*†], Yuan Jing[1*], Xiangjun Yang[1], Hejiang Xu[1] and Yuelin Ren[1]

[1]School of Economics and Management, Guangxi Normal University, Guilin, China, [2]Jinan Liangong Testing Technology Co., Ltd, Jinan, China, [3]Key Laboratory of Digital Empowerment Economic Development, Guangxi Normal University, Guilin, China

The healthcare industry plays a crucial role in global economic development and public health, but the healthcare cross-border e-commerce supply chain often faces numerous risks due to various disruptive events. We employ panel data from 2013 to 2022 for provincial-level regions in China to investigate the impact mechanisms of the digital economy on supply chain resilience in cross-border healthcare e-commerce. The results indicate that the digital economy significantly enhance supply chain resilience, with reduced reliance on foreign trade, increased export technology complexity, and decreased export concentration being key pathways for this improvement. The impact of the digital economy is stronger in the western regions than in central and eastern areas, and the establishment of comprehensive cross-border e-commerce pilot zones can further empower the supply chain. These findings offer valuable insights for the sustainable development of healthcare cross-border e-commerce supply chain resilience and the digital economy.

KEYWORDS

digital economy, healthcare industry, cross-border e-commerce, supply chain resilience, impact mechanisms

1 Introduction

The advent of digital technologies has fundamentally reconfigured conventional production, manufacturing, and operational paradigms, engendering the evolution of emergent industrial ecosystems and innovative development frameworks. The digital economy relies on the integration of data resources and digital technologies to promote economic development and enhance construction efficiency. The cross-border e-commerce supply chain in healthcare is an important application of the digital economy in the medical field, playing a vital role in global health initiatives. As digital technology and e-commerce continue to develop, the digital economy and healthcare cross-border e-commerce supply chain will further deepen and expand, injecting new vitality and momentum into global health efforts.

However, the instability and uncertainty of the VUCA environment pose challenges to the management of cross-border e-commerce supply chains. For example, the COVID-19 pandemic has revealed the vulnerability of supply chains due to shortages of medical supplies, highlighting the urgent need for improved management to achieve sustainable development. Although cross-border e-commerce supply chains are similar to traditional supply chains, they display diverse and decentralized characteristics influenced by the unique aspects of international trade.

As attention to supply chain resilience and risk management increases, researchers and practitioners are gradually focusing more on healthcare supply chains. Studies have explored resilience mechanisms from various perspectives, including the digital transformation of healthcare enterprises (1, 2) and lean management (3). However, there is still a lack of specific applications and theoretical research concerning the healthcare cross-border e-commerce supply chain. The complexity of the healthcare cross-border e-commerce supply chain and its significance in public health crises emphasize the necessity for further exploration and practical application.

This study centers on the core proposition of cross-border e-commerce development in the healthcare industry during the digital economy era, systematically addressing the critical scientific question of "how to develop adaptive mechanisms driven by digital technologies to enhance the resilience of cross-border medical supply chains." Grounded in industrial and regional economics perspectives, the research deconstructs the multidimensional impact mechanisms of the digital economy on cross-border healthcare supply chains—encompassing three structural dimensions: foreign trade dependence, export technological sophistication, and export trade concentration—to establish an integrated analytical framework of "digital technologies–economic structures–supply chain synergies." The potential contributions and innovations of this study are as follows: First, existing research primarily focuses on the impact of digital economy development on the socio-economic landscape, with an emphasis on its effects on domestic economic circulation. However, we focus on the resilience of healthcare cross-border e-commerce supply chains and explore the enabling mechanisms of the digital economy on external economic circulation. This approach will help to provide a more comprehensive assessment of the multidimensional impact of the digital economy on economic development. Second, this research is the first to establish an evaluation system for the resilience of healthcare cross-border e-commerce supply chains, contributing to the comprehensive theoretical framework related to supply chain resilience in the healthcare and cross-border e-commerce industries. Third, by analyzing the impact mechanisms of digital economy development on the resilience of healthcare cross-border e-commerce supply chains at the provincial level, this study can uncover the relational mechanisms between the digital economy and supply chain management. This enriches the theoretical research in both the digital economy and supply chain management fields and has significant practical and economic implications for promoting the development of the digital economy and the healthcare industry across different regions.

2 Literature review

2.1 Research of digital economy

2.1.1 Definition of digital economy

The digital economy emerged as a new engine for global economic development in the 1990s. During this period, the rise of internet technology gave birth to e-commerce, with the emergence of industry giants like Amazon and eBay marking the embryonic form of the digital economy. Initially, the definition of the digital economy was confined to output related to the Information and Communication Technology (ICT) industry, representing the earliest narrow conception of the digital economy. As internet technologies became widely adopted across economic and social spheres, the U.S. Department of Commerce and OECD defined the digital economy as an integrated system encompassing IT production, application industries, and e-commerce. However, with the continuous advancement of new-generation information technologies, the essence and scope of the digital economy have been progressively expanding. Kling and Lamb (4) defined digital economic activities from the perspective of digital technology applications in the production, distribution, and exchange of products or services. Knickrehm and Daugherty (5) suggested that the portion of new additional output resulting from investments in information technology is termed the digital economy.

2.1.2 Integration of digital economy and cross-border e-commerce

The digital economy has transcended traditional business models, inevitably impacting economic and social structures as well as enterprise operational paradigms (6, 7). Cross-border e-commerce, a novel application of international trade integrating information and communication technologies with internet technologies, has garnered significant attention globally. From the perspective of cross-border e-commerce supply chains, the digital economy also drives digitalization in supply chain management. Nunez-Merino et al. (8) emphasized the importance of enterprises leveraging digital technologies for continuous optimization and innovation in supply chain management within the context of the digital economy. Modern digital technologies enhance the capabilities for information sharing and collaboration in supply chains (9, 10), increase supply chain integration (11), and reduce negative value processes in supply chain economic activities (12). Numerous scholars have studied the role of digital technologies in empowering supply chains (13):suggested that the adoption of digital tools such as big data analytics can enhance the flexibility of product flows, thereby improving supply chain performance and resilience; Hazen et al. (14) and argued that big data analytics can enhance supply chain performance and drive innovation; Matthias et al. (15) also suggested that big data analytics can lower overall supply chain costs, enabling better decision-making and product and service offerings.

2.2 Research of supply chain resilience

2.2.1 Definition of supply chain resilience

Rice and Caniato were among the first to propose the concept of supply chain resilience. Christopher and Peck (16) defined "supply chain resilience" as "the ability of a supply chain to recover to its original state or a more ideal state after being disrupted." This concept has also been employed by many scholars to investigate supply chain security management at the enterprise level.

Some scholars have elevated the enhancement of supply chain resilience to the level of national economic strategy, defining it as the ability to flexibly respond to new crises and rapidly recover (17). Currently, most scholars tend to define supply chain resilience from the perspective of dynamic capabilities. According to Larin et al. (18), supply chain development strategies should ensure that each link can efficiently respond to adverse factors. Furthermore, supply chain

resilience places greater emphasis on the ability to respond promptly and continuously improve when facing uncertainty and risks (19).

2.2.2 Influencing factors and measurement of supply chain resilience

Research on the factors influencing supply chain resilience has been conducted extensively by scholars, focusing on both internal and external factors. External factors encompass political, social, economic, and environmental aspects. Globalization has driven supply chain resilience to become a national strategy, with social systems and political regimes between countries potentially impacting the flow of capital, information, and logistics within supply chains (20). Wieland (21) noted that uncontrollable factors such as social culture and public opinion have also emerged as major sources of supply chain risk. Compared to external factors, internal factors influencing supply chain resilience are more complex and encompass a broader range of research areas. From an organizational perspective, integration capability (22), collaborative cooperation (23), and communication (24)all positively influence supply chain resilience. From a technological perspective, big data analytics (13) and digital technologies (25) enhance the predictive and management capabilities of supply chains, thereby playing a crucial role in supply chain resilience.

For cross-border e-commerce supply chain resilience, environmental uncertainties—including geopolitical conflicts (e.g., China-U.S. trade frictions), natural disasters (26), and global public health crises (27)—constitute critical disruption factors. Cross-border logistics delays and tariff fluctuations further exacerbate emerging markets' vulnerability, thereby significantly compromising supply chain resilience. Structurally, supplier diversification (28) enhances resilience through risk dispersion. At the organizational level, joint contingency protocols (29)and cross-cultural management competencies (30)serve as pivotal soft enablers for resilience augmentation.

Existing scholars have primarily constructed supply chain resilience indicators around five main dimensions: prediction, adaptation, response, recovery, and learning, with distinctions made in the sub-dimensions of these five capabilities (31). In terms of research methodologies, many validated and widely applied scales have been used to measure supply chain resilience. However, these scales often rely on subjective assessments and micro-level expressions.

2.3 Research of healthcare supply chain

Most existing research on the healthcare industry primarily focuses on technological perspectives, with fewer scholars approaching it from a management science viewpoint. Considering the characteristics of the healthcare industry, it is known for being technology-intensive, knowledge-intensive, patent-dependent, and globally innovative. Consequently, many countries classify the healthcare industry as a strategic emerging industry (32). As a knowledge-intensive industry, the healthcare industry is typically patent-dependent, encompassing pharmaceutical manufacturing, medical technology, and biotechnology. It is characterized by high investment, high risk, high return, and long cycles (33). The majority of current research on the healthcare industry primarily adopts a technological perspective, focusing on cutting-edge fields such as new drug development (34), medical device innovation (35), and breakthroughs in diagnostic and therapeutic technologies (36). However, a limited number of studies have analyzed the healthcare industry from a management standpoint. For instance, Alotaibi and Wilson (37)explored the factors influencing the digital competencies of healthcare professionals, while Ahmed and Hamdan (38) investigated the resilience and digital transformation strategies of healthcare supply chain in emerging economies. These studies provide valuable insights for our subsequent research.

The healthcare supply chain involves numerous participants, particularly in the pharmaceutical supply chain, making its structure relatively complex. Current research on healthcare supply chains primarily focuses on pricing and profit coordination decisions. Zandkarimkhani et al. (39)investigated the design of a perishable pharmaceutical supply chain network under uncertainty. Similarly, Zahiri et al. (40) studied the design of pharmaceutical supply chain networks under uncertainty, considering product perishability and substitutability within the context of sustainable and resilient supply chains. Settanni et al. (41)proposed an improved interactive multi-objective fuzzy programming method to establish and optimize a multi-period, multi-objective pharmaceutical supply chain model, enriching the healthcare system. Benneyan et al. (42) developed optimization strategies for healthcare supply chains and pre-positioning storage locations to address the demand of home healthcare patients experiencing periodic interruptions. Ma et al. (43) examined the quality of work in healthcare supply chains from the perspective of patient benefits and suggested that optimizing quality work can enhance supply chain profitability.

2.4 Research commentary

Existing literature indicates that research on the digital economy has achieved significant breadth and depth, systematically exploring its integration with cross-border e-commerce, including business models, development promotion, and supply chain digital transformation. It provides a theoretical foundation for this study.

However, existing studies predominantly adopt a "technology-economy" dualistic analytical framework, failing to adequately reveal the differentiated mechanisms of digital economy in specialized industries like healthcare. A tripartite analytical model integrating industrial characteristics, digital economy, and regional development remains notably absent. Supply chain resilience has emerged as a key research focus in supply chain management, with scholars examining its influencing factors and evaluation systems from multiple perspectives. Nevertheless, current research—particularly on manufacturing enterprises—overwhelmingly emphasizes firm-level analyses, focusing on organizational and operational models while neglecting macro-industrial dimensions and external economic circulation. In healthcare industry research, the predominance of technological perspectives and case-study methodologies has led to excessive focus on individual institutions' operational optimization. This approach lacks systematic consideration of regional or industry-wide healthcare supply chain resilience, revealing critical gaps in both theoretical frameworks and practical applications.

Therefore, we innovatively develop a supply chain resilience evaluation system for cross-border e-commerce in the healthcare sector from macro-industrial and regional economic perspectives. Methodologically, it enriches healthcare industry research by

integrating industrial characteristics, digital economy development, and regional coordination into a unified analytical framework to examine their impacts and mechanisms on supply chain resilience. These theoretical breakthroughs not only expand the application boundaries of cross-border e-commerce supply chain resilience theory, but also provide critical policy implications for the global deployment of healthcare industries in the post-pandemic era.

3 Theoretical basis and research hypothesis

3.1 Digital economy and resilience of cross-border e-commerce supply chains in healthcare

Driven by the new wave of technological revolution, the digital economy has emerged as a novel economic paradigm characterized by digital technologies (e.g., internet, big data, and artificial intelligence) as its core driver and data as its key production factor. As a product of deep integration between information technology and traditional economies, it fundamentally restructures production, distribution, and consumption patterns through digital transformation. This paradigm significantly influences supply chain operations and production efficiency while creating new opportunities for value generation in supply chain (44). Supply chain resilience emphasizes a system's ability to rapidly adapt, recover, and continuously optimize in response to internal and external disruptions. Its essence lies in enabling supply chain to achieve higher levels of equilibrium and competitiveness amid uncertainty. The most direct impact of the digital economy on healthcare cross-border e-commerce supply chain manifests in the application of digital technologies, which enhance resilience across four key dimensions: risk early warning, operational flexibility, collaborative efficiency, and compliance management.

From the perspective of risk early warning, big data analytics enables organizations to process vast operational datasets, effectively identifying and assessing risks. This capability improves planning timeliness and facilitates risk mitigation (45, 46). By efficiently integrating and processing information data, digital technologies can help enterprises obtain rapidly changing customer demand information and supplier inventory status information, significantly improving the visibility (47) and traceability (48) of the supply chain. This facilitates precise demand–supply matching and enables dynamic optimization of resource allocation. In addition to integrating information, digital technologies can also facilitate experiential learning from data. Technologies such as blockchain and artificial intelligence enable the digitization and standardization of existing knowledge and experience, providing supply chain members with information, knowledge, and experience to handle disruptive events, thereby enhancing their resilience (49, 50)and enhancing operational management efficiency.

From the perspective of collaborative efficiency, the high innovation, strong penetration, and wide coverage of the digital economy have profoundly changed the total factor productivity at various levels of the real economy (51), driving the development of digital platforms and digital infrastructure. This can overcome the limitations of resource scarcity and homogeneity within cross-border e-commerce and cross-border logistics enterprises (52), accelerate the flow of resources and information between cross-border e-commerce and cross-border logistics, reduce information asymmetry, and significantly improve inefficiencies and unnecessary resource wastage in the supply–demand matching process, thereby lowering the coordination costs between them (53). From a compliance management perspective, the unique regulatory requirements of healthcare products make certification and supervision a critical component in cross-border e-commerce supply chain. The deep integration of digital technologies has significantly enhanced intelligent regulatory capabilities: AI-powered certification engines automatically align products with target market regulations, reducing compliance review cycles and improving audit efficiency; blockchain-based traceability systems enable end-to-end monitoring from raw material procurement to final sales, ensuring each healthcare product meets the quality standards and regulatory requirements of destination markets. This digital regulatory framework not only mitigates compliance risks but also transforms safety control from reactive responses to proactive prevention. By establishing a robust quality assurance mechanism, it provides a foundational safeguard for the sustainable development of healthcare cross-border e-commerce. Therefore, the following hypothesis is proposed:

> *Hypothesis 1*: The development of the digital economy can enhance the resilience of the cross-border e-commerce supply chain in healthcare.

3.2 Digital economy, foreign trade dependence, and resilience of cross-border e-commerce supply chains in healthcare

Foreign trade dependence on typically refers to the degree to which a country or region's national economy relies on international trade, reflecting both the depth of its participation in global division of labor and its level of economic openness. From the perspective of the broader developmental environment, China's marginal contribution of foreign trade to GDP is diminishing, with the growth rate of dependence on foreign trade gradually slowing down, and even showing a downward trend (54). Foreign trade dependence is influenced by multiple factors, including the stage of economic development, industrial structure characteristics, market size, and policy orientation. However, the digital economy era is driving transformative changes: digital technologies are reshaping the traditional mechanisms behind foreign trade dependence by enhancing domestic industrial chain coordination efficiency and accelerating the digital transformation of trade in services. The impact of the digital economy on foreign trade dependence is primarily manifested in two aspects: traditional trade patterns and domestic market influences. Firstly, concerning traditional trade patterns, the digital economy has propelled the development of service trade, whereby digital technologies enable the provision of globalized services across borders. By developing service trade, nations can reduce reliance on goods trade and mitigate risks associated with foreign trade. Simultaneously, through technologies such as the internet, big data, and artificial intelligence, enterprises can achieve intelligent management of supply chains, thereby becoming more independent in production and supply, and reducing reliance on external supply chains. For the

domestic market, the permeability, integration, and synergy of the digital economy continuously enhance the digitization level of China's information and communication industry, which facilitating the domestic circulation. Concurrently, through the digital transformation of industries, it increases the output and efficiency of traditional industries and the real economy, thereby enhancing domestic enterprises' supply capacity and their ability to accurately match market demand. Additionally, the digital economy has given rise to new consumer formats such as platform economy and sharing economy, creating new consumption patterns and driving continuous expansion in domestic demand (55).

The Resource Dependence Theory posits that organizations must acquire critical resources from external environments to sustain operations, with such dependence creating power dynamics among entities—where the criticality and scarcity of resources determine the bargaining advantage of external actors (56). To mitigate dependency risks, firms adopt strategies like supply diversification, vertical integration, and strategic alliances to reconfigure their resource networks. From the perspective of this theory, lower foreign trade dependence essentially reflects a regional economic system's deep embeddedness in internal resource endowments and market structures. This inward-oriented resource acquisition pattern drives cross-border e-commerce enterprises in the healthcare sector to construct localized resource pools, thereby reducing reliance on external critical resource providers.

Specifically, in the dimension of resource acquisition, cultivating local supplier ecosystems creates alternative resource nodes, enabling medical cross-border e-commerce firms to overcome the "resource dependence dilemma" (56) by establishing polycentric supply networks to disperse operational risks arising from environmental uncertainty. Secondly, in terms of power balancing, an evenly distributed supply chain structure diminishes the bargaining leverage of suppliers from specific (external) regions, allowing these firms to dynamically adjust procurement strategies based on resource importance and substitutability, thereby achieving a rebalancing of resource control. Finally, regarding organizational adaptability, the implementation of localized management systems essentially responds to the need for "boundary-spanning" (57). Through on-site supply chain teams and infrastructure, healthcare cross-border e-commerce enterprises can more effectively absorb and translate local market knowledge, enhancing their agile responsiveness to fluctuations in cross-border demand. This organizational restructuring, rooted in deepening local resource integration, not only reduces information asymmetry costs in cross-border transactions but also establishes an institutional buffer mechanism for emergencies, ultimately leading to a structural enhancement in the resilience of medical cross-border e-commerce supply chain. Hence, the following hypothesis is proposed:

> *Hypothesis 2*: The digital economy enhances the resilience of medical cross-border e-commerce supply chains by reducing foreign trade dependence.

3.3 Digital economy, export technological complexity, and resilience of cross-border e-commerce supply chains in healthcare

Global Value Chain (GVC) theory serves as a critical analytical framework for examining the division of labor and cooperation in the global economy, with its core focus on deconstructing and coordinating the entire process—from conceptual design to final consumption—of products or services across different countries and firms. From the perspective of GVC theory, export technological sophistication not only reflects, to some extent, the technological content and production efficiency of exported goods (58), but also indicates a country's or firm's position and competitiveness within the GVC division of labor. Some scholars further regard it as a key measure of trade structure optimization (59). A higher level of export technological sophistication indicates that firms within a country are better positioned to occupy strategic, high-value-added segments of the global value chain (GVC), such as R&D and design. The digital economy can significantly enhance the efficiency of information flows and coordination capabilities across GVC segments by reshaping the operational dynamics of global value chains. Specifically, digital technologies break down the spatial and temporal barriers inherent in traditional GVC, reducing information asymmetry and coordination costs for firms engaged in global production networks. This facilitates the cross-border integration of innovation factors across R&D, production, and logistics, thereby driving the technological upgrading of export products (60). Furthermore, the development of the digital economy has facilitated deeper integration in global technology markets. Through digital platforms, firms can more efficiently access cutting-edge international technological knowledge, which stimulates their R&D activities and increases investment in innovation (61), thereby enhancing their competitive advantage in global value chain. The construction of new digital infrastructure not only reduces communication, transaction, and information search costs but also drives trade upgrading through technology spillover effects (62), helping firms break free from the "low-end lock-in" dilemma and achieve upward mobility in GVC. Beyond technological capability, infrastructure, and trade costs, the digital economy also strengthens firms' absorptive capacity for advanced GVC technologies by improving the digital skills of human capital, providing sustained talent support for the continuous advancement of export technological sophistication.

While high technological complexity may pose challenges in supply chain management, in the healthcare industry, mastery of highly complex export technologies contributes to enhancing product quality and safety. In the global value chain of the healthcare industry, products with high technological sophistication typically correspond to core control segments of the value chain. Such products must comply with stringent international certification standards (e.g., FDA, GMP), and their manufacturing processes involve complex technical procedures and quality control systems. By enhancing export technological sophistication, firms can better meet these international standards, ensuring consistent product quality across all GVC stages—from R&D to final consumption. Particularly in cross-border logistics, the application of advanced temperature-control technologies and digital traceability systems enables firms to monitor product flows in real time throughout the GVC, allowing timely responses to potential quality risks. This capability strengthens the overall resilience and reliability of the value chain. Hence, the following hypothesis is proposed:

> *Hypothesis 3*: The digital economy enhances the resilience of healthcare cross-border e-commerce supply chains by elevating export technological complexity.

3.4 Digital economy, export trade concentration, and resilience of cross-border e-commerce supply chains in healthcare

Export trade concentration reflects the degree of agglomeration in export commodities or target markets across product categories and geographical dimensions. This concept encompasses two dimensions: product concentration, which measures the extent to which export earnings are concentrated in a limited number of commodity categories; and market concentration, which characterizes the dispersion level of export destinations. High concentration is often associated with comparative advantages in resource endowments or specialized division of labor, while low concentration reflects a diversification strategy. The digital transformation serves as a crucial driving force for enhancing the diversification of enterprise exports (63). External risks contribute to the highly dynamic and complex nature of the international market, making adaptability to new environments a critical capability for enterprises in responding to external dynamic changes. Under the advancement of the digital economy, digital technologies enable organizations to swiftly and accurately capture changes in the external environment (64). By influencing internal organization, production methods, management costs, information dissemination methods, etc., digital technologies endow organizations with acute international market insights and robust resource acquisition capabilities (65), thereby providing favorable conditions for expanding the diversity of international markets. The reduction of trade costs facilitates the formation of new trade connections, thereby lowering the concentration of exports and enhancing the level of export diversification (66). Specifically, the application of digital financial technologies can streamline cross-border trade payment and settlement processes, reducing transaction costs. This enables small enterprises and emerging market countries to more easily participate in international trade, thereby promoting export diversification.

The core proposition of portfolio theory posits that by allocating capital across diversified assets with low return correlations, investors can either minimize risk at a given return level or maximize returns at an acceptable risk threshold. This theoretical framework demonstrates that investment diversification reduces unsystematic risk due to heterogeneous responses of different assets to market shocks. When transposed to international trade, this financial paradigm suggests that export structures essentially constitute "trade portfolios": export product categories function as distinct assets, while target markets represent alternative investment channels. Excessive concentration in either export products or markets (analogous to "overweight positions" in financial portfolios) may engender export instability (67, 68), exposing trade flows to idiosyncratic risks including demand volatility, technological substitution, or policy barriers that could trigger significant export earnings fluctuations. Conversely, diversification across products and markets has been empirically shown to mitigate export volatility (69), effectively constructing an "efficient trade portfolio" that employs risk-hedging mechanisms to cushion external shocks—when returns from certain products/markets decline, the stable performance of others creates compensatory effects.

For cross-border e-commerce healthcare supply chain, regional diversity in healthcare medical products functions analogously to an investment portfolio holding stocks across different sectors. When specific product categories encounter technical barriers or regulatory scrutiny, other product lines can maintain stable cash flows. This approach not only mitigates market risks but also reduces dependency on particular products or markets. In the event of external shocks affecting certain healthcare products, the performance of alternative export commodities can compensate for losses, thereby enhancing supply chain stability and risk resilience. Moreover, greater export product diversity reflects stronger regional market competitiveness and contributes to sustainable regional development.

Therefore, the following hypothesis is proposed:

> *Hypothesis 4*: The development of the digital economy enhances the resilience of healthcare cross-border e-commerce supply chains by reducing export concentration.

Based on the aforementioned theoretical analysis and research hypotheses, the theoretical model diagram of this study is shown in Figure 1.

4 Research design

4.1 Model assumptions

To examine the impact of the digital economy on the resilience of healthcare cross-border e-commerce supply chains, we set the following baseline model (Equation 1):

$$Revl_{it} = \alpha + \beta_1 Digde_{it} + \sum_j \beta_j Control_{it} + \mu_i + \gamma_t + \varepsilon_{it} \quad (1)$$

Where: the subscripts i and t represent provinces and years, respectively; Revl denotes the level of resilience of medical cross-border e-commerce supply chains; Digde represents the level of development of the digital economy; Control represents the control variable group; μ_i and γ_t represent province fixed effects and time fixed effects, respectively; ε_{it} is the random error term. If the regression coefficient β_j is significantly positive, it indicates a direct positive and significant impact of digital economy development on the resilience of healthcare cross-border e-commerce supply chains.

4.2 Variables description

4.2.1 Dependent variable: the level of resilience of healthcare cross-border e-commerce supply chains (Revl)

Currently, the construction of resilience indicators for supply chains typically includes dimensions such as prediction, adaptation, recovery, response, and innovation capabilities. In light of this, this study measures the resilience level of healthcare cross-border e-commerce supply chains primarily from four dimensions: responsiveness, adaptability, recovery, and learning and innovation capabilities, based on the dynamic capability theory. Responsiveness, adaptability, and recovery capabilities mainly refer to the ability of the supply chain to respond to disturbances, while learning and innovation capability pertains to the ability of the supply chain to

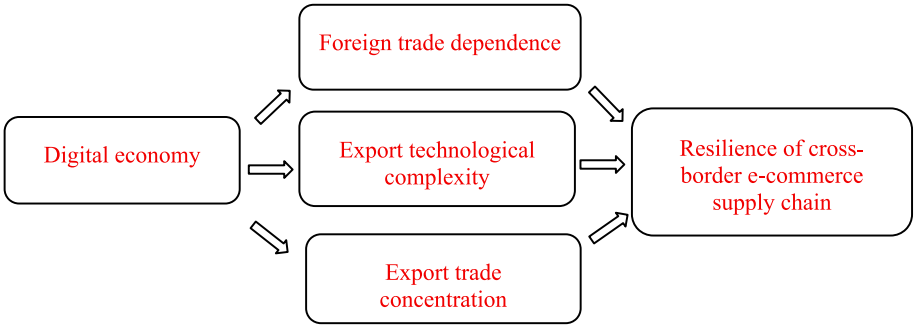


FIGURE 1
Theoretical model.

adapt after disturbances. Corresponding indicators are selected for measurement in each dimension, and principal component analysis is employed to calculate the resilience level of healthcare cross-border e-commerce supply chains for each province and time period.

Recovery capability, as referenced by WEI et al. (65), is primarily reflected by the rate of change in healthcare exports. The numerical fluctuations and trend variations in healthcare exports essentially serve as a "barometer" of the synergistic efficacy across supply chain segments, with their data dynamics precisely capturing the entire process from localized disruptions to systemic recovery within the supply chain. When the fluctuation rate of export volume is low, it indicates that the supply chain can quickly adjust and recover in the face of external shocks or emergencies, demonstrating strong resilience.

Supply chain resistance refers to the ability of the supply chain system to effectively withstand and maintain normal operation when facing external shocks, risks, or changes. The cargo capacity and transportation capability of a region reflect its logistical distribution competence and overall regulatory capacity, which indirectly demonstrates the development level of regional supply chain and their "resilience redundancy" when facing supply chain disruptions. From an ecosystem perspective, the quantitative scale of healthcare enterprises within a region directly determines the nodal density of the supply chain network. This density effect inherently possesses risk dispersion characteristics and innovation multiplier effects, thereby enhancing supply chain flexibility.

Responsiveness refers to the supply chain system's ability to quickly respond and adjust to changes in market demand, external environmental factors, and emergencies. Inventory functions as an "emergency response reserve pool," where strategic inventory deployment plays a crucial role in providing operational buffers for supply chain systems. Given the high-value and time-sensitive nature of healthcare products, inventory management must achieve "precision redundancy"—avoiding expiration losses from overstocking while ensuring rapid response during emergencies. This balancing capability serves as a key metric for evaluating supply chain responsiveness. Consequently, the inventory turnover rate of regional healthcare industries reflects the response capacity of cross-border e-commerce healthcare supply chain. Furthermore, a diversified network of collaborative partners establishes "distributed response hubs." A broader base of partners provides cross-border e-commerce operations with increased resources and alternatives. In scenarios of sudden demand surges or regional supply chain disruptions, the ability to quickly activate alternative partners enables production capacity substitution and logistics channel switching. This mechanism significantly enhances the flexibility and stability of the supply chain.

Learning and innovation capability reflects the strength and endurance of supply chain organizations. Higher levels of innovation indicate stronger technical support for cross-border e-commerce supply chains, as well as more innovation resources and talent in the region. Additionally, it can promote information sharing and collaboration. The development level and innovation capacity of the technological market most directly reflect the knowledge flow and innovation synergy effects within a region. Consequently, we will employ these two dimensions—technological market development and innovation performance—as metrics to evaluate the learning and innovation capabilities of cross-border e-commerce healthcare supply chain. Specific indicators are detailed in Table 1.

4.2.2 Core explanatory variable: level of digital economy development (Digde)

Drawing on the measurement methods proposed by Wang et al. (70) and Zhao et al. (71), a comprehensive evaluation system comprising four primary dimensions—digital infrastructure, digital industrialization, industrial digitalization, and digital innovation capability—and 10 secondary dimensions, totaling 21 detailed indicators, was constructed as shown in Table 2 below. The entropy weight method (entropy value method) was then employed to calculate the level of digital economy development for each time period.

Digital infrastructure, as a fundamental indicator, incorporates hard metrics such as internet broadband access and mobile communication coverage (e.g., port capacity, base station density). These parameters directly determine data flow efficiency and connectivity breadth, serving as the physical foundation for digital economy operations. Digital industrialization focuses on scale indicators of the information and communication technology (ICT) sector (e.g., software revenue share, total telecom services), which objectively quantify the maturity and economic contribution of core digital industries. Industrial digitalization is measured through enterprise digital penetration rates (e.g., e-commerce transaction ratio, computer utilization density), reflecting the practical outcomes of traditional industry transformation and revealing the depth of digital technology's empowerment in the real economy. Digital

10.3389/fpubh.2025.1570338

TABLE 1 Evaluation indicators for the resilience of healthcare cross-border e-commerce supply chains.

Primary Indicators	Secondary Indicators	Description of Indicators
Recovery Capability	Fluctuation degree of healthcare product export volume	Absolute value of export volume change rate
Resistance Capability	Regional goods carrying capacity	Goods turnover volume
	Scale of cross-border healthcare e-commerce enterprises	Number of cross-border healthcare e-commerce enterprises
	Regional transportation capacity	Freight volume
Responsiveness	Regional healthcare product inventory turnover rate	Sales amount/Average inventory
	Supplier network relationships	Number of bilateral trade partnerships
Learning and Innovation Capability	Level of technological market development	Total value of technology contracts
	Level of innovation	Logarithm of patent applications

innovation capability employs R&D intensity indicators (e.g., R&D expenditure, full-time equivalent research personnel), as these directly represent sustainable drivers of technological iteration and constitute core elements for assessing long-term digital economy competitiveness.

The entropy weight method is an objective quantitative approach that automatically calculates indicator weights based on data dispersion characteristics. Compared with subjective methods like expert scoring, it effectively avoids weighting biases. In this study, we first applied range standardization to eliminate dimensional effects. Since all indicators are positively oriented, we standardized them using the Equation 2:

$$X'_{ij} = \frac{x_{ij} - \min\left(x_j\right)}{\max\left(x_j\right) - \min\left(x_j\right)} \tag{2}$$

Let x_{ij} represent the value of the j-th indicator for the i-th sample.

Subsequently, we calculate the proportion of each indicator, see Equation 3 for details:

$$p_{ij} = \frac{x'_{ij}}{\sum_{i=1}^{n} x'_{ij}} \tag{3}$$

Where $p\ Z_{ij} \in (0,1)$, and $\sum p_{ij} = 1$;

Subsequently, the entropy value for each indicator is determined using the information entropy formula, see Equation 4 for details:

$$e_j = -k\sum_{i=1}^{n} p_{ij} \ln p_{ij} \tag{4}$$

Where: k = 1/ln(n) serves as the normalization constant;

Finally, the objective weight for each indicator is derived through the weighting formula, followed by a weighted calculation of the composite score, refer to Equation 5:

$$w_j = \frac{1 - e_j}{\sum_{j=1}^{m}\left(1 - e_j\right)} \tag{5}$$

4.2.3 Mediating variables

This study focuses on healthcare exports as the research subject, and therefore selects foreign trade dependence (Ftrd), export technological complexity (Expt), and export trade concentration (Dexp) as the mediating variables. Foreign trade dependence (Ftrd) is represented by the ratio of the total import and export volume of a province to the GDP of that province.

The export technological complexity (Expt) is measured following the approach of Hausmann et al. (72), calculating the export technological complexity at the provincial level. Firstly, the export technological complexity at the product level for a given year ($\mathrm{Prody_p}$) is calculated as the Equation 6:

$$Prody_p = \sum_m \frac{\frac{X_{mp}}{X_m}}{\sum_m \frac{X_{mp}}{X_m}} Y_m \tag{6}$$

Where $\mathrm{Prody_p}$ represents the technological complexity of export product p, $\mathrm{Y_m}$ denotes the per capita GDP of region m, and $\mathrm{X_{mp}}$ and $\mathrm{X_m}$ represent the export value of product p and the total export value of all products from country m, respectively. Based on this, the export technological complexity at the provincial level in China is further constructed by considering the export structure of each province. The detailed calculation procedure is shown in Equation 7:

$$Expt_{it} = \sum_{c=1}^{n} \frac{X_{ipt}}{X_{it}} Prody_p \tag{7}$$

Where $\mathrm{Expt_{it}}$ represents the export technological complexity of province i in year t, $\mathrm{X_{ipt}}$ denotes the export value of product p from province i in year t, and $\mathrm{X_{it}}$ represents the total export value of province i in year t.

Export diversification and export trade concentration (Dexp) is measured using the Herfindahl–Hirschman Index (HHI). This index reflects the distribution characteristics of the proportions of traded products and can indirectly indicate the degree of diversification. Consequently, it is utilized by the economics community and government management departments as a measure of diversification. The Herfindahl–Hirschman Index (HHI) is defined as the sum of the squares of the percentages of the total export value for various products relative to the total export value, reflecting the concentration of import and export trade. The specific calculation formula is as the Equation 8:

$$HHI = \sum_{i=1}^{n} s_{ijt}^2 ; s_i = \frac{x_{ijt}}{x_{git}} \tag{8}$$

TABLE 2 Composite index of digital economy development.

Primary Indicators	Secondary Indicators	Description of Indicators
Digital infrastructure	Level of internet penetration	Number of internet broadband access ports
		Number of internet broadband access users
		Number of internet domain names
	Level of mobile phone penetration	Density of mobile phone base stations
		Mobile phone penetration rate
	Breadth of information transmission	Length of long-distance optical cables per unit area
Digital industrialization	Software and information technology services industry	Proportion of software business revenue to GDP
		Number of employees in the information transmission, software, and information technology services industry
	Development level of the electronic information manufacturing industry	Proportion of information technology service revenue to GDP
		Proportion of total telecommunications business to GDP
		Per capita total telecommunications business
	Development level of the postal and telecommunications industry	Per capita total postal business
		Volume of express delivery
		E-commerce transaction value of enterprises
Industrial digitalization	Degree of enterprise digitalization	Proportion of enterprises engaged in e-commerce activities
		Number of computers used per 100 employees in enterprises
		Number of websites owned per 100 enterprises
	Digital inclusive finance	Digital inclusive finance index
Digital innovation capability	Level of research and experimental development	Full-time equivalent of R&D personnel in industrial enterprises above designated size
		R&D expenditure of industrial enterprises above designated size
		Number of R&D projects (topics) in industrial enterprises above designated size

Where s_{ijt} represents the proportion of the export value of product i from province j in period t to the total export value of province j; x_{ijt} denotes the export value of product i from province j in period t, and x_{git} represents the total export value of province j in period t. The HHI index ranges between 0 and 1, with a smaller index indicating lower export concentration, i.e., greater export diversification. It serves as an inverse indicator of export diversification.

4.2.4 Control variables

Drawing from existing literature and the availability of data, the specific control variables selected for this study include: Human capital level (HC): represented by the average years of education; Level of transportation infrastructure (Inft): represented by the logarithm of highway mileage and the logarithm of total freight volume; Labor level (Labor): represented by the natural logarithm of the number of employed persons; Level of industrial structure upgrading (Inds): represented by the logarithm of the ratio of the value added of the tertiary industry to the secondary industry; Government fiscal expenditure (Gov): represented by general government expenditure; Level of industrialization (Indu): represented by the ratio of industrial output value to regional total output value.

4.3 Data source

Data pertaining to export transactions are sourced from the customs database, which comprises complete sample data from customs ports, covering detailed information from all export regions. Export technological complexity and the resilience of the cross-border healthcare e-commerce supply chain, calculated using customs data, are considered highly reliable. Given the focus of this study on the healthcare industry, which mainly encompasses pharmaceutical manufacturing and medical devices, export product inquiries primarily involve selected products from these two categories. Other indicators related to the development of the digital economy and resilience assessments are primarily sourced from the "China Statistical Yearbook" and various provincial and local statistical yearbooks. As pharmaceutical manufacturing and medical devices are part of China's high-tech industries, some data are also obtained from the "China High-Tech Industry Statistical Yearbook." For the limited missing data, interpolation methods were employed for imputation, while logarithmic transformations were applied to specific variables (e.g., Human capital level) to normalize distributions.

5 Empirical analysis

5.1 Benchmark regression

Table 3 presents the benchmark regression results for the levels of digital economy and resilience of the healthcare cross-border e-commerce supply chain. Column (1) reports the regression results of the univariate relationship between the digital economy and the resilience of the healthcare cross-border e-commerce supply chain

after controlling for bidirectional fixed effects. Columns (2) and (3) display the regression results after including control variables and alternatively incorporating time fixed effects and provincial fixed effects. Column (4) reports the regression results after including control variables and simultaneously incorporating both fixed effects. The results indicate that in Column (4), the coefficient for digital economy development (Digde) is 4.818 and statistically significant at the 1% level. This suggests that digital economy development significantly positively influences the resilience of the healthcare cross-border e-commerce supply chain. Moreover, coefficients in Columns (1) to (4) are all positively significant at the 1% level, confirming Hypothesis 1. The variation in the coefficient of digital economy development across Columns (1) to (4) indicates that the extent to which the digital economy promotes the resilience of the healthcare cross-border e-commerce supply chain is influenced by the year and province. This variability may be attributed to policy differences among provinces and external shocks in different years, but overall, it does not affect the significance of the results.

5.2 Robustness tests

We examined the robustness of the research results using five methods: replacing the core explanatory variable, adding control variables, lagging one period, GMM model test and conducting endogeneity tests.

5.2.1 Replacing the core explanatory variable, adding control variables and lagging one period

Since this paper uses the entropy method to measure the level of digital economic development, the principal component analysis (PCA) method will be employed in this section to reassess the development level of the digital economy. First, data standardization preprocessing is required to transform the original indicators with different units into standard scores with a mean of 0 and a standard deviation of 1, thereby eliminating the impact of unit differences on the analysis results. The second step involves constructing a correlation coefficient matrix. By calculating the degree of correlation between each indicator, highly correlated indicator groups are identified. The third step is eigenvalue decomposition, where the eigenvalues and eigenvectors of the correlation coefficient matrix are solved. The size of the eigenvalues represents the ability of each principal component to explain the variation in the original data. The fourth step determines the number of principal components. We select the first few principal components with eigenvalues greater than 1 and a cumulative variance contribution rate exceeding 85%, which significantly reduces dimensionality while retaining most of the effective information. Finally, the comprehensive score is calculated by performing a weighted summation of the standardized data based on the variance contribution rate of each principal component. The recalculated digital economy development levels of each province are denoted as Digde_new.

And the added control variable is the level of economic development (Eco). Additionally, we lagged the level of digital economy development by one period (L. Digde). The results are presented in Table 4, which shows that the coefficients for the level of digital economy development are consistent with the benchmark regression results, passing the robustness test.

5.2.2 GMM model test

To eliminate the impact of endogeneity, the basic panel model was transformed into a system GMM model for re-estimation. In this model, we treated the dependent variable lagged by 1–2 periods as endogenous variables, while the independent variables lagged by one period and all control variables were treated as exogenous variables. The regression results of the GMM model are shown in Table 5. The regression coefficient of "Digde" remains significantly positive at the 1% level, consistent with the results of the basic panel model. Moreover, the AR2 is greater than 0.05, failing to reject the null hypothesis of no second-order autocorrelation in the residuals, and the Hansen value is also greater than 0.1, failing to reject the null hypothesis of valid instrumental variables. This indicates that the GMM model is valid, and the earlier analysis results remain robust.

TABLE 3 Benchmark regression results.

Variables	(1)	(2)	(3)	(4)
	Revl	Revl	Revl	Revl
Digde	4.818*** (10.00)	1.466*** (3.13)	3.669*** (6.68)	2.842*** (4.99)
HC		1.865*** (3.00)	2.043*** (3.06)	0.801 (0.93)
Inft		1.257*** (9.53)	1.169*** (9.62)	1.298*** (8.92)
Labor		−0.204 (−0.84)	0.037 (0.23)	−0.197 (−0.73)
Inds		−0.002 (−0.24)	0.000 (0.02)	0.001 (0.07)
Gov		0.000*** (5.20)	0.000*** (3.66)	0.000*** (3.88)
Indu		0.346 (0.78)	0.244 (0.57)	−0.002 (−0.00)
_cons	2.177*** (38.14)	−15.218*** (−5.72)	−16.428*** (−8.85)	−13.262*** (−4.80)
FE	Yes	No	Yes	Yes
TE	Yes	Yes	No	Yes
N	300	300	300	300
R2	0.700	0.764	0.7872	0.793

*, **, and *** denote significance levels at 10, 5, and 1%, respectively. Values in parentheses represent t-statistics. The same applies to the subsequent tables.

TABLE 4 Robustness test results.

Variables	(1) Replacement of the Core Explanatory Variable	(2) Addition of Control Variable	(3) Lagging by One Period
Digde _new	0.432*** (5.25)		
Digde		2.899*** (5.07)	
L. Digde			2.533*** (3.89)
HC	0.689 (0.81)	0.751 (0.87)	−0.121 (−0.13)
Inft	1.235*** (8.52)	1.297*** (8.91)	1.321*** (8.22)
Labor	−0.067 (−0.25)	−0.218 (−0.80)	−0.134 (−0.46)
Inds	0.001 (0.13)	0.001 (0.08)	−0.002 (−0.27)
Gov	0.000*** (7.56)	0.000*** (3.70)	0.000*** (3.44)
Indu	0.018 (0.04)	0.176 (0.37)	−0.236 (−0.47)
Eco		0.093 (1.06)	
_cons	−13.532*** (−4.92)	−14.034*** (−4.91)	−11.900*** (−3.86)
FE	Yes	Yes	Yes
TE	Yes	Yes	Yes
N	300	300	270
R2	0.795	0.794	0.768

TABLE 5 GMM model test results.

Variables	(1) Revl
L. Revl	0.593*** (5.13)
Digde	3.453*** (3.83)
HC	0.233 (0.32)
Inft	0.374* (1.78)
Labor	0.024 (0.12)
Inds	0.009 (0.94)
Gov	0.000 (0.68)
Indu	0.516 (0.74)
Constant	−4.761 (−1.60)
FE	Yes
TE	Yes
AR1	0.000
AR2	0.225
Hansen	0.137

5.2.3 Endogeneity test

To avoid biases in the estimated results due to endogeneity, we followed the approach of HUANG et al. (73) and Zhao et al. (71) by selecting the interaction term of the total volume of postal and telecommunications services in 1984 and the internet usage rate in each province from the previous year as the instrumental variable, denoted as Iv. The specific regression results are shown in Table 6. The Anderson canonical correlation LM statistic p-value for the instrumental variable Iv is significant at the 1% level, rejecting the null hypothesis of insufficient identification of the instrumental variable. The Cragg-Donald Wald F statistic is greater than the critical value for the Stock-Yogo test at the 1% significance level, thus also rejecting the null hypothesis of weak instruments. The endogenous variables correspond one-to-one with the instrumental variables, so there is no issue of over-identification of the instrumental variable.

6 Mechanism tests

We will further examine the underlying mechanism through which the digital economy influences the resilience of the healthcare cross-border e-commerce supply chain, and analyze the impact pathways of different dimensions of the digital economy on the resilience of the healthcare cross-border e-commerce supply chain. Specifically, we will first examine the impact of the digital economy development level on foreign trade dependence, export technological complexity, and export diversification. Then, we will separately examine the impact of these three dimensions on the resilience of the healthcare cross-border e-commerce supply chain. Finally, all dimensions and the level of digital economy development will be included in the regression model to examine the changes in the coefficient and significance of the impact of the digital economy development level on supply chain resilience. The specific model is as follows:

$$Revl_{it} = \alpha + \beta_1 Digde_{it} + \sum_j \beta_j Control_{it} + \mu_i + \gamma_t + \varepsilon_{it} \quad (9)$$

$$med_{it} = \alpha + \beta_1 Digde_{it} + \sum_j \beta_j Control_{it} + \mu_i + \gamma_t + \varepsilon_{it} \quad (10)$$

10.3389/fpubh.2025.1570338

TABLE 6 Endogeneity test results.

Variables	(1) First Stage Digde	(2) Second Stage Revl
Digde		2.7136** (2.10)
LnIv	−0.1191*** (−7.08)	
Constant	1.9200*** (5.09)	−12.2514*** (−4.86)
Controls	Yes	Yes
FE	Yes	Yes
TE	Yes	Yes
Anderson canon. corr. LM statistic	49.449***	
Cragg-Donald Wald F statistic	50.129 [16.38]	
Observations	300	300
R-squared		0.987

*, **, and *** denote significance levels at 10, 5, and 1%, respectively. Values in parentheses are t-statistics. Values within curly brackets are critical values for significance levels of the Stock-Yogo test.

$$Revl_{it} = \alpha + \beta_1 med_{it} + \beta_2 Digde_{it} + \sum_j \beta_j Control_{it} + \mu_i + \gamma_t + \varepsilon_{it} \quad (11)$$

Model 9 investigates the relationship between the digital economy and the resilience of the healthcare cross-border e-commerce supply chain. Model 10 considers the relationship between the mediator variable and the digital economy. Model 11 examines the joint effects of the digital economy and the mediator variable on the resilience of the cross-border medical e-commerce supply chain. "med" represents the mediator variable, which includes foreign trade dependence (Ftrd), export technological complexity (Expt), and export diversification (Dexp).

6.1 Mediation mechanism test

The regression results are shown in Table 7. Columns (1), (2), and (3) of Table 7 indicate that the estimated coefficients are significantly correlated, and the signs of the coefficients suggest that the development of the digital economy can reduce dependence on foreign trade, ultimately enhancing the resilience of the healthcare cross-border e-commerce supply chain. These results indicate that reducing dependence on foreign trade is one of the mediating channels through which the digital economy influences the resilience of the healthcare cross-border e-commerce supply chain, thereby validating Hypothesis 2.

Columns (1), (6), and (7) of Table 7 show that the estimated coefficients are significant at the 1% level. The signs of these coefficients imply that the development of the digital economy can reduce the concentration of export products, thereby increasing export diversity, which ultimately enhances the resilience of the healthcare cross-border e-commerce supply chain. These findings indicate that export product concentration is one of the mediating channels through which the digital economy contributes to the resilience of the healthcare cross-border e-commerce supply chain, validating Hypothesis 4.

Results from Columns (4) and (5) of Table 7 demonstrate that after introducing the mediating variables, the coefficient of the core explanatory variable increases, and the coefficient of the mediating variable is inversely related to that of the core explanatory variable. According to the explanation by WEN and YE (74), this situation can be attributed to a certain degree of masking effect. Specifically, export technology complexity plays a masking role between the level of digital economy development and the resilience of the healthcare cross-border e-commerce supply chain, obscuring the direct impact of digital economy development on the resilience of the healthcare cross-border e-commerce supply chain. However, whether it is a mediating effect or a masking effect, it indicates an indirect effect exists between export technology complexity, the digital economy, and the resilience of the healthcare cross-border e-commerce supply chain. In other words, the development of the digital economy can promote the resilience of the healthcare cross-border e-commerce supply chain by enhancing export technology complexity, thus validating Hypothesis 3.

6.2 Sobel test and bootstrap test

To strengthen the verification of the mediation mechanism, we conducted further tests: the Sobel test and the Bootstrap test. As shown in Table 8, the Sobel test results indicate that the Sobel statistic for the mediation path of Mediating Mechanism 1 ("digital economy—foreign trade dependence—healthcare cross-border e-commerce supply chain resilience") is not significant at any conventional level. In contrast, the Sobel statistics for the other two mediation paths are significant at the 10% level. This suggests that Hypothesis 2 is not supported by the Sobel test, which deviates from the earlier three-step mediation test results. The Sobel test assumes that the sampling distribution of the mediation effect approximates normality. However, in practice—especially in small samples—the distribution of the product term is often skewed, which can lead to biased test results. Therefore, the Bootstrap method provides greater accuracy and robustness in assessing mediation effects.

As shown in Table 9, the Bootstrap test results indicate that neither the direct nor indirect effects of the three mediation mechanisms include zero within the 95% confidence interval, rejecting the null hypothesis at valid significance levels. This confirms the existence of mediation (or suppression) effects, providing further support for Hypotheses 2, 3, and 4. Based on both the Sobel and Bootstrap test results, the following conclusions can be drawn: foreign trade dependence mediates the relationship between the digital economy and healthcare cross-border e-commerce supply chain resilience, accounting for 17.11% of the total effect; export technological complexity exhibits a suppression effect (as the signs of the indirect and direct effects are opposite), with the suppression effect amounting to 10.91% (the absolute value of the ratio of the indirect effect to the direct effect); export product concentration mediates the relationship between the digital economy and healthcare cross-border e-commerce supply chain resilience, explaining 12.12% of the total effect.

10.3389/fpubh.2025.1570338

TABLE 7 Mechanism test results.

Variables	(1)	(2)	(3)	(4)	(5)	(6)	(7)
	Revl	Ftrd	Revl	lnExpt	Revl	Dexp	Revl
Digde	2.842*** (4.99)	−0.977*** (−7.17)	2.356*** (3.79)	−0.205** (−2.50)	3.184*** (5.68)	−0.444*** (−3.10)	2.535*** (4.43)
Ftrd			−0.498* (−1.91)				
lnExpt					1.672*** (3.95)		
Dexp							−0.692*** (−2.81)
_cons	−13.262*** (−4.80)	1.579** (2.39)	−12.476*** (−4.49)	8.404*** (21.09)	−27.311*** (−6.13)	−0.547 (−0.79)	−13.641*** (−5.00)
Controls	Yes	Yes	Yes	Yes	Yes	Yes	Yes
FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes
TE	Yes	Yes	Yes	Yes	Yes	Yes	Yes
N	300	300	300	300	300	300	300
R2	0.793	0.433	0.796	0.980	0.805	0.122	0.799

TABLE 8 Sobel test results.

Measurement items	Mediating Mechanism 1	Mediating Mechanism 2	Mediating Mechanism 3
Sobel Value	0.486 (1.843)	−0.348* (−2.150)	0.307* (2.082)
Mediating Effect Coefficient	0.486 (1.843)	−0.348* (−2.150)	0.307* (2.082)
Direct Effect Coefficient	2.356*** (3.791)	3.190*** (5.6984)	2.535*** (4.428)
Total Effect	2.842*** (4.990)	2.842*** (5.004)	2.842*** (3.791)
Mediation Effect Ratio	17.109%	−10.914%	12.120%

*, **, and *** denote significance levels at 10, 5, and 1%, respectively. Values in parentheses are t-statistics.

TABLE 9 Bootstrap test results.

Mechanisms	Effect category	Observed coefficient	Bias	Bootstrap std. err.	[95% conf. interval]
Mediating Mechanism 1	Indirect	0.4861913	−0.0647742	0.25446265	(0.0531118, 1.16549)
	Direct	2.355598	−0.038791	0.84588663	(0 0.6913589,4.035667)
Mediating Mechanism 2	Indirect	−0.34247298	−0.003599	0.18389279	(−0.8521886, −0.0719047)
	Direct	3.1842618	−0.0020825	0.85674249	(1.5771,4.889731)
Mediating Mechanism 3	Indirect	0.30720395	−0.0096761	0.15284604	(0.093417,0.7069903)
	Direct	2.5345849	−0.000544	0.87673567	(0.8889207,4.353372)

7 Heterogeneity analysis

7.1 Regional heterogeneity

Geographical location can influence the economic development of a region. Areas located at transportation hubs or rich in resources are generally more favourable for economic development, attracting investment and commercial activities. This study divides the full sample into eastern and central regions versus the western region for analysis. The results are shown in Columns (1) and (2) of Table 10: the impact coefficient of the digital economy on the resilience of the healthcare cross-border e-commerce supply chain in the western region (3.979) is greater than that in the eastern and central regions (2.021), indicating a more pronounced positive enabling effect of the digital economy in the western region.

China's eastern and central regions are situated at the nation's economic centre, which facilitate logistics and the movement of people, featuring developed transportation networks and convenient transportation conditions. Additionally, these regions are densely populated, offering vast potential for commercial and market development. These inherent conditions have allowed the digital economy in China's eastern and central regions to start earlier and develop to a relatively higher level, significantly enhancing the positive promotive effects of the digital economy. In recent years, China has been vigorously implementing the "Western Development" strategy. Compared to the relatively saturated state of digital economy development in the eastern and central regions, the western region is still in the stage of increasing marginal returns from digital economy development. Therefore, the western region can more significantly absorb the positive impact of the digital

TABLE 10 Heterogeneity analysis results.

Variables	(1)	(2)	(3)	(4)
	Eastern and Central Regions	Western Region	Pre-Policy Implementation	Post-Policy Implementation
Digde	2.021*** (2.88)	3.979*** (2.65)	0.856 (0.38)	1.955*** (2.88)
_cons	−21.842*** (−5.65)	2.180 (0.50)	−7.579 (−0.95)	−12.231*** (−3.43)
FE	Yes	Yes	Yes	Yes
TE	Yes	Yes	Yes	Yes
N	190	110	90	210
R^2	0.831	0.814	0.632	0.741

economy on the resilience of the healthcare cross-border e-commerce supply chain.

7.2 Policy heterogeneity

Since 2015, China has established comprehensive pilot zones for cross-border e-commerce. These zones serve as pioneering areas aimed at exploring the technical standards, business processes, regulatory models, and informatization construction of various aspects of cross-border e-commerce. To assess the effectiveness of these comprehensive pilot zones, this study regards 2015 as a watershed year and divides the sample into periods before and after the implementation of policies. The results, as shown in Columns (3) and (4) of Table 10, indicate that the impact of the digital economy on the resilience of the healthcare cross-border e-commerce supply chain was not statistically significant before the establishment of comprehensive pilot zones for cross-border e-commerce. However, after the establishment of these zones, the digital economy significantly promotes the resilience of the healthcare cross-border e-commerce supply chain. This suggests that the establishment of comprehensive pilot zones for cross-border e-commerce has facilitated the role of the digital economy in enhancing the resilience of the healthcare cross-border e-commerce supply chain, providing strong support and impetus for the development of the healthcare cross-border e-commerce industry.

8 Conclusions and policy recommendations

This study utilizes provincial-level panel data from China to investigate the impact of the digital economy on the resilience of the cross-border e-commerce supply chain in the healthcare industry and its underlying mechanisms. Research demonstrates that digital economy development significantly enhances the resilience of healthcare cross-border e-commerce supply chain through three key mechanisms: reducing foreign trade dependence, increasing export technology complexity, and optimizing export concentration. This effect is particularly pronounced in western regions, with cross-border e-commerce comprehensive pilot zones further amplifying the impact. Policy recommendations focus on four dimensions: Industrial integration calls for government policies supporting big data and AI applications in supply chain optimization, along with establishing industry-academia-research platforms for digital solutions. Trade optimization advocates implementing the "dual-circulation" strategy with tax incentives and R&D subsidies to stimulate innovation, complemented by export credit insurance to mitigate risks. Regional coordination emphasizes prioritizing digital infrastructure in western China and establishing east–west collaboration mechanisms for global value chain integration. Institutional innovation recommends replicating successful pilot zone experiences, advancing "single-window" systems for streamlined customs, and encouraging policy experimentation. These measures will effectively foster synergistic development between the digital economy and healthcare cross-border e-commerce.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

JL: Conceptualization, Validation, Writing – review & editing. SM: Conceptualization, Data curation, Methodology, Validation, Writing – original draft, Writing – review & editing. LL: Conceptualization, Validation, Writing – review & editing, Data curation, Methodology, Writing – original draft. YJ: Methodology, Validation, Writing – review & editing. XY: Writing – review & editing, Conceptualization, Validation. HX: Methodology, Validation, Writing – review & editing. YR: Data curation, Methodology, Writing – review & editing.

Funding

The author(s) declare that financial support was received for the research and/or publication of this article. This work was supported by the Innovation Project of Guangxi Graduate Education (Project No: JGY2024045) and by the Guangxi Normal University Campus level Scientific Research Project (2022PY) and by Guangxi Key R&D Plan (Project No: 2022AB34029): The Key Technologies and

Industrialization of Intelligent Traceability in the Whole Link of High-quality Seedling Seed Supply Chain in Lijiang River Basin and by the Research Fund Project of Development Institute of Zhujiang-Xijiang Economic Zone, Key Research Base of Humanities and Social Sciences in Guangxi Universities (Project No: ZX2023051).

Acknowledgments

The authors would like to acknowledge all colleagues and friends who have voluntarily reviewed the survey's translation and this study's manuscript.

Conflict of interest

JL was employed by Jinan Liangong Testing Technology Co., Ltd.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The author(s) declare that no Gen AI was used in the creation of this manuscript.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2025.1570338/full#supplementary-material

References

1. Furstenau LB, Zani C, Terra SX, Sott MK, Choo K-KR, Saurin TA. Resilience capabilities of healthcare supply chain and supportive digital technologies. *Technol Soc*. (2022) 71:102095. doi: 10.1016/j.techsoc.2022.102095

2. Junaid M, Zhang Q, Cao M, Luqman A. Nexus between technology enabled supply chain dynamic capabilities, integration, resilience, and sustainable performance: an empirical examination of healthcare organizations. *Technol Forecast Soc Chang*. (2023) 196:122828. doi: 10.1016/j.techfore.2023.122828

3. Alemsan N, Tortorella GL. 42, lean and resilience in healthcare supply chain: a mediation analysis. *IFAC-PapersOnLine*. (2022) 55:436–41. doi: 10.1016/j.ifacol.2022.09.432

4. Kling R, Lamb R. IT and organizational change in digital economies: a socio-technical approach. *ACM SIGCAS Comput Soc*. (1999) 29:17–25. doi: 10.1145/572183.572189

5. Knickrehm MBB, Daugherty P. Digital disruption: The growth multiplier Oxford Economics (2016). Ed. Thomasina Heath, Oxford.

6. Chen J, Huang S, Liu Y. Operations Management in the Digitization era:from empowering to enabling. *Manag World*. (2020) 36:117–128+222. Available at: http://www.mwm.net.cn/web/xq?leafid=933&docid=3071

7. Wei J, Liu J, Liu Y. Digital economy: connotations, theoretical basis and future research. *Sci Technol Progress Policy*. (2021) 38:1–7. doi: 10.6049/kjjbydc.2021010096

8. Nunez-Merino M, Manuel Maqueira-Marin J, Moyano-Fuentes J, Jose Martinez-Jurado P. Information and digital technologies of industry 4.0 and lean supply chain management: a systematic literature review. *Int J Prod Res*. (2020) 58:5034–61. doi: 10.1080/00207543.2020.1743896

9. Schallmo D, Williams CA, Boardman L. Digital transformation of business models — best practice, enablers, and roadmap. *Int J Innov Manag*. (2017) 21:740014. doi: 10.1142/S136391961740014X

10. Gnimpieba CZDR, Nait-Sidi-Moh A, Durand D, Fortin J. Using internet of things technologies for a collaborative supply chain: application to tracking of pallets and containers. *Proc Comp Sci*. (2015) 56:550–557. doi: 10.1016/j.procs.2015.07.251

11. Li Q, Liu L-g, Shao J-b. The effects of digital transformation and supply chain integration on firm performance: the moderating role of entrepreneurship. *Econ Manag*. (2021) 43:5–23. doi: 10.19616/j.cnki.bmj.2021.10.001

12. Yasmin M, Tatoglu E, Kilic HS, Zaim S, Delen D. Big data analytics capabilities and firm performance: an integrated MCDM approach. *J Bus Res*. (2020) 114:1–15. doi: 10.1016/j.jbusres.2020.03.028

13. Brandon-Jones E, Squire B, Autry CW, Petersen KJ. A contingent resource-based perspective of supply chain resilience and robustness. *J Supply Chain Manag*. (2014) 50:55–73. doi: 10.1111/jscm.12050

14. Hazen BT, Boone CA, Ezell JD, Jones-Farmer LA. Data quality for data science, predictive analytics, and big data in supply chain management: an introduction to the problem and suggestions for research and applications. *Int J Prod Econ*. (2014) 154:72–80. doi: 10.1016/j.ijpe.2014.04.018

15. Matthias O, Fouweather I, Gregory I, Vernon A. Making sense of big data – can it transform operations management? *Int J Oper Prod Manag*. (2017) 37:37–55. doi: 10.1108/IJOPM-02-2015-0084

16. Christopher M, Peck H. Building the resilient supply chain. *Int J Logist Manag*. (2004) 15:1–14. doi: 10.1108/09574090410700275

17. Behzadi G, O'Sullivan MJ, Olsen TL. On metrics for supply chain resilience. *Eur J Oper Res*. (2020) 287:145–58. doi: 10.1016/j.ejor.2020.04.040

18. Larin O, Tarasov D, Mirotin L, Rublev V, Kapski D. Resilient supply chain management model. *SHS Web Confer*. (2021) 93:03005. doi: 10.1051/shsconf/20219303005

19. Um J, Han N. Understanding the relationships between global supply chain risk and supply chain resilience: the role of mitigating strategies. *Supply Chain Manag Int J*. (2021) 26:240–55. doi: 10.1108/SCM-06-2020-0248

20. Wang Z. The paradox of resilient supply chain strategy and China 's policy responses. *Pac J Theol*. (2022) 30:36–50. doi: 10.14015/j.cnki.1004-8049.2022.01.004

21. Wieland A. Dancing the supply chain: toward transformative supply chain management. *J Supply Chain Manag*. (2021) 57:58–73. doi: 10.1111/jscm.12248

22. Ji L, Yuan C, Feng T, Wang C. Achieving the environmental profits of green supplier integration: the roles of supply chain resilience and knowledge combination. *Sustain Dev*. (2020) 28:978–89. doi: 10.1002/sd.2050

23. Juan S-J, Li EY, Hung W-H. An integrated model of supply chain resilience and its impact on supply chain performance under disruption. *Int J Logist Manag*. (2022) 33:339–64. doi: 10.1108/IJLM-03-2021-0174

24. Dubey R, Gunasekaran A, Childe SJ, Papadopoulos T, Blome C, Luo Z. Antecedents of resilient supply chains: an empirical study. *IEEE Trans Eng Manag*. (2019) 66:8–19. doi: 10.1109/TEM.2017.2723042

25. Chatterjee S, Chaudhuri R, Vrontis D. Examining the impact of adoption of emerging technology and supply chain resilience on firm performance: moderating role of absorptive capacity and leadership support. *IEEE Trans Eng Manag*. (2022) 71:10373–10386. doi: 10.1109/TEM.2021.3134188

26. Bednarski L, Samuel R, Constantin B, Schleper MC. Geopolitical disruptions in global supply chains: a state-of-the-art literature review. *Prod Plan Control*. (2025) 36:536–62. doi: 10.1080/09537287.2023.2286283

27. Ozdemir D, Sharma M, Dhir A, Daim T. Supply chain resilience during the COVID-19 pandemic. *Technol Soc*. (2022) 68:101847. doi: 10.1016/j.techsoc.2021.101847

28. Ivanov D, Dolgui A, Sokolov B. Ripple effect in the supply chain: definitions, frameworks and future research perspectives In: D Ivanov, A Dolgui and B Sokolov, editors. Handbook of ripple effects in the supply chain. Cham: Springer International Publishing (2019) 276:1–33. doi: 10.1007/978-3-030-14302-2_1

29. Sheffi Y. Preparing for disruptions through early detection. *MIT Sloan Manag Rev*. (2015) 57:30–42. Available at: http://mitsmr.com/1OV6aJu

30. Kraude R, Narayanan S, Talluri S, Singh P, Kajiwara T. Cultural challenges in mitigating international supply chain disruptions. *IEEE Eng Manag Rev*. (2018) 46:98–105. doi: 10.1109/EMR.2018.2809910

31. Ali A, Mahfouz A, Arisha A. Analysing supply chain resilience: integrating the constructs in a concept mapping framework via a systematic literature review. *Supply Chain Manag Int J*. (2017) 22:16–39. doi: 10.1108/SCM-06-2016-0197

32. Guo C, Xu T. Research on the resilience and safety of China's pharmaceutical industrial chain and supply chain. *Econ Manag*. (2023) 37:82–93. doi: 10.3969/j.issn.1003-3890.2023.03.010

33. DiMasi JA, Grabowski HG, Hansen RW. Innovation in the pharmaceutical industry: new estimates of R&D costs. *J Health Econ*. (2016) 47:20–33. doi: 10.1016/j.jhealeco.2016.01.012

34. Jiménez-Luna J, Francesca G, Nils W, Schneider G. Artificial intelligence in drug discovery: recent advances and future perspectives. *Expert Opin Drug Discov*. (2021) 16:949–59. doi: 10.1080/17460441.2021.1909567

35. Gao W, Yu C. Wearable and implantable devices for healthcare. *Adv Healthc Mater*. (2021) 10:2101548. doi: 10.1002/adhm.202101548

36. Kaminski MM, Abudayyeh OO, Gootenberg JS, Zhang F, Collins JJ. CRISPR-based diagnostics. Nature. *Biomed Eng*. (2021) 5:643–56. doi: 10.1038/s41551-021-00760-7

37. Alotaibi N, Wilson CB, Traynor M. Enhancing digital readiness and capability in healthcare: a systematic review of interventions, barriers, and facilitators. *BMC Health Serv Res*. (2025) 25:500. doi: 10.1186/s12913-025-12663-3

38. Ahmed NSJI, Hamdan AMM. Enhancing resilience and digital transformation in the healthcare supply chain: an exploratory study in emerging economies In: A Hamdan and A Harraf, editors. Business development via AI and digitalization: volume 1. Cham: Springer Nature Switzerland (2024) 538:141–9. doi: 10.1007/978-3-031-62102-4_12

39. Zandkarimkhani S, Mina H, Biuki M, Govindan K. A chance constrained fuzzy goal programming approach for perishable pharmaceutical supply chain network design. *Ann Oper Res*. (2020) 295:425–52. doi: 10.1007/s10479-020-03677-7

40. Zahiri B, Jula P, Tavakkoli-Moghaddam R. Design of a pharmaceutical supply chain network under uncertainty considering perishability and substitutability of products. *Inf Sci*. (2018) 423:257–83. doi: 10.1016/j.ins.2017.09.046

41. Settanni E, Harrington TS, Srai JS. Pharmaceutical supply chain models: a synthesis from a systems view of operations research. *Operat Res Persp*. (2017) 4:74–95. doi: 10.1016/j.orp.2017.05.002

42. Benneyan JC, Sonuc SB, Krishnan RPR. Optimization of medical supply chains and forward store locations for recurrent homecare patient demand with periodic interruptions. *Am J Operat Res*. (2018) 8:203–20. doi: 10.4236/ajor.2018.83012

43. Ma P, Gong Y, Jin M. Quality efforts in medical supply chains considering patient benefits. *Eur J Oper Res*. (2019) 279:795–807. doi: 10.1016/j.ejor.2019.06.030

44. Chen X, Liu Y, Zhou K. Research on the path of digital economy to improve China's industrial chain resilience. *Reform Econ Syst*. (2022) 1:95–102.

45. El Baz J, Ruel S. Can supply chain risk management practices mitigate the disruption impacts on supply chains' resilience and robustness? Evidence from an empirical survey in a COVID-19 outbreak era. *Int J Prod Econ*. (2021) 233:107972. doi: 10.1016/j.ijpe.2020.107972

46. Wang G, Gunasekaran A, Ngai EWT, Papadopoulos T. Big data analytics in logistics and supply chain management: certain investigations for research and applications. *Int J Prod Econ*. (2016) 176:98–110. doi: 10.1016/j.ijpe.2016.03.014

47. Williams BD, Roh J, Tokar T, Swink M. Leveraging supply chain visibility for responsiveness: the moderating role of internal integration. *J Oper Manag*. (2013) 31:543–54. doi: 10.1016/j.jom.2013.09.003

48. Song H. The implication of the novel coronavirus outbreak to supply chain flexibility management. *China Busin Market*. (2020) 34:11–6. doi: 10.14089/j.cnki.cn11-3664/f.2020.03.002

49. Ambulkar S, Blackhurst J, Grawe S. Firm's resilience to supply chain disruptions: scale development and empirical examination. *J Oper Manag*. (2015) 33-34:111–22. doi: 10.1016/j.jom.2014.11.002

50. Xue L, Zhang C, Ling H, Zhao X. Risk mitigation in supply chain digitization: system modularity and information technology governance. *J Manag Inf Syst*. (2013) 30:325–52. doi: 10.2753/MIS0742-1222300110

51. Wu F, Hu H, Lin H, Ren X. Enterprise digital transformation and capital market performance: empirical evidence from stock liquidity. *Manag World*. (2021) 37:130-144+10.

52. Zhang X. New development pattern of dual circulation promoted by cross-border E-commerce: theoretical mechanism, development ideas and relevant measures. *Contemp Econ Manag*. (2021) 43:59–65. doi: 10.13253/j.cnki.ddjjgl.2021.10.008

53. Sun Y, Yu M, Zhao L. Research on the impact of regional digital trade rules on trade flows of ICT products. *World Econ Stud*. (2021) 8:49–64+136. doi: 10.13516/j.cnki.wes.2021.08.004

54. Lin JY, He D, Fan C, Tian G, Guo Q, Wan G. Special articles for studying and lmplementing the Spirit of the fifth plenary session of the 19th CPC central committee. *Econ Res J*. (2021) 56:4–25.

55. Zhu H-L, Li X-W. Mechanism, motivation and countermeasures of developing the strong domestic market driven by digital economy——based on condition and dilemma facing the development of China's strong domestic market. *China Busin Market*. (2022) 36:25–36.

56. Pfeffer J, Salancik GR. The external control of organizations: a resource dependency perspective. *Econ J*. (1979) 89:969–970. doi: 10.2307/2231527

57. Thompson JD. Organizations in action: Social science bases of administrative theory (2003). New York: Routledge.

58. Huang X, Chen X, Liu H. Measurement of industrial export complexity and analysis of its dynamic evolution mechanism: an empirical study on the export of metal products from 52 economies during the period of 1993 to 2006. *Manag World*. (2010) 3:44–55.

59. Dai X, Jin B. Intra-product specialization, Insitution quality and export sophistication. *Econ Res J*. (2014) 49:4-17+43.

60. Paunov C, Rollo V. Has the internet fostered inclusive innovation in the developing world? *World Dev*. (2016) 78:587–609. doi: 10.1016/j.worlddev.2015.10.029

61. Dai K-Z. The impact of the development of technology market on the export technical sophistication and its mechanism. *China Indust Econ*. (2018) 7:117–135. doi: 10.19581/j.cnki.ciejournal.2018.07.006

62. Chao X, Xue Z, Sun Y. How the new digital infrastructure affects the upgrading of foreign trade: evidence from Chinese cities. *Econ Sci*. (2020) 42:46–59.

63. Wang M, Song Y, Yan H, Zhang X. Impact of digital transformation on the scope of firm internationalization: the mediating role of dynamic capability. *For Econ Manag*. (2022) 44:33–47. doi: 10.16538/j.cnki.fem.20211212.204

64. Hansen R, Sia SK. Hummel's digital transformation toward Omni channel retailing: key lessons learned. *MIS Q Exec*. (2015) 14:51–66. Available at: https://api.semanticscholar.org/CorpusID:32441362

65. Wei Y, Gong X, Liu C. Does digital transformation improve firms' export resilience. *J Int Trade*. (2022) 10:56–72. doi: 10.13510/j.cnki.jit.2022.10.010

66. Liu H, Xiao Y, Zhang P. Digital trade, export diversification and Enterprise output fluctuation—quasi-natural experiments based on joining the cross-border E-commerce platform. *J Int Trade*. (2022) 12:54–69. doi: 10.13510/j.cnki.jit.2022.12.007

67. Corcoles D, Diaz-Mora C, Gandoy R. Export survival in global production chains. *World Econ*. (2015) 38:1526–54. doi: 10.1111/twec.12249

68. Hausmann R, Klinger B. Structural transformation and patterns of comparative advantage in the product space. *Int Trade*. (2006) 128:1–39. doi: 10.2139/ssrn.939646

69. Lu X, Li L. Diversification and volatility in the Chinese Firms' exports: a study on product mix and market portfolio. *Stat Res*. (2018) 35:56–67.

70. Wang J, Zhu J, Luo X. Research on the measurement of China's digital economy development and the characteristics. *J Quant Tech Econ*. (2021) 38:26–42. doi: 10.13653/j.cnki.jqte.2021.07.002

71. Zhao T, Zhang Z, Liang S. Digital economy, entrepreneurship, and high-quality economic development: empirical evidence from urban China. *Manag World*. (2020) 36:65–76. doi: 10.19744/j.cnki.11-1235/f.2020.0154

72. Hausmann R, Hwang J, Rodrik D. What you export matters. *J Econ Growth*. (2007) 12:1–25. doi: 10.1007/s10887-006-9009-4

73. Huang Q-H, Yu Y-Z, Zhang S-L. Internet development and productivity growth in manufacturing industry:internal mechanism and China experiences. *China Indust Econ*. (2019) 8:5–23. doi: 10.19581/j.cnki.ciejournal.2019.08.001

74. Wen Z, Ye B. Analyses of mediating effects: the development of methods and models. *Adv Psychol Sci*. (2014) 22:731–45. doi: 10.3724/SP.J.1042.2014.00731

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 27 May 2025
DOI 10.3389/fpubh.2025.1574780

Check for updates

OPEN ACCESS

EDITED BY
Jing Yuan,
Fudan University, China

REVIEWED BY
Davi Rumel,
Retired, São Paulo, Brazil
Aleksandra Kovačević,
Military Medical Academy, Serbia

*CORRESPONDENCE
Lihui Ouyang
✉ xiangyuexiang123@163.com
Jun Meng
✉ 657156451@qq.com

RECEIVED 11 February 2025
ACCEPTED 30 April 2025
PUBLISHED 27 May 2025

CITATION
Hong J, Zeng X, Chen W, Zhou Z, He Y, Meng J and Ouyang L (2025) Cost-effectiveness analysis of rezvilutamide versus bicalutamide and androgen-deprivation therapy in patients with high-volume, metastatic, hormone-sensitive prostate cancer: a Markov's model-based evaluation.
Front. Public Health 13:1574780.
doi: 10.3389/fpubh.2025.1574780

COPYRIGHT
© 2025 Hong, Zeng, Chen, Zhou, He, Meng and Ouyang. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

Cost-effectiveness analysis of rezvilutamide versus bicalutamide and androgen-deprivation therapy in patients with high-volume, metastatic, hormone-sensitive prostate cancer: a Markov's model-based evaluation

Juan Hong[1], Xiaohui Zeng[2], Wenjun Chen[1], Ziyuan Zhou[1], Yuming He[3], Jun Meng[1]* and Lihui Ouyang[4]*

[1]Department of Pharmacy, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital & Shenzhen Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Shenzhen, China, [2]Department of Nuclear Medicine/PET Image Center, The Second Xiangya Hospital of Central South University, Changsha, China, [3]School of Pharmacy, Guangdong Medical University, Dongguan, China, [4]Department of Pharmacy, The Affiliated Changsha Hospital of Xiangya School of Medicine, Central South University, Changsha, China

Objectives: Rezvilutamide, an androgen-receptor inhibitor, has been approved by the Chinese National Medical Products Administration as a first-line treatment for high-volume metastatic hormone-sensitive prostate cancer (mHSPC). This study aims to assess the cost-effectiveness of rezvilutamide plus androgen-deprivation therapy (ADT) compared to bicalutamide plus ADT for the first-line treatment of high-volume mHSPC in China.

Methods: A Markov model with three health states was developed to evaluate the health and economic outcomes of first-line treatment for high-volume mHSPC. Efficacy data were sourced from the CHART trial. Quality-adjusted life-years (QALYs) and incremental cost-effectiveness ratios (ICERs) were calculated. To address modeling uncertainties, one-way sensitivity analysis and probabilistic sensitivity analysis were performed.

Results: Compared with bicalutamide plus ADT, rezvilutamide plus ADT resulted in an additional 2.16 QALYs, with an ICER of $39,122.16/QALY. At a willingness-to-pay (WTP) threshold of three times the gross domestic product per capita in China for 2023 ($37,256.3/QALY), the probability of cost-effectiveness for rezvilutamide plus ADT was 30%. One-way sensitivity analysis revealed that the results were most sensitive to the cost of rezvilutamide. Scenario analysis indicated that rezvilutamide could be considered cost-effective if priced below $705.46 per cycle.

Conclusion: From the perspective of Chinese payers, rezvilutamide plus ADT appears to be a less cost-effective strategy compared to bicalutamide plus ADT for the first-line treatment of high-volume mHSPC in China.

KEYWORDS

cost-effectiveness, rezvilutamide, bicalutamide, high-volume mHSPC, Markov model

Introduction

Prostate cancer is a prevalent genitourinary malignancy, particularly among older men. According to the Global Cancer Statistics 2022, prostate cancer is the second most frequently diagnosed malignancy in men worldwide and the fifth leading cause of cancer-related deaths among men (1). In China, it accounts for 13.42% of male cancer incidence and 4.75% of cancer-related deaths (2). Although the 5-year survival rate for clinically localized prostate cancer in China increased from 53.8% to 66.4% between 2003 and 2015, it remained significantly lower compared to developed countries such as the United States, where the survival rate was close to 100% (3). However, only 30% of cases are diagnosed at an early stage, while the majority of prostate cancer cases in China are diagnosed in the intermediate to advanced stages (3). The prognosis for metastatic prostate cancer is generally poor, with a 5-year survival rate of approximately 36.6% (4, 5). As a result, innovative therapeutic approaches are critically needed to improve survival outcomes for patients with metastatic prostate cancer.

For many years, androgen deprivation therapy (ADT), which includes both surgical and chemical castration, has been the standard of care for advanced prostate cancer (6). However, most patients with metastatic hormone-sensitive prostate cancer (mHSPC) who received ADT alone are at risk of developing metastatic castration-resistant prostate cancer (mCRPC) within 2 years (7). Recent advances have revealed the considerable potential of combining docetaxel with ADT. This combination therapy has demonstrated remarkable superiority over ADT alone (8–10). Bicalutamide, a first-generation androgen receptor (AR) inhibitor approved in the United States in 1995, has been commonly used for metastatic prostate cancer. However, first-generation AR inhibitors exhibit weak affinity for the AR, leading to limited efficacy in blocking AR activity and potential drug resistance due to AR overexpression or mutation (11). Consequently, first-generation AR inhibitors in combination with ADT, as well as ADT alone, were not recommended as standard treatment options for mHSPC in the 2021 European Association of Urology Guidelines (12). Second-generation AR inhibitors, such as enzalutamide (approved in the US in 2012), apalutamide (approved in 2018), and darolutamide (approved in 2019), have been shown to effectively delay the onset of castration resistance and improve overall survival for patients (13–16). In June 2022, the Chinese National Medical Products Administration (NMPA) approved rezvilutamide for the treatment of high-volume mHSPC. This treatment approach is also recommended by the Chinese Society of Clinical Oncology (CSCO) diagnosis and treatment of prostate cancer guideline (17).

The clinical efficacy of rezvilutamide in combination with ADT was evaluated in the CHART study (18). CHART was a randomized, open-label, phase 3 study conducted across 72 hospitals in China, Poland, the Czech Republic, and Bulgaria. The study aimed to assess the efficacy and safety of rezvilutamide plus ADT as a first-line therapy for patients with high-volume mHSPC who had not previously received chemotherapy or other localized treatments. Total of 654 patients were eligible and randomly assigned to either the rezvilutamide group (240 mg orally once daily in a 4-week cycle; $n = 326$) or the bicalutamide group (50 mg orally once daily in a 4-week cycle; $n = 326$). All patients received background therapy with either surgical ADT or luteinizing hormone-releasing hormone (LHRH) agonists or antagonists, in accordance with the package insert, throughout the study period. The co-primary endpoints of the study were radiographic progression-free survival (rPFS) and overall survival (OS). The results showed that the rezvilutamide group significantly improved rPFS compared with the bicalutamide group [not reached vs. 25.1 months; hazard ratio = 0.44, 95% confidence interval (CI) 0.33–0.58, $p < 0.0001$]. Furthermore, rezvilutamide significantly improved OS compared to bicalutamide (not reached vs. not reached; hazard ratio = 0.58, 95% CI 0.44–0.77, $p < 0.0001$).

The findings of the CHART trial formed the basis for the regulatory approval of rezvilutamide in combination with ADT for the treatment of high-volume mHSPC in China. However, clinical treatment decisions and national health policy require evidence of cost-effectiveness. Since existing economics assessment studies have used partitioned survival model and reached controversial conclusions (19, 20). The objective of this study conducted a Markov model to evaluate the cost-effectiveness of rezvilutamide plus ADT versus bicalutamide plus ADT for high-volume mHSPC, based on the data from the CHART trial, from the perspective of the Chinese healthcare system.

Methods

Model overview

This study adhered to the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) reporting guidelines (21, 22). A Markov model was developed to simulate the costs and health benefits associated with the treatment of high-volume mHSPC using rezvilutamide plus ADT versus bicalutamide plus ADT. The model included three distinct health states: progression-free survival (PFS), progressive disease (PD), and death (Figure 1). The cycle length of the Markov model was set to 28 days, aligning with the treatment periods. The average life expectancy in China in 2020 was 77.93 years (23). Given that the median age of patients in the CHART study was 69.2 years (range: 64–74 years), a 13-year time horizon was selected to better represent long-term survival of patients. All patients began in the PFS state and transitioned to either the PD state or death. Patients in the PD state could remain there or transition to death. The model's outcomes included life years, quality-adjusted life years (QALYs), and costs. According to Chinese pharmacoeconomic evaluation guidelines, both costs and QALYs were discounted at an annual rate of 5%. Incremental cost-effectiveness ratios (ICERs) were calculated to represent the cost per additional QALY gained. The cost-effectiveness threshold in China was defined as $37,256.3, equivalent to three times the per capita gross domestic product (GDP) of China in 2023 (24, 25).

Clinical efficacy

Survival parameters were primarily derived from the Kaplan–Meier (KM) curve of the CHART trial (18). We used the Engauge Digitizer software to extract digitized data points from the PFS and OS KM curves of the CHART study. Individual patient data were then reconstructed using standard statistical methods as outlined by Guyot et al. (26). Several parametric survival functions were evaluated, including the Exponential, Weibull, Log-logistic, Gompertz, and Log-normal distributions. The model selection was based on the Akaike information criterion (AIC), Bayesian information criterion

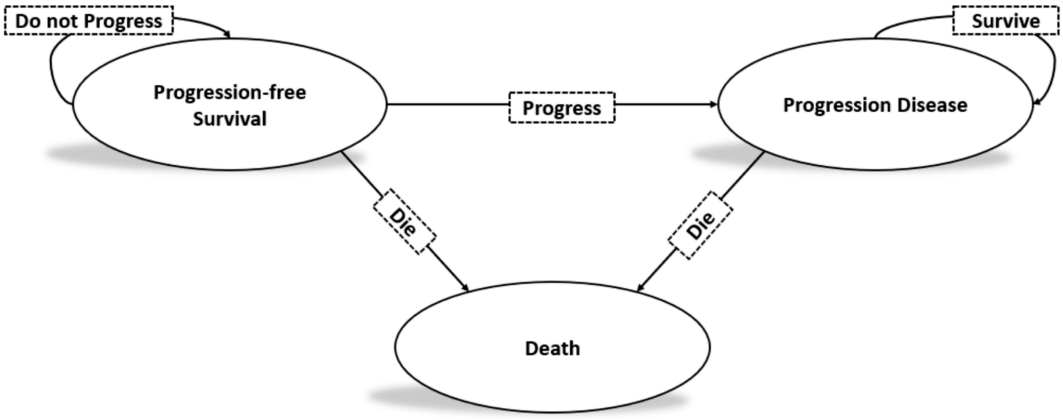


FIGURE 1
The Markov state transition model.

(BIC), and visual inspection of the parametric extrapolation and long-term survival estimates. The distribution with the lowest AIC or BIC values was chosen as the best-fit model (27).

Cost estimates

This analysis focused solely on direct medical costs, which included drug costs, costs for managing treatment-related adverse events (AEs), subsequent treatment costs, and disease management costs (outpatient visits, supportive care, nursing, laboratory tests). Drug costs were estimated based on patient dosing schedules and unit prices, calculated per treatment cycle. Unit drug costs were sourced from Hunan Public Resources Trading Service Platform (28). Costs associated with subsequent treatments, AE management, and end-of-life care were either estimated or referenced from published literature (29–31). For AE management costs, only grade ≥ 3 events from the CHART trials were included (18). According to the CHART study, the incidence of treatment-emergent AEs was 7% for hypertension and 2% for hypertriglyceridemia in the rezvilutamide plus ADT group, compared to 8% and 7%, respectively, in the bicalutamide plus ADT group. Upon disease progression, 27 and 62% of patients received subsequent treatments, including hormonal therapy, abiraterone acetate, enzalutamide, and docetaxel; the others received supportive care. All costs were adjusted to US dollars for 2024. Chinese Yuan was converted to US dollars using the exchange rate formula: 1 US $ = 7.1954 CNY (32). Key costs are shown in Table 1.

Utility estimates

Quality-adjusted life-years were estimated by adjusting survival time with health-related quality of life. Separate health state utility (HSU) values were applied for patients in the PFS and PD states. The HSU values for these different health states in the CHART trial population were derived from published literature (33). The values and sources for HSU were detailed in Table 1.

Sensitivity analysis

The robustness of the results was tested with a series of one-way sensitivity analysis on several parameters. In the one-way sensitivity analysis, the cost parameters ranged between −20% and +20% and the utility parameters were variable at 10% efficiency, as detailed in Table 1. The results of the one-way sensitivity analysis are presented as tornado diagrams. Moreover, probabilistic sensitivity analysis were conducted using Monte Carlo simulations with 10,000 replicated outcomes. The results of these are presented as cost-effectiveness acceptability curves. For the model, different distribution types were applied to each parameter: Gamma distributions for cost inputs and Beta distributions for utility values.

Results

Base-case analysis

The results of the deterministic analysis are showed in Table 2. In patients with high-volume mHSPC, compared to bicalutamide plus ADT, rezvilutamide plus ADT yielded an additional 2.16 QALYs (5.46 QALYs vs. 3.31 QALYs), corresponding to an incremental cost of $84,417.48. The calculated ICER was $39,122.16/QALY gained, which exceeded the WTP threshold of three times the GDP per capita in China.

Sensitivity analysis

According to the one-way deterministic sensitivity analysis (DSA), the model was most sensitive to the cost of rezvilutamide (Figure 2). In the probabilistic sensitivity analysis (PSA), the cost-effectiveness plane illustrated the results of 10,000 Monte Carlo simulations (Figure 3).

Comparing rezvilutamide plus ADT with bicalutamide plus ADT the cost-effectiveness acceptability curve indicated a nearly 30% probability of cost-effectiveness at the WTP threshold of $37,256.30, consistent with the base-case analysis results (Figure 4).

10.3389/fpubh.2025.1574780

TABLE 1 Model parameters of clinical data, costs and utilities: baseline values, ranges, and distributions.

Unit	Baseline value (range)	Distribution	Source
Survival model for rezvilutamide			
PFS	AIC = −111.95, BIC = −109.12	Log-normal	Estimated
OS	AIC = −268.95, BIC = −263.40	Log-normal	Estimated
Survival model for bicalutamide			
PFS	AIC = −80.94, BIC = −77.96	Log-normal	Estimated
OS	AIC = −329.31, BIC = −323.51	Log-normal	Estimated
Rezvilutamide	823.03(658.42–987.63)	Gamma	Local database
Bicalutamide	120.75(96.60–144.90)	Gamma	Local database
Goserelin	149.23(119.38–179.07)	Gamma	Local database
Leuprolide	176.86(141.49–212.23)	Gamma	Local database
Triptorelin	163.90(131.12–196.68)	Gamma	Local database
Degarelix	104.23(83.39–125.08)	Gamma	Local database
Average	148.55(118.84–178.26)	Gamma	Estimated
Subsequent antitumor therapy			
Abiraterone	177.89(142.31–213.47)	Gamma	Local database
Enzalutamide	1083.36(866.69–1300.03)	Gamma	Local database
Docetaxel	815.74(652.59–978.89)	Gamma	Local database
Prednisone	0.49(0.39–0.59)	Gamma	Local database
Apalutamide	917.25(733.80–1100.70)	Gamma	Local database
Darolutamide	1044.00(835.20–1252.80)	Gamma	Local database
Surgical ADT	1389.78(1111.82–1667.73)	Gamma	Estimated
Cost of routine treatment and Checklist per unit	642.89(514.32–771.47)	Gamma	Estimated
Testosterone concentrations	4.17(3.34–5.00)	Gamma	Estimated
Prostate specific antigen	16.68(13.34–20.01)	Gamma	Estimated
CT	27.80(22.24–33.35)	Gamma	Estimated
Cost of supportive care per cycle	117.1(93.68–140.52)	Gamma	(28)
Routine follow-up of patients per unit	51.5(41.2–61.8)	Gamma	Estimated
AE			
Hypertension	12.15(9.72–14.58)	Gamma	(8)
Hypertriglyceridemia	13.23(10.58–15.88)	Gamma	(8)
Health state utility			
PFS	0.76(0.684–0.836)	Beta	(31)
PD	0.68(0.612–0.748)	Beta	(31)
Discount rate	0.05(0.00–0.08)	Beta	(22)

AIC, Akaike information criterion; BIC, Bayesian information criterion; OS, overall survival; PFS, progression-free survival. ADT, androgen deprivation therapy; AE, adverse event.

Discussion

The introduction of second-generation AR inhibitors has brought a new ray of hope to the treatment of high-volume mHSPC. The combination of AR inhibitors with ADT has been recommended as a first-line treatment in the guideline of the CSCO for prostate cancer (17). The recommended first-line treatment for patients with high-volume mHSPC includes ADT combined with an antiandrogen, such as bicalutamide, rezvilutamide, abiraterone, enzalutamide, or apalutamide. Despite these positive developments, many of these second-generation AR inhibitors were imported medications, and the clinical studies that have been registered primarily focused on Western populations. The CHART trial demonstrated that rezvilutamide, in combination with ADT, significantly improved the prognosis of patients with high-volume mHSPC when compared with bicalutamide plus ADT (18).

The purpose of this study, which employed a Markov model, was to assess the cost-effectiveness of rezvilutamide plus ADT compared with bicalutamide plus ADT in the treatment of high-volume mHSPC. The results suggest that, compared with bicalutamide plus ADT, rezvilutamide plus ADT was associated with an incremental survival of 2.16 QALYs and an incremental cost of $84,417.28. The calculated ICER was $39,122.16 per QALY. The

TABLE 2 Summary of results of the base-case analysis.

Regimens	Costs ($)	Incremental Cost ($)	QALYs	Incremental QALYs*	ICER*
Rezvilutamide	126510.14	84417.48	5.46	2.15	39122.16
Bicalutamide	42092.66	NA	3.31	NA	NA

QALYs, Quality-adjusted life years; ICER, Incremental cost-effectiveness ratio.

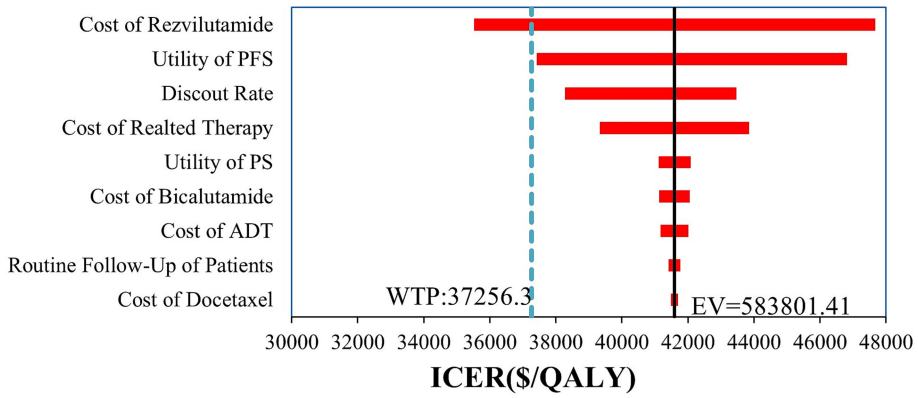


FIGURE 2
Tornado plot generated in the one-way deterministic sensitivity analysis. Only the top 9 most influential parameters are presented. PFS, progression-free survival; PS, progression survival; ADT, androgen deprivation therapy; WTP, willingness-to-pay; QALY, quality-adjusted life-year; ICER incremental cost-effectiveness ratio; EV, expect value.

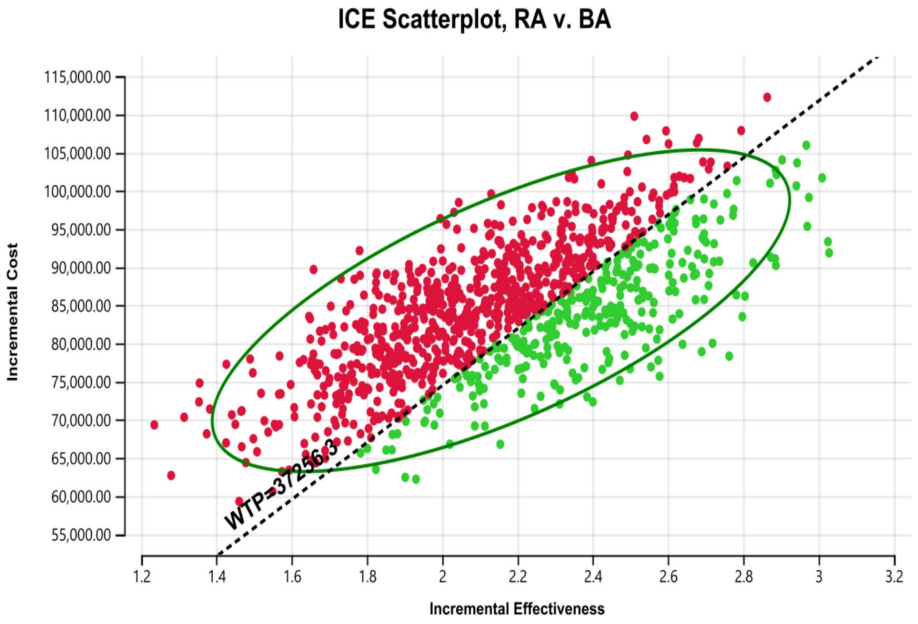


FIGURE 3
Cost-effectiveness plane generated in the probabilistic sensitivity analysis. WTP, willingness to pay; RA, rezvilutamide; BA, bicalutamide. Red: ICER value greater than WTP. Green: ICER value less than WTP.

cost-effectiveness acceptability curve revealed that rezvilutamide plus ADT was not cost-effective when the WTP threshold was set at $37,256.3 per QALY. However, these findings should not be used as a basis for limiting the use of rezvilutamide, as this may result in missed opportunities for beneficial treatment options. Instead, they should be regarded as economic considerations for informing the implementation of China's national pricing negotiation policies. To address the issue of high drug prices, promote patient access, and ensure the sustainability of the medical insurance fund, China formally launched national reimbursement-linked price

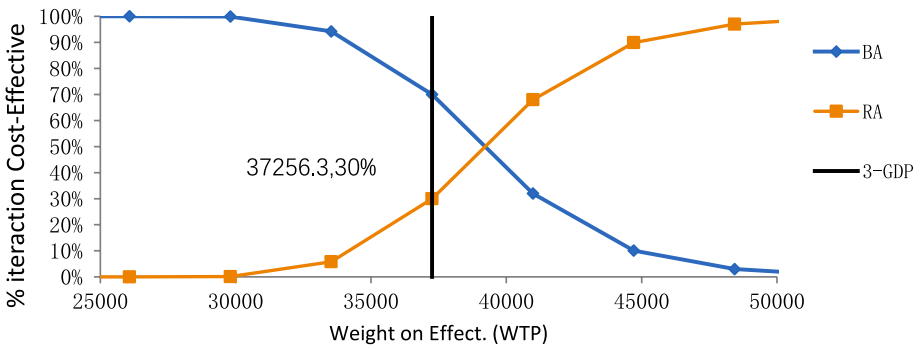


FIGURE 4
The cost-effectiveness acceptability curve for rezvilutamide versus bicalutamide. BA, bicalutamide; RA, rezvilutamide; WTP, willingness-to-pay; GDP, gross domestic product.

negotiations in 2017 (34, 35). Such a policy could significantly improve the cost-effectiveness of rezvilutamide.

The results of the one-way sensitivity analysis showed that the cost of rezvilutamide was the most sensitive factor affecting the ICER. The analysis revealed that the cost-effectiveness of rezvilutamide plus ADT compared to bicalutamide plus ADT could be influenced by the price of rezvilutamide. Rezvilutamide can be considered cost-effective only when priced below $705.46 per cycle at a WTP threshold of $37,256.3 per QALY. The results of both the one-way sensitivity analysis and probabilistic sensitivity analysis demonstrate the robustness of these findings. These results provide important insights for China's health insurance policymakers when determining the price of rezvilutamide following its launch.

Several studies have assessed the cost-effectiveness of first-line treatments for high-volume mHSPC, including two Chinese studies focusing on the cost-effectiveness of rezvilutamide. As a novel therapy, rezvilutamide was associated with a high economic burden, highlighting the need for pharmacoeconomic research based on the CHART trial to evaluate its cost-effectiveness (19, 20, 36, 37). Ding et al. (20) previously conducted a partitioned survival model to evaluate the cost-effectiveness of rezvilutamide combined with ADT for high-volume mHSPC in China. Their study demonstrated that rezvilutamide plus ADT was more cost-effective compared to bicalutamide plus ADT as the first-line treatment for high-volume mHSPC from the perspective of the Chinese healthcare system (20). In contrast, Wu et al. (19) conducted a similar study using a partitioned survival model and concluded that rezvilutamide plus ADT is unlikely to be cost-effective for most adults when compared to bicalutamide plus ADT, considering a WTP threshold of $38,223.3 per QALY from the perspective of the Chinese healthcare system. However, they suggested that a promising economic advantage could be achieved if rezvilutamide were included in the National Reimbursement Drug List (NRDL) with a 10% price reduction (19). Due to the discrepancies between the findings of these two studies, we constructed a Markov model to assess the cost-effectiveness of rezvilutamide plus ADT versus bicalutamide plus ADT as a first-line treatment for high-volume mHSPC from the perspective of the Chinese healthcare system. Our results indicated that rezvilutamide treatment regimen would be considered cost-effective only when priced below $705.46 per cycle at a WTP threshold of $37,256.3 per QALY, yielding findings consistent with those of Wu et al. (19). This provided new evidence to inform clinical decision-making regarding antiandrogen drugs for Chinese patients with high-volume mHSPC based a Markov model cost-effectiveness comparison.

The present study has several limitations. First, the pharmacoeconomic evaluation was based on the CHART trial, which unfortunately had a limited follow-up period. As a result, we obtained progression-free survival PFS and OS data by fitting parameter distributions. Although extrapolation could obtain relevant data outside the follow-up period of the CHART trial, this would increase model uncertainty. To mitigate this, we conducted a comparative analysis using the Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC) to select the best-fitting distribution, and performed sensitivity analysis to assess the robustness of the model results. Second, the study only focused on the two most serious AEs related to treatment, neglecting other potential AEs. As a result, there may be some degree of bias between the calculated costs and those in real-world settings. Third, several key parameters in the analysis, including utility scores, were obtained from the literature. However, a comprehensive search of existing studies did not identify utility scores specific to the Chinese population, which may impact the accuracy of the model results. Finally, this analysis was conducted while Rezvilutamide was still under patent protection. The pricing of generic equivalents may influence the cost-effectiveness analysis in future studies.

Conclusion

In conclusion, our analysis indicates that rezvilutamide plus ADT is not cost-effective at the current price compared to bicalutamide plus ADT. However, it becomes cost-effective if the price of rezvilutamide is reduced by 14.29%.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding authors.

Author contributions

JH: Conceptualization, Formal analysis, Methodology, Validation, Writing – original draft. XZ: Formal analysis, Methodology, Validation, Writing – original draft. WC: Data curation, Investigation, Writing – original draft. ZZ: Data curation, Investigation, Writing – original draft. YH: Data curation, Investigation, Writing – original draft. JM: Conceptualization, Formal analysis, Methodology, Project administration, Resources, Supervision, Validation, Writing – review & editing. LO: Conceptualization, Formal analysis, Methodology, Project administration, Resources, Supervision, Validation, Writing – review & editing.

Funding

The author(s) declare that financial support was received for the research and/or publication of this article. This study was supported by Shenzhen High-level Hospital Construction Fund and the Natural Science Foundation of Hunan Province (2021JJ80080).

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The authors declare that no Gen AI was used in the creation of this manuscript.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

References

1. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. (2024) 74:229–63. doi: 10.3322/caac.21834

2. Zheng RS, Chen R, Han BF, Wang SM, Li L, Sun KX, et al. Cancer incidence and mortality in China, 2022. *Zhonghua Zhong Liu Za Zhi*. (2024) 46:221–31. doi: 10.3760/cma.j.cn112152-20240119-00035

3. He J, Chen WQ, Li N, Cao W, Ye DW, Ma JH, et al. China guideline for the screening and early detection of prostate cancer (2022, Beijing). *Zhonghua Zhong Liu Za Zhi*. (2022) 44:29–53. doi: 10.3760/cma.j.cn112152-20211226-00975

4. Zeng H, Chen W, Zheng R, Zhang S, Ji JS, Zou X, et al. Changing cancer survival in China during 2003-15: a pooled analysis of 17 population-based cancer registries. *Lancet Glob Health*. (2018) 6:e555–67. doi: 10.1016/S2214-109X(18)30127-X

5. National Cancer Institute Surveillance, Epidemiology, and end results (SEER) program. Cancer Stat Facts Prostate Cancer. Available online at: https://seer.cancer.gov/statfacts/html/prost.html (Accessed October 20, 2024).

6. Virgo KS, Rumble RB, Talcott J. Initial Management of Noncastrate Advanced, recurrent, or metastatic prostate Cancer: ASCO guideline update. *J Clin Oncol*. (2023) 41:3652–6. doi: 10.1200/JCO.23.00155

7. Lin TT, Chen YH, Wu YP, Chen SZ, Li XD, Lin YZ, et al. Risk factors for progression to castration-resistant prostate cancer in metastatic prostate cancer patients. *J Cancer*. (2019) 10:5608–13. doi: 10.7150/jca.30731

8. Kyriakopoulos CE, Chen YH, Carducci MA, Liu G, Jarrard DF, Hahn NM, et al. Chemohormonal therapy in metastatic hormone-sensitive prostate Cancer: long-term survival analysis of the randomized phase III E3805 CHAARTED trial. *J Clin Oncol*. (2018) 36:1080–7. doi: 10.1200/JCO.2017.75.3657

9. James ND, Sydes MR, Clarke NW, Mason MD, Dearnaley DP, Spears MR, et al. Addition of docetaxel, zoledronic acid, or both to first-line long-term hormone therapy in prostate cancer (STAMPEDE): survival results from an adaptive, multiarm, multistage, platform randomised controlled trial. *Lancet*. (2016) 387:1163–77. doi: 10.1016/S0140-6736(15)01037-5

10. Gravis G, Fizazi K, Joly F, Oudard S, Priou F, Esterni B, et al. Androgen-deprivation therapy alone or with docetaxel in non-castrate metastatic prostate cancer (GETUG-AFU 15): a randomised, open-label, phase 3 trial. *Lancet Oncol*. (2013) 14:149–58. doi: 10.1016/S1470-2045(12)70560-0

11. Prostate Cancer Trialists' Collaborative Group. Maximum androgen blockade in advanced prostate cancer: an overview of the randomised trials. *Lancet*. (2000) 355:1491–8. doi: 10.1016/S0140-6736(00)02163-2

12. Cornford P, van den Bergh RCN, Briers E, Van den Broeck T, Cumberbatch MG, De Santis M, et al. EAU-EANM-ESTRO-ESUR-SIOG guidelines on prostate Cancer. Part II-2020 update: treatment of relapsing and metastatic prostate Cancer. *Eur Urol*. (2021) 79:263–82. doi: 10.1016/j.eururo.2020.09.046

13. Smith MR, Hussain M, Saad F, Fizazi K, Sternberg CN, Crawford ED, et al. Darolutamide and survival in metastatic, hormone-sensitive prostate Cancer. *N Engl J Med*. (2022) 386:1132–42. doi: 10.1056/NEJMoa2119115

14. Hussain M, Tombal B, Saad F, Fizazi K, Sternberg CN, Crawford ED, et al. Darolutamide plus androgen-deprivation therapy and docetaxel in metastatic hormone-sensitive prostate Cancer by disease volume and risk subgroups in the phase III ARASENS trial. *J Clin Oncol*. (2023) 41:3595–607. doi: 10.1200/JCO.23.00041

15. Chi KN, Chowdhury S, Bjartell A, Chung BH, de Santana P, Gomes AJ, et al. Apalutamide in patients with metastatic castration-sensitive prostate Cancer: final survival analysis of the randomized, double-blind, phase III TITAN study. *J Clin Oncol*. (2021) 39:2294–303. doi: 10.1200/JCO.20.03488

16. Armstrong AJ, Iguchi AAT. Final overall survival (OS) analysis from ARCHES: a phase III, randomized, double-blind, placebo (PBO)-controlled study of enzalutamide (ENZA) + androgen deprivation therapy (ADT) in men with metastatic hormone-sensitive prostate cancer (mHSPC). *Ann Oncol*. (2021) 32:S1300–1. doi: 10.1016/j.annonc.2021.08.2101

17. CSCO. Guidelines of Chinese society of clinical oncology (CSCO) diagnosis and treatment of prostate cancer guideline. People's Medical Publishing House Press. (2024).

18. Gu W, Han W, Luo H, Zhou F, He D, Ma L, et al. Rezvilutamide versus bicalutamide in combination with androgen-deprivation therapy in patients with high-volume, metastatic, hormone-sensitive prostate cancer (CHART): a randomised, open-label, phase 3 trial. *Lancet Oncol*. (2022) 23:1249–60. doi: 10.1016/S1470-2045(22)00507-1

19. Wu H, Sun L, Feng R, Zhang H, Tang K, Wang S, et al. Cost-effectiveness of rezvilutamide versus bicalutamide and androgen-deprivation therapy in patients with highvolume, metastatic, hormone-sensitive prostate cancer. *Front Pharmacol*. (2023) 14:1269129. doi: 10.3389/fphar.2023.1269129

20. Ding H, Li S, Xu X, Xu W, He C, Xin W, et al. Cost-effectiveness analysis of rezvilutamide versus bicalutamide in the treatment of metastatic hormone-sensitive prostate cancer. *BMJ Open*. (2024) 14:e073170. doi: 10.1136/bmjopen-2023-073170

21. Husereau D, Drummond M, Petrou S, Carswell C, Moher D, Greenberg D, et al. Consolidated health economic evaluation reporting standards (CHEERS) statement. *Eur J Health Econ*. (2013) 14:367–72. doi: 10.1007/s10198-013-0471-6

22. Husereau D, Drummond M, Augustovski F, de Bekker-Grob E, Briggs AH, Carswell C, et al. Consolidated health economic evaluation reporting standards 2022 (CHEERS 2022) statement: updated reporting guidance for health economic evaluations. *BMC Med*. (2022) 20:23. doi: 10.1186/s12916-021-02204-0

23. National Health Commission. China health statistics yearbook. China: Union Medical University Press (2022).

24. Liu GE. China guidelines for pharmacoeconomic evaluation China Market Press (2020).

25. National Bureau of Statistics of China. Available online at: https://data.stats.gov.cn/search.htms=GDP (accessed October 20, 2024)

26. Guyot P, Ades AE, Ouwens MJ, Welton NJ. Enhanced secondary analysis of survival data: reconstructing the data from published Kaplan-Meier survival curves. *BMC Med Res Methodol*. (2012) 12:9. doi: 10.1186/1471-2288-12-9

27. Latimer NR. Survival analysis for economic evaluations alongside clinical trials extrapolation with patient-level data National Institute for Health and Care Excellence (NICE). (2013).

28. Hunan Public Resources Trading Service Platform. Available online at: https://jyjy.hnsggzy.com/ (accessed October 20, 2024).

29. Zhao J, Jiang K, Li Q, Zhang Y, Cheng Y, Lin Z, et al. Cost-effectiveness of olanzapine in the first-line treatment of schizophrenia in China. *J Med Econ*. (2019) 22:439–46. doi: 10.1080/13696998.2019.1580714

30. Zhang PF, Xie D, Li Q. Adding enzalutamide to first-line treatment for metastatic hormone-sensitive prostate Cancer: a cost-effectiveness analysis. *Front Public Health*. (2021) 9:608375. doi: 10.3389/fpubh.2021.608375

31. Ming J, Wu Y, Han R, Xu X, Waldeck R, Hu S. Cost-utility analysis of Darolutamide combined with androgen deprivation therapy for patients with high-risk non-metastatic castration-resistant prostate Cancer in China. *Adv Ther*. (2023) 40:1087–103. doi: 10.1007/s12325-022-02389-7

32. Bank of China. Foreign exchange rate Available online at: https://www.boc.cn/sourcedb/whpj/ (accessed October 20, 2024)

33. Liu M, Qu S, Liu Y, Yao X, Jiang W. Comparative clinical effects and cost-effectiveness of maximum androgen blockade, docetaxel with androgen deprivation therapy and ADT alone for the treatment of mHSPC in China. *J Comp Eff Res*. (2019) 8:865–77. doi: 10.2217/cer-2018-0133

34. Zhou J, Lan T, Lu H, Pan J. Price negotiation and pricing of anticancer drugs in China: an observational study. *PLoS Med*. (2024) 21:e1004332. doi: 10.1371/journal.pmed.1004332

35. Liu GG, Wu J, He X, Jiang Y. Policy updates on access to and affordability of innovative medicines in China. *Value Health Reg Issues*. (2022) 30:59–66. doi: 10.1016/j.vhri.2021.12.003

36. Yoo M, Nelson RE, Haaland B, Dougherty M, Cutshall ZA, Kohli R, et al. Cost-effectiveness analysis of 7 treatments in metastatic hormone-sensitive prostate cancer: a public-payer perspective. *J Natl Cancer Inst*. (2023) 115:1374–82. doi: 10.1093/jnci/djad135

37. Gupta N, Gupta D, Vaska KG, Prinja S. Cost-effectiveness analysis of systemic therapy for intensification of treatment in metastatic hormone-sensitive prostate cancer in India. *Appl Health Econ Health Policy*. (2024) 22:415–26. doi: 10.1007/s40258-023-00866-w

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 30 May 2025
DOI 10.3389/fpubh.2025.1569855

Check for updates

OPEN ACCESS

EDITED BY
Jing Yuan,
Fudan University, China

REVIEWED BY
Valentin Marian Antohi,
Dunarea de Jos University, Romania
Chen Li,
Shanghai University of Engineering Sciences, China
Xinyi Xu,
Guangxi Medical University, China

*CORRESPONDENCE
Huishu Tian
✉ smiling-tian@163.com

†These authors have contributed equally to this work and share first authorship

RECEIVED 11 February 2025
ACCEPTED 01 May 2025
PUBLISHED 30 May 2025

CITATION
Chang J, Chen S, Li A, Yang X, Luo H, Yilamu M, Fu B, Xu N, Liu J and Tian H (2025) Facilitators and barriers to the implementation of DIP payment methodology reform in a public hospital in Guangzhou: a qualitative study based on the implementation of the meta-framework for research (CFIR) framework.
Front. Public Health 13:1569855.
doi: 10.3389/fpubh.2025.1569855

COPYRIGHT
© 2025 Chang, Chen, Li, Yang, Luo, Yilamu, Fu, Xu, Liu and Tian. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

Facilitators and barriers to the implementation of DIP payment methodology reform in a public hospital in Guangzhou: a qualitative study based on the implementation of the meta-framework for research (CFIR) framework

Jinghui Chang[1†], Siyi Chen[1†], Anqi Li[1], Xixi Yang[1], Hualian Luo[1], Maidina Yilamu[1], Bingqian Fu[1], Nuoyan Xu[1], Jing Liu[2] and Huishu Tian[2*]

[1]School of Health Management, Southern Medical University, Guangzhou, China, [2]Guangzhou First People's Hospital, Guangzhou, China

Background: The Diagnosis-Intervention Packet (DIP), a medical insurance payment management system utilizing big data, has been piloted in 12 cities by the National Healthcare Security Administration in China starting in 2021. Guangzhou is one of the pilot cities, and it has demonstrated significant success in the DIP payment reform, with its practical experience being affirmed and promoted by the National Health Department. In this study, researchers conducted field visits to a public hospital in Guangzhou to understand the internal responses to the DIP reform and the cognitive attitudes of relevant personnel. The analysis of the positive and negative factors affecting the implementation of the reform and the proposed measures to optimize internal hospital management are expected to provide practical evidence for the implementation of DIP payment reform in other public hospitals.

Methods: This study develops an interview guide based on the Consolidated Framework for Implementation Research (CFIR) and conducts one-on-one semi-structured interviews offline with personnel from a Grade A tertiary public hospital in Guangzhou. Employing rapid qualitative analysis techniques and utilizing NVivo 14.0 for coding CFIR-structured texts related to implementation, the study integrates five dimensions: innovation, inner and outer context, individuals, and the implementation process. It identifies factors that facilitate and hinder the implementation of the Diagnosis-Intervention Packet (DIP) payment reform, thereby proposing optimized internal management strategies for public hospitals to cope with DIP payment reforms.

Discussion: This study will provide significant insights for optimizing the internal management of public hospitals in the context of DIP payment reform. It offers a reference for optimizing internal management in tertiary public hospitals in China, aiming to achieve standardized, healthy, collaborative, and high-quality development.

KEYWORDS

public hospitals, internal management, DIP Medicare payment methodology, meta-framework for implementation research (CFIR) framework, public health policy

Background

The stable and efficient operation of medical insurance funds is crucial for as well as. Changes significantly on allocating and coordinating medical resources and services, and changes in medical insurance payment methods significantly impact the efficiency of medical insurance fund utilization (1) Therefore, the reform of medical insurance payment methods occupies an important position in the medical reform process (2). Since 2009, China has been exploring the implementation of Diagnosis Related Group (DRG) payment reform, progressively eliminating the excessive medical practices associated with the traditional fee-for-service model (3). In 2019, the National Health Department, in collaboration, issued the technical specifications and grouping schemes for DRG pilot programs, designating 30 cities as national pilot cities for DRG payment (4).

China's exploration of localized medical cost containment strategies began in 2018, based on authentic domestic data. It objectively summarized the characteristics of various diseases and their treatment paradigms and, from these common features, established a Diagnosis-Intervention Packet (DIP) system that aligns with the current state of medical services in China. Gradually, a medical payment framework was constructed that supports a "total budget for normal growth; disease category points to guide rational treatment, payment reflects incentive mechanisms, and intelligent monitoring to strengthen process management" (5). Consequently, in 2020, the National Medical Insurance Administration issued the "Regional Point Method Total Budget and DIP Pilot Work Plan," officially launching DIP pilot programs in 71 cities nationwide. To date, the National Medical Insurance Administration has published seven policy documents, emphasizing from the national health strategy level the construction of a "practical and efficient medical insurance payment mechanism" adapted to the national conditions.

In 2021, the National Healthcare Security Administration, guided by developmental objectives, comprehensively and concurrently advanced DRG/DIP payment methodologies reform, issuing the "Three-Year Action Plan for DRG/DIP Payment Method Reform" (6, 7). It proposed that by 2022–2024, the reform tasks for DRG/DIP payment methods would be fully completed, thereby promoting high-quality development in medical insurance. By the end of 2024, all regions under the unified management had initiated the reform of DRG/DIP payment methodologies (8). By the end of 2025, the DRG/DIP payment method is expected to cover all eligible medical institutions providing inpatient services nationwide, achieving comprehensive coverage across four aspects: unified regions, medical institutions, disease groupings, and medical insurance funds (9).

By the strategic planning of the National Healthcare Security Administration, regions are advancing medical insurance payment reforms in a phased and batched manner, implementing them steadily through a combination of national unified deployment and local practice. Observations from the practices in various provinces and cities indicate that the DRG/DIP payment system has achieved certain effects. By the end of 2021, it had entered the actual payment phase, which can essentially ensure that medical institutions retain a certain surplus (10). Taking Zhejiang Province, which entered the actual payment phase earlier, as an example, the province has included inpatient costs across the entire province, encompassing all demographics and aspects of diagnosis and treatment within the scope of DRG payment reform (11). The DIP reform has also yielded preliminary results: in pilot cities of Guangdong, Jiangsu, Fujian, and Shandong provinces, there has been a significant reduction in the growth rate of medical expenses and average inpatient costs, with the growth rate of medical insurance payments for inpatient costs decreasing by up to 4.8%, thereby alleviating the pressure on fund expenditures to a certain extent (12).

Guangzhou, with the richest medical resources in southern China, with the number of top-tier hospitals ranking only after Beijing and Shanghai nationwide. As one of the first pilot cities for the Diagnosis-Intervention Packet (DIP) payment reform, since January 2018, it has fully implemented a big data-based case-based payment system, covered 334 medical institutions and saved 1.1 billion yuan in medical insurance costs in that year alone, establishing an integrated payment supervision mechanism of "retaining surpluses and sharing deficits" (13). In 2020, as a national advanced pilot for DIP, the National Healthcare Security Administration promoted the "Guangzhou Experience" to the national level. By 2023, the average inpatient cost and out-of-pocket expenses in Guangzhou had decreased by over 10%, reducing unnecessary hospitalizations by 56,000 person-times annually, and the average number of hospital stays per patient declined by 5.8%. This effectively controlled the irrational increase in medical expenses and promoted the rational allocation of medical resources (14). The DIP payment reform in Guangzhou, Guangdong Province, has covered all designated inpatient hospitals, benefiting 14 million insured individuals in the city.

The effectiveness of the Diagnosis-Intervention Packet (DIP) payment reform has garnered widespread attention, as it not only meets the basic medical needs of the population but also alleviates the financial burden on medical institutions (15). Many scholars believe that DIP payment, as an indigenous innovation in the management model of medical insurance funds, will effectively address issues such as excessive medical treatment and the extensive development of hospitals (16). A bundled pricing approach achieves precise pricing and reasonable compensation for medical services, playing a positive role in controlling the irrational increase in medical expenses (17). However, the implementation of DIP still faces certain obstacles. The shift in payment methods and the management pressure due to overly detailed categorization have increased the operational burden on hospitals. Under the pressure of reform targets (18), profit-driven behaviors such as patient referral and conservative treatment are hard to avoid. Weak support from electronic medical record platforms, benefit disparities between disease categories, and insufficient awareness among medical staff and patients constrain the promotion and implementation of DIP (19). Profit-driven behaviors such as patient referral and conservative treatment are hard to avoid. Weak support from electronic medical record platforms, benefit

disparities between disease categories, and insufficient awareness among medical staff and patients constrain the promotion and implementation of DIP.

Against the backdrop of medical reform, scholars often begin their investigation with the operational effects of the Diagnosis-Intervention Packet (DIP) reform on medical institutions, examining its impact on aspects such as medical quality, medical expenses, and hospital stay duration. From a research perspective, domestic and international scholars focus on policy orientation, system construction, and multi-stakeholder collaboration (20), emphasizing macro-level policy analysis. In contrast, studies on individual policy cognition and evaluation at the implementers' level are relatively scarce (21). However, the in-depth implementation of DIP requires a combined qualitative approach from both macro and individual perspectives to better explore how health policies can be effectively implemented within hospitals.

The Consolidated Framework for Implementation Research (CFIR), initially introduced in 2009, comprises five dimensions and 39 domains that influence the implementation process and outcomes (22). After a decade and a half of application and evolution, in 2022, the CFIR development team updated the framework in response to feedback from research scholars, resulting in CFIR 2.0. This updated version expanded the framework by adding 21 new constructs and 19 secondary constructs. It refined some of the existing constructs and their definitions (23, 24), enhancing their utility and applicability. Worldwide, in the assessment of healthcare service quality, the CFIR framework is extensively applied in practical investigations across various fields such as nursing implementation, screening interventions, clinical decision-making, medical platform evaluation, and health analytics, promoting a more profound integration of implementation science theory with empirical research (25, 26).

The CFIR used in this study provides a theoretical and methodological basis for analyzing DIP payment reform. Compared to frameworks such as RE-AIM or PARIHS, CFIR provides a more structured approach to assessing the contextual, behavioral, and organizational dynamics that influence implementation outcomes (22, 27). When involving multiple levels of participants in the policy, institutional, and clinical arenas, CFIR is better suited than the Theoretical Domains Framework (TDF) to study complex policy reforms, capturing the interplay between policy characteristics, institutional context, and individual behaviors that are critical to understanding the real-world challenges of healthcare system reforms (28) CFIR's five-domain structural design allows for a better layered understanding of how reforms are perceived (innovations), experienced at the institutional and inter-institutional levels (internal and external environments), implemented by individuals, and how the adaptation process takes shape - dimensions that are highly relevant to the context of top-down policy diffusion and local adaptation in China. In addition, CFIR has been successfully applied to implementation studies of DRG-based payment reforms in multiple countries, enhancing its cross-country and cross-system applicability. For example, in South Korea, Kim et al. (29) used CFIR to assess how hospitals are responding to bundled DRG-based payments, identifying organizational leadership and system infrastructure as key enablers. In Germany, Linn et al. (30) utilized CFIR to explore the implementation of digital health in a DRG environment. Similarly, in France, Dufour et al. (31) used CFIR to examine behavioral responses to performance-based hospital grants.

By adopting CFIR in the context of China's DIP reforms, this study can serve to fill a comparative gap in how developing health systems respond to complex payment reforms. CFIR's cross-country relevance and its flexibility in integrating micro- and macro-implementation determinants strengthen its applicability in this study.

Although there has been a great deal of research on the institutional design and macro-effectiveness (e.g., cost control, efficiency improvement) of the DIP payment reform, most of the literature focuses on the macro-policy level or the analysis of quantitative economic indicators, and there is a lack of qualitative research on the complexity of the healthcare reform in the process of hospitalization, the resistance and adaptive mechanism of the implementation of the healthcare reform, especially from the perspectives of the main actors of the implementation -- hospital administrators and clinical staff. However, most of the literature focuses on the macro policy level or quantitative economic indicators to analyze the complexity, resistance and adaptation mechanism of the implementation of the reform in the frontline of hospitals, especially from the perspective of the implementation subjects - hospital administrators and clinical staff. This "implementation gap" limits our in-depth understanding of the actual operation mechanism of DIP reform and is not conducive to the identification and optimization of system adaptation problems at the micro level.

Therefore, using CFIR as a theoretical framework, researchers conducted semi-structured interviews with administrators, clinical department heads, and clinical technicians. Unlike studies that rely on large samples of data or disease-specific analyses, this type of holistic frame analysis and coding comparison for a single sample of healthcare organizations can reveal facilitators and major barriers to policy implementation in hospitals. In contrast to questionnaires and quantitative data analysis methods, interviews can provide insights into the perceptions and feedback of hospital insiders on the current status of DIP payment reform, and further explore the major issues faced by this tertiary care public hospital in the implementation of DIP payment reform.

This study focuses on the internal implementation process of DIP reform in a public tertiary hospital, aiming to answer the following core research questions:

- How do medical staff and administrators perceive and adapt to the DIP payment reform?
- What are the organizational, process, and individual challenges and facilitators faced by hospitals in the implementation of DIP reform?
- How can recommendations be made to optimize the path of reform implementation from the perspective of the implementers?

Through semi-structured interviews and framework-oriented coding analysis, this research attempts to fill the gap of the lack of micro-mechanisms explored in existing studies at the implementer level and provides empirical insights and strategic references for the policy implementation of DIP reform and the continuous optimization of the health insurance payment system.

Methods

Research design

This study employs the five-dimensional structure of the Consolidated Framework for Implementation Research (CFIR), which

includes Innovation, Outer setting, Inner setting, Roles, Characteristics, and Process, to guide future implementation and evaluation. This comprehensive framework facilitates a structured and systematic approach to guiding and assessing policy execution, and it actively assists in identifying potential and actual factors that influence the progress and outcomes of implementation (23). By integrating a hierarchical exploration from the macro (senior hospital management) to meso (department and unit managers) to micro (medical, technical personnel, individual implementers) levels, we can gain a clearer understanding of how the DIP system disseminates information and develops signals to affect internal hospital decision-making and direction, thereby influencing operational models and reward and punishment mechanisms, ultimately manifesting in the policy cognition, strategic thinking, and medical behaviors of healthcare professionals.

Researchers collected perceptions and evaluations of implementing the Diagnosis-Intervention Packet (DIP) through semi-structured interviews with participants. By inductively coding the viewpoints of each interviewee across the five dimensions, we synthesized the interactions at different levels, elucidating how medical institutions implement policies and objectives through internal adjustments and coordination. We also explored individuals' reactions and implementation status at the micro-level to management at the meso-level. From the acquisition and organization of this information, we identified the barriers and facilitators to the implementation of DIP.

Study setting

In the study, we selected a large public hospital in Guangzhou, one of the first batch of tertiary-level hospitals in Guangdong Province, with a history of operation spanning over a century, making it representative. The research team conducted in-depth investigations within the medical institution, carrying out on-site field interviews with nine participants. Before the implementation of the field investigation, the team leader organized the division of labor among team members to collect and organize background information on the case hospital. The supervising instructor provided interview training for all personnel, standardizing the interview execution criteria and working group assignments.

The selection of interview subjects is based on the relevant departmental sections implementing DIP as a clue, combining the background of the hospital system, on-site tracking, and literature search. Full consideration was given to the work content of the personnel in different departments, the balance of their backgrounds, and the personal wishes of the respondents.

Data collection

Between November 17 and November 30, 2023, 16 separate semi-structured qualitative interviews were conducted. To increase methodological rigor, this study used purposeful theoretical sampling to select interviewees from administrative and clinical departments directly related to DIP reform. Interviews were continued until theoretical saturation was reached, i.e., three consecutive interviews in which no new themes emerged. Two interviewers were assigned to one interview unit, and each interview lasted 45–60 min while being audio-recorded and transcribed offline. Electronic interview transcripts were backed up and transcribed in groups. A total of 16 valid interview texts were collected and organized, integrating one copy of each hospital background collection material and the DIP interview research guidebook.

Data analysis

The 16 valid interview texts were cross-checked and cleaned by the four groups of interview unit staff and imported into NVivo.14.0 software by four data coders for manual organization and coding. In terms of coding consistency, two researchers with qualitative research backgrounds independently carried out the initial coding, and consensus was reached on the divergent parts through discussion and guided review by qualitative research experts to ensure the stability of the coding results. The coding process used CFIR as the main coding framework to summarize and arrange the qualitative texts by five dimensions and 36 domains. This enabled the researchers to take the qualitative, stand-alone texts and build them into a salient structure of positive and negative contributing factors to policy implementation. The distribution and frequency of the key domains were statistically analyzed as a reference point for comparison, and the factors were hierarchically categorized in conjunction with affective words and attitudes in the textual content. Triangulation was also used in this study to enhance reliability and validity. Interviews were cross-checked with relevant hospital documents and information (e.g., performance notices, implementation rules, etc.), and interviews with key informants were confirmed, thus strengthening the reliability and robustness of data interpretation.

The coding process identified 27 parent nodes and 83 child nodes across the five dimensions of CFIR 2.0. Parent nodes corresponded to core constructs (e.g., 5–6 nodes under Innovation, such as "Comparative Advantage" and "Complexity"), while child nodes were derived through granular thematic analysis (e.g., "Theoretical Complexity" and "Clinical Adaptability" under "Complexity"). Node density analysis revealed the highest concentration in *Inner Setting* (32%, primarily reflecting departmental collaboration [IC01] and resource allocation [H01]) and *Innovation* (28%, aligned with DIP policy design discussions [Ge01, CM01]). Inter-coder reliability was confirmed with Cohen's $\kappa = 0.78$ (95%CI 0.72–0.84) based on dual independent coding of 30% transcripts.

Ethical considerations

Ethical approval for this research was obtained from the First People's Hospital of Guangzhou, with the approval number (K-2024-099-01). Before the interviews, the researchers assured the interviewees of the anonymization of their personal information.

Results

Summary of interviewees

We conducted semi-structured interviews with implementers of the in-hospital DIP medical payment reform in a locally representative

public hospital, covering eight clinical medical departments (joint surgery, neurology, hematology, obstetrics, traditional Chinese medicine, pediatrics, geriatrics, and obstetrics, and gynecology) as well as six administrative functions (medical insurance office, medical record department, quality control department, economic management department, complaint management department, information center) covered a total of 16 implementers. Their basic information is described and organized in Table 1.

Facilitators and barriers

The study was coded using the dimensions and corresponding domains of the Comprehensive Framework for Implementation Research (CFIR) as a reference, it analyzed the interview texts, distilling the five thematic results and disaggregating the facilitators and impediments to the implementation of DIP reform policies. The interview texts were analyzed, the five thematic results were distilled, and the facilitators and impediments to the implementation of DIP reform policies were disaggregated based on the qualitative textual results. The disaggregated results can be seen in Table 2.

Domain 1: Innovation

The dimension of innovation lies in exploring the differences between the Diagnosis-Intervention Packet (DIP) and previous medical insurance payment systems. Respondents assess the execution status of regarding effectiveness, comparative advantage, adaptability, applicability, and complexity. A positive factor is that respondents generally agree that the DIP reform policy is the most important policy at the current stage of the hospital in terms of medical insurance. Recognizing the policy's importance leads to higher compliance and trust among implementers. The comparative advantage of DIP lies in controlling overall medical expenses to improve medical efficiency and resource utilization while also strengthening medical standards. Still, there are also concerns about its limitations on high-end medical care. The DIP reform still faces issues, such as the need for rational optimization of disease groupings.

The interviewees' policy implementation assessments and opinions are coded, starting with the English abbreviation of the department or section, followed by 01 for department managers and 02 for medical staff.

- ***Ge01:*** *The impact of DIP payments on clinical care is currently evident and is arguably one of the most important factors. There is no doubt that DIP payments are dominant and that they play the role of the baton in clinical work.*
- ***CM01:*** *DIP is in line with clinical needs and use. It was originally designed to maximize savings at the national level and minimize unneeded tests and treatments.*
- ***EM01:*** *We are increasingly facing insurance reform, which is becoming increasingly significant. As a source of funding, this affects everything. Hospital management needs to be more sophisticated; managers face greater operational management costs and pressures.*
- ***MR01:*** *The DIP payment reform is a kind of innovation; the process of reform is more tortuous, but in the other, process of reform is more tortuous, but from another perspective, it is a forward and progressive.*
- ***COM01:*** *Medical insurance reform is reform and the most important policy at this stage. The most important aspect of medical insurance is ensuring basic coverage. Early preventive care and early intervention are also very important but rarely mentioned.*

Domain 2: Outer setting

Outer setting factors pertain to the external impact events and societal collaborative relationships (policies, legal environment, public attitudes) that the DIP reform encounters. Regarding the facilitation of DIP reform implementation, there has been an intensified supervision and review of medical institutions by higher authorities following the policy's enactment. For hospitals, this has led to heightened demands for refined management, necessitating adjustments in their management approaches to align with the standardized requirements of the DIP system regarding diagnosis, treatment, and cost control. Regarding collaborative facilitation, hospitals engage in feedback with higher medical insurance

TABLE 1 Interviewed departments and interviewees included in November 2023.

Interview subject		Departments/Interviewees (%)
Departments (n = 14)	**Administrative departments** (Economic Management, Medical Records, Quality Control, Complaints Management, Information Center)	6(43)
	Clinical departments (Hematology, Geriatrics, Pediatrics, Obstetrics, Chinese Medicine, Neurology, Joint Surgery, Gynecology)	8 (57)
Individuals (n = 16)	**Responsibility**	
	Managerial staff	12 (75)
	Operational staff	4 (25)
	Roles	
	Administrative Staff	6 (38)
	Clinical staff	10 (62)

TABLE 2 Factors that promote and hinder the implementation of DIP payment.

CFIR construct		CFIR domain	Determinants facilitator/Barrie/Mixed
Innovation		Effectiveness	Mixed
		Comparative advantage	Facilitator
		Trust	Facilitator
		Applicability	Mixed
		Complexity	Barrier
		Supporting policies	Facilitator
Outer setting		Important events (outer pressure)	Barrier
		Outer attitudes	Mixed
		Local policy conditions	Mixed
		Collaborative relationships	Facilitator
		Policy and Laws	Mixed
		Outer incentives (financial aid)	Facilitator
Inner setting		Team structure	Mixed
		Collaboration within the hospital	Facilitator
		Information sharing	Facilitator
		Culture	Mixed
		Urgency of reform	Facilitator
		Compatibility	Mixed
		Relative priority	Facilitator
		Incentive system	Barrier
		Goal alignment	Mixed
		Available Resources	Barrier
		Accessibility of knowledge and information	Facilitator
Individuals	Roles	Leaders, team members, supporters	Mixed
		Individual's adaptability to reform	Barrier
		Individual abilities	Mixed
	Characteristics	Scope of individual power (available resources)	Barrier
		Individual motivation	Barrier
Implementation process		Teamwork	Facilitator
		Needs assessment	Barrier
		Environmental assessment	Mixed
		Planning	Facilitator
		Adjust strategy	Facilitator
		Mobilization	Barrier
		Execute	Mixed
		Reflection and evaluation	Facilitator

Facilitators to implementation were predominantly high (39%), with 22% barriers to implementation.

departments and share reform experiences with peer institutions. The resulting hindrances include increased operational management costs and pressures for hospitals, exacerbating the operational burden and leading to inefficiencies in policy execution at the departmental level.

- ***MI02:*** *The oversight and evaluation of DIP are primarily conducted through two methods: supervision by higher authorities and self-inspection; performance is assessed mainly by the hospital's economic management department, with regulatory scrutiny becoming increasingly stringent.*
- ***IC01:*** *Our information center mainly provides active support for policy implementation, studying policy changes in conjunction with the construction and renovation of information systems, and engages in training and exchange activities with higher authorities.*
- ***H01:*** *Departments within the hospital report to the medical insurance department, which then feeds back to higher authorities; the timeliness of issue resolution depends on the specific*

circumstances. The degree of response to the reform and the pressure faced by different departments varies, *which is related to the characteristics of their business operations.*

Domain 3: Inner setting

Inner setting factors emphasize the conduction and feedback mechanisms within hospital management, detailing how strategies are deployed, and policies are implemented at every level. Although the DIP payment reform has altered the payment method, it remains consistent with the hospital's overall operational objectives. Respondents have indicated that the DIP reform acts as a "conductor's baton" within the hospital, with internal adjustments made in response to policy learning, thereby promoting dynamic implementation. The hospital's medical insurance department primarily handles policy training (combining online and offline approaches) and collecting feedback. Personnel performance and reward, and punishment systems are adjusted with DIP requirements and medical insurance funds. Implementation hindrances are reflected in the varying completion rates of DIP reform indicators across different departments and sections, due to real differences in disease categorization and diagnostic behaviors. This leads to significant differences in the adaptability of various departments to the reform.

Differences in the completion rates of the DIP indicators in different departments actually reflected the essential differences in their patient composition and treatment controllability. The interviews revealed that the hematology and geriatrics departments often faced greater challenges in implementing DIP indicators and insufficient DIP balances due to the complexity of patients' conditions, the combination of multiple chronic diseases, and more uncontrollable treatment pathways, while joint surgery and Chinese medicine departments had better DIP matching and better implementation due to the relative stability of their disease types and the standardization of their treatment pathways. Furthermore, the DIP indicators are linked to personnel performance, departments with lower completion rates exhibit more pronounced emotional responses to the policy and, thus, are more prone to inefficiencies in execution.

- ***CM01:*** *Poor performance will lead to financial penalties. The prospect of deductions by medical insurance serves as the most primal motivation for us. Previously, the hospital primarily relied on a reward system, which led to a more cursory approach to work; now, there is increased attention to cost control and adherence to protocols.*
- ***MR01:*** *The hospital has appointed medical insurance specialists, also known as medical insurance administrators, in each department. These specialists form small teams with department heads to implement relevant policies. When conducting a detailed analysis of the operational status of departments, we employ a* variety *of management tools. For instance, when analyzing disease types, we utilize the Pareto Principle, Alpha Analysis, and the Boston Matrix, along with various information systems.*
- ***EM01:*** *The performance assessment for our hospital staff has not changed significantly; it has been adjusted to accommodate and align with the existing performance and medical insurance cost systems.*
- ***Ge01:*** *The operational goals of the departments have not seen a drastic shift, but there is a greater emphasis on addressing the primary contradictions, moving away from the previous approach of conducting comprehensive examinations and treatments. This means that when facing patients with multiple coexisting conditions, the focus may be on resolving the most severe issue rather than managing all conditions simultaneously.*
- ***MR01:*** *The medical insurance office first understands the policies before arranging training for personnel in* various *departments. They regularly visit clinical departments to address queries. Our hospital conducts two to three internal audits per year, and they adopt multiple formats to train frontline staff.*

Domain 4: Individuals

The individual dimension is bifurcated into the sub-dimensions of roles and characteristics. On the roles sub-dimension, emphasis is placed on the role of middle and senior managers within the organization. In the implementation of DIP, hospital administrators recognize its benefits as being closely intertwined with the hospital's operational management, thereby leading and facilitating the execution of policies as opinion leaders. In the characteristics sub-dimension, the focus is on the adaptability and motivation of individual implementation units. The role of individual factors in promoting the implementation of DIP lies in enhancing the implementation personnel's emphasis on disease diagnosis grouping and the completion of medical records. Interviewees involved in the DIP implementation widely accept that DIP reform is a process of gradual adaptation. Concurrently, regarding individual performance, different departments face varying pressures, with some interviewees indicating that the reform has increased the burden of clinical work, effectively hindering the implementation of individuals' proactivity and the mobilization of individual available resources.

- ***EN01:*** *Our department staff always discuss whether DIP will restrict the development of new clinical technologies in clinical practice. Some departments have this concern because, in terms of business development, they employ new technologies, especially new materials, but are constrained by the impact of DIP payment.*
- ***Ge01:*** *The incentive direction of the reform may lead to polarization among physicians. When dealing with patients whose conditions are neither severe nor mild, medical staff may be reluctant to provide comprehensive medical services and consider the point value when choosing the primary diagnosis. This could lead to an inaccurate grasp of the patient's actual condition, affecting treatment outcomes and patient satisfaction due to unmet medical needs. Medical staff can submit their opinions and suggestions through specific channels. However, the lack of a concrete mechanism to handle this feedback and advice on improvement measures is challenging.*
- ***MR01:*** *Our approach is primarily one of cooperation and support. But work pressure increases, and we can only go with the flow and enhance our capabilities.*
- ***H01:*** *The DIP reform has added a significant amount of extra workload to our department. Our department frequently*

encounters issues with cost settlements exceeding budgets, thus increasing the workload. Everyone can only do their best, but if the policies are too restrictive and cannot be met, doctors will have grievances. We believe that special cases should be resolved according to the actual situation. For example, it is not reasonable to deduct money from doctors for patients who can afford to pay for their medication out-of-pocket.

- ***N01:*** *When clinical medical staff encounter unreasonable situations, such as uncontrollable, excessive-cost patients, apart from feeding back opinions to the department head and the medical insurance office, we can only choose to compromise and cooperate, adjusting our medical practices to follow the policy. The channels for feedback are few and singular.*

Domain 5: Implementation process

Research on the implementation process serves to holistically delineate the execution and propagation pathways of the DIP policy (32). The implementation of the DIP reform is led primarily by the hospital's medical insurance department, with administrative personnel responsible for oversight and self-auditing. Various departments within the hospital are tasked with policy implementation and upward feedback. The hospital integrates the DIP implementation framework into constructing its information systems to advance cost estimation, monitoring, and quality control. Adjustments to the reform's implementation are made through the aggregation of departmental feedback and regular self-audits. This collaboration has effectively facilitated the control of medical insurance costs and the maintenance of financial balance. However, impeding factors are not to be overlooked, including inefficient execution due to unclear policies and undefined responsibilities within the hospital departments, and inaccurate needs assessment of implementing individuals, leading to some personnel failing to adjust promptly.

- ***MI02:*** *The medical insurance Bureau's settlement is based on the whole hospital as a unit, the settlement of medical expenses, the balance of the hospital, and the amount of excess fees. The hospital's management is subdivided into* various *departments.*
- ***EN01:*** *DIP reform has a neutral effect on hospital efficiency, depending on how the hospital is managed. Management in place will benefit the hospital, which means we must pay more attention to improving medical quality.*
- ***IC01:*** *Some of the medical insurance department's requirements for the information system are not practical, such as the requirement that the system be improved in 5 days. In fact, the system cannot be changed in 20 days, and the change is more complicated. People who make policies do not understand information technology, often leading to unrealistic information requirements.*
- ***JS01:*** *In the early days, the hospital staff faced many problems and disagreements regarding DIP. Later, we gradually adapted and cooperated with the policy, improved the compliance degree of medical records, and progressively standardized them.*
- ***COM01:*** *The effect of policy implementation is also closely related to the understanding of patients and medical staff to the policy, and the actual change is not significant with the reform of medical insurance settlement.*
- ***QC01:*** *There are differences in implementation standards between departments. The medical insurance management department manages from the perspective of funds, and the medical management department considers the overall medical quality and medical process. There are some data differences in the process of implementing clinical pathways.*

Discussion

Under the safeguarding impetus of national policy and platform construction, the reform of the DIP payment method is advancing steadily. Its leverage effect has effectively prompted medical institutions to gradually shift from extensive, expansionary operations to refined cost control and internal optimization (33). To date, the reform of medical payment methods has essentially achieved full coverage, and initial success is being seen in local practices. The next planning phase involves conducting practices with a more systematic and comprehensive depth and breadth (34).

Compared to most domestic and international scholars who focus on quantitative studies surrounding medical costs or hospital operational efficiency when researching the DIP payment reform, this study conducts a qualitative investigation into the internal response of a representative public tertiary hospital in the region to explore the status and challenges of the reform's implementation in hospital operations. In contrast to previous studies, this research places greater emphasis on the responses of hospital staff to the DIP payment reform and its impact on policy implementation.

The synthesis of qualitative interview results indicates that, in the dimension of innovation, positive factors include the comparative advantages of the policy, its credibility, and supporting policies. In contrast, the complexity of the policy tends to hinder its implementation. Among outer setting factors, collaborative relationships and external incentives play a facilitating role, and significant events, as external pressure factors, impede policy implementation to some extent. From the inner setting dimension, active internal collaboration, information sharing, the urgency of reform, relative priority, and access to information and knowledge are conducive to implementing DIP innovation but also reveal a lack of internal incentive systems and available resources within the hospital. From an individual perspective, the adaptability of the implementing units to reform and their access to resources and scope of authority are somewhat limiting in policy implementation. In terms of the overall dimension of the implementation process, the effective execution of teamwork, planning, strategy adjustment, feedback, and evaluation is beneficial in demonstrating positive policy outcomes. However, there is still a need to pay attention to assessing individual needs and mobilization.

The DIP payment is an innovative measure in payment reform; its innovative design and empirical basis are crucial to the success of its implementation (35). Observations from field

investigations indicate that external environmental factors such as policy, economy, and patient demand influence the implementation of the DIP payment method. Internal factors within the hospital, including organizational culture, resources, and system management, significantly impact the acceptance and enforcement of the DIP payment method (36). At the level of individual roles and characteristics, the cognition, capabilities, and attitudes of medical staff toward the reform affect the actual effectiveness of policy advancement. The overall implementation process, encompassing planning, strategy development, execution, and confirmation, requires the active participation of hospital management and medical personnel.

Overall, implementing the DIP reform has achieved positive effects in reducing the medical burden on the population, guiding the allocation of medical resources, and standardizing diagnostic and treatment practices (37). The reform of the DIP payment method in public hospitals, supported and supervised by national policies, is progressing gradually but still faces multifaceted challenges. Through analysis using the CFIR framework, hospital administrators and policy researchers can more systematically identify and address these challenges, facilitating the smooth implementation of the DIP payment reform.

The findings of this study echo the international experience with the implementation of value-oriented payment models such as disease-based payment (DRG) or packaged payment. Since the implementation of the G-DRG system in Germany in 2004, it has been noted that while controlling healthcare costs, the system has triggered controversies about limited clinical autonomy, especially in departments with diverse treatment modalities and complex patient conditions (38). France's performance-oriented inpatient payment reform, while improving efficiency, also faced problems with "diagnostic upcoding" behavior and insufficient attention to patients with slow and complex diseases (39). Similarly, in the United States, the BPCI-A (Bundled Payments for Care Improvement-Advanced) program, while effective in reducing healthcare expenditures in some departments (orthopedics, cardiology, etc.), has also reduced the focus on access to care for high-risk patients (40).

Although China's DIP reform is a homegrown original payment model, its core challenges are highly common to the countries mentioned above. DIP's classification of disease groups based on cost homogeneity may be insufficient to adequately reflect clinical complexity, which, in turn, may lead to physicians' tendency to engage in harm avoidance behaviors. These responses may affect the quality of patient-centered care, especially for the older adults, multimorbid coexisting individuals, and lower socioeconomic groups (41).

From an ethical perspective, payment reforms such as DIP need to strike a balance between cost efficiency and equity of access. International experience suggests that one-size-fits-all cost containment may exacerbate inequalities in access to healthcare if there is a lack of contextual flexibility. Therefore, policymakers should consider introducing approaches such as "risk adjustment mechanisms," "high-complexity elasticity bands," and patient-reported outcomes (PROs) to improve the system's responsiveness to patients' actual needs (42). Some regions in China have already begun to pilot reforms - for example, Zhejiang Province's 2024 DIP reform program has included PRO data in 10% of the payment score, reflecting an initial exploration of DIP fairness calibration (43).

Faced with the tension between cost containment and clinical autonomy, DIP should increase its flexibility. The French T2A system can be modeled on the "clinical exception clause" that protects physicians' professional judgment, while Germany requires the recording of patient-physician shared decision-making in the G-DRG system (44).

To address the identified challenges and support the long-term implementation of DIP payment reform, the following multi-tiered strategies are proposed, structured around three levels: hospital-based adaptation, payment system refinement, and national strategy integration.

Hospital management optimization recommendations (short term, 1–3 years)

Optimize performance incentives:

> Interviews showed that the implementation of the DIP payment reform may lead to behavioral adjustments when doctors face complex cases (Domain 3 CM01), affecting the quality of treatment. It is recommended that a "fault tolerance zone" be introduced into the performance appraisal to alleviate the subjective pressure on doctors and improve the acceptability and efficiency of the policy.

Implementing differentiated assessment weights:

> There are differences in the adaptability of different departments in the DIP payment reform, and uniform assessment standards may lead to greater pressure on certain departments. Thus, Differentiated assessment weights should be implemented according to the actual situation, and flexible thresholds (e.g., ±15%) should be adopted for special departments such as geriatrics and oncology to avoid "one size fits all.

Suggestions for improving the medical reform system (medium-term 3–5 years)

Dynamic adjustment mechanism for disease grouping:

> Jointly establish expert committees on DIP grouping at the level of diagnostic and treatment institutions at all levels with clinical, medical insurance, and case departments to review and adjust disease groupings on a regular basis in order to gradually optimize the rationality of the groupings.

Strengthening financial support for information technology construction:

> The effective operation of the DIP payment system relies on high-quality medical data and information systems. However, medical institutions are under both financial and technological pressure to build informatization (Domain 5IC01 Policymakers do not understand informatization needs) It is recommended that the government increase financial investment in hospital informatization construction to improve data collection and disease identification capabilities.

National strategy-oriented recommendations (long-term more than 5 years)

DRG/DIP synergistic development:

> Given that DRG is applicable to acute diseases and short-term hospitalization, and DIP is applicable to chronic diseases and multiple treatments, it is recommended to establish a "categorized and segmented payment mechanism," adopting DRG in the acute stage and DIP for chronic disease management, so as to adapt to the needs of different service pathways and payment efficiencies.

Enhancing patient participation:

> The current DIP assessment mechanism is dominated by the medical service provider, and it is recommended to introduce patient cost satisfaction survey data as a payment correction factor, and to explore the doctor-patient balance sharing mechanism to enhance the public acceptance of the policy and the sense of fairness.

Limitations

This study also has its limitations. Firstly, the research was conducted solely within one medical institution without the introduction of a control group. Thus, it is not possible to rule out the possibility that certain specific factors may alter the behavior of patients and the hospital. Secondly, due to the inherent limitations of qualitative research, the number of subjects is small, which includes the potential risk of selection bias. The subjective responses of the subjects may not accurately reflect the true situation. Thirdly, this study did not involve patient visits, and patient feedback on the reform, which is the ultimate indicator of implementation effectiveness, was not included. Additionally, there may be a degree of social desirability bias among the administrative and clinical staff interviewed when talking about sensitive or performance-related issues such as health care reform, and some of the interviewees may be inclined to express "positive attitudes" consistent with the policy rather than fully revealing the reality of the difficulties or their realities. To a certain extent, this limits the insights of this study on the individual dimension. Future research may consider combining anonymous questionnaires and third-party observation to reduce such bias. Meanwhile, the study population on which the conclusions of this paper are based is a tertiary public hospital in Guangzhou City, and its results still need to be treated with caution when generalized to other regions or different levels of healthcare institutions.

However, the results of this study are still representative and reliable; the management case of DIP in public hospitals and the interview data formed can reflect the internal response strategies and transmission pathways within the hospital, still providing a multi-dimensional perspective for exploring subsequent optimization of the reform. As the reform process deepens and policies are updated, further assessment of the long-term impact and overall effectiveness of DIP will be needed in the future.

Conclusion

Our results highlight the key facilitators of the implementation of DIP payment in hospitals: the emphasis placed on DIP reform by hospital leadership, high compliance among implementing personnel, smooth communication with higher-level medical insurance departments and other hospitals, and the establishment of an information-based measurement and quality control system adapted to the DIP framework. The main obstacles to implementation include restrictions on high-end medical care, the need to optimize disease groupings, high demands for refined hospital management, and increased burden on clinical work. Additionally, due to the linkage of physician performance incentives to the surplus medical insurance funds, there is a significant variation in the adaptability of different departments within the hospital to the DIP reform. Currently, under the DIP payment reform, the hospital has been effective in controlling overall medical insurance costs, achieving a balance between income and expenditure.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Author contributions

JC: Conceptualization, Data curation, Investigation, Project administration, Resources, Software, Supervision, Writing – original draft, Writing – review & editing. SC: Data curation, Formal analysis, Investigation, Software, Writing – original draft, Writing – review & editing. AL: Data curation, Investigation, Software, Writing – review & editing. XY: Data curation, Investigation, Writing – review & editing. HL: Data curation, Investigation, Software, Writing – review & editing. MY: Data curation, Investigation, Software, Writing – review & editing. BF: Data curation, Investigation, Software, Writing – review & editing. NX: Data curation, Investigation, Software, Writing – review & editing. JL: Investigation, Resources, Supervision, Writing – review & editing. HT: Writing – review & editing, Data curation, Investigation, Project administration, Resources.

Funding

The author(s) declare that financial support was received for the research and/or publication of this article. This work was supported by the Harvard University HCHP China Healthcare Organization Internal Management Survey Project, the Guangdong University Student Innovation and Entrepreneurship Competition (202312121370). Guangzhou Philosophy and Social Science Development "14th Five-Year Plan" 2023 Project (2023GZGJ109), the Key Laboratory of Philosophy and Social Sciences of Guangdong Higher Education Institutions for Health Policies Research and Evaluation (grant number 2015WSY0010), and the Research Base for Development of Public Health Service System of Guangzhou.

Acknowledgments

The author would like to express his heartfelt thanks to the professors who participated in the writing and the students who participated in the interview. Special thanks to the interview participants and the staff of Guangzhou First People's Hospital of Guangdong Province for their valuable help and support during the interview.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The author(s) declare that no Gen AI was used in the creation of this manuscript.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

References

1. Wang Y. Study on the influence of medical insurance payment modes on public hospital operational performance. Changsha: Central South University (2022).

2. Min S. Analysis of Physicians' medical behavior and changes in medical expenditure under the background of integrated tri-medical collaboration. *Huazhong University of Science and Technology*. (2018). doi: 10.7666/d.D01542664

3. Xie H, Cui X, Ying X, Hu X, Xuan J, Xu S. Development of a novel hospital payment system - big data diagnosis & intervention packet. *Health Policy Open*. (2022) 3:100066. doi: 10.1016/j.hpopen.2022.100066

4. Xing J, Li X, Shi L, Wang Y, Zhang H, Liu M, et al. Understanding and countermeasures of DRG payment reform. *Sci Technol Econ Market*. (2021) 11:149–50.

5. Liu W. DIP payment reform: realities and ideals. *Journal*. (2021) 17:32–41.

6. Zhang X, Chen Y, Li J, Wang L, Zhao Q, Liu H, et al. Research on the performance distribution of public hospitals based on the payment method reform. *Chinese Health Economics*. (2022) 41:4.

7. DRG/DIP application guidance expert Group of Private Hospitals of Beijing Zhong Wei Yun Institute of Medical Data Analytics and Application Technology. A study on the current status of private Hospitals' response to medical insurance payment reform in China. (2024).

8. Yang R, Xing R. Research on the application of medical insurance intelligent auditing and monitoring platform in hospital information construction. *China Health Standard Management*. (2023) 14:6–9.

9. Deng Q, Wang C, Jin J, Liu Y, Zhang S, Li M, et al. An empirical study on the implementation effect of diagnosis-intervention packet in pilot cities based on the method of difference-in-difference. *Chinese Hospital Management*. (2023) 43:6–9.

10. Luo X, Liu X, Dong S, Zhang Y, Chen L, Wang J, et al. DIP grouping study based on decision tree model: a case study of patients with premature rupture of membranes. *J Guangxi Med Univ*. (2023) 40:682–9.

11. Zhou Z, Lv C. Discussion on DRG case grouping error and fee settlement appeal in Zhejiang Province. *Hospital Management Forum*. (2023) 40:19–21.

12. Li Q, Yang C, Zhao Z, Chen Z, Feng Z, Huang D, et al. Research on the policy of diagnosis-intervention packet (DIP) in China: a comparative analysis based on the national, provincial and municipal levels. *Chin J Health Policy*. (2022) 15:8–15.

13. Ma J. Research on the construction and application of dynamic evaluation model for disease performance. Guangzhou: Southern Medical University (2022).

14. Zeng Y. Research on current situation and countermeasures of basic medical insurance payment methods in China. *Chin J Soci Med*. (2020) 37:19–22.

15. Zhang Y, Teng L, Wang C. Diagnosis-intervention packet-based Pareto chart of the proportion of high-cost cases and the analysis of the structure of hospitalization expenses. *Technol Health Care*. (2023) 31:1355–64. doi: 10.3233/THC-220647

16. Hong D, Lv D, Wu J, Li X, Zhao Q, Lu X, et al. The influence of diagnosis intervention packet policy intervention on medication structure and drug cost of elderly hypertensive inpatients in China: a multicenter interrupted time-series analysis. *Risk Manag Health Policy*. (2023) 16:1781–90. doi: 10.2147/RMHP.S418541

17. Ding Y, Yin J, Zheng C, Dixon S, Sun Q. The impacts of diagnosis-intervention packet payment on the providers' behavior of inpatient care-evidence from a national pilot city in China. *Front Public Health*. (2023) 11:1069131. doi: 10.3389/fpubh.2023.1069131

18. Chen YJ, Zhang XY, Tang X, Yan JQ, Qian MC, Ying XH. How do inpatients' costs, length of stay, and quality of care vary across age groups after a new case-based payment reform in China? An @interrupted time series analysis. *BMC Health Serv Res*. (2023) 23:160. doi: 10.1186/s12913-023-09109-z

19. Huang Y, Zhu Y. Enlightenments and reflections from Guangdong's experience for the diagnosis intervention packet national pilot cities. *West China Med J*. (2021) 36:1739–43. doi: 10.7507/1002-0179.202104235

20. Zhang X, Tang S, Wang R, Qian M, Ying X, Maciejewski ML. Hospital response to a new case-based payment system in China: the patient selection effect. *Health Policy Plan*. (2024) 39:519–27. doi: 10.1093/heapol/czae022

21. Shi H, Cheng Z, Liu Z, Zhang Y, Zhang P. Does a new case-based payment system promote the construction of the ordered health delivery system? Evidence from a pilot city in China. *Int J Equity Health*. (2024) 23:55. doi: 10.1186/s12939-024-02146-y

22. Damschroder LJ, Reardon CM, Opra WM, Lowery J. Conceptualizing outcomes for use with the consolidated framework for implementation research (CFIR): the CFIR outcomes addendum. *Implement Sci*. (2022) 17:7. doi: 10.1186/s13012-021-01181-5

23. Yakovchenko V, Lamorte C, Chinman MJ, Goodrich DE, Gibson S, Park A, et al. Comparing the CFIR-ERIC matching tool recommendations to real-world strategy effectiveness data: a mixed-methods study in the veterans health administration. *Implement Sci*. (2023) 18:49. doi: 10.1186/s13012-023-01307-x

24. Huang JJ, Lai HH, Sun MY, Wang Q, Li Y, Zhang T, et al. Interpretation of update on consolidated framework for implementation research (CFIR 2.0). *Chin Med Practice*. (2023) 26:3863–75. doi: 10.12114/j.issn.1007-9572.2023.0082

25. Liu Y, Ma Z, An Z. Interpretation of update on consolidated framework for implementation research (CFIR 2022). *Chin J Evid Based Med*. (2023) 23:738–44. doi: 10.7507/1672-2531.202303071

26. Nevedal AL, Reardon CM, Opra Widerquist MA, Jackson GL, Cutrona SL, White BS, et al. Rapid versus traditional qualitative analysis using the consolidated framework for implementation research (CFIR). *Implement Sci*. (2021) 16:67. doi: 10.1186/s13012-021-01111-5

27. Birken SA, Powell BJ, Shea CM, Haines ER, Alexis Kirk M, Leeman J, et al. Criteria for selecting implementation science theories and frameworks: results from an international survey. *Implement Sci*. (2017) 12:124. doi: 10.1186/s13012-017-0656-y

28. Nilsen P. Making sense of implementation theories, models and frameworks. *Implement Sci*. (2015) 10:53. doi: 10.1186/s13012-015-0242-0

29. Kim B, Kim CY, Kim J, Park E. Implementation of diagnosis-related group-based payment system in Korea: using the CFIR framework to explore hospital responses. *BMC Health Serv Res*. (2021) 21:1023.

30. Linn AJ, Kooij L, Maat HP, Dijkstra A, Smit EG. Applying the CFIR to understand the implementation of digital health interventions in a DRG context in Germany. *Int J Qual Health Care*. (2020) 32:447–55.

31. Dufour JC, Boucekine M, Peretti-Watel P, Sambuc R. Using the CFIR to evaluate performance-based hospital funding reform in France. *Implement Sci*. (2018) 13:112.

32. Zhang Q, Pang D, Hu J, Wang Z, Jin S, Yang W, et al. Interpretation of consolidate framework for implementation research (CFIR). *Chin J Evid Based Med*. (2021) 3:355–60. doi: 10.7507/1672-2531.202008076

33. Deng Y. Data empowerment: pioneering DIP reform and innovation. *China Health*. (2022) 11:32–3.

34. Qu J, Zhou D, Du H, Li X, Wang Y, Zhang L, et al. Analysis of influencing factors on medical insurance revenue and expenditure balance under DIP payment: a case study of a tertiary Hospital in Chifeng City. *China Health Insurance*. (2023) 5:78–83.

35. Li X, Han Y, Yang W. Research on policy synergies of 17 DRG pilot cities in China. *Chinese Health Economics*. (2024) 43:37–42.

36. Li Y, Yang Y, Yang Y, Chen Z, Liu X, Wang H, et al. Research on multi-dimensional linkage lean operation Management of Hospitals under the reform of DIP medical insurance payment method. *Chinese Hospital Management*. (2024) 44:29–32.

37. Guo P, Zhuang Z. Analysis and exploration of disease benefits in public hospitals under DIP payment method. *Hospital Management Forum*. (2024) 41:27–30.

38. Geissler A, Scheller-Kreinsen D, Quentin W, Busse R. Germany: understanding G-DRGs In: R Busse, A Geissler, W Quentin and M Wiley, editors. Diagnosis-related groups in Europe: Moving towards transparency. Efficiency and Quality in Hospitals: Open University Press (2011). 243–64.

39. Or Z, Renaud T, Sicot C. Performance-based hospital financing in France: challenges and lessons after 17 years. *Health Policy*. (2022) 126:20–7.

40. Navathe AS, Troxel AB, Liao JM, Nan N, Zhu J, Zhong W, et al. Cost of joint replacement using bundled payment models. *JAMA Intern Med*. (2019) 179: 924–32.

41. Zhao Y, Liu Q, Xiong W, Guo W. Challenges and equity risks in China's DIP payment reform: An analysis from the perspective of multimorbidity and vulnerable populations. *Chinese Health Economics*. (2023) 42:44–8.

42. Eijkenaar F, Emmert M, Scheppach M, Schöffski O. Effects of pay-for-performance in healthcare: a systematic review of systematic reviews. *Health Policy*. (2013) 110:115–30. doi: 10.1016/j.healthpol.2013.01.008

43. Zhejiang Provincial Healthcare Security Administration, (2024). Guidelines on enhancing DIP payment equity via patient-reported outcomes (trial version).

44. Hofmann H, Kraus M, Rothgang H. Balancing efficiency and clinical autonomy: patient-physician decision making under Germany's G-DRG system. *Heal Econ Rev*. (2024) 14:5.

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 09 June 2025
DOI 10.3389/fpubh.2025.1567838

Check for updates

OPEN ACCESS

EDITED BY
Kevin Lu,
University of South Carolina, United States

REVIEWED BY
Valentin Marian Antohi,
Dunarea de Jos University, Romania
Wenhao Qi,
Jilin Agriculture University, China
Liming Liu,
Capital Medical University, China

*CORRESPONDENCE
Xuehui Meng
✉ mengxuehui@aliyun.com

RECEIVED 29 January 2025
ACCEPTED 08 May 2025
PUBLISHED 09 June 2025

CITATION
Tao Y, Shen K, Chen Y, Li C, Wu D and Meng X (2025) A study of the impact of DIP payment reform on coronary heart disease hospitalization costs and equity. *Front. Public Health* 13:1567838. doi: 10.3389/fpubh.2025.1567838

COPYRIGHT
© 2025 Tao, Shen, Chen, Li, Wu and Meng. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

A study of the impact of DIP payment reform on coronary heart disease hospitalization costs and equity

Yingying Tao, Keyi Shen, Yating Chen, Chengcheng Li, Dan Wu and Xuehui Meng*

School of Humanities and Management, Zhejiang Chinese Medical University, Hangzhou, China

Background: To control the growth of healthcare costs, the Chinese government introduced a diagnosis-intervention package (DIP)-based health insurance payment reform. This study evaluated the impact of the DIP policy on hospitalization costs, Length of Hospital Stay, and Out-of-Pocket Ratio for patients with coronary heart disease (CHD).

Methods: Hospitalization claims data from 2020 to 2023 in City S, central China, were selected and analyzed using interrupted time series (ITS), covering 264 hospitals with January 2022 as the intervention point.

Results: After the implementation of DIP, hospitalization costs decreased from 8.81 to 8.57 for employee health insurance (UEBMI) ($p < 0.001$) and from 8.18 to 7.97 for resident health insurance (URRBMI) ($p < 0.001$), with even greater decreases for primary and secondary hospitals. The number of days of hospitalization decreased, from 8.82 to 7.78 ($p < 0.001$) for UEBMI and from 8.24 to 7.46 ($p < 0.001$) for URRBMI, with the largest decrease in primary hospitals. As for out-of-pocket ratio, the URRBMI increased from 20.71 to 25.2% ($p < 0.001$), and the UEBMI decreased from 28.67 to 23.57% ($p < 0.001$).

Conclusion: The DIP policy was effective in controlling hospitalization costs and days, especially in primary and secondary hospitals. However, the out-of-pocket ratio of URRBMI increased and UEBMI decreased, suggesting differential impact of the policy. It is recommended that policy makers pay attention to differences in health insurance types and hospital grades to optimize the fairness and effectiveness of the policy.

KEYWORDS

DIP payment reform, interrupted time series analysis, types of health insurance, healthcare cost control, healthcare equity

1 Introduction

Coronary heart disease (CHD) is a prevalent cardiovascular disease globally, characterized by high morbidity and mortality rates, which pose significant threats to human health and life safety (1). In China, the increasing prevalence of CHD is attributed to population aging and widespread unhealthy lifestyles, resulting in a yearly rise in the number of affected individuals (2). Hospitalization, which constitutes a substantial part of CHD treatment, entails high costs that impose considerable financial burdens on patients and their families (3). This escalating healthcare expenditure presents a formidable challenge to national healthcare systems (4), prompting countries to seek methods for rationalizing healthcare costs (5), For instance,

Germany's German Diagnosis-Related Groups (G-DRG) System, the Accountable Care Organizations (ACOs) model in the United States, Japan's Diagnosis Procedure Combination (DPC) System, and France's Tarification à l'Activité (T2A) system, etc. These reforms have achieved some success in controlling healthcare costs and improving healthcare efficiency, yet they also give rise to certain problems and challenges, such as the transfer of high - cost cases and a decline in healthcare service quality (6–9). Australia also implemented the Activity-Based Funding (ABF) payment system nationwide during the 2011–2012 fiscal year. Research shows that ABF has achieved some success in controlling medical expenses. However, the implementation effects vary across states and hospitals. Some hospitals, in a bid to optimize fund allocation, have been selective in patient admission. Subsequently, Australia also carried out several Diagnosis-Related Groups (DRG) reforms to address the issues caused by the ongoing refinement of DRG (10, 11). The UK's Payment by Results (PbR) system, which is based on DRG, also faces similar problems. Although it has contributed to improving hospital efficiency, it has also raised concerns about the potential impact on the quality of healthcare services (12).

In China, Basic Medical Insurance (BMI) coverage expanded to 1.3 billion people by 2021, prompting reforms in healthcare payment methods to address escalating healthcare costs (13). The traditional fee-for-service (FFS) model is inadequate, leading to service overutilization and heightened healthcare costs (14).

In 2019, the Chinese government initiated Diagnosis-Related Group (DRG) payment reforms to balance cost containment and healthcare efficiency. However, a one-year evaluation in pilot cities revealed that although the DRG reform reduced healthcare spending, it also increased patient hospitalization rates and neglected acutely ill patients (15–17). Thus, the Chinese government has been consistently exploring novel solutions, leading to the introduction of the Diagnosis-Intervention Packet (DIP) payment system, which categor patientsizes based on specific cases (18). The theoretical framework of the system originates from the "risk selection theory" of Germany's DRG reform and the "institutional response hypothesis" of the ACO model in the US (19, 20). Compared with the "hospital - grading exemption mechanism" of Japan's DPC system and the "global budget buffer design" of France's T2A system, the particularity of China's DIP reform lies in that it achieves a balance between total control of medical insurance funds and the autonomy of medical institutions through "dynamic adjustment of case - based scores" (21). China currently has a dual - track system of DRG and DIP payment methods. The DIP payment system is now being piloted in 71 cities (22). The DIP categorizes patients using ICD-10 and ICD-9-CM3 codes to form a disease portfolio, focusing on major disease diagnoses and treatment modalities (23).

The implementation of the DIP system in China demonstrates that DIP offers advantages over DRG in comprehensively covering healthcare services. DIP payments foster internal competition and stringent control among providers through the establishment of payment coefficients and "health insurance fund pools" (21). However, the effectiveness of DIP varies by region, depending on historical cost data to determine disease group weights, which leads to variations in implementation across regions.

The effectiveness of implementing DIP reforms varies across regions and types of healthcare organizations. Some studies have shown that DIP reforms significantly reduced average hospitalization and drug costs per patient in economically developed regions, but did not achieve the desired effect in other regions, and even led to an increase in patient healthcare costs in the short term (24, 25). Previous studies have examined the impact of payment reforms on other chronic conditions, but fewer have focused on coronary heart disease.

While emphasizing innovative payment methods, Chinese policymakers and researchers have also prioritized health equity. Within China's health insurance system, UEBMI and URRBMI constitute the two primary components. Studies have demonstrated that disparities in population coverage, financing mechanisms, and reimbursement policies between these two health insurance systems can lead to health inequities among patients. Since DIP is a reform targeting healthcare providers, initial considerations did not include whether residents with different health insurance types are affected by health equity. Due to differences in contributions, benefit coverage, and medical expenditures between China's UEBMI and URRBMI, budget caps were set based on health insurance types. At the time of DIP implementation, UEBMI had a sufficient budget, while URRBMI faced budget constraints. Consequently, whether innovative payment methods impact healthcare equity for patients with different health insurance types remains an important question for exploration (4).

In this study, a pilot city sample was selected from S city in central China, one of the initial pilot areas. UEBMI and URRBMI CHD patients in S city were selected to assess the impact of DIP policy implementation across various healthcare institutions on patients with both insurance types. This study aims to provide a deeper understanding of the practical application effects of the DIP payment method reform in different healthcare systems, offer a scientific basis for optimizing healthcare policies, enhance the efficiency of healthcare fund utilization, alleviate the economic burden on patients, and promote the rational allocation of healthcare resources.

2 Methods

2.1 Study design

City S, situated in Hubei Province in central China, was among the first cities in China to fully implement the DIP payment methodology across all healthcare organizations. Owing to the successful implementation of this pilot, City S has been designated as a model unit by the National Health Security Bureau. Given its pioneering and prominent status, this study utilizes data from the Medical Protection Bureau of City S to conduct the empirical analysis.

City S comprises 10 urban districts and 59 rural districts, with a resident population of 3.15 million and a 2023 GDP per capita of 73,489.10 RMB. These statistics indicate that the City S is at a medium level of economic and social development and is representative of a typical prefecture-level city in China. City S, as one of 71 pilot cities undergoing DIP reform, has a designated DIP disease catalog that includes 5,393 core diseases and 928 comprehensive diseases. Regarding health insurance, the city has 545,400 UEBMI participants and 2,459,100 URRBMI participants, with a social insurance coverage rate of 95.3%.

In January 2022, the local Medicare authority in City S formally implemented DIP payments for all providers in the city. To ensure the validity of this study, we conducted a comprehensive review of published literature and relevant policies to identify and consider any

potential confounding policies that might affect hospital inpatient service behaviors. We selected interrupted time series (ITS) analysis as our research methodology. The main reason for using an interrupted time - series (ITS) design in this study is its unique policy evaluation advantages. First, the policy was city - wide and lacked a natural control group. Second, ITS models trends before and after intervention, distinguishing policy effects from time - related confounders like seasonal fluctuations and long - term trends. Lastly, ITS is widely used in payment reform evaluation and proven effective in health policy research (26–28). Based on the relevant policy documents, we used January 2022 as the intervention point for this study and employed an interrupted time series design to assess the impact of DIP payment reforms on hospital services for differently insured patients at all levels of hospitalization in City S. This provides insights into whether DIP reforms are likely to affect health equity between UEBMI and URRBMI hospitalized patients.

2.2 Data sources and samples

City S did not experience a major outbreak during the COVID-19 epidemic, thus its healthcare activities were minimally impacted, facilitating time series analysis. The data utilized in this study were sourced from the city's Medicare information platform, which collated monthly Medicare claims data from January 2020 to December 2023 and anonymized the data to safeguard patient privacy. Each claims data record primarily included details such as the patient's gender, type of health insurance, occupational status, length of hospitalization, discharge information, diagnosis, amount of Medicare reimbursement, and the hospital level in question. During the data cleaning phase, datasets with missing entries, irregular hospitalization or discharge lengths, and unusual expenditure figures were excluded. The final dataset used for our analysis comprised a total of 107,714 participants.

2.2.1 Coronary heart disease

Coronary atherosclerosis (CHD) is a prevalent cardiovascular disease characterized by lipid deposition and plaque formation on the inner lining of coronary arteries, resulting in the narrowing or blockage of blood vessels. CHD is currently the leading cause of death globally.

Treatment for CHD primarily involves lifestyle modification, drug therapy, and, for patients with poor drug therapy outcomes, percutaneous coronary intervention or coronary artery bypass grafting. CHD has a substantial patient population and is less influenced by environmental factors such as seasons. Previous studies have conducted limited research on individual diseases. Therefore, this paper selects data coded as I25 in the ICD-10 disease codes and compiles it into a dataset following data cleansing.

2.2.2 Types of health insurance

After the upgrade of China's medical insurance system to an integrated level, the primary insurance types are UEBMI and URRBMI. UEBMI is medical insurance for urban employees, with premiums paid jointly by the organization and the individual. It primarily covers outpatient and hospitalization costs and is mandatory for all workers with regular employment. URRBMI, conversely, is medical insurance for urban and rural residents, encompassing both urban and rural populations. It is government-led, with voluntary individual participation, and primarily covers hospitalization costs and some outpatient expenses.

2.2.3 Hospital level

In China, hospitals are categorized into three levels based on their functions, facilities, and technical capabilities: primary hospitals, secondary hospitals, and tertiary hospitals.

Primary hospitals are primary care hospitals or health clinics, mainly providing basic medical, preventive, rehabilitation, and health care services to communities. They are relatively small in scale, with fewer than 100 beds, and are primarily responsible for the initial diagnosis and treatment of common and frequently occurring diseases, as well as referring difficult and severe cases to higher-level hospitals.

Secondary hospitals are regional hospitals, usually county-level, district-level, or city-level hospitals, with bed numbers ranging from 101 to 500. They offer more comprehensive medical services, including specialized treatments and advanced surgeries. Secondary hospitals not only accept referrals from primary hospitals but also undertake certain teaching and research tasks.

Tertiary hospitals are large comprehensive hospitals, with more than 501 beds, providing high-level specialized medical services. Tertiary hospitals possess comprehensive capabilities in medical care, teaching, and research, are able to handle critical and difficult cases, and accept referrals from secondary hospitals.

2.3 Measurement variables

This study aims to examine the impact and differences of the DIP reform on healthcare expenditures, quality, and treatment for inpatients with two types of social health insurance across different hospital levels. To this end, the study employs three variables: hospitalization costs, hospital days, and out-of-pocket ratios, to conduct the necessary assessments. To account for the impact of inflation and other factors on hospitalization costs, we standardized hospitalization costs using China's annual Consumer Price Index (CPI) with 2020 as the base year, ensuring that our findings reflect actual changes in healthcare costs. Given the typically skewed distribution of healthcare expenditure costs, we log-transformed the total healthcare costs per hospitalized patient. This transformation stabilizes the variance, facilitating statistical analysis and highlighting trends and outliers in healthcare spending more effectively. The number of hospitalization days was determined by calculating the variance between the patient's admission and discharge dates. To ensure the accuracy of our statistical analyses, hospital days data following a normal distribution were appropriately processed. Out-of-pocket ratios were calculated on a cost-standardized basis, with total costs as the denominator and out-of-pocket costs as the numerator, to reflect the level of treatment for different health insurance types.

2.4 Statistical analysis

In this study, SPSS 24.0 software was used, with continuous variables presented as means ± standard deviations and categorical variables expressed as percentages. To analyze the impact of DIP policy implementation on patient characteristics and outcome

variables in the sample, we performed t-tests and chi-square tests before and after the DIP reform, considering the effects of health insurance category and hospital level variables. Additionally, to assess the impact of the DIP policy intervention on patients' total healthcare costs, hospital days, and out-of-pocket ratios, we employed a segmented regression model from interrupted time series analysis, with January 2021 designated as the intervention point. The general form of our ITS regression model is shown below:

$$Y_t = \beta_0 + \beta_1 Tt + \beta_2 DIPt + \beta_3 DIPtTt + \varepsilon_t$$

In the interrupted time series analysis conducted in this study, the outcome variable Yt represents the outcome at a specific time point t. β0 estimates the baseline level of the outcome variable at the study's inception. β1 represents the monthly slope of the outcome variable before the DIP policy intervention. β2 represents the immediate change in the outcome variable at the moment of the DIP reforms. Furthermore, β3 indicates the post-intervention change in the outcome variable compared to the expected trend change based on the pre-intervention period. The combination of β1 and β3 reflects the post-intervention trend. The time variable Tt spans from the study's initiation to its conclusion, while DIPt is a binary variable indicating the occurrence of the DIP policy intervention (0 before the intervention and 1 after the intervention). Meanwhile, DIPtTt represents another time variable from the initiation of the DIP intervention to the study's conclusion. Finally, εt represents the random error estimator at time t. To address potential autocorrelation in the model, we initially employed the Newey-West estimator with zero lags to fit an ordinary least squares (OLS) model. We subsequently tested for autocorrelation using the 'actest' command. If first-order autocorrelation is detected, the regression is re-estimated using the Prais-Winston method, and the validity of adjusting for autocorrelation is assessed using Durbin-Watson (DW) values. For second-order and higher-order autocorrelation, the Newey-West method was applied to adjust, specifying the necessary number of lags. For statistical significance tests, we used two - sided tests in the segmented regression model and set $\alpha = 0.05$ as the significance threshold. All analyses were performed using STATA17.0.

3 Results

3.1 Sample characteristics

In this study, data pertaining to CHD patients with various insurance types in City S from 2020 to 2023 were selected. The data for employee health insurance were 9,955 before and 8,207 after the reform, and the data for URRBMI were 47,870 before and 41,682 after the reform. The table also presents the male-to-female ratio of the two insured populations, along with the number and percentage of visits to hospitals at all levels.

Supplementary Table 1 also presents the changes in medical costs, hospitalization days, and out-of-pocket ratio for insured UEBMI and URRBMI before and after the DIP reform, with significant differences observed in these variables before and after the reform. Specifically, the average hospitalization cost for patients enrolled in UEBMI decreased from 8.81 to 8.57, and for those enrolled in URRBMI, it decreased from 8.18 to 7.97. The average hospitalization time for patients enrolled in UEBMI decreased from 8.82 days to 7.78 days, and for those enrolled in URRBMI, it decreased from 8.24 days before the reform to 7.46 days after the reform. Regarding the out-of-pocket ratio, it decreased from 28.67 to 23.57% for patients enrolled in the UEBMI program, while it increased from 20.71 to 25.2% for those enrolled in the URRBMI.

3.2 Total cost of hospitalization

The cost trend of healthcare expenditures for CHD patients enrolled in URRBMI and UEBMI in City S before and after the DIP reform is illustrated in Figure 1a and Supplementary Table 2. The initial levels of URRBMI and UEBMI were significantly different, and both experienced a decrease in overall costs after the reform. URRBMI hospitalization costs were initially at 8.196 before the DIP reform, with a non-significant decrease of 0.06 per month before the reform, and a significant decrease of 0.008 per month after the implementation of the DIP reform compared to the pre-intervention level. UEBMI hospitalization costs were initially at 8.783 before the DIP reform, with a non-significant decrease of 0.067 per year before the reform. After the implementation of the DIP reform, costs decreased significantly by 0.016 per month from the pre-intervention level.

Figures 1a–c and Supplementary Table 2 illustrate the cost trend of healthcare expenditures before and after the DIP reform for CHD patients enrolled in URRBMI and UEBMI in City S across hospitals of different levels. In primary hospitals, the initial level of URRBMI inpatient costs was 7.64, and the changes before and after the reform were not significant, but both were on a downward trend, with a greater decrease after the reform than before. In primary hospitals, the initial level of hospitalization costs for UEBMI was 7.89; the changes before and after the reform were not significant, but both were on a downward trend, with a greater decline after the reform than before.

In secondary hospitals, the initial level of hospitalization costs for patients enrolled in URRBMI was 8.699, which decreased significantly in the first month after the implementation of the DIP reform, and showed a more pronounced downward trend in subsequent years compared to the pre-implementation trend, although not significant. The initial level of hospitalization costs for patients using UEBMI was 8.709, with costs trending downward but not significantly both before and after the DIP reform, decreasing by 0.005 per month after the DIP reform compared to the pre-reform trend.

In tertiary hospitals, the initial level of hospitalization costs for URRBMI was 8.825, with a significant increase of 0.01 per month before the DIP reform, and a significant decrease of 0.02 per month after the implementation of the DIP reform compared to the pre-reform level. The initial level of hospitalization costs for UEBMI was 9.210, with a non-significant increase of 0.002 per month in hospitalization costs before the implementation of DIP, and a significant decrease of 0.013 per month in hospitalization costs after the implementation of the DIP compared to the pre-reform level. Costs decreased significantly by a margin of 0.013 per month from the pre-reform level.

3.3 Average length of hospitalization

The trend of the average length of hospitalization before and after the DIP reform for CHD patients enrolled in URRBMI and UEBMI

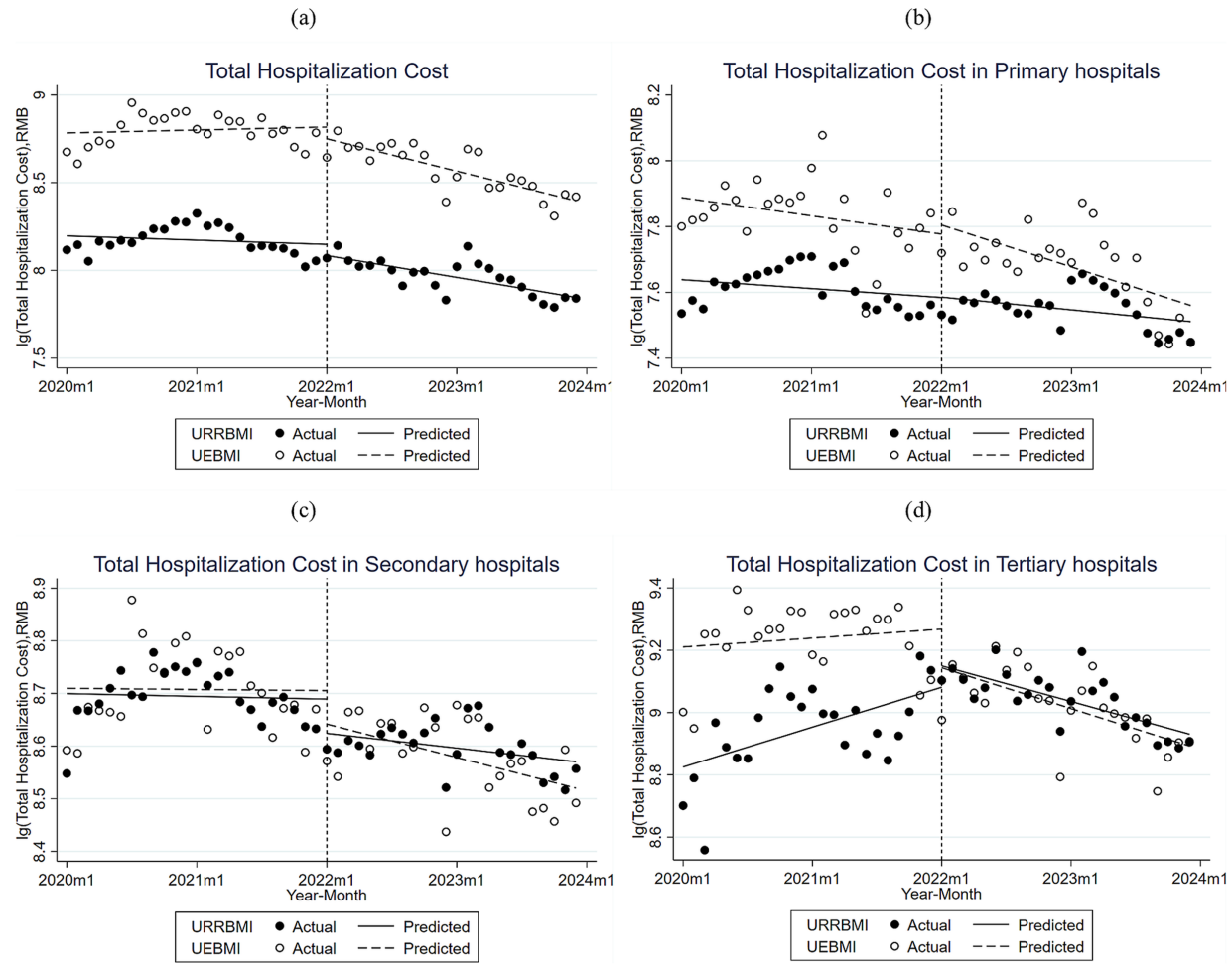


FIGURE 1
(a) Monthly trends in adjusted total cost per case for inpatients with UEBMI and URRBMI in all hospitals of City S; **(b)** Monthly trends in adjusted total cost per case for inpatients with UEBMI and URRBMI in primary hospitals of City S; **(c)** Monthly trends in adjusted total cost per case for inpatients with UEBMI and URRBMI in secondary hospitals of City S; **(d)** Monthly trends in adjusted total cost per case for inpatients with UEBMI and URRBMI in tertiary hospitals of City S.

in City S is illustrated in Figure 2a and Supplementary Table 3. The initial mean difference in hospitalization days between URRBMI and UEBMI was not significant, and the two were not significantly different before the DIP reform. However, in terms of trends, both experienced a decrease in overall length of stay after the DIP reform. The average number of total hospitalization days for URRBMI was 8.413 days before the DIP reform, with a non-significant decrease of 0.215 days per month in hospitalization days before the reform. After the implementation of the DIP reform, the number of hospitalization days did not change significantly from the pre-reform period, but showed an overall downward trend. UEBMI hospitalization days averaged 9.072 days before the DIP reform, with a non-significant monthly decrease of 0.341 days per month before the reform. After the implementation of the DIP reform, the number of hospitalization days did not change significantly from the pre-reform period, but showed an overall downward trend.

Figures 2b–d and Supplementary Table 3 illustrate the trend of hospitalization lengths for CHD patients enrolled in URRBMI and UEBMI in City S before and after the DIP reform across hospitals of different levels. The initial level of hospitalization days in primary hospitals using URRBMI was 7.922 days, and hospitalization days decreased before and after the implementation of the DIP reform, with a greater decrease after the implementation of the DIP reform. The initial level of inpatient days for primary hospitals using UEBMI was 9.651 days, showing a non-significant decrease by 0.06 days per month before the DIP reforms, and still showing a decreasing trend after the implementation of the DIP reforms, but at a slower rate than before the reforms.

The initial average length of hospitalization for URRBMI among cases attending secondary hospitals was 9.108 days, with a non-significant decrease in the length of hospitalization by 0.019 days per month before the implementation of the DIP reform, and an even greater decrease after the implementation of the DIP reform compared to the pre-reform period, with an additional decrease of 0.011 days per month. The initial average length of hospitalization for UEBMI was 9.336 days, with a slow non-significant upward trend in the length of hospitalization for UEBMI patients prior to the implementation of the DIP reform, and after the implementation of the reform, the length of hospitalization declined by a trend of 0.038 days per month less than prior to the implementation of the reform.

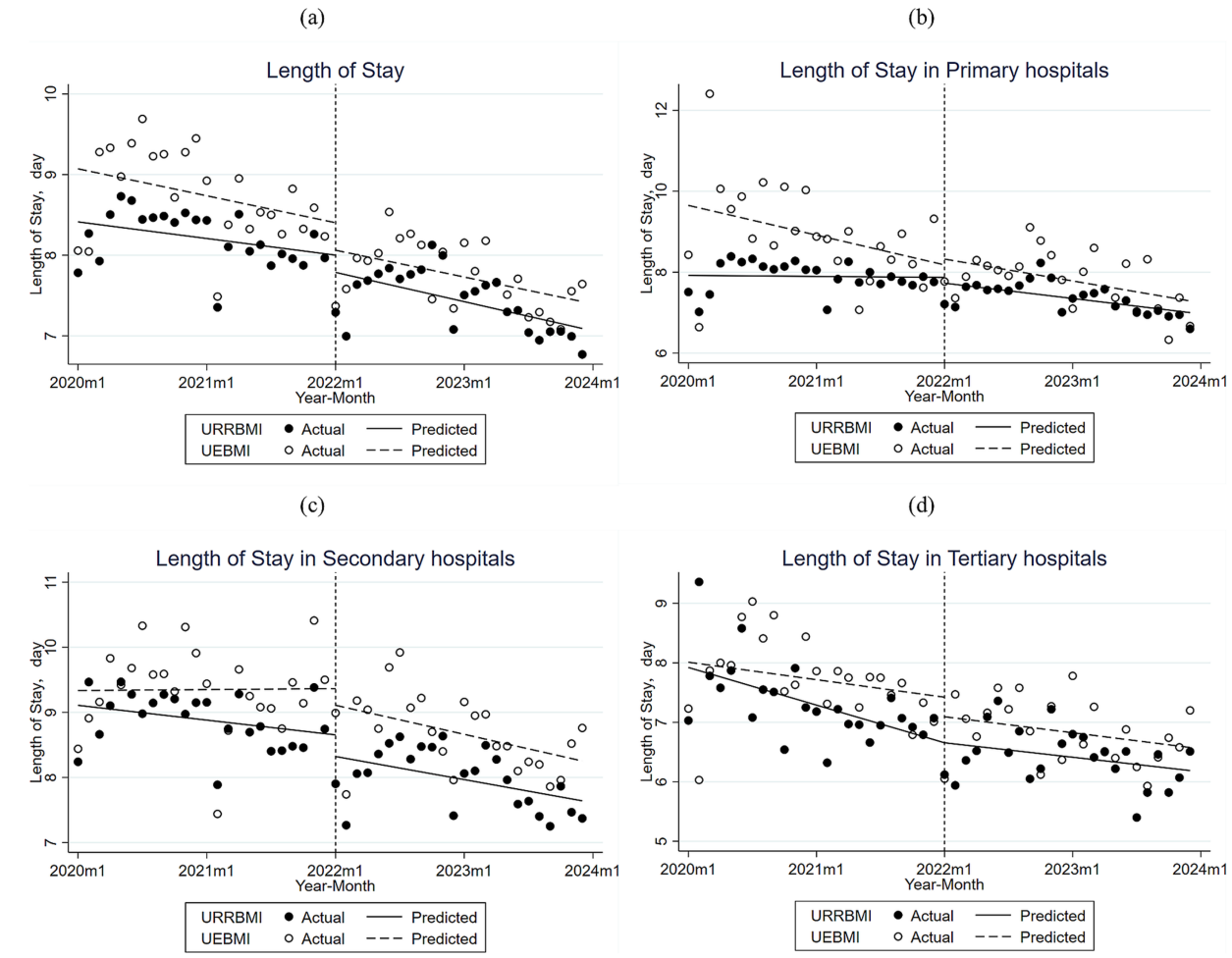


FIGURE 2
(a) Monthly trends in inpatient days for URRBMI and UEBMI inpatients in all hospitals of City S; **(b)** Monthly trends in inpatient days for URRBMI and UEBMI inpatients in primary hospitals of City S; **(c)** Monthly trends in inpatient days for URRBMI and UEBMI inpatients in secondary hospitals of City S; **(d)** Monthly trends in inpatient days for URRBMI and UEBMI inpatients in tertiary hospitals of City S.

In tertiary hospitals, the initial average length of stay for URRBMI was 7.922 days, and before the DIP reform, the number of hospitalization days was decreasing significantly with a trend of about 0.05 days per month, and after the implementation of DIP, the number of hospitalization days, although decreasing, decreased more slowly than before the implementation of DIP. The initial average number of hospitalization days for UEBMI was 8.01 days, and before the DIP reform, the number of hospitalization days was decreasing with a trend of about 0.02 days per month, and after the implementation of the DIP, the number of hospitalization days, although decreasing, decreased with a slower trend compared to the pre-implementation period.

3.4 Out-of-pocket ratio

As shown in Figure 3a and Supplementary Table 4, the trend of the average out-of-pocket ratio of CHD patients enrolled in URRBMI and UEBMI in City S before and after the DIP reform is demonstrated. The difference in the initial average between the URRBMI and UEBMI out-of-pocket ratios was significant, as was the difference in the pre-reform period. The difference remained significant in the first month of DIP reform implementation. The average out-of-pocket ratio for URRBMI was 20.16% before the DIP reform, and the change in the out-of-pocket ratio from month to month was not significant before the reform. In the year of implementation of the DIP reform, the out-of-pocket ratio increased by 5.02%, and then decreased by an average of 0.15% per year from the pre-reform trend. The average out-of-pocket ratio of UEBMI was 30.74% before the DIP reform, declining at a rate of 0.18% per month before the reform, and increasing slowly by 0.16% per month after the implementation of the DIP reform over the pre-reform out-of-pocket ratio.

Figures 3a–c and Supplementary Table 4 demonstrate the trend of out-of-pocket ratio for CHD patients enrolled in URRBMI and UEBMI in City S before and after the DIP reform across hospitals of different levels. In primary hospitals, the initial level of out-of-pocket ratio for URRBMI was 12.54%, and the out-of-pocket ratio showed a significant monthly increase in the pre-implementation period, with an increase of 4.92% in the month of implementation of the DIP reform, and the overall out-of-pocket ratio in subsequent months was higher than the pre-implementation period. Cases increased, but showed a certain downward trend. The out-of-pocket expense ratio for UEBMI in primary hospitals was initially 21.13%, decreasing by 5.53% immediately after the implementation of DIP, and the overall out-of-pocket expense ratio decreased in subsequent years compared to the pre-implementation level, but showed a certain upward trend.

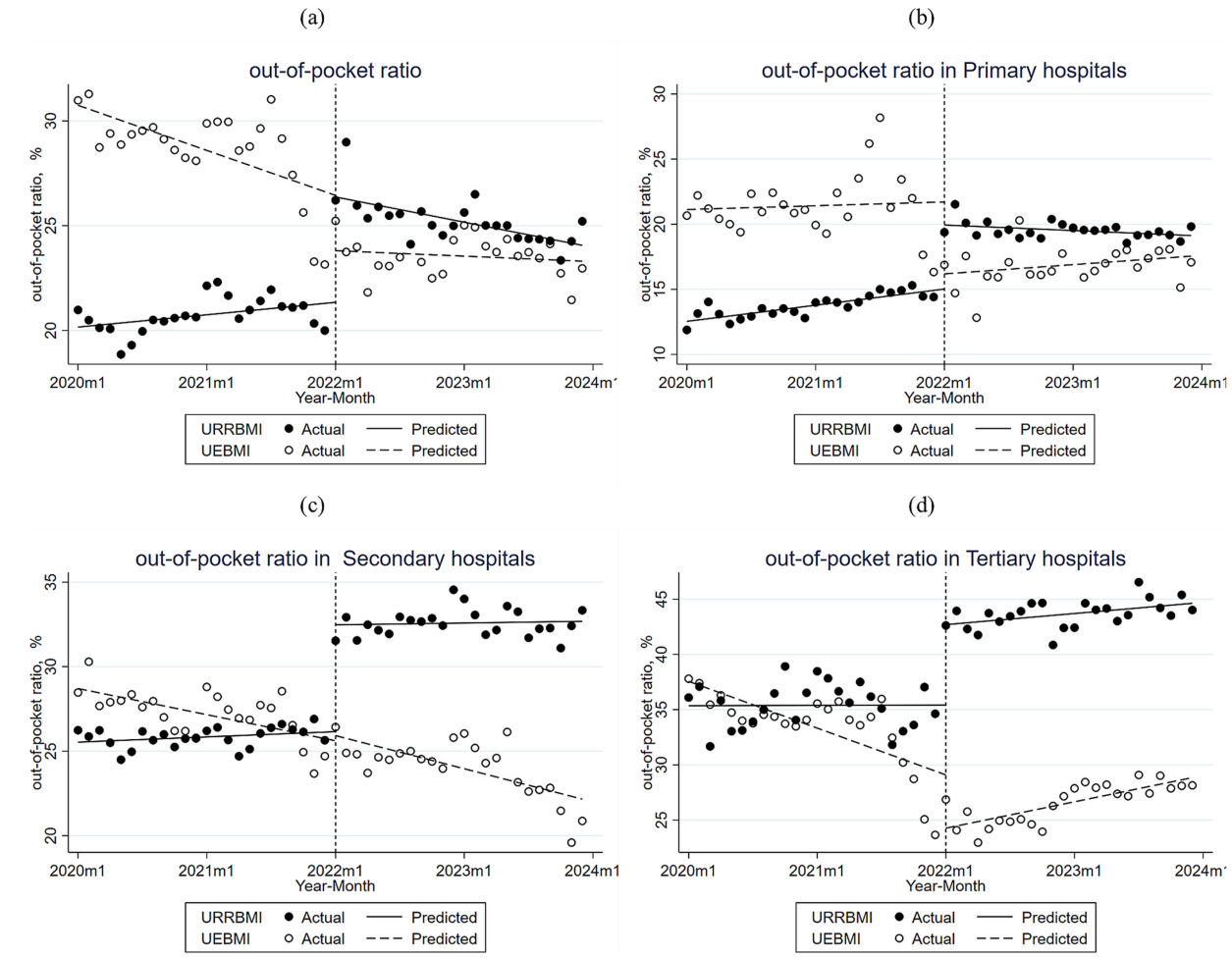


FIGURE 3
(a) Monthly trends in the proportion of out-of-pocket payments for inpatients with URRBMI and UEBMI in all hospitals of City S; **(b)** Monthly trends in the proportion of out-of-pocket payments for inpatients with URRBMI and UEBMI in primary hospitals of City S; **(c)** Monthly trends in the proportion of out-of-pocket payments for inpatients with URRBMI and UEBMI in secondary hospitals of City S; **(d)** Monthly trends in the proportion of out-of-pocket payments for inpatients with URRBMI and UEBMI in tertiary hospitals of City S.

In secondary hospitals, the initial level of out-of-pocket ratio for URRBMI was 25.54%, increasing significantly by 0.02% per month before the implementation of the reform, and increasing significantly by about 6.3% in the first month of the implementation of the DIP reform, with the general trend in the subsequent months of the implementation of the reform not significant compared to the pre-initial level, and the overall upward trend slowed down. The initial level of out-of-pocket expenses for UEBMI was 28.7%, decreasing significantly by 0.23% per month before the implementation of the reform, and the overall trend after the implementation of the DIP reform was the same as before the reform, with a greater decrease than before the implementation.

In tertiary hospitals, the initial level of the URRBMI out-of-pocket ratio was 35.36%, with a significant increase of about 7.3% in the first month of implementation of the DIP reform, and a non-significant monthly increase of 0.08% in the ongoing phase of implementation. The initial level of out-of-pocket ratio for UEBMI was 37.56%, showing a significant and gradual decrease in the pre-implementation level; in the first month of the implementation of the DIP reform, the out-of-pocket ratio decreased significantly by about 4.8%, and in the continuation phase of the program, the out-of-pocket ratio showed a slow increase, significantly different from the pre-implementation trend.

3.5 Robustness tests

Supplementary Tables 1–3 in the additional file show the results of the test using September 2021 as the intervention point to test the stability of the experiment. Among the results against the changes before and after the reform show that the results are insignificant, proving the reliability of the experiment and verifying the robustness of the experiment. Some of the results for the pre-intervention period show significant changes, which may be due to related policies such as the price adjustment of medical services.

4 Discussion

In this study, data pertaining to patients with CHD in City S from 2020 to 2023 were selected, encompassing two types of enrollment:

employee health insurance (UEBMI) and resident health insurance (URRBMI). The data results indicate that hospitalization costs and hospitalization days in both UEBMI and URRBMI have declined compared with the pre-reform period, and the DIP reform has achieved significant results in controlling healthcare costs and hospitalization days. This finding echoes the "payment - method - insurance - type interaction effect" seen in France's T2A reform. However, China's DIP reform has led to a larger drop in costs, which may be related to hospitals adjusting their behavior due to the pressure of total control over medical insurance funds (29, 30). However, as in Australia's ABF reform, DIP reform may also lead to hospitals selectively accepting patients, requiring further attention and study (11). However, in terms of out-of-pocket ratios, the performance of different health insurance types varies.

The DIP reform has demonstrated significant results in controlling treatment costs, consistent with the effects of previous DRG implementations (31, 32). The hospitalization costs of both URRBMI and UEBMI patients decreased after the reform, with a larger decrease in hospitalization costs for UEBMI, which may be related to both hospital choice and patient choice. In terms of the nature of the insurance itself, China's URRBMI is primarily funded by the government and individuals, and is a universal bottom-up health insurance. Therefore, the amount of health insurance premiums paid is low, and the corresponding treatment is lower than that of those who pay the UEBMI (33). Hospital treatment costs are lower due to the low budget and large number of URRBMI patients. After the DIP reform, hospitals have to bear the excess due to the low cost of treatment and medication (34). The health insurance premiums for UEBMI are higher, so hospitals tend to choose more expensive treatments due to short-term income and other factors to make higher profits and obtain higher points in the next year's point calculation (4). This choice will, to a certain extent, cause inequality in health among populations (35). Secondly, on the subjective side, the UEBMI population may also have higher budgets for expected treatment costs due to better treatment, resulting in treatment costs being at a higher level (36, 37). Regarding the difference between the cost of residential health insurance and that of UEBMI, some studies have shown that although the integration of residential health insurance reforms has promoted health equity, the impact on different regions and income groups varies, and the low-income group still suffers from more serious health inequalities (38). This phenomenon resembles the "high - cost case transfer" in Germany's DRG reform and the divergent evolution of commercial and national health insurance under Japan's DPC system (39). It is recommended to refer to the risk - adjustment mechanism in the US ACO model and apply weight correction based on the Charlson Comorbidity Index for URRBMI patients admitted to hospitals (40).Previous studies on DRG have also mentioned the existence of reforms that have reduced drug costs but increased overall treatment costs for chronic conditions. Since the research on DIP in this study is biased toward its short-term effects, it is possible to conduct a long-term follow-up study to examine the total cost of treatment for chronic conditions over multiple years (41). The downward trend in hospitalization costs is reflected in different levels of hospitals. These results suggest that the DIP reform has been effective in curbing the increase in hospitalization costs in different levels of hospitals, especially in primary and secondary hospitals. Long - term studies on Japan's DPC and Germany's DRG reform show a 3 to 5-year lag between payment reform and healthcare - quality changes, indicating that our three year study may be limited by an "effect-observation window period" (7, 39).The fact that primary and secondary hospitals have better cost containment results than tertiary hospitals can be attributed to several factors. Previous studies have shown that DRG has different cost-control effects on different levels of hospitals (42, 43), Primary and secondary hospitals are more advantageous in terms of cost control due to their simple cost structure, single type of disease treated, and more standardized treatment protocols. Compared to DRG, hospitals have more initiative in payment coefficients during the DIP reform, and primary and secondary hospitals can adjust payment coefficients by optimizing historical data to reduce inpatient costs. Tertiary hospitals, on the other hand, are less effective in controlling costs due to the complexity of patients' illnesses, the volume of historical data, and the complicated cost structure. However, studies have also shown that tertiary hospitals are able to avoid sacrificing profitability by lowering the price of services to attract patients in the competition due to their better cost control ability (44).

The results on length of stay before and after the DIP reform also provide some evidence for the corresponding view on hospitalization costs described above. The average length of stay for both residents' and UEBMI declined after the reform, and the declining trend was reflected in different levels of hospitals. Specifically, the decline in hospital days was more pronounced for UEBMI patients than for URRBMI patients. This result is somewhat inconsistent with previous studies (4, 45, 46), which may be related to factors such as the study's regional and demographic and health resource allocations (47), but both reflect good cost control in DIP. The reason for the larger decrease in hospital days for UEBMI patients than for URRBMI patients after the implementation of the DIP payment method may be related to several factors. First, the post-payment price of UEBMI is usually higher than that of URRBMI, which incentivizes hospitals to be more motivated to improve efficiency by reducing the number of inpatient days in treating UEBMI patients, thus reducing the use of healthcare resources without compromising the quality of treatment. Second, from the patient's perspective, employee patients are mostly active workers, relatively young, and usually have milder conditions, so it is easier to achieve a reduction in the number of hospitalization days under the DIP payment method. URRBMI patients, on the other hand, include the unemployed, farmers, and the older adult. These groups may have more complex conditions and require longer hospitalization. In addition, hospitals may prefer UEBMI patients in resource allocation due to the higher post-payment price of UEBMI, which may result in less significant reductions in hospital days for URRBMI patients than for employee patients (4), These factors together resulted in a greater decrease in hospital days for UEBMI patients after the implementation of the DIP payment method. The data on length of stay in different levels of hospitals showed a high degree of consistency with the reduction in hospitalization costs. From previous studies related to DRG, it was found that hospitals may increase the number of hospitalizations to obtain additional subsidies (16, 48). In this study, because readmission rates were not included in the study variables, it was not possible to ensure whether any hospitals obtained corresponding benefits by disaggregating hospitalizations.

The DIP reform showed different effects in terms of out-of-pocket expenses. The out-of-pocket ratio for URRBMI increased after the reform, while the out-of-pocket ratio for UEBMI decreased after the reform. Specifically, the out-of-pocket ratio for URRBMI was 20.16%

before the DIP reform, rose by 5.02% after the reform, and subsequently declined by an average of 0.15% per year from the pre-reform trend. The out-of-pocket ratio for UEBMI was 30.74% before the DIP reform, and has been rising slowly by 0.16% per month since the reform compared to the pre-reform out-of-pocket ratio. The increase in the out-of-pocket ratio of the URRBMI may be related to the corresponding policy of the health insurance pool. Previous studies have pointed out that a single health care provider can sometimes lead to an increase in out-of-pocket medical expenses or an increase in other medical expenditures (49, 50). The lack of a comprehensive and rational policy mechanism may also lead hospitals to cut reimbursement budgets to cope with the risk (51). Because the aging of Chinese society has led to the expansion of the URRBMI group, in order to ensure the sustainability of the health insurance fund, some regions have made certain policy adjustments, such as raising the starting line and lowering the reimbursement rate to cope with the risk of bottoming out the fund (52), and these adjustments may directly lead to an increase in the out-of-pocket expenses of the URRBMI. However, when linked to the overall cost trend of URRBMI, the out-of-pocket costs have still decreased compared to the pre-reform period. The increase in out-of-pocket expenses may also be related to the characteristics of the population enrolled in the URRBMI, which has a higher probability of suffering from other chronic and basic diseases due to its older age on average, while the persistence of medication for basic diseases and the adjustments of some drug catalogs may also lead to a certain degree of increase in the out-of-pocket expenses. Among different levels of hospitals, the changes in the out-of-pocket ratios of URRBMI patients and UEBMI patients in level 1 hospitals and level 2 hospitals are basically the same as the overall. The out-of-pocket ratios for URRBMI in tertiary hospitals, on the other hand, showed a trend of increasing in the month after the reform and then decreasing on a monthly basis. Previous studies have shown that the risk adjustment mechanism established will be more compatible with the payment standards of tertiary hospitals, thus providing more reasonable treatment and services to patients while alleviating the pressure of cost control (53), a finding consistent with the results of this study. The decrease in out-of-pocket ratios for URRBMI patients in tertiary hospitals after the implementation of DIP is also attributed to the fact that tertiary hospitals usually have a higher institutional factor in the DIP reform and are able to receive more financial support for Medicare payments. The health insurance department has also given certain policy support and fund tilts to tertiary hospitals to encourage them to admit and treat critically ill patients and difficult cases, and this support has enabled tertiary hospitals to obtain more funds in health insurance payments, thus reducing the out-of-pocket proportion of patients.

This study has its strengths. First, the data covered all hospitalization claims from January 2020 to December 2023 for all patients with coronary artery disease in the city. This ensured the adequacy of the assessment data. Second, all data were obtained from the hospitalization claims records of the S. City Health Protection Bureau, which ensured the quality of the data. Third, ITSA of the corresponding outcome variables for UEBMI and URRBMI hospitalized patients allowed for a more effective investigation of the respective impacts before and after the DIP reform. This study also has its limitations. First, it was obtained from only one city, a single source. Second, it lacks its own control group to make its own comparison. Third, because the variables are more crude, it may ignore the influence of other factors and cannot find the influence mechanism of more potential factors.

5 Conclusion

The DIP reform has achieved significant results in controlling hospitalization costs and hospital days, especially in Primary and secondary hospitals. The decline in hospitalization costs and hospital days reflects the short-term and more favorable cost-control effects of the DIP reform. The DIP reform has performed differently in terms of out-of-pocket ratios. Out-of-pocket ratios for URRBMI increased after the reform, while those for UEBMI decreased. Among the different levels of hospitals, Primary and secondary hospitals experienced larger declines in hospitalization costs and length of stay, which were attributed to their simple cost structures, standardized treatment protocols, and cost-control incentives under the DIP payment methodology. The downward trend in the length of stay in Tertiary hospitals slowed down after the reform, but the out-of-pocket ratio of URRBMI patients instead declined after the reform, which was mainly attributed to the fact that Tertiary hospitals had higher institutional coefficients under the DIP reform and were able to obtain more financial support for health insurance payments, while the policy support and fund tilting of health insurance departments toward Tertiary hospitals also lowered the out-of-pocket ratio of patients.

Overall, the DIP reform has effectively reduced the financial burden for patients and enhanced the operational efficiency of hospitals. When further promoting the DIP reform, policymakers should consider the fairness of medical treatment for patients with different types of health insurance and other circumstances, and seek the optimal solution whereby patients with different types of health insurance can receive good medical services, so as to optimize the provision of medical services while ensuring the universality and fairness of medical treatment. Future research can combine clinical - quality metrics, like 30 - day readmission rates, to build a DIP composite - performance index. It can also apply mixed - methods to explore how payers and patients adapt to payment rules.

Data availability statement

The datasets presented in this article are not readily available because it is from a public institution, institutional review is required. Requests to access the datasets should be directed to Yingying Tao, 15168340102@163.com.

Ethics statement

The data for this study were obtained from the Hubei Provincial Healthcare Security Information Platform, covering hospitalization claims records in S City, Hubei Province, from January 1, 2020, to December 31, 2023. Patients' information was fully anonymized, with only unique identifiers retained for analysis purposes. The data were accessed on June 10, 2024, after obtaining approval from the Ethics Committee of Zhejiang University of Traditional Chinese Medicine

(Approval Number: 20240516–3).The authors had no access to any personally identifiable information during or after the study. The Bureau of Medical Security authorized the use of the anonymized dataset for research purposes. The requirement for individual informed consent was waived due to the retrospective nature of the study. This study adhered strictly to the ethical principles outlined in the Declaration of Helsinki, and all data processing methods complied with relevant legal and ethical standards.

Author contributions

YT: Data curation, Writing – original draft. KS: Formal analysis, Writing – original draft. YC: Writing – review & editing. CL: Writing – review & editing. DW: Writing – review & editing. XM: Formal analysis, Supervision, Writing – review & editing.

Funding

The author(s) declare that financial support was received for the research and/or publication of this article. This study was supported by the Medical Science and Technology Project of Zhejiang Province (Grant No. 2024KY1190) and the Zhejiang Provincial Xinmiao Talent Program (Grant No. 2024R410A053). We gratefully acknowledge the support provided by these funding organizations, which made this research possible.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The author(s) declare that no Gen AI was used in the creation of this manuscript.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2025.1567838/full#supplementary-material

References

1. Wang L, Ai D, Zhang N. Exercise benefits coronary heart disease In: J Xiao, editor. Exercise for cardiovascular disease prevention and treatment: From molecular to clinical, part 2. Singapore: Springer Singapore (2017). 3–7.

2. Liu L, Xu Y, Yu J, Man X, Jiang Y, Zhao L, et al. The impact of comprehensive public hospital reforms on the direct medical cost of inpatients with coronary heart disease. *Front Public Health*. (2022) 10:891186. doi: 10.3389/fpubh.2022.891186

3. Yan J, Shi Y, Zhang J, Chen S, Huo X, Shen Y, et al. Impact of capitation prepayment on the medical expenses and health service utilization of patients with coronary heart disease: a community policy intervention program in a county in China. *BMC Public Health*. (2023) 23:2224. doi: 10.1186/s12889-023-17161-x

4. Lin K, Li Y, Yao Y, Xiong Y, Xiang L. The impact of an innovative payment method on medical expenditure, efficiency, and quality for inpatients with different types of medical insurance: evidence from a pilot city, China. *Int J Equity Health*. (2024) 23:115. doi: 10.1186/s12939-024-02196-2

5. Wang H, Gao C, Dantona C, Hull B, Sun J. DRG-LLaMA: tuning LLaMA model to predict diagnosis-related group for hospitalized patients. *Npj Digi Med*. (2024) 7:16. doi: 10.1038/s41746-023-00989-3

6. Yasunaga H, Ide H, Imamura T, Ohe K. Impact of the japanese diagnosis procedure combination-based payment system on cardiovascular medicine-related costs. *Int Heart J*. (2005) 46:855–66. doi: 10.1536/ihj.46.855

7. Wang K, Li P, Chen L, Kato K, Kobayashi M, Yamauchi K. Impact of the japanese diagnosis procedure combination-based payment system in Japan. *J Med Syst*. (2010) 34:95–100. doi: 10.1007/s10916-008-9220-2

8. Strehl R. Gesundheitsreform 2000 – auswirkungen auf die stationäre versorgung. *Chirurg*. (2000) 71:417–21. doi: 10.1007/s001040051074

9. Quentin W, Stephani V, Berenson RA, Bilde L, Grasic K, Sikkut R, et al. How Denmark, England, Estonia, France, Germany, and the USA pay for variable, specialized and low volume care: a cross-country comparison of in-patient payment systems. *Int J Health Policy Manag*. (2022) 11:2940–50. doi: 10.34172/ijhpm.2022.6536

10. Dimitropoulos V, Yeend T, Zhou Q, McAlister S, Navakatikyan M, Hoyle P, et al. A new clinical complexity model for the australian refined diagnosis related groups. *Health Policy*. (2019) 123:1049–52. doi: 10.1016/j.healthpol.2019.08.012

11. Jackson T, Dimitropoulos V, Madden R, Gillett S. Australian diagnosis related groups: drivers of complexity adjustment. *Health Policy*. (2015) 119:1433–41. doi: 10.1016/j.healthpol.2015.09.011

12. Charlton V. NICE and fair? Health technology assessment policy under the UK's National Institute for health and care excellence, 1999–2018. *Health Care Anal*. (2020) 28:193–227. doi: 10.1007/s10728-019-00381-x

13. Li X, Zhang Y, Zhang X, Li X, Lin X, Han Y. Effects of fee-for-service, diagnosis-related-group, and mixed payment systems on physicians' medical service behavior: experimental evidence. *BMC Health Serv Res*. (2022) 22:870. doi: 10.1186/s12913-022-08218-5

14. Gao C, Xu F, Liu GG. Payment reform and changes in health care in China. *Soc Sci Med*. (2014) 111:10–6. doi: 10.1016/j.socscimed.2014.03.035

15. Jian W, Lu M, Liu G, Chan KY, Poon AN. Beijing's diagnosis-related group payment reform pilot: impact on quality of acute myocardial infarction care. *Soc Sci Med*. (2019) 243:112590. doi: 10.1016/j.socscimed.2019.112590

16. Kutz A, Gut L, Ebrahimi F, Wagner U, Schuetz P, Mueller B. Association of the swiss diagnosis-related group reimbursement system with length of stay, mortality, and readmission rates in hospitalized adult patients. *JAMA Netw Open*. (2019) 2:e188332. doi: 10.1001/jamanetworkopen.2018.8332

17. Yuan S, Liu W, Wei F, Zhang H, Wang S, Zhu W, et al. Impacts of hospital payment based on diagnosis related groups (DRGs) with global budget on resource use and quality of care: a case study in China. *IJPH*. (2019). doi: 10.18502/ijph.v48i2.818

18. Cao Z, Liu X, Wang X, Guo M, Guan Z. Impacts of DRG-based prepayment reform on the cost and quality of patients with neurologic disorders: evidence from a quasi-experimental analysis in Beijing, China. *Risk Manag Healthc Policy*. (2024) 17:1547–60. doi: 10.2147/RMHP.S458005

19. Schreyögg J, Stargardt T, Tiemann O, Busse R. Methods to determine reimbursement rates for diagnosis related groups (DRG): a comparison of nine european countries. *Health Care Manag Sci*. (2006) 9:215–23. doi: 10.1007/s10729-006-9040-1

20. Fernandez-Alonso V, Gil-Prieto R, Amado-Anton-Pacheco M, Hernández-Barrera V, Gil-De-Miguel Á. Hospitalization burden associated with anus and penis neoplasm in Spain (2016-2020). *Hum Vaccin Immunother*. (2024) 20:2334001. doi: 10.1080/21645515.2024.2334001

21. Xie H, Cui X, Ying X, Hu X, Xuan J, Xu S. Development of a novel hospital payment system – big data diagnosis & intervention packet. *Health Policy OPEN*. (2022) 3:100066. doi: 10.1016/j.hpopen.2022.100066

22. Policy and regulations of the National Medical Insurance Administration: Notice from the Office of the National Medical Insurance Administration on the issuance of the

list of pilot cities for regional point-based Total budget and diagnosis-related group payment. Available online at: https://www.nhsa.gov.cn/art/2020/11/4/art_37_3812.html (Accessed January 20, 2025).

23. Lai Y, Fu H, Li L, Yip W. Hospital response to a case-based payment scheme under regional global budget: the case of Guangzhou in China. *Soc Sci Med*. (2022) 292:114601. doi: 10.1016/j.socscimed.2021.114601

24. Hong D, Lv D, Wu J, Li X, Zhao Q, Lu X, et al. The influence of diagnosis intervention packet policy intervention on medication structure and drug cost of elderly hypertensive inpatients in China: a multicenter interrupted time-series analysis. *Risk Manag Healthc Policy*. (2023) 16:1781–90. doi: 10.2147/RMHP.S418541

25. Tang X, Zhang X, Chen Y, Yan J, Qian M, Ying X. Variations in the impact of the new case-based payment reform on medical costs, length of stay, and quality across different hospitals in China: an interrupted time series analysis. *BMC Health Serv Res*. (2023) 23:568–10. doi: 10.1186/s12913-023-09553-x

26. Bernal JL, Cummins S, Gasparrini A. Corrigendum to: interrupted time series regression for the evaluation of public health interventions: a tutorial. *Int J Epidemiol*. (2020) 49:1414. doi: 10.1093/ije/dyaa118

27. Hategeka C, Ruton H, Karamouzian M, Lynd LD, Law MR. Use of interrupted time series methods in the evaluation of health system quality improvement interventions: a methodological systematic review. *BMJ Glob Health*. (2020) 5:e003567. doi: 10.1136/bmjgh-2020-003567

28. Xiong X, Huo Z, Zhou S, Bai G, He S, Zhou Y, et al. Short- and long-term impacts of the national essential medicines policy on drug availability, price, and usage in a deprived rural county in southwestern China: an interrupted time series analysis across 8 years. *Front Public Health*. (2024) 12:1355239. doi: 10.3389/fpubh.2024.1355239

29. Quentin W, Scheller-Kreinsen D, Geissler A, Busse RGroup on behalf of the E. Appendectomy and diagnosis-related groups (DRGs): patient classification and hospital reimbursement in 11 european countries. *Langenbeck's Arch Surg*. (2011) 397:317–26. doi: 10.1007/s00423-011-0877-5

30. Gaughan J, Kobel C. Coronary artery bypass grafts and diagnosis related groups: patient classification and hospital reimbursement in 10 european countries. *Health Econ Rev*. (2014) 4:4. doi: 10.1186/s13561-014-0004-8

31. Ma W, Qu J, Han H, Jiang Z, Chen T, Lu X, et al. Statistical insight into China's indigenous diagnosis-related-group system evolution. *Health Care*. (2023) 11:2965. doi: 10.3390/healthcare11222965

32. Li Q, Fan X, Jian W. Impact of diagnosis-related-group (DRG) payment on variation in hospitalization expenditure: evidence from China. *BMC Health Serv Res*. (2023) 23:688. doi: 10.1186/s12913-023-09686-z

33. Yang Y, Nicholas S, Maitland E, Huang Z, Chen X, Ma Y, et al. An equity evaluation in stroke inpatients in regard to medical costs in China: a nationwide study. *BMC Health Serv Res*. (2021) 21:425. doi: 10.1186/s12913-021-06436-x

34. Yashi LI, Wenlong ZHANG, Zhang YUAN, Jianguo LI. Analysis on the equity of benefits of medical insurance between employees and residents ——evidence from China Famliy panel studies. *Health Economics Research*. (2022) 39:13–7. doi: 10.14055/j.cnki.33-1056/f.2022.03.004

35. Chandra A, Cutler D, Song Z. "Chapter six - who ordered that? The economics of treatment choices in medical care", In: MV Pauly, TG Mcguire and PP Barros, editors. *Handbook of health economics*. Elsevier (2011). 397–432. doi: 10.1016/B978-0-444-53592-4.00006-2

36. Zhou T, Gao Y, Zuo X. On the benefit equity of basic medical insurance under the background of common prosperity:empirical evidence from CHARLS data. *J East China Normal University*. (2024) 56:182. doi: 10.16382/j.cnki.1000-5579.2024.02.014

37. Gu X, Hui W. A study on universal health care coverage and equity in health care utilization: an analysis based on multiple rounds of data from the China household tracking survey. *J Soochow Univ*. (2024) 45:28–38. doi: 10.19563/j.cnki.sdzs.2024.05.004

38. Meng Y, Yu R, Bai H, Han J. Evidence from the China family panel studies survey on the effect of integrating the basic medical insurance system for urban and rural residents on the health equity of residents: difference-in-differences analysis. *JMIR Public Health Surveillance*. (2024) 10:e50622. doi: 10.2196/50622

39. Messerle R, Schreyögg J. Country-level effects of diagnosis-related groups: evidence from Germany's comprehensive reform of hospital payments. *Eur J Health Econ*. (2023) 25:1013–30. doi: 10.1007/s10198-023-01645-z

40. Lin M-Y, Hanchate AD, Frakt AB, Burgess JF, Carey K. Do accountable care organizations differ according to physician-hospital integration? A retrospective observational study. *Medicine*. (2021) 100:e25231. doi: 10.1097/MD.0000000000025231

41. Wang H, Xiang X. Evaluating the effect of health insurance reform on health equity and financial protection for elderly in low- and middle-income countries: evidences from China. *Glob Health*. (2024) 20:57. doi: 10.1186/s12992-024-01062-8

42. Meng Z, Ma Y, Song S, Li Y, Wang D, Si Y, et al. Economic implications of Chinese diagnosis-related group-based payment Systems for Critically ill Patients in ICUs. *Crit Care Med*. (2020) 48:e565–73. doi: 10.1097/CCM.0000000000004355

43. Hu W-Y, Yeh C-F, Shiao A-S, Tu T-Y. Effects of diagnosis-related group payment on health-care provider behaviors: a consecutive three-period study. *J Chin Med Assoc*. (2015) 78:678–85. doi: 10.1016/j.jcma.2015.06.012

44. Tan H, Zhang X, Bi S, Chen Y, Guo D. How significant is cost-shifting behavior under the diagnosis intervention packet payment reform? Evidence from the coronary heart disease market. *Front Public Health*. (2024) 12:1431991. doi: 10.3389/fpubh.2024.1431991

45. Qin Z, Liu S, Zhou M, Chen L, Huang W, Shen L. Impacts of unifying urban and rural residents' medical insurance on the hospitalisation expenses of rural patients in eastern China: an interrupted time series analysis. *BMJ Open*. (2023) 13:e067198. doi: 10.1136/bmjopen-2022-067198

46. Lin X, Cai M, Tao H, Liu E, Cheng Z, Xu C, et al. Insurance status, inhospital mortality and length of stay in hospitalised patients in Shanxi, China: a cross-sectional study. *BMJ Open*. (2017) 7:e015884. doi: 10.1136/bmjopen-2017-015884

47. Dai G, Li R, Ma S. Research on the equity of health resource allocation in TCM hospitals in China based on the Gini coefficient and agglomeration degree: 2009–2018. *Int J Equity Health*. (2022) 21:145–14. doi: 10.1186/s12939-022-01749-7

48. Vuagnat A, Yilmaz E, Roussot A, Rodwin V, Gadreau M, Bernard A, et al. Did case-based payment influence surgical readmission rates in France? A retrospective study. *BMJ Open*. (2018) 8:e018164. doi: 10.1136/bmjopen-2017-018164

49. Dong Y, Chen J, Jing X, Shi X, Chen Y, Deng X, et al. Impact of capitation on outpatient expenses among patients with diabetes mellitus in Tianjin, China: a natural experiment. *BMJ Open*. (2019) 9:e024807. doi: 10.1136/bmjopen-2018-024807

50. Yan J, Lin H-H, Zhao D, Hu Y, Shao R. China's new policy for healthcare cost-control based on global budget: a survey of 110 clinicians in hospitals. *BMC Health Serv Res*. (2019) 19:84. doi: 10.1186/s12913-019-3921-8

51. He R, Miao Y, Zhang L, Yang J, Li Z, Li B. Effects of expanding outpatient benefit package on the rationality of medical service utilisation of patients with hypertension: a quasi-experimental trial in rural China. *BMJ Open*. (2019) 9:e025254. doi: 10.1136/bmjopen-2018-025254

52. Tao X, Zeng Y, Jiao W. The impact of medical insurance and old-age security on the utilization of medical services by the older population with disabilities. *BMC Health Serv Res*. (2024) 24:892. doi: 10.1186/s12913-024-11323-2

53. Ding Y, Yin J, Zheng C, Dixon S, Sun Q. The impacts of diagnosis-intervention packet payment on the providers' behavior of inpatient care—evidence from a national pilot city in China. *Front Public Health*. (2023) 11:1069131. doi: 10.3389/fpubh.2023.1069131

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 11 June 2025
DOI 10.3389/fpubh.2025.1587028

Check for updates

OPEN ACCESS

EDITED BY
Kevin Lu,
University of South Carolina, United States

REVIEWED BY
Valentin Marian Antohi,
Dunarea de Jos University, Romania
Michail Tsangas,
CDA College, Cyprus

*CORRESPONDENCE
Jiajing Li
a19103292811@163.com

RECEIVED 03 March 2025
ACCEPTED 26 May 2025
PUBLISHED 11 June 2025

CITATION
Li J (2025) Can the Marketing Authorisation Holder system improve the ESG performance of pharmaceutical manufacturers?
Front. Public Health 13:1587028.
doi: 10.3389/fpubh.2025.1587028

COPYRIGHT
© 2025 Li. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

Can the Marketing Authorisation Holder system improve the ESG performance of pharmaceutical manufacturers?

Jiajing Li*

School of Public Economics and Administration, Shanghai University of Finance and Economics, Shanghai, China

Introduction: The Marketing Authorisation Holder (MAH) system is an advanced drug registration mechanism widely adopted globally Nevertheless, there is a scarcity of in-depth empirical investigations concerning MAH within the context of pharmaceutical manufacturing enterprises.

Methods: This research endeavors to investigate the influence of MAH on the environmental, social and corporate governance (ESG) performance of companies through the application of the difference-in-differences model, leveraging firm data from China's A-share-listed pharmaceutical manufacturing sector spanning from 2012 to 2019.

Results: First, MAH markedly enhances the ESG performance of pharmaceutical manufacturing entities. Secondly, MAH impacts firms' ESG performance via three pathways, namely, boosting research and development (R & D) investment, diminishing the internal pay disparity, and lowering supply chain concentration. Thirdly, the effect of MAH on firms' ESG performance is more pronounced in non-state-owned firms, those with elevated management shareholding, and firms with enhanced internal control levels. Furthermore, this study ascertained that MAH exerted no influence on firm ESG variance and real earnings management.

Discussion: The results offer actionable policy recommendations for refining the MAH system and promoting the sustainable development of pharmaceutical manufacturing firms. This study not only expands the research boundary of the economic consequences of the MAH system, but also affirms the key role of institutional innovation in the sustainable development of enterprises.

KEYWORDS

Marketing Authorisation Holder system, ESG performance, R & D investment, internal pay gap, supply chain concentration

1 Introduction

Good health and medical conditions are fundamental to disease prevention, diagnosis, and treatment, playing a pivotal role in enhancing societal well-being. With the growing global population, aging population, and emphasis on health, the demand for medicines is increasing, especially innovative medicines. *PrecedenceResearch* data shows that innovative Active Pharmaceutical Ingredients (APIs) account for the largest share of the global active pharmaceutical ingredient market in 2022 (1). According to the data released by Frost and Sullivan, as of September 2024, the global innovative drug market has reached 1.7 trillion yuan. The COVID-19 pandemic underscored the critical importance of pharmaceutical innovation, reinforcing its role in addressing global health challenges.

Despite this growing demand, pharmaceutical manufacturers face significant hurdles, particularly in innovation and research and development (R & D). One of the key problems is the lack of innovation and the high cost of R & D in pharmaceutical manufacturing companies, which leads to high selling prices. As a result, the social benefits of pharmaceutical innovation are not high enough to generate positive externalities. According to *Evaluate Pharma* data, global pharmaceutical R & D expenses grew from $168.4 billion in 2017 to $203.9 billion in 2024, a Compound Annual Growth Rate (CAGR) of about 2.7%. The cost of R & D for individual new drugs has been on a significant upward trend over the past few decades. High drug prices have distorted the significance of R & D, which has led pharmaceutical manufacturing companies to emphasize more on financial benefits than health benefits (2).

Beyond financial challenges, pharmaceutical R&D and production pose severe environmental and ecological risks. Advances in medical technology have escalated the generation of medical waste, which, if improperly managed, can lead to environmental contamination and biodiversity loss (3). For instance, the incineration of biomedical waste contains polycyclic aromatic hydrocarbons (PAH) and high levels of heavy metals, which generate unfavorable amounts of hazardous substances that contaminate surface and groundwater (4). Beigaite et al. (5) contend that the existence of pharmaceutical substances and their movement in aquatic ecosystems have a considerable environmental impact worldwide.

To address these issues, scholars have explored strategies to enhance innovation performance in pharmaceutical enterprises. Gridchyna et al. (6) contends that the French Diagnosis Related Groups (DRG) paid funding fails to keep up with the development of innovative technologies or the progress of costly innovative medicines. Schuhmacher et al. (7) asserts that companies need to strengthen their core competencies in drug discovery and development, and they need to establish connections with academic partners and service providers to construct external networks and guarantee sustainable investment in R & D to produce a continuous flow of innovative drugs. Niwash et al. (8), relying on data from Jordanian pharmaceutical and medical supply companies, discovered that knowledge elements boost firms' competitive edge through mechanisms like business intelligence, innovation speed, and innovation quality, and that high levels of human capital, relational capital, and structural capital. Li and Xu (9) discover that the policy of centralized volume-based drug procurement compels pharmaceutical firms to increase innovation inputs and enhances the quality of innovation outputs by exerting existential pressure on them.

In this context, China's Marketing Authorization Holder (MAH) system represents a significant institutional innovation. Piloted in 10 provinces in November 2015 and implemented nationwide in December 2019, MAH decouples drug marketing authorization from production authorization. Before the implementation of MAH, China linked the marketing authorisation of medicines with the production authorisation, and the approval number of a medicine was only granted to the medicine manufacturer. Under this system, drug developers lacking their own production capacity had to either cooperate with a production-qualified company or transfer their R & D results to a manufacturing company. This hindered developers from obtaining the full value of their innovations. Correspondingly, the manufacturing company bore full responsibility for the quality of the drug, resulting in inadequate attention being given to the quality and safety of the drug in the R & D process. The binding of registration and production has caused overcapacity in some large-scale production firms. At the same time, some small innovative firms have difficulty in converting their R & D results into actual products due to their inability to obtain production licenses. The implementation of the MAH system aims to break through these constraints and facilitate the innovative development of the pharmaceutical industry.

This study investigates whether China's MAH system enhances the Environmental, Social, and Governance (ESG) performance of pharmaceutical manufacturers.

This study is driven by the following aspects. First, as the world's second-most populous nation with a rapidly aging demographic, China's pharmaceutical sector sustainability is critical to global health. The annual total number of deaths in China is approximately 10 million, and in 2023, China's pharmaceutical market sales exceed $2 trillion. If MAH is effective, it will contribute significantly to improving the health security of approximately 17.4 percent of the world's population and provide a reference experience for many more countries. Secondly, in China, institutional problems are one of the key reasons for the dilemma of drug innovation (10), which are similar to those in many countries. China's previous drug review and approval process was cumbersome and time - consuming. If China can promote R & D innovation and ESG performance of Chinese pharmaceutical manufacturing companies through institutional innovation, it will furnish guidelines for emerging economies across the globe. Thirdly, China's pilot execution of MAH in 10 provinces from 2015 to 2019 furnishes us with a splendid research opportunity. We employ it as a quasi-natural experiment to probe into the effect of the MAH system on the ESG performance of pharmaceutical manufacturing firms through the difference-in-differences (DID) model.

Leveraging panel data from Chinese A-share listed pharmaceutical firms, we employ a difference-in-differences (DID) model to assess MAH's impact on ESG performance and its underlying mechanisms. Our study has three main contributions. First, we concentrate on investigating the influence of MAH on the ESG performance of Chinese pharmaceutical manufacturing enterprises, augmenting the pertinent research on the efficacy of MAH. China's MAH was rolled out nationwide in 2020, over 4 years ago, yet empirical evidence regarding its effectiveness remains scant. Presently, there is merely a limited amount of literature that examines the function of MAH on R & D innovation via empirical tests (11, 12), and we broaden the discourse on its impact. We discover that MAH propels pharmaceutical manufacturing firms in the pilot region to enhance their ESG performance.

Second, we decipher the 'black box' of the connection between MAH and firms' ESG performance from the viewpoints of R & D, remuneration, and supply chain management, and probe into the impact mechanism, which enables us to gain a more lucid comprehension of the policy logic behind the positive impacts of MAH, and assists us in putting forward relevant insights for firm management. Our findings imply that MAH spurs pharmaceutical manufacturing firms to augment R & D investment, narrow internal pay disparities, and decrease customer concentration, but the effect on supplier concentration is not significant.

Third, based on a series of findings, we provide not only insights for pharmaceutical manufacturing firm managers, but also recommendations for policy - makers. Although these recommendations come from the Chinese scenario, as we mentioned earlier, China, as the second - largest country in terms of population and a representative emerging country, these recommendations may be relevant for many countries.

2 Literature review and hypothesis

2.1 Literature review

2.1.1 Research on MAH

The MAH system represents a more comprehensive drug registration framework compared to traditional models that bundle marketing and manufacturing licenses. Central to the MAH system is the separation of these licenses, granting greater independence to holders of marketing authorizations (13).

The MAH system has been widely promoted globally, especially in European countries such as Germany, Italy, and Israel (14–18). However, its implementation has revealed variations in regulatory compliance and effectiveness. For instance, Handa et al. (19) found that while MAH in Japan mandated adverse event (AE) reporting, communication of these events to healthcare providers was often inadequate. Conversely, Alsaleh and Alshammari (20) asserted that MAH in Saudi Arabia distributed direct healthcare professional communication (DHPC) letters to guidelines with a satisfactory level of compliance.

In 2015, China initiated a pilot program for the MAH system, prompting scholarly exploration of its implications. China's MAH will bring great changes and effects to the drug technology transfer system, drug commissioned production system, drug business licensing system, adverse drug reaction monitoring and pharmacovigilance system, drug damage liability system and other supporting regulatory systems (21). Based on the inter - provincial panel data of China's pharmaceutical manufacturing industry, Liu et al. (11) used the synthetic control method to detect that MAH has a remarkable positive influence on the quality of innovation in pilot provinces. Based on data from A - share pharmaceutical manufacturing listed companies, Wan et al. (12) used the DID model to ascertain that MAH significantly boosted innovation inputs and outputs of pharmaceutical companies. However, MAH in China still has some flaws in promoting new drug development. In particular, drugs in China's MAH are mainly chemicals - based, with most dosage forms being tablets and injections, and the amount of drugs varies widely across provinces (22).

While existing research has established the theoretical relationship between MAH and pharmaceutical companies, empirical evidence remains limited. On the one hand, empirical researches on MAH are scarce in quantity, both for China and other countries. On the other hand, these scarce empirical studies have merely concentrated on the influence of MAH on pharmaceutical innovation. Therefore, more empirical evidence is required to investigate the various impacts of MAH on pharmaceutical manufacturing companies.

2.1.2 Research on ESG performance of pharmaceutical manufacturing firms

In recent years, firm ESG performance has garnered increasing attention from investors, prompting a growing body of scholarly research. The pharmaceutical manufacturing sector has numerous environmental, social and governance issues that pose challenges to its long-term sustainability (23), thus research on its ESG performance is of great significance.

The literature has approached this topic from two main perspectives. First, numerous studies have identified and analyzed the key dimensions of ESG performance in pharmaceutical manufacturing. Yu et al. (24) put forward a comprehensive MCDM framework for assessing the ESG sustainability performance of listed companies and discovered that the most crucial criteria in environmental, social, and governance aspects were pollution treatment, health and safety, and risk management. Lee et al. (25) carried out an online survey of 1,298 respondents. Two categories of firm social responsibility (CSR), promotion of public health and emergency disaster relief support, had the highest preference. Bae et al. (26) found that pharmaceutical companies in South Korea complied with ethical, legal, and economic responsibilities only, but did not contribute enough beyond these, such as innovative drug development.

Second, empirical studies have substantiated the strategic importance of ESG performance for pharmaceutical manufacturers. Based on Fuzzy - set Qualitative Comparative Analysis (fsQCA) and Necessary Condition Analysis (NCA), Tan and Wei (27) found that pharmaceutical firms can improve their overall ESG performance by strategically allocating resources and capabilities while considering ESG performance and financial leverage, among other factors, to improve total factor productivity. Based on Chinese A - share listed pharmaceutical manufacturing data from 2012 to 2021, Tan et al. (53) found that their firm ESG performance directly affects firm value.

Despite these valuable contributions, we identify an important gap in the literature. While existing research has established the importance of ESG performance and identified its key components, few studies have investigated concrete mechanisms for its improvement. Therefore, it is innovative and important for us to explore the effect of MAH on ESG performance of pharmaceutical manufacturing companies and its mechanism.

2.2 Policy background

In August 2015, China released *the Opinions on Reforming the Review and Approval System for Drugs and Medical Devices*, which for the first time suggested carrying out the pilot work of MAH (56). By November 2015, ten provinces and municipalities, Beijing, Tianjin, Hebei, Shanghai, Jiangsu, Zhejiang, Fujian, Shandong, Guangdong, and Sichuan, were selected for the three-year pilot program. In June 2016, China issued the *Notice on the Issuance of the Pilot Programme for the System of Holders of Listed Permits for Pharmaceuticals*, which clarified the scope of the pilot medicines, the conditions, obligations, and liabilities of each subject (54). In October 2018, China determined to extend the three-year pilot period of MAH by 1 year. In 2019, China enacted the newly revised *Drug Administration Law,* which clearly states that the state implements MAH for the administration of drugs (11).

The MAH system is characterized by three key innovations. Firstly, MAH broadens the scope of subjects of commissioned production, while enhancing the production efficiency of firms. MAH allows more types of subjects to participate in drug production, including R & D organisations that are not drug manufacturers, etc., which solves the problem of the scope of subjects in traditional entrusted production. The authorisation holder is legally responsible for the commissioned production firm, which allows the firm to have greater scale and resources for drug R & D and production. Secondly, MAH offers better protection for the intellectual property rights of R & D institutions and personnel. Holders of drug approval numbers

can directly commission production to manufacturing enterprises that have obtained certification in line with the Good Manufacturing Practice (GMP) for pharmaceuticals. This measure provides R & D institutions with cutting - edge knowledge and technologies more room for development, enabling them to have greater control over the drug R & D and production processes. It also reduces intellectual property disputes arising from technology transfer. Third, MAH enhances the quality control of drug production. In contrast to the original system, MAH can alleviate the issue of information loss and distortion during the transmission process, thereby enhancing the quality and safety of drug production. Authorization holders are accountable for the entire supply chain and they have an incentive to guarantee the quality of their products. This also diminishes the ambiguity of risk and responsibility and boosts the effectiveness of quality management.

China has attained remarkable outcomes since the comprehensive implementation of the MAH system. According to the data from the *China Pharmaceutical Innovation and Research Development Association*,[1] as of 30 November 2023, the number of B - license (Drug Manufacturing License Category B, which represents the holder of a marketing authorisation for commissioned production) firms in China had reached 1,172. With respect to regional distribution, aside from the ten centrally-administered provinces and municipalities where the pilot implementation was executed in 2015, Hainan, Hubei, Heilongjiang and other provinces have observed the most considerable increase in the number of B certificates.

2.3 Hypothetical development

Stakeholder theory states that business managers should understand and respect all individuals who are closely involved in the organization's actions and outcomes, and try to balance and satisfy their interests as comprehensively as possible, rather than focusing only on the accumulation of shareholder wealth. According to this theory, the inclusion of various stakeholders in organizational decision - making is both a strategic resource and an ethical imperative, both of which contribute to the overall competitive advantage of the organization (28, 29).

The MAH builds a stakeholder system that includes listed company holders, contract - manufacturing companies and drug supervision and management authorities. Firstly, MAH enables the range of drug - listing license holders to be extended to drug R&D institutions and researchers, which promotes R&D incentives. Secondly, MAH allows the holder to entrust part or all of the drug production to other drug manufacturers. Thirdly, the governmental subjects of interest involved in MAH include the drug regulatory agency where the holder is located, the drug regulatory agency where the entrusted firm is located, and the State Drug Administration.

Stakeholders in pharmaceutical enterprises are concerned about environmental performance, such as the waste of raw materials and discarded packaging generated by the enterprises. A large amount of chemical waste generated during the production process of pharmaceutical enterprises, if discharged directly without effective treatment, will lead to the deterioration of the surrounding ecological environment, affect the quality of life of residents, and increase the cost of social environmental governance (30). Therefore, enterprises need to adopt green production technologies, enhance the utilization rate of raw materials, optimize packaging design, reduce waste generation, and achieve green and sustainable development to meet the expectations of the government and the public for environmental protection.

Stakeholders are concerned about the social performance of pharmaceutical enterprises. On the one hand, the public, as an important stakeholder, is highly concerned about whether enterprises can continuously innovate and provide innovative drugs that maintain social health (31). With the development of medical standards and changes in the disease spectrum, the public's demand for innovative drugs is constantly increasing. Innovative drugs can bring better therapeutic effects to patients and improve the overall health level of society. On the other hand, as internal stakeholders of the enterprise, employees care about their own security during the process of drug research and development and production, including safety guarantees, salary guarantees, etc. (32). A safe working environment is the foundation for employees to work efficiently, and reasonable salary and benefits are the recognition of the value of employees' labor, which directly affects their work enthusiasm and loyalty.

Stakeholders pay attention to the governance performance of pharmaceutical enterprises. Suppliers and customers, as stakeholders with close economic ties, expect to cooperate with enterprises that operate stably and have lasting competitiveness. A stable cooperative relationship is conducive to ensuring the smooth operation of the supply chain, reducing transaction costs, and achieving mutual benefit and win-win results. Investors and drug consumers will also make value judgments based on the financial performance and governance of enterprises, thereby influencing their investment decisions and consumption behaviors (33). A sound governance structure and financial status of an enterprise can enhance investor confidence and attract more funds to support its development.

Based on this, this study proposes the following hypotheses:

> *H1*: MAH is conducive to promoting ESG performance in pharmaceutical manufacturing companies.

For the treatment of pharmaceutical pollution, it is better to strengthen front - end treatment than end - of - pipe treatment, as the removal of pharmaceuticals once they enter the environment will consume a lot of resources and present many technical difficulties. A more effective approach is to promote innovation in pharmaceutical production and to strengthen the management of pharmaceutical production, use and disposal. MAH protects the intellectual property rights of R & D organizations and personnel better, which helps to promote increased R & D investment by pharmaceutical manufacturing companies, reduce waste generation during the production of pharmaceuticals, and reduce the environmental pollution caused by pharmaceuticals during their use and disposal. Therefore, while MAH helps to reduce environmental pollution by promoting pharmaceutical innovation (34), it meets the regulatory needs of the government's environmental protection department and responds positively to the concerns of international environmental organizations about environmental protection.

1 https://www.phirda.com/

The government calls for quality and innovation in pharmaceuticals. In response, MAH will promote deeper specialization in the division of labor among pharmaceutical manufacturing companies and enhance their innovation capacity. R & D organizations will invest more resources in drug innovation, and manufacturing companies will be more committed to improving production efficiency and quality. Management will have to give up some of its profits to increase the salaries of production managers and R & D staff, thereby strengthening the quality management and innovation capacity of the firms. MAH will help pharmaceutical manufacturing firms to narrow the internal pay gap, and will also enhance the sense of belonging of their employees, which will promote their motivation in production and R & D, and bring sustained competitive advantages and economic benefits to the firms.

Besides, MAH may have a positive impact on the supply chain management of pharmaceutical manufacturing firms. On the one hand, in the traditional model, pharmaceutical manufacturing firms are responsible for both R & D and production, and the entire supply of pharmaceuticals will be seriously affected in the event of any problems in the firms, such as production equipment failure, quality control problems, and broken capital chain. MAH allows the holder to entrust different firms to produce. This provides pharmaceutical manufacturing firms with the possibility of reducing risks through supply chain management and promotes more efficient and safer pharmaceutical R & D and manufacturing. On the other hand, with the advancement of specialized division of labor and R & D innovation, pharmaceutical manufacturing firms in each segment will significantly improve their core competitiveness, increasing their competitive advantages in the face of suppliers and customers. This helps firms reduce the concentration of the supply chain and further diversify business risks (35).

> *H2*: The channels through which MAH promotes ESG performance in pharmaceutical manufacturing firms are increasing R & D investment, reducing internal pay gaps, and reducing supply chain concentrations.

To verify these hypotheses, we constructed the DID model to implement the strategy of hypothesis testing. The acceptance or rejection of a hypothesis depends on the statistical significance and sign direction of the coefficients of the key variables in the model. All tests were conducted using two-sided tests, and the significance levels were set at 0.1, 0.05, and 0.01. The following text specifically describes the settings of the model and variables.

3 Methodology

3.1 Model and variables

We take China's implementation of MAH in 10 pilot regions as an exogenous policy shock and employ the DID model to evaluate its influence on the ESG performance of pharmaceutical manufacturing firms. The DID model has been extensively utilized in the assessment of the impacts of the pilot policies, and it can effectively relieve the endogeneity problem in empirical studies (36). The benchmark regression equation is shown below:

$$ESG_{i,t+1} = \alpha + \beta Time_t \times Treat_i + \gamma X_{i,t} + \delta_i + \mu_t + \varepsilon_{i,t} \quad (1)$$

In Equation 1, i represents firms and t represents years. δ is an individual fixed effect, μ is a year fixed effect, and ε is a random disturbance term. We lag Treat×Time and all control variables by one period to further mitigate the effects of endogeneity.

Regarding ESG as an explanatory variable, referring to Li and Zhu (55), we first use ESG rating data from Bloomberg as a proxy variable. Bloomberg began to gradually establish an ESG rating system and conduct scoring since 2009. It covers thousands of listed enterprises worldwide, integrates data on environmental (E), social (S), and corporate governance (G) aspects, and assesses the ESG performance of enterprises through standardized scores (0–100), with higher scores indicating better performance. Its greatest advantage is that it takes into account the characteristics of the industry. For the pharmaceutical industry, it takes into account environmental aspects such as the traceability of raw materials by pharmaceutical enterprises and R&D investment to reduce the use of toxic reagents; social aspects such as the protection against exposure to high-risk chemicals by laboratories and production personnel; and corporate governance issues such as intellectual property rights and supply chains.

Besides, studies on ESG performance usually use ESG rating data from Sino-Securities Index Information Service (Shanghai) Co. Ltd. Later, we use this ESG rating data as a proxy variable for the robustness test.

Treat × Time is the explanatory variable that calculates the average effect of MAH on the ESG performance of pharmaceutical manufacturing enterprises in the pilot area. And deem the pilot implementation of MAH in China as a quasi - natural experiment. Group dummy variable; it gets the value of 1 if the enterprise's registration is in the pilot area of MAH, and 0 otherwise. Time dummy variable; it attains the value of 1 if the year is after the implementation of MAH, and 0 otherwise.

We set Time as a dummy variable based on the year around 2016 for two reasons. First, the MAH pilot program was proposed only in November 2015, which was already the end of the year. Moreover, it usually takes some time for enterprises to carry out research and development and strategic challenges. Therefore, it is very likely that enterprises will start to adjust their strategies some time after the end of 2015. Secondly, in November 2015, China merely proposed to conduct a pilot program, but the implementation methods and key points were not clarified. It was not until June 2016 that the relevant content was determined. Besides, our approach is also in line with that of many other scholars (37). Therefore, we take 2016 as the starting year for the implementation of the MAH pilot.

X denotes a set of control variables which might exert an influence on the ESG performance of firms. In order to regulate the impact of other firm - and region - specific traits on the ESG performance of firms, we introduce the following control variables, including the ltime (the number of years since listing), the size of the firm, financial leverage (lev), profitability level (roa), the number of board of directors (board), the independence of the board of directors (ind_r), shareholding concentration (top1), the nature of property rights (soe), regional economic level (grp), and regional industrial structure (industry) (38). The specific definitions are exhibited in Table 1.

TABLE 1 Variable definition.

Notation	Name	Measurement
ESG	Firm ESG performance	See 3.1
Treat×Time	MAH system	See 3.1
ltime	Number of years listed	Natural logarithm of the number of years since the firm was listed (ln)
size	Firm size	total assets (ln)
lev	Financial leverage	Total liabilities/total assets (%)
roa	Profit level	Net profit/total assets (%)
board	Number of Board of Directors	Natural logarithm of the number of board members (ln)
ind_r	Board independence	Number of independent directors/number of board of directors (%)
top1	Shareholding concentration	Shareholding ratio of the largest shareholder (%)
soe	Nature of property rights	A value of 1 is assigned if the firm is state - owned, and 0 otherwise
grp	Regional economic level	Regional GDP (ln)
industry	Regional industrial structure	Percentage of GDP in the secondary sector (%)

3.2 Data sources

We selected Chinese A - share - listed pharmaceutical companies from 2012 to 2019 for the study. Further, following the general practice, we excluded sample data of companies with ST, ST* designations and a gearing ratio greater than 1. Eventually, this study obtained 81 sample companies with a total of 491 observations.

We chose 2012–2019 as our sample period because, first, MAH was fully implemented in China from 2020 onwards (11). On 1 December 2019, China started to implement a revised version of the *Drug Administration Law*, which has a special chapter on 'marketing authorisation holders of drugs', and in January 2020, it reviewed and passed the *Measures for the Administration of Drug Registration*, which came into effect from July 2020 onwards. Second, starting in 2020, China suffered the full brunt of COVID - 19. In 2020 and beyond, people's health was under great threat, and there was a significant impact on pharmaceutical companies. By setting the end of the sample period in 2019, we were able to evade the impact of COVID - 19 on the study. Third, China's MAH was implemented on a pilot basis from 2016, and we set the first period of the sample to 2012, which ensures the symmetry of the sample period.

Data on firm ESG performance are from Bloomberg, and data on other financial indicators are from the CSMAR database. Data at the regional level are from the *China Statistical Yearbook*. We processed the data using STATA17.

4 Empirical analysis

4.1 Descriptive statistics

The descriptive statistics of the main variables are presented in Table 2. Throughout the sample period, the mean value of ESG performance for listed companies amounts to 30.013, with the standard deviation being 9.479, the minimum value standing at 10.744, and the maximum value reaching 67.206. This suggests that the ESG performance within the sample exhibits a relatively significant disparity, which holds value for its study. At the same time, the mean value of Treat × Time is 0.364, signifying that the pilot firms possess 36.4 per cent of observations subsequent to the implementation of the MAH system, making it highly appropriate for the application of the DID model.

TABLE 2 Descriptive statistics.

Variable	Obs	Mean	Std. Dev.	Min	Max
ESG	491	30.013	9.479	10.744	67.206
Treat×Time	491	0.364	0.482	0	1
Treat	491	0.624	0.485	0	1
Time	491	0.566	0.496	0	1
ltime	491	2.334	0.764	0	3.258
size	491	22.591	0.84	20.185	25.056
lev	491	0.299	0.156	0.025	0.697
roa	491	0.088	0.066	−0.364	0.34
board	491	2.16	0.175	1.609	2.708
ind_r	491	0.37	0.05	0.25	0.625
top1	491	0.362	0.152	0.068	0.891
soe	491	0.321	0.467	0	1
grp	491	10.223	0.794	6.553	11.587
industry	491	0.407	0.092	0.162	0.563

4.2 Benchmark regression analysis

4.2.1 Parallel trend test

In order to verify whether the study satisfies the parallel trend assumption, we conducted a dynamic effects test (39), constructing the model as follows:

$$ESG_{i,t+1} = \alpha + \sum_{t=2012}^{2019} \beta_t T_t \times Treat_i + \gamma X_{i,t} + \delta_i + \mu_t + \varepsilon_{i,t} \quad (2)$$

In Equation 2, we substitute the dummy variable Time in model (1) with a series of dummy variables T representing each year from 2012 to 2019. We take 2015, the year prior to the implementation of

MAH, as the base period to examine whether there is a significant disparity between the experimental group and the control group in terms of ESG performance before and after 2016.

In Figure 1, we mark the estimated coefficients of the dummy variables for each year as dots, and the dashed segments signify 95 per cent confidence intervals. The disparity in ESG performance between the pre - policy experimental group and the control group is insignificant, which implies that the study fulfills the parallel trend hypothesis. Meanwhile, we discover that the impact effect of the MAH regime is delayed by 1 year, which might be attributed to the long R & D cycle.

4.2.2 Regression results

Table 3 shows the baseline regression results. We discover that, upon controlling for year fixed effects and individual fixed effects, the coefficient on Treat × Time is significantly positive at the 1 per cent level, irrespective of whether control variables are incorporated. Moreover, pharmaceutical manufacturing firms in the pilot region improved on average by 4.7% after 2016 (2.957*0.482/30.013), which is highly economically significant. This suggests that the MAH system contributes to the significant improvement of ESG performance of pharmaceutical manufacturing companies by constructing a stakeholder system of listed company holders, trustee manufacturers, and drug regulatory authorities.

The impact of the MAH system on the ESG performance of pharmaceutical manufacturing enterprises is specific. In terms of the environment, it can be reflected in the increased investment of enterprises in environmental protection measures. For instance, pharmaceutical enterprises can adopt more environmentally friendly raw materials and production technologies, reduce the generation and discharge of medical chemical waste, and increase investment in waste treatment facilities, thereby minimizing the impact on the surrounding ecological environment.

In terms of social performance, enterprises may invest more resources in research and development innovation, including increasing the recruitment and training of scientific researchers, establishing a more complete research and development incentive mechanism, and attracting more outstanding talents to participate in the research and development of innovative drugs. Meanwhile, enterprises pay more attention to the welfare and rights of R & D and production employees, increase salary and benefits, and improve the working environment to enhance employee satisfaction and loyalty.

In terms of corporate governance, enterprises may further improve their corporate governance structure and enhance the scientificity and fairness of decision-making. At the same time, enterprises may also enhance the transparency of information disclosure, promptly and accurately revealing their ESG performance and development strategies to investors and other stakeholders.

4.3 Robustness check

4.3.1 Placebo test

To prevent the impact of MAH on the ESG performance of pharmaceutical manufacturing firms from being influenced by unobservable omitted variables, we carry out a placebo test (40). We repeated the aforementioned process 500 times. In each repetition, we randomly picked the same quantity of units as the treatment group in the total sample to constitute a dummy treatment group, and considered the remainder as the control group.

The outcomes are presented in Figure 2, in which the majority of the estimated coefficients of the placebo test cluster around 0 and are insignificant, and the genuine estimated coefficients are outliers. This implies that the robustness of the baseline regression results, which

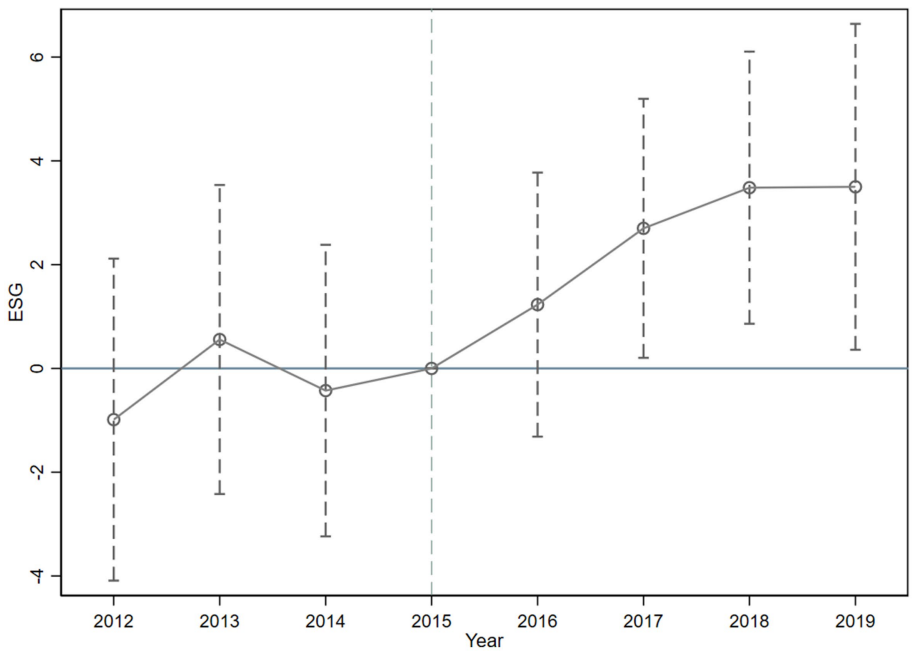


FIGURE 1
Dynamic effects plot.

TABLE 3 Baseline regression results.

	Without Control Variables	With Control Variables
	ESG	ESG
Treat×Time	2.933***	2.957***
	(0.753)	(0.746)
ltime		−1.598
		(1.011)
size		−0.924
		(0.848)
lev		0.591
		(3.218)
roa		11.776***
		(3.987)
board		−0.863
		(3.147)
ind_r		−0.848
		(8.915)
top1		2.951
		(5.322)
soe		1.644
		(1.337)
grp		4.546*
		(2.723)
industry		11.019
		(11.801)
_cons	28.996***	2.006
	(0.317)	(32.326)
Year FE	Yes	Yes
Individual FE	Yes	Yes
N	491	491
R^2	0.877	0.883

***, * indicate significant at the 1 per cent, 5 per cent and 10 per cent levels, with robust standard errors in parentheses.

constitutes the baseline conclusion, cannot be acquired following the placebo test for the randomized treatment group.

4.3.2 Difference-in-Difference-in-Differences model test

Based on the DID model, we brought in a new set of experimental and control groups to build a Difference-in-Difference-in-Differences (DDD) model, which is beneficial for further removing the impact of potential confounding factors (41). The specific model is as follows:

$$ESG_{i,t+1} = \alpha + \beta Time_t \times Treat_i \times Medicine_{i,t} + \theta Time_t \times Treat_i + \rho Time_t \times Medicine_{i,t} + \sigma Treat_i \times Medicine_{i,t} + \varphi Medicine_{i,t} + \gamma X_{i,t} + \delta_i + \mu_t + \varepsilon_{i,t} \quad (3)$$

In Equation 3 medicine serves as a dummy variable indicating whether firm i pertains to the pharmaceutical manufacturing industry in year t. If it does, it is assigned 1; otherwise, it is 0. The outcomes are presented in column (1) of Table 4. The estimated coefficients of the interaction term Treat × Time × Medicine in the DDD model are significantly positive at the 1% level, which validates the robustness of the findings.

4.3.3 PSM-DID test

Taking into account potential biases between the treatment and control groups that might impact the study results, we employed the propensity score matching (PSM) method to modify the sample (42). Firstly, we selected all control variables as matching variables. Secondly, we opted for the nearest - neighbor matching method to create a new dataset in two ratios of 1:2 and 1:4 respectively, in order to re - evaluate the effect of MAH on the ESG performance of pharmaceutical manufacturing enterprises.

The outcomes, as presented in columns (2) and (3) of Table 4, demonstrate that the positive impact of MAH on the ESG performance of pharmaceutical manufacturing enterprises is significant at the 5 per cent level at both scales, which aligns with the estimation of the baseline regression model and validates the robustness of the findings.

4.3.4 Control the impact of the centralized drug purchasing pilot policy

When exploring the impact effect of a pilot policy, we usually need to consider the interference of the same type of policy. In December 2018, China launched the '4 + 7' *Centralised Drug Purchasing Pilot Policy*. The policy is similar in timing to the MAH, and the policy has had a huge impact on the production and operation of pharmaceutical companies (43). Therefore, we use the DID model to generate its proxy variable CDPPP and include it as a new control variable in model (1).

The outcomes, as presented in column (4) of Table 4, indicate that the positive influence of CDPPP on the ESG performance of pharmaceutical manufacturing enterprises is insignificant. Meanwhile, the positive impact of MAH on the ESG performance of pharmaceutical manufacturing enterprises remains significant at the 1 per cent level, which further validates the robustness of the findings.

4.3.5 Replacement of measurement

To examine the sensitivity of the measurement approach of the benchmark results, this paper substitutes the measurement method of the explained variable with the comprehensive score of Sino-Securities Index Information Service (Shanghai) Co. Ltd. ESG (44). As presented in column (5) of Table 4, following the replacement of the explained variable, the impact coefficient of the MAH on the ESG performance of pharmaceutical manufacturing enterprises remains significantly positive. This suggests that the benchmark conclusion is not susceptible to the measurement method of the explained variable.

4.3.6 Cluster analysis

We are concerned that the treatment of standard errors may have influenced the benchmark conclusions. Since the MAH was piloted and implemented at the provincial and municipal levels in China, we grouped the standard errors at the provincial level where the enterprises are situated for analysis. As presented in column (6) of Table 4, the impact coefficient of the MAH on the ESG performance of pharmaceutical manufacturing enterprises remains significantly positive, which further illustrates the robustness of the research findings.

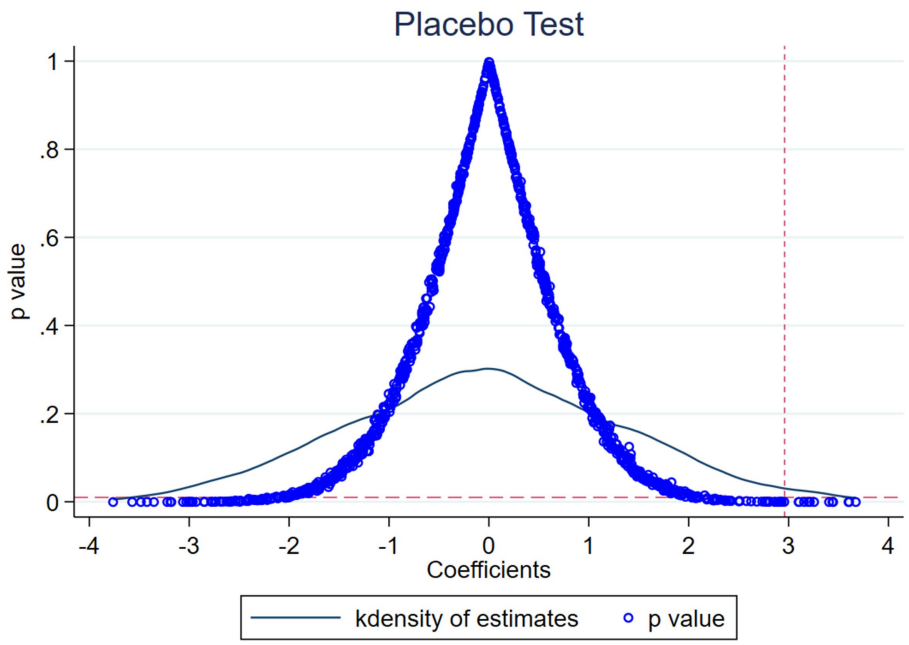


FIGURE 2
Placebo test.

5 Expansion analysis

5.1 Mechanism testing

To test the three potential influencing mechanisms, we use the methods commonly employed in economic literature to construct the following model:

$$Mechanism_{i,t} = \alpha + \beta Time_t \times Treat_i + \gamma X_{i,t} + \delta_i + \mu_t + \varepsilon_{i,t} \quad (4)$$

In Equation 4, "Mechanism" stands for the three mechanism variables. Firstly, the R&D expense ratio is utilized to gauge R&D investment (Innovation). Secondly, the disparity between the average salary of the top three senior executives and the average salary of employees is computed, and then this value is divided by total assets to measure the internal wage gap (Wage_gap). We also measure it (Wage_gap2) by the ratio of the average salary of the top three senior executives to the average salary of employees to enhance robustness. Thirdly, we measure the degree of supply chain concentration from two aspects: the proportion of the largest customer (Consume) and that of the largest supplier (Vendor).

Table 5 presents the outcomes of the mechanism test. The MAH markedly enhances the R&D expense ratio of firms, narrows the internal wage gap, and reduces the proportion of the largest customer. However, the negative impact of the MAH on the proportion of the largest supplier is not significant. A possible reason is that some leading firms have emerged among the upstream suppliers of Chinese pharmaceutical manufacturing firms. These leading firms have grasped most of the orders in the market, including raw material suppliers, intermediate and excipient suppliers, as well as production equipment suppliers. Therefore, the change in the proportion of suppliers is relatively small.

5.2 Heterogeneity analysis

5.2.1 Nature of property rights

We hold the view that the MAH system has a stronger ability to enhance the performance in terms of ESG of private enterprises as opposed to public enterprises. This is attributed to the fact that, on the one hand, private enterprises are more acutely responsive to the responses of the capital market. Consequently, they place greater emphasis on the performance in terms of ESG, which can yield substantial benefits from the capital market. On the other hand, in contrast to public enterprises that possess inherent advantages, private enterprises need to acquire enduring competitive edge through research and development innovation. Hence, the MAH system is more favorable for prompting private enterprises to enhance drug innovation.

As depicted in column (1) of Table 6, within the group of private enterprises, the estimated coefficient is markedly positive at the 1% level. As illustrated in column (2), in the group of public enterprises, the estimated coefficient is not significant. This validates our conjecture that the facilitating effect of MAH on the performance in terms of ESG of private enterprises is more evident.

5.2.2 Management ownership

We consider that management ownership might serve as an efficient means to magnify the influence of the MAH. Owing to the presence of the agency issue, management typically refrains from taking risks in firm innovation. The setback of innovation has the potential to harm the management's standing in the market, which explains why they frequently withdraw when confronted with innovation prospects. On the contrary, if the management possesses a larger share of stocks, they will attach greater significance to the

TABLE 4 Robustness tests.

	DDD Model	PSM-DID 1:2	PSM-DID 1:4	Control the CDPPP	Measurement	Cluster Analysis
	ESG	ESG	ESG	ESG	ESG2	ESG
Treat×Time×Medicine	2.825***					
	(0.796)					
Treat×Time	0.179	4.924**	3.583**	2.920***	0.201*	2.957**
	(0.207)	(2.226)	(1.807)	(0.785)	(0.120)	(1.057)
Time×Medicine	−0.462					
	(0.546)					
Treat×Medicine	−5.823***					
	(1.721)					
Medicine	2.285**					
	(1.092)					
CDPPP				0.123		
				(0.930)		
_cons	8.305	2.053	−23.894	2.115	−0.511	2.006
	(6.049)	(51.663)	(48.982)	(32.465)	(4.772)	(34.370)
Controls	Yes	Yes	Yes	Yes	Yes	Yes
Year FE	Yes	Yes	Yes	Yes	Yes	Yes
Individual FE	Yes	Yes	Yes	Yes	Yes	Yes
N	7,496	157	225	491	491	491
R^2	0.855	0.928	0.909	0.883	0.705	0.883

***, **, and * represent significance levels of 0.01, 0.05, and 0.1, respectively. The values in parentheses in columns (1)–(5) are robust standard errors, and the value in parentheses in column (5) is the robust standard error clustered at the provincial level (53).

TABLE 5 Mechanism testing.

	R & D Investment	Internal Pay Gap		Supply Chain Concentrations	
	Innovation	Wage_gap	Wage_gap2	Consume	Vendor
treat×time	0.011***	−0.006***	−0.835*	−0.038***	−0.020
	(0.003)	(0.002)	(0.433)	(0.011)	(0.017)
_cons	−0.024	0.847***	−103.577***	0.194	−1.426*
	(0.142)	(0.222)	(18.651)	(0.405)	(0.827)
Controls	Yes	Yes	Yes	Yes	Yes
Year FE	Yes	Yes	Yes	Yes	Yes
Individual FE	Yes	Yes	Yes	Yes	Yes
N	491	491	491	491	491
R^2	0.759	0.756	0.629	0.775	0.705

***, and * represent significance levels of 0.01, 0.05, and 0.1, respectively. The values in parentheses are robust standard errors.

long-term growth of the enterprise and augment investment in research, development, and innovation.

As indicated in column (3) of Table 6, within the group where the management ownership ratio is below the median, the estimated coefficient is insignificant. As demonstrated in column (4), in the group with a management ownership ratio no less than the median, the estimated coefficient is notably positive at the 1% level. This implies that the method of management ownership can motivate pharmaceutical manufacturing companies to engage more actively in the MAH, thereby markedly enhancing their ESG performance.

5.2.3 Internal control

We hold the view that enhancing a company's internal control could also be one of the effective approaches to motivate the company to engage in the MAH system. The degree of internal control dictates a company's operational and management effectiveness. Companies with a superior level of internal control are inclined to place more emphasis on the long-term benefits of the company. Consequently, a company's internal control might exert an influence on its R&D strategy, salary allocation, and supply chain management.

TABLE 6 Heterogeneity analysis.

	Nature of property rights		Management ownership		Internal control	
	(1) non-SOEs	(2) SOEs	(3) less	(4) more	(5) lower	(6) higher
treat×time	4.475***	0.857	−0.760	2.720***	1.856	4.484***
	(0.936)	(2.004)	(2.235)	(1.000)	(1.538)	(1.048)
_cons	15.974	−44.597	−93.497	46.139	−20.638	−9.765
	(33.819)	(76.632)	(57.075)	(43.256)	(62.609)	(40.382)
Controls	Yes	Yes	Yes	Yes	Yes	Yes
Year FE	Yes	Yes	Yes	Yes	Yes	Yes
Individual FE	Yes	Yes	Yes	Yes	Yes	Yes
N	330	157	165	322	214	249
R^2	0.902	0.875	0.873	0.912	0.889	0.910

*** denote significance levels of 0.01, 0.05, and 0.1, respectively. The values inside the parentheses are robust standard errors.

TABLE 7 Additional analyses.

	Impression Management	Earnings Management
	ESG performance differences	Real earnings management
treat×time	−0.008	−0.031
	(0.201)	(0.035)
_cons	0.653	−0.808
	(9.061)	(1.714)
Controls	Yes	Yes
Year FE	Yes	Yes
Individual FE	Yes	Yes
N	491	491
R^2	0.643	0.850

***, **, and * represent significance levels of 0.01, 0.05, and 0.1, respectively. The figures in parentheses are robust standard errors.

We employ the firm internal control index from the DIB database as a metric. The greater the index, the higher the level of internal control (45). As depicted in column (5) of Table 6, within the group with a lower internal control level (below the median), the estimated coefficient is insignificant. As illustrated in column (6), in the group with a higher internal control level (not less than the median), the estimated coefficient is notably positive at the 1% level. This suggests that internal control profoundly impacts the strategic decisions of pharmaceutical manufacturing firms and affects the connection between MAH and firm ESG performance.

5.3 Additional tests

5.3.1 Variations in ESG performance

We investigated the effect of MAH on the disparities in ESG ratings among pharmaceutical manufacturing enterprises. Firstly, we computed the Bloomberg ESG[2] and Sino-Securities Index Information Service (Shanghai) Co. Ltd. ESG[3] variations. This was achieved by deducting the sample mean from each ESG value and subsequently dividing by the standard deviation. The discrepancy between these two computed values was employed to gauge the variations in firm ESG ratings (46). As illustrated in column (1) of Table 7, it was discovered that MAH did not exert a substantial influence on the differences in ESG ratings of pharmaceutical manufacturing firms.

5.3.2 Real earnings management

Real earnings management reflects a company's accounting information quality and earnings motivation. Generally speaking, when a company faces significant performance pressure, its management has a stronger incentive to implement real earnings management. Also, it is more likely to conduct impression management (the act of using false ESG disclosures to create a positive but potentially misleading image) through false ESG disclosures (47). As shown in column (2) of Table 7, we found that MAH also did not have a significant impact on the level of real earnings management of pharmaceutical manufacturing firms.

In recent years, there have been increasing doubts about companies using ESG for impression management (48). To address such concerns, we conducted the above two tests to explore whether the impact of MAH on the ESG performance of pharmaceutical manufacturing firms stems from impression management. The above results indicate that the firms affected by MAH do not have the motivation to conduct impression management through ESG disclosures.

6 Discussion

Compared with the existing research, the conclusion of this study shows unique theoretical value and practical significance. Regarding the impact of MAH on enterprises, previous studies have mostly focused on the single dimension of MAH on enterprise innovation or market performance. For instance, Liu et al. (11) pointed out that MAH has a significant positive impact on the innovation quality of the pharmaceutical manufacturing industry by increasing R&D investment. Wan et al. (12) found that the separation of marketing authorization

2 https://www.bloombergchina.com/product/indices/

3 https://www.chindices.com/

and production authorization can promote pharmaceutical innovation, but few studies have approached it from the comprehensive perspective of ESG. This study found that MAH has a significant positive impact on the ESG performance of pharmaceutical manufacturing enterprises. It not only expands the research boundary of the economic consequences of the MAH system, but also confirms the key role of system innovation in promoting the sustainable development of enterprises.

From the perspective of institutional innovation, the MAH system promotes systematic improvement of enterprises in the dimensions of environment, society and governance by reconstructing the stakeholder system, including marketing authorization holders, entrusted manufacturing enterprises and regulatory authorities. This conclusion echoes the theory of institutional gaps in emerging economies (49), that is, in a market environment where the system is not yet perfect, institutional innovation can fill the gaps in regulation and resource allocation. MAH breaks the traditional "R&D - production binding" model and achieves the optimal allocation of resources through contract manufacturing, prompting enterprises to incorporate ESG goals into their strategic planning. This confirms the theory proposed by North (50) that "institutions promote economic development by reducing transaction costs and shaping incentive mechanisms," indicating that emerging economies can guide the transformation of enterprise behaviors toward a sustainable direction through institutional innovation.

Enterprise heterogeneity analysis further reveals the mechanism of MAH. In non-state-owned enterprises, enterprises with high management holding shares and enterprises with good internal control, the improvement effect of MAH on ESG performance is more significant. This conclusion is highly consistent with the theory of ownership structure in emerging economies (51). Compared with state-owned enterprises, non-state-owned enterprises are more responsive to institutional changes due to their shorter decision-making chains and higher market sensitivity. Managing high-holding enterprises directly link ESG goals with management incentives by strengthening the binding of interests. In addition, a sound internal control system helps enterprises efficiently implement ESG strategies and reduce the friction costs of system implementation. These findings provide a theoretical basis for how enterprises with different owner-ownership and governance structures in emerging economies can maximize institutional dividends.

Furthermore, this study confirmed that there is no ESG performance greenwashing phenomenon in pharmaceutical manufacturing enterprises, which contrasts with the research conclusion that some industries "obtain policy dividends through superficial ESG behaviors" (52), and indirectly reflects the constraining effect of the strong regulatory nature of the pharmaceutical industry on the behavior of enterprises.

7 Conclusions, recommendations and limitations

7.1 Conclusion

Health issues have turned into a global concern. Especially after the eruption of COVID - 19, how to deal with sudden global diseases has become a central focus for all nations. Pharmaceutical manufacturing companies, as vital entities in protecting human health, urgently need scholars' profound research on ways to boost their innovation and high - quality development. China initiated the piloting of the Marketing Authorization Holder (MAH) system in 2016 and fully implemented it in 2020. Based on the data of Chinese A - share listed pharmaceutical manufacturing enterprises from 2012 to 2019, we employed the DID model to examine the influence of MAH on the firms' ESG performance, along with its underlying mechanisms and boundary conditions.

We discovered that, firstly, MAH has a markedly positive effect on the ESG performance of pharmaceutical manufacturing companies. Secondly, MAH drives the R&D investment of pharmaceutical manufacturing companies, narrows the internal salary gap within firms, and decreases the concentration of firm supply chains, thereby enhancing ESG performance. Thirdly, the impact of MAH is more evident in non - state - owned companies, companies with a higher proportion of management shareholding, and companies with a higher level of internal control, leading to a greater enhancement in ESG performance. Fourthly, MAH has no significant impact on the disparities in firm ESG ratings and real earnings management. There is no evidence of "greenwashing" in terms of ESG performance or the motivation for such behavior among pharmaceutical manufacturing companies.

7.2 Policy and management recommendations

7.2.1 Policy recommendations

For China, based on the MAH system, the government ought to further introduce supportive policies to stimulate innovation in pharmaceutical manufacturing enterprises. Firstly, the government can offer assistance like tax incentives, R&D subsidies, and innovation awards to pharmaceutical manufacturing enterprises with outstanding innovation performance. This can lower their innovation costs and risks, and boost their enthusiasm and quality of innovation. Secondly, the government can help pharmaceutical manufacturing enterprises with good innovation performance in expanding their financing channels. The government can actively guide financial institutions to specially create financial products and services to encourage innovation in pharmaceutical manufacturing enterprises, such as intellectual property pledge financing and equity financing. Thirdly, the government is required to enhance the intellectual property protection mechanism in the field of pharmaceutical research and development. The government should establish a sound and reasonable system to protect drug innovation, safeguard the legitimate rights and interests of intellectual property owners, and promote healthy market competition.

We also recommend that the government should guide pharmaceutical manufacturing firms to actively fulfill their social responsibilities. Besides the research and development of innovative drugs, drug quality is also one of the core factors affecting the sustainable survival and development of pharmaceutical manufacturing firms. Firstly, the government can leverage the MAH system to encourage pharmaceutical manufacturing firms to enhance their efforts in attracting and cultivating innovative talents, as this is an internal driving force directly influencing the firms' sustainable innovation. Secondly, the government should strengthen drug quality management and improve relevant systems. Through

measures such as supervision and punishment, the government can enhance firms' attention to and investment in drug quality. Thirdly, the government can streamline the social supervision and management mechanism. By setting up hotlines and mailboxes for reporting, the government can strengthen public supervision over pharmaceutical manufacturing firms and encourage the reporting of their improper behaviors.

In addition to this, we suggest that the government should optimize the supply chain of pharmaceuticals from R&D to manufacturing and distribution in a number of ways. Firstly, we suggest that the government can establish a comprehensive supplier information platform for the pharmaceutical industry. The government can integrate raw material suppliers, intermediates and excipients suppliers, and production equipment suppliers and other types of information, including product quality, price, capacity, reputation, etc., to provide detailed supplier information resources for pharmaceutical manufacturers, reducing the degree of information asymmetry. The government can also use the platform for dynamic monitoring of the operating conditions, reputation and quality of suppliers of pharmaceutical manufacturing firms, and timely release of relevant information and early warning signals. Second, the government should strengthen the macro-control of the pharmaceutical R&D and manufacturing market to guide healthy competition. In particular, the government needs to pay real-time attention to market monopoly behavior, and once firms are found to have gained or maintained an excessive market share through improper means, such as abusing a dominant market position and engaging in price monopoly, the government should investigate and punish them in a timely manner.

For other countries, the conclusions of this study also have certain reference value for their policy systems. For countries like Europe that have implemented the MAH system in the past, first of all, they can promote the establishment of a cross-border MAH regulatory collaboration mechanism. For instance, these countries can promote the standardized sharing of MAH data among EU member states, including drug safety data, credit records of holders, etc. Secondly, establish and improve the full life cycle liability insurance for MAH. The government can collaborate with insurance companies to develop differentiated insurance products, such as high-risk and high-coverage innovative drugs and low-premium generic drugs, to diversify the risks of the holders.

For some countries that have not yet implemented the MAH system, we suggest that these countries can give priority to piloting the limited MAH system in the field of generic drugs, allowing domestic research and development institutions to act as the holders and entrust local branches or regional cmos of multinational pharmaceutical companies to produce. In addition, these countries can cooperate with the international patent pool to authorize local enterprises to produce specific drugs whose patents have expired. The MAH qualification will only be granted to enterprises that commit to local supply, and regulatory personnel will be trained simultaneously.

7.2.2 Management recommendations

We advise pharmaceutical manufacturing companies to strengthen R & D and cooperation. First, pharmaceutical manufacturing firms should enhance cooperation with other enterprises in R & D. Firms with technological and equipment advantages can cooperate with those having market and channel advantages. This cooperation can accelerate the process of new drugs from R & D to sales, and also give full play to their comparative advantages. Meanwhile, domestic firms can establish a cooperation with internationally renowned pharmaceutical firms. By doing so, they can introduce advanced foreign technology and management experience, participate in international drug R & D projects and standard - setting, thus enhancing the visibility and competitiveness of domestic pharmaceutical manufacturing firms in the international arena. Secondly, we suggest that pharmaceutical manufacturing firms strengthen their cooperation with universities and research institutes. Firms can integrate the resources of all parties to establish an industry - university - research platform. They can combine the financial and business advantages of state - owned firms with the R & D resources of scientific research institutes to jointly carry out major drug innovation projects, improving the efficiency of innovation.

We also urge that pharmaceutical manufacturing firms formulate a reasonable compensation system and other incentive measures. Firstly, to fully leverage the institutional advantages of MAH, pharmaceutical manufacturing firms must increase the compensation and other incentives for R & D personnel. Only by attracting, retaining, and motivating R & D talents can these firms ensure a strong innovation impetus. Secondly, apart from R & D personnel, firms must ensure and continuously improve the salary guarantees for front - line production workers. Production workers play a crucial role in pharmaceutical manufacturing firms, and their attitudes directly determine the quality of drugs. Based on meeting their basic needs, firms should use various incentive measures to enhance their sense of identity and belonging. Coupled with strict production management systems, this can ensure that drug production quality meets the standards.

In addition, we suggest that pharmaceutical manufacturing firms strengthen their supply chain management. Firstly, although we have not found that MAH has a significant impact on the supplier concentration of pharmaceutical manufacturing firms, we recommend that these firms enhance their management of suppliers. Pharmaceutical innovation carries high risks. Once suppliers encounter issues such as raw material shortages, contract disputes, or quality problems, purchasers will face significant production and operational risks. Furthermore, we suggest that pharmaceutical manufacturing firms appropriately strengthen their management of customers. Every link, from R & D to production and then to sales, is of vital importance. Pharmaceutical manufacturing firms should not only actively respond to market demands by researching and developing targeted new drugs but also increase promotional efforts based on genuine product features to enhance market competitiveness and promote continuous innovation.

7.3 Limitations

Our research has certain unaddressed limitations. Firstly, we primarily focused on the impact of MAH on the Chinese pharmaceutical market. In advanced countries such as those in Europe and America, MAH was implemented long ago and they have already entered the next stage. While our empirical evidence offers reference for many similar emerging countries, there is a lack of discussion on developed countries. Secondly, China fully implemented MAH after

2020, and some new issues emerged during this process. Meanwhile, after the COVID - 19 pandemic, global pharmaceutical research, development, and manufacturing have entered a new phase. We must admit that in order to respond to major sudden diseases, pharmaceutical - related systems (e.g., pharmaceutical regulatory systems) need further innovation. Relevant research should continuously pay attention to new systems. Thirdly, our research did not fully support the claim that MAH has a significant impact on the supplier concentration of pharmaceutical manufacturing firms. This conclusion may be affected by variable measurement and data quality. Perhaps subsequent research can provide evidence to support this view.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

JL: Conceptualization, Data curation, Formal analysis, Funding acquisition, Methodology, Software, Visualization, Writing – original draft, Writing – review & editing.

Funding

The author(s) declare that no financial support was received for the research and/or publication of this article.

Conflict of interest

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The author(s) declare that no Gen AI was used in the creation of this manuscript.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

References

1. Market C. M.. (2022). Precedence research. Available online at:https://www.precedenceresearch.com/cryptocurrency-mining-market (data zvernennia: 15.07. 2023).

2. Annett S. Pharmaceutical drug development: high drug prices and the hidden role of public funding. *Biologia Futura*. (2021) 72:129–38. doi: 10.1007/s42977-020-00025-5

3. He X, Xie Z, Wang CH. Selection of new employees in environmental technology company by MCDM. *J Environ Prot Ecol*. (2021) 22:1220–6.

4. Al-Omran K, Abahussain A, Khan E. Integrated environmental assessment of medical waste management in the Kingdom of Bahrain. *Sustain For*. (2023) 15:2397. doi: 10.3390/su15032397

5. Beigaite R., Baranauskaite-Fedorova I., Dvarioniene J. (2021). Assessment and management of pharmaceutical substances in the environment. In Computational Science and Its Applications–ICCSA 2021: 21st International Conference, Cagliari, Italy

6. Gridchyna I, Aulois-Griot M, Maurain C, Bégaud B. How innovative are pharmaceutical innovations? The case of medicines financed through add-on payments outside of the French DRG-based hospital payment system. *Health Policy*. (2012) 104:69–75. doi: 10.1016/j.healthpol.2011.11.007

7. Schuhmacher A, Gassmann O, Hinder M. Changing R & D models in research-based pharmaceutical companies. *J Transl Med*. (2016) 14:1–11. doi: 10.1186/s12967-016-0838-4

8. Niwash MNK, Cek K, Eyupoglu SZ. Intellectual capital and competitive advantage and the mediation effect of innovation quality and speed, and business intelligence. *Sustain For*. (2022) 14:3497. doi: 10.3390/su14063497

9. Li X, Xu J. Does China's national volume-based drug procurement policy promote or hinder pharmaceutical innovation? *Front Pharmacol*. (2024) 15:1392239. doi: 10.3389/fphar.2024.1392239

10. Liu GG, Wu J, He X, Jiang Y. Policy updates on access to and affordability of innovative medicines in China. *Value Health Reg Issues*. (2022) 30:59–66. doi: 10.1016/j.vhri.2021.12.003

11. Liu Q, Wang S, Huang Z. The impact of the drug marketing authorization holder system on sustainable improvement of innovation quality in the pharmaceutical manufacturing industry in China—An empirical study using synthetic control methods. *PLoS One*. (2024) 19:e0304056. doi: 10.1371/journal.pone.0304056

12. Wan P, He F, Zhang H. Can the separation of marketing authorization from manufacturing authorization stimulate pharmaceutical innovation? Evidence from China's pharmaceutical industry reform. *Econ Anal Policy*. (2024) 83:734–48. doi: 10.1016/j.eap.2024.07.020

13. Han QQ, Zhang Q. The study on implementation and suggestions of drug marketing authorization holder in China. *Zhongguo Xin Yao Za Zhi*. (2019) 28:593–7.

14. Gallo V, Alessi E, Montilla S, Altamura G, Traversa G, Trotta F. The timelines for the price and reimbursement authorization in Italy 2018–2020. *Front Med*. (2022) 9:1055359. doi: 10.3389/fmed.2022.1055359

15. Ribeiro J. P. S. (2017) Internship reports and monograph entitled "the regulatory world of generic medicines and patents" (Order No. 29195743). Available from ProQuest Dissertations & Theses Global A&I: The Sciences and Engineering Collection. (2700777682). Retrieved from https://www-proquest-com-443.wvpn.hrbeu.edu.cn/dissertations-theses/internship-reports-monograph-entitled-regulatory/docview/2700777682/se-2

16. Schwartzberg E, Ainbinder D, Vishkauzan A, Gamzu R. Drug shortages in Israel: regulatory perspectives, challenges and solutions. *Isr J Health Policy Res*. (2017) 6:1–8. doi: 10.1186/s13584-017-0140-9

17. Sickmüller B, Thurisch B, Kaszkin-Bettag M. Proposal for publishing and parallel reporting of case reports on adverse drug reactions to authorities by physicians. *Global Adv Health Med*. (2013) 2:7. doi: 10.7453/gahmj.2013.007

18. Stammwitz V, Honnens Ä, Hochhuth D, Schuberth HJ. Increase of adverse events after intravenous injection of gentamicin in horses between 2015 and 2017—from marketing authorization holder's point of view. *Front Vet Sci*. (2021) 8:710571. doi: 10.3389/fvets.2021.710571

19. Handa N, Ishii K, Matsui Y, Ando Y. Reporting of cardiovascular medical device adverse events to pharmaceuticals and medical devices agency, Japan. *EBioMedicine*. (2015) 2:1211–6. doi: 10.1016/j.ebiom.2015.07.011

20. Alsaleh H, Alshammari TM. Direct healthcare professional communications: a quantitative assessment study. *Pharmacol Res Perspect*. (2021) 9:e00763. doi: 10.1002/prp2.763

21. Xie JP, Sun YY, Peng N, Shao R. The influence and cohesion suggestions of the MAH system on the current regulatory systems. *Chin J Health Policy*. (2018) 12:1–6. doi: 10.3969/j.issn.1674-2982.2018.12.001

22. Haishi Y., Yingzhu J., Weijun Z. (2020). Status analysis on the marketing authorization holder of China's drugs. In E3S Web of Conferences (185, p. 04009).

23. Furtner D, Hutas G, Tan BJW, Meier R. Journey from an enabler to a strategic leader: integration of the medical affairs function in ESG initiatives and values. *Pharma Med*. (2023) 37:405–16. doi: 10.1007/s40290-023-00485-9

24. Yu K, Wu Q, Chen X, Wang W, Mardani A. An integrated MCDM framework for evaluating the environmental, social, and governance (ESG) sustainable business performance. *Ann Oper Res*. (2024) 342:987–1018. doi: 10.1007/s10479-023-05616-8

25. Lee H, Kim SY, Kim G, Kang HY. Public preferences for corporate social responsibility activities in the pharmaceutical industry: empirical evidence from Korea. *PLoS One*. (2019) 14:e0221321. doi: 10.1371/journal.pone.0221321

26. Bae G, Ahn JH, Lim KM, Bae S. Corporate social responsibility of pharmaceutical industry in Korea. *Front Pharmacol*. (2022) 13:950669. doi: 10.3389/fphar.2022.950669

27. Tan J, Wei J. Configurational analysis of ESG performance, innovation intensity, and financial leverage: a study on total factor productivity in Chinese pharmaceutical manufacturing firms. *J Knowl Econ*. (2023) 15:1–25. doi: 10.1007/s13132-023-01678-y

28. Ho VH. Enlightened shareholder value: corporate governance beyond the shareholder-stakeholder divide. *J Corp L*. (2010) 36:59.

29. Thayer CE, Fine AH. Evaluation and outcome measurement in the non-profit sector: stakeholder participation. *Eval Program Plann*. (2001) 24:103–8. doi: 10.1016/S0149-7189(00)00051-3

30. Pal P. Treatment and disposal of pharmaceutical wastewater: toward the sustainable strategy. *Sep Purif Rev*. (2018) 47:179–98. doi: 10.1080/15422119.2017.1354888

31. Petrova E. Innovation in the pharmaceutical industry: the process of drug discovery and development In: Editors Ding M, Eliashberg J, Stremersch S. Innovation and Marketing in the Pharmaceutical Industry: Emerging Practices, Research, and Policies. New York, NY: Springer New York (2013). 19–81.

32. Muhr SM. Exploring job placement in the BioCapital pharmaceutical industry: a quantitative analysis. Minneapolis, Minnesota, USA: Capella University (2007).

33. Grewal R, Chakravarty A, Ding M, Liechty J. Counting chickens before the eggs hatch: associating new product development portfolios with shareholder expectations in the pharmaceutical sector. *Int J Res Mark*. (2008) 25:261–72. doi: 10.1016/j.ijresmar.2008.07.001

34. Li Y, Zhu C. Regional digitalization and corporate ESG performance. *J Clean Prod*. (2024) 473:143503. doi: 10.1016/j.jclepro.2024.143503

35. Xu Y, Zhu C. Do green supply chains promote firm environmental information disclosure? *Pol J Environ Stud*. (2024) 34:1807–22. doi: 10.15244/pjoes/188065

36. Zhu C, Cheng Z, Li J. Is it possible for government intervention to support low-carbon transition in agriculture through Agri-environmental protection? Evidence from the waste agricultural film recycling pilot. *Pol J Environ Stud*. (2024) 34:1973–93. doi: 10.15244/pjoes/187140

37. Dong F, Dai Y, Zhang S, Zhang X, Long R. Can a carbon emission trading scheme generate the porter effect? Evidence from pilot areas in China. *Sci Total Environ*. (2019) 653:565–77. doi: 10.1016/j.scitotenv.2018.10.395

38. Zhang Z. Can energy internet improve corporate ESG performance?--evidence from Chinese high energy-consuming companies. *Heliyon*. (2024) 10. doi: 10.1016/j.heliyon.2024.e24175

39. Kong R, Zhu C. Green agriculture: an assessment of the effectiveness of centralized management of contaminated cropland in China. *Pol J Environ Stud*. (2024). doi: 10.15244/pjoes/192362

40. Cheng Z, Zhu C. Positive impacts of green finance on environmental protection investment: evidence from green finance reform and innovations pilot zone. *Heliyon*. (2024) 10:e33714. doi: 10.1016/j.heliyon.2024.e33714

41. Du Z, Zhu C, Zhou Y. Increasing quantity or improving quality: can soil pollution control promote green innovation in China's industrial and mining enterprises? *Sustain For*. (2022) 14:14986. doi: 10.3390/su142214986

42. Li Y, Zhu C, Zhang K, Yang Z. The impact of electricity marketization reform on carbon emission-a quasi-natural experiment based on electricity spot market construction. *Pol J Environ Stud*. (2024). doi: 10.15244/pjoes/193583

43. Hua YF, Lu J, Bai B, Zhao HQ. Can the profitability of medical enterprises be improved after joining China's centralized drug procurement? A difference-in-difference design. *Front Public Health*. (2022) 9:809453. doi: 10.3389/fpubh.2021.809453

44. Huang X. The impact of green stock indices and ESG considerations on sustainable finance—a study of Chinese green indices. *Financ Eng Risk Manage*. (2023) 6:143–50.

45. Chan KC, Chen Y, Liu B. The linear and non-linear effects of internal control and its five components on corporate innovation: evidence from Chinese firms using the COSO framework. *Eur Account Rev*. (2021) 30:733–65. doi: 10.1080/09638180.2020.1776626

46. Lin X, Zhu H, Meng Y. ESG greenwashing and equity mispricing: evidence from China. *Finance Res Lett*. (2023) 58:104606. doi: 10.1016/j.frl.2023.104606

47. Ronen J. Earnings management. New York, NY: Springer (2008).

48. Hamza S, Jarboui A. Esg performance and disclosure quality: does a well-balanced board of directors matter when impression management occurs? *EuroMed J Bus*. (2024). doi: 10.1108/EMJB-05-2023-0140

49. Treviño L. J. (2016). Institutional theory and institution building in emerging economies. Editors Merchant H. Handbook of contemporary research on emerging markets (pp. 62–87). UK: Edward Elgar Publishing.

50. North DC. Institutions, institutional change and economic performance. Cambridge, England: Cambridge university press (1990).

51. Chen VZ, Li J, Shapiro DM, Zhang X. Ownership structure and innovation: an emerging market perspective. *Asia Pac J Manag*. (2014) 31:1–24. doi: 10.1007/s10490-013-9357-5

52. Zhu F, Fan H, Zheng Z. The disclosure fog: institutional investors and corporate greenwashing. *Int J Finance Econ*. (2025). doi: 10.1002/ijfe.3096

53. Tan W, Cai Y, Luo H, Zhou M, Shen M. ESG, technological innovation and firm value: evidence from China. *Int Rev Financ Anal*. (2024) 96:103546. doi: 10.1016/j.irfa.2024.103546

54. GOV CN. Notice on the issuance of the pilot programme for the system of holders of listed permits for pharmaceuticals. Available online at:https://www.gov.cn/gongbao/content/2016/content_5086349.htm (accessed on May 26th, 2016).

55. Li Y, Zhu C. Unlocking the value of data: the impact of market allocation of data elements on corporate green innovation. *Pol J Environ Stud*. (2024). doi: 10.15244/pjoes/191960

56. Liu Y, Zhang N, Xie C, Jiang Y, Qin Y, Zhou L, et al. Evolution of drug regulations and regulatory innovation for anticancer drugs in China. *Acta Pharm Sin B*. (2022) 12:4365–77. doi: 10.1016/j.apsb.2022.08.004

frontiers | Frontiers in Health Services

TYPE Original Research
PUBLISHED 12 June 2025
DOI 10.3389/frhs.2025.1621018

Check for updates

OPEN ACCESS

EDITED BY
Kevin Lu,
University of South Carolina, United States

REVIEWED BY
Valentin Marian Antohi,
Dunarea de Jos University, Romania
Davi Rumel,
Retired, Brazil
Xinyi Xu,
Guangxi Medical University, China

*CORRESPONDENCE
Weizhang Huang
66191322@qq.com

†These authors have contributed equally to this work

RECEIVED 06 May 2025
ACCEPTED 26 May 2025
PUBLISHED 12 June 2025

CITATION
Wu B, Wu W, Wang X, Huang W, Luo Z and Li J (2025) Evaluating and enhancing the service capacity of secondary public hospitals in urban China: a multi-method empirical analysis based on Guangzhou (2019–2023). Front. Health Serv. 5:1621018. doi: 10.3389/frhs.2025.1621018

COPYRIGHT
© 2025 Wu, Wu, Wang, Huang, Luo and Li. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

Evaluating and enhancing the service capacity of secondary public hospitals in urban China: a multi-method empirical analysis based on Guangzhou (2019–2023)

Baoling Wu[1,2†], Wenbo Wu[1†], Xi Wang[2], Weizhang Huang[1*], Zhenni Luo[3] and Jifeng Li[4]

[1]The Second Affiliated Hospital, Guangzhou Medical University, Guangzhou, Guangdong, China, [2]Faculty of Humanities and Social Sciences, Macau Polytechnic University, Macau, China, [3]School of Health Management, Guangzhou Medical University, Guangzhou, Guangdong, China, [4]School of Public Health, Guangzhou Medical University, Guangzhou, Guangdong, China

Background: Secondary public hospitals play a pivotal role in China's hierarchical medical system, serving as a critical intermediary tier. However, in rapidly urbanizing cities such as Guangzhou, these hospitals face mounting challenges including widening efficiency disparities, imbalanced resource allocation, and weak governance structures. This study aims to systematically evaluate the evolution and spatial dynamics of service capacity among secondary general public hospitals in Guangzhou, offering empirical evidence to support capacity improvement and policy optimization.

Methods: A composite evaluation framework was constructed across three dimensions: medical quality, operational efficiency, and sustainability. Based on panel data from 12 secondary general public hospitals in Guangzhou between 2019 and 2023, we applied a combination of Entropy-TOPSIS model, Kernel Density Estimation (KDE), and the Dagum Gini Coefficient to assess overall service capacity levels, temporal trends, and spatial inequalities.

Results: The findings indicate a general upward trend in service capacity; however, disparities among hospitals have intensified. While indicators of medical safety (e.g., mortality and complication rates) have steadily improved, there remains significant divergence in surgical ratios and pharmaceutical service coverage—particularly in peripheral areas. KDE analysis reveals a transition from unimodal to bimodal distribution, indicating stratification of service capacity. Decomposition of the Dagum Gini Coefficient shows that transvariation (inter-group overlaps) is the main source of inequality, underscoring increasing cross-regional capacity divergence.

Conclusions: Although Guangzhou's secondary public hospitals have shown overall improvement, challenges remain in terms of regional coordination and internal structural disparities. This study recommends differentiated interventions such as specialty alliances, performance-based resource allocation, and workforce optimization to enhance system resilience and equity. The proposed evaluation model demonstrates strong applicability and scalability, offering theoretical and empirical insights for healthcare system governance in other rapidly urbanizing regions.

KEYWORDS

secondary public hospitals, healthcare service capacity evaluation, entropy-topsis, kernel density estimation, Dagum Gini coefficient

1 Introduction

Amid the deepening reform of global health systems, enhancing the service capacity of public hospitals—particularly secondary-level general public hospitals in urban areas—has become a focal issue in health policy development worldwide. These hospitals, positioned between primary care institutions and tertiary hospitals, are essential for receiving referrals from the community level and managing moderately complex conditions. They serve a bridging role within China's hierarchical diagnosis and treatment system.

However, in the context of rapid urbanization, secondary hospitals in many developing countries face significant challenges, including underdeveloped resource allocation and insufficient attention to their service capacity. Studies have shown that in Nanjing, China, for example, healthcare resources are unevenly distributed, with high concentration in central districts and much weaker capacity in peripheral areas (1). In Nigeria, urbanization has resulted in medical personnel migrating toward cities, thereby reducing healthcare accessibility in rural areas—especially for the elderly (2). Similarly, in Thailand, urban expansion has widened the accessibility gap between urban and rural medical facilities, highlighting the need for spatial planning interventions to ensure more equitable resource distribution (3). These cases reflect a common challenge: urbanization places significant pressure on the equity and sustainability of healthcare systems.

To respond to these challenges, the global community is increasingly recognizing the need to strengthen hospital service capacity, especially by empowering "middle-tier" institutions. As urbanization alters the structure of healthcare demand, scientifically evaluating and optimizing resource allocation and hospital capacity has become a shared concern among health policymakers.

In recent years, various international organizations and research institutes have introduced frameworks to support performance-based resource planning. The World Health Organization (WHO) has promoted performance-oriented allocation models that emphasize service integration to improve the efficiency of healthcare systems. Strengthening secondary hospitals is a key part of this effort, with WHO advocating for them to act as regional service "hubs" that support integration with primary care and public health services, thereby optimizing resource use for specific populations (4). In 2003, the WHO Regional Office for Europe developed the Performance Assessment Tool for Quality Improvement in Hospitals (PATH), which evaluates hospital performance across dimensions such as clinical effectiveness, efficiency, and staff orientation. After being piloted in six countries between 2004 and 2006, PATH expanded in 2007–2008 to 140 hospitals across eight European countries including Belgium, France, and Germany (5, 6). In 2010, the WHO and USAID jointly launched the Service Availability and Readiness Assessment (SARA), offering manuals (7) and implementation guides (8) to assess the accessibility and readiness of health services. This framework has since been adopted in Bangladesh, Burkina Faso, Ghana, Mozambique, and other countries (9–13).

Meanwhile, methodological innovations in healthcare capacity evaluation are trending toward diversification and integration. These methods are widely used in assessing service efficiency, optimizing resource allocation, and analyzing regional equity. Multi-Criteria Decision Analysis (MCDA) approaches, including entropy-weighted TOPSIS, Analytic Hierarchy Process (AHP), and Stochastic Frontier Analysis (SFA), have been broadly applied in hospital performance evaluation and healthcare efficiency comparisons (14, 15).

In pursuit of Sustainable Development Goal 3—"Ensure healthy lives and promote well-being for all at all ages"—scholars are increasingly integrating spatial and inequality analytics. For example, Kernel Density Estimation (KDE), a non-parametric method, has been widely used to explore spatial clustering and evolution of healthcare capacity (16). In contrast, the Dagum Gini coefficient offers decomposable metrics that allow more detailed examination of within-region, between-region, and transvariation (overlap) inequality, outperforming the traditional Gini index in explaining structural disparities (17).

China's healthcare system is structured into three levels, with secondary general public hospitals playing a central role in the implementation of hierarchical diagnosis and treatment. These hospitals primarily serve urban and peri-urban populations by offering general diagnostic, inpatient, and outpatient care. They are also essential in public health initiatives such as chronic disease management and epidemic response. However, compared with tertiary hospitals, secondary hospitals often fall into a "resource valley"—marked by shortages in manpower, equipment, and policy attention. Moreover, their contribution is frequently overlooked in policy prioritization and funding, which leads to weakened functional roles. Although academic interest in secondary hospitals has grown, most studies remain focused on single-year financial or performance metrics, lacking insight into the dynamic evolution of capacity or structural inequality—especially in megacities with pronounced development imbalances (18, 19). Furthermore, the COVID-19 pandemic exposed the vulnerabilities of hospital systems, prompting a re-evaluation of the resilience and load-bearing capacity of non-core hospitals. Secondary hospitals played a crucial role in initial diagnosis and triage, yet lacked the tertiary hospitals' infrastructure and resources—highlighting the need for more refined evaluation tools and targeted governance strategies (20, 21).

In light of this context, this study focuses on Guangzhou, a major city in South China, and examines 12 secondary general public hospitals from 2019 to 2023. A comprehensive evaluation framework is developed based on three key dimensions:

- Medical Quality (e.g., average length of stay, surgical complication rates),
- Operational Efficiency (e.g., income structure, cost containment),
- Sustainability (e.g., staffing ratios, physician workload intensity).

Methodologically, the study integrates three analytical tools:

- Entropy-weighted TOPSIS, which enables objective weighting and ranking of hospitals based on service capacity;

- Kernel Density Estimation (KDE), to examine the evolution of score distributions over time;
- Dagum Gini Coefficient decomposition, to measure and decompose spatial inequality in service capacity.

By triangulating results from these methodologies, this study proposes a replicable and transferable evaluation framework tailored to secondary hospitals in urban China. It aims to support local policy evaluation in Guangzhou and offer insights for improving healthcare system governance in other rapidly urbanizing regions. In addressing the global challenges of "filling the gaps" and "strengthening mid-tier institutions," this study seeks to contribute reform strategies and analytical methods that are both empirically grounded and globally applicable.

2 Materials and methods

2.1 Data sources

This study targets 12 secondary general public hospitals located within the administrative boundaries of Guangzhou. A comprehensive evaluation index system was developed to assess their healthcare service capacity (see Table 1). The index system is structured into three primary dimensions, each representing a core pillar of institutional performance:

- Medical Quality: This dimension evaluates clinical outcomes and safety. Indicators include average length of stay, low-risk group mortality rate, surgical rate, complication rate. These measures reflect the hospital's ability to deliver safe, effective, and timely care—essential to meeting patient expectations and improving health outcomes.
- Operational Efficiency: This component assesses resource use and cost containment. It includes the ratio of service revenue to total revenue, personnel cost ratio, asset-liability ratio, outpatient and inpatient cost growth. These indicators are crucial for evaluating financial sustainability and responsiveness to health payment reforms, such as Diagnosis-Related Group (DRG)–based funding.
- Sustainability: This dimension captures human resource adequacy and service resilience. It includes nurse-to-doctor ratio, physician workload, pharmacist staffing. These indicators help identify whether hospitals possess the staffing capacity to maintain stable service delivery under both routine and emergency conditions.

The selection of these three dimensions ensures a balanced and policy-relevant assessment framework. It integrates clinical effectiveness, economic performance, and long-term institutional resilience—aligning with national healthcare reform goals and international standards in health systems evaluation.

Each secondary indicator is defined with its unit, orientation (positive/negative), and coded numerically (X_1–X_{14}). The indicators collectively form a multidimensional representation of hospital service capacity. Data were drawn from multiple sources spanning 2019 to 2023, including the *Guangzhou Statistical Yearbook*, official reports from the Guangzhou Health Commission, and municipal government publications.

TABLE 1 Evaluation index system for healthcare service capacity of secondary public hospitals.

Primary dimension	Secondary indicator	Unit	Indicator orientation	Code
Medical quality	Average length of stay	Days	Negative	X_1
	Mortality rate of low-risk patients	%	Negative	X_2
	Proportion of discharged patients who underwent surgery	%	Positive	X_3
	Complication rate among surgical patients	%	Negative	X_4
Operational efficiency	Proportion of medical service revenue (excluding drugs, consumables, and diagnostic fees)	%	Positive	X_5
	Personnel expenditure as a proportion of operational expenditure	%	Positive	X_6
	Asset-liability ratio	%	Negative	X_7
	Growth rate of per outpatient visit cost	%	Negative	X_8
	Growth rate of per outpatient drug cost	%	Negative	X_9
	Growth rate of per inpatient cost	%	Negative	X_{10}
	Growth rate of per inpatient drug cost	%	Negative	X_{11}
Sustainability	Nurse-to-doctor ratio	%	Positive	X_{12}
	Average daily inpatient workload per licensed physician	Bed-days	Negative	X_{13}
	Number of pharmacists per 100 hospital beds	Persons	Positive	X_{14}

2.2 Research methods

To ensure robustness and multidimensional insights, three quantitative methods were employed:

2.2.1 Entropy weight-TOPSIS method

The Entropy-Weighted TOPSIS method integrates entropy-based weight assignment with the TOPSIS (Technique for Order Preference by Similarity to Ideal Solution) approach to handle multi-criteria decision-making problems (22–24). It addresses challenges associated with subjective weighting and correlation among indicators, and is widely applied in healthcare, construction, and industrial evaluation scenarios (23, 25–27, 28). Stepwise procedure:

Step 1: Normalization of the Original Data Matrix

Let there be n evaluation objects (e.g., hospitals) and m evaluation indicators. The original data matrix is denoted as:

$$X = \begin{Bmatrix} x_{11} & x_{12} & \dots & x_{1m} \\ x_{21} & x_{22} & \dots & x_{2m} \\ \dots & \dots & \dots & \dots \\ x_{n1} & x_{n2} & \dots & x_{nm} \end{Bmatrix} n \times m$$

To standardize the original matrix X, we apply min-max normalization to obtain the normalized matrix $R = (r_{ij})n \times m$, where $r_{ij} \in [0, 1]$ represents the normalized score of the i -th object on the j-th indicator:

- For positive indicators (the higher, the better): $r_{ij} = \frac{x_{ij} - \min(x_j)}{\max(x_j) - \min(x_j)}$
- For negative indicators (the lower, the better): $r_{ij} = \frac{\max(x_j) - x_{ij}}{\max(x_j) - \min(x_j)}$
- Step 2: Entropy-Based Weight Calculation and Weighted Matrix Construction

Let l_{ij} denote the normalized proportion of indicator j for object i, computed from matrix R:

$$l_{ij} = \frac{r_{ij}}{\sum_{i=1}^{n} r_{ij}}$$

Define e_j as the entropy value for indicator j. The weight w_j is then calculated as:

$w_j = \frac{1 - e_j}{\sum_{j=1}^{m} (1 - e_j)}$, $0 \le w_j \le 1$, $\sum_{j=1}^{m} w_j = 1$

The weighted normalized matrix Z is obtained by:

$$Z = w_j \times R = \begin{Bmatrix} w_1 r_{11} & w_2 r_{12} & \dots & w_m r_{1m} \\ w_1 r_{21} & w_2 r_{22} & \dots & w_m r_{2m} \\ \dots & \dots & \dots & \dots \\ w_1 r_{n1} & w_2 r_{n2} & \dots & w_m r_{nm} \end{Bmatrix} = \begin{Bmatrix} z_{11} & z_{12} & \dots & z_{1m} \\ z_{21} & z_{22} & \dots & z_{2m} \\ \dots & \dots & \dots & \dots \\ z_{n1} & z_{n2} & \dots & z_{nm} \end{Bmatrix}$$

Step 3: Identify Ideal and Anti-Ideal Solutions

For each indicator j, determine the best (ideal) and worst (anti-ideal) values:

- Ideal solution: $z_j^+ = \max(z_{jj})$, thus $z_j^+ = (z_1^+, z_2^+, \dots, z_m^+)$
- Anti-ideal solution: $z_j^- = \min(z_{jj})$, thus $z_j^- = (z_1^-, z_2^-, \dots, z_m^-)$
- Step 4: Calculate Euclidean Distances

For each evaluation object i, compute its distance to the ideal and anti-ideal solutions:

- Distance to ideal: $d_i^+ = \sqrt{\sum_{j=1}^{m} (z_{ij} - z_j^+)^2}$
- Distance to anti-ideal: $d_i^- = \sqrt{\sum_{j=1}^{m} (z_{ij} - z_j^-)^2}$
- Step 5: Compute Relative Closeness to the Ideal Solution

The relative closeness coefficient v_i is calculated as:

$$v_i = \frac{d_i^-}{d_i^+ + d_i^-},\ 0 \le v_i \le 1$$

A higher v_i indicates stronger service capacity of the corresponding hospital. The ranking of v_i values reflects the comparative performance across all evaluated hospitals.

2.2.2 Kernel density estimation (KDE)

KDE is a non-parametric method for estimating the probability density function of a continuous variable, offering flexibility in modeling data distributions without assuming a parametric form (29–31). It is especially valuable in visualizing temporal evolution and regional heterogeneity in healthcare quality assessments (32–34).

The Gaussian kernel function is adopted:

$$\widehat{f}_h(x) = \frac{1}{\mathrm{nh}} \sum_{n=1}^{n} K\left(\frac{x_i - \bar{x}}{h}\right)$$

where $K(\cdot)$ is the Gaussian kernel, h is the bandwidth, and n is the sample size.

KDE allows the visualization of capacity distribution shifts and stratification patterns across years, highlighting convergence or divergence trends.

2.2.3 Dagum Gini coefficient decomposition

The Dagum Gini coefficient, proposed by Argentine-Canadian economist Camilo Dagum in the 1970s, represents a significant advancement over the traditional Gini index. It is based on the three-parameter Dagum probability distribution, which offers superior fitting performance—particularly in capturing inequalities at both tails of a distribution. Its key advantage lies in its decomposability, enabling the total inequality to be separated into within-group inequality, between-group inequality, and transvariation (overlapping) inequality components. This makes the Dagum Gini model a powerful analytical tool for examining the structural dimensions of inequality (35, 36). Due to its enhanced explanatory capacity, it has been widely applied across economics, social sciences, public policy, and healthcare resource allocation to investigate the deep structures and dynamic mechanisms underlying inequality (37, 38).

In this study, the Dagum Gini coefficient is applied using subgroup decomposition to assess the spatial differentiation in healthcare service capacity among secondary public general hospitals in Guangzhou. The total inequality G is composed of the following three components:

$$G = G_w + G_{nb} + G_t$$

The respective formulas are defined as follows:

- Total Gini Coefficient:

$$G = \frac{\sum_{j=1}^{k}\sum_{h=1}^{k}\sum_{i=1}^{n_j}\sum_{r=1}^{n_h}|y_{ji} - y_{hr}|}{2n^2\bar{y}}$$

- Within-Region Inequality:

$$G_{jj} = \frac{\sum_{i=1}^{n_j}\sum_{r=1}^{nj}|y_{ji} - y_{hr}|}{2\bar{y_j}n_j^2}$$

- Between-Region Inequality:

$$G_{jh} = \frac{\sum_{i=1}^{n_j}\sum_{r=1}^{nh}|y_{ji} - y_{hr}|}{n_j n_h(\bar{y_j} + \bar{y_h})}$$

- Decomposition of Within-Region Inequality:

$$G_w = \sum_{j=1}^{k} G_{jj}p_j s_j$$

- Decomposition of Between-Region Inequality:

$$G_{nb} = \sum_{j=2}^{k}\sum_{h=1}^{j-1} G_{jh}(p_j s_h + p_h s_j)D_{jh}$$

- Transvariation (Overlapping Component):

$$G_t = \sum_{j=2}^{k}\sum_{h=1}^{j-1} G_{jh}(p_j s_h + p_h s_j)(1 - D_{jh})$$

Where y_{ji} and y_{hr} denote the healthcare service capacity of hospital i in region j and hospital r in region h, respectively. $\bar{y}$ represents the overall average service capacity across all hospitals, while $\bar{y}_j$ denotes the mean capacity within region j. n is the total number of hospitals, and n_j , n_h are the number of hospitals in regions j and h, respectively. The term $p_j = \frac{n_j}{n}$ indicates the proportion of hospitals in region j, and $s_j = \frac{n_j\bar{y}_j}{n\bar{y}}$ reflects the weighted contribution of region j to the overall capacity level. D_{jh} is a directional influence index that measures the relative dominance of region j compared to region h in terms of healthcare service capacity.

3 Results and analysis

3.1 Descriptive analysis of Key indicators

Based on the statistical summary in Table 2, the healthcare service capacity of Guangzhou's 12 secondary general public hospitals demonstrated a combination of progress and divergence across the three key dimensions between 2019 and 2023.

3.1.1 Medical quality (X_1–X_4)

- The average length of stay (X_1) increased from 7.93 days in 2019 to 9.68 days in 2023, indicating a slowdown in patient turnover efficiency. The substantial rise during 2020–2021 corresponds to COVID-19 control policies that extended hospitalization duration. The increasing standard deviation over time suggests growing variability in treatment efficiency among hospitals.
- The mortality rate for low-risk patients (X_2) dropped sharply from 0.999% to 0.247%, alongside a dramatic decrease in variance. This reflects notable improvements in medical safety and standardization in treatment practices across facilities.
- The surgical discharge ratio (X_3), which peaked at 26.97% in 2020, dropped significantly to 16.88% in 2023. This could be attributed to shifts in disease case-mix, surgical policy adjustments, or redistribution of surgical resources during the pandemic.
- The surgical complication rate (X_4) decreased modestly throughout the period, indicating an overall improvement in surgical safety and intraoperative risk management.

TABLE 2 Descriptive statistics of Key evaluation indicators for 12 secondary public hospitals in Guangzhou (2019–2023).

Code	Indicator	2019	2020	2021	2022	2023
X_1	Average length of stay (days)	7.93 ± 2.56	9.18 ± 2.45	9.18 ± 2.55	8.94 ± 2.54	9.68 ± 2.78
X_2	Mortality rate of low-risk patients (%)	1.00 ± 0.94	0.59 ± 0.37	0.42 ± 0.33	0.29 ± 0.15	0.25 ± 0.11
X_3	Surgical discharge ratio (%)	21.66 ± 9.16	26.97 ± 9.30	24.57 ± 9.80	23.02 ± 9.01	16.88 ± 5.78
X_4	Complication rate among surgical patients (%)	0.64 ± 0.31	0.57 ± 0.32	0.50 ± 0.29	0.51 ± 0.32	0.46 ± 0.29
X_5	Proportion of service revenue (non-drug, non-consumable, %)	33.88 ± 4.76	34.21 ± 3.75	33.66 ± 4.24	33.54 ± 3.38	33.78 ± 4.04
X_6	Personnel cost ratio (%)	50.42 ± 4.13	47.11 ± 4.30	45.61 ± 5.21	43.09 ± 5.28	39.53 ± 6.24
X_7	Asset-liability ratio (%)	28.62 ± 6.79	29.18 ± 6.33	28.84 ± 6.49	28.95 ± 6.64	27.49 ± 7.31
X_8	Outpatient cost growth rate (%)	2.73 ± 4.52	3.37 ± 3.70	4.79 ± 3.98	5.25 ± 4.12	41.77 ± 20.86
X_9	Outpatient drug cost growth rate (%)	3.06 ± 5.81	2.54 ± 5.17	4.66 ± 4.77	4.15 ± 4.69	43.94 ± 21.57
X_{10}	Inpatient cost growth rate (%)	6.58 ± 5.31	7.35 ± 4.74	−2.69 ± 6.17	−2.18 ± 5.87	−3.17 ± 6.99
X_{11}	Inpatient drug cost growth rate (%)	6.17 ± 6.09	7.01 ± 5.33	−1.83 ± 5.64	−2.10 ± 5.13	−2.73 ± 6.44
X_{12}	Nurse-to-doctor ratio (%)	1.44 ± 0.24	1.50 ± 0.26	1.52 ± 0.24	1.54 ± 0.25	1.59 ± 0.25
X_{13}	Inpatient workload per physician (bed-days/day)	3.23 ± 0.51	3.22 ± 0.49	3.18 ± 0.50	3.13 ± 0.49	3.11 ± 0.47
X_{14}	Pharmacists per 100 beds (persons)	4.29 ± 1.20	4.17 ± 1.08	4.01 ± 0.96	3.98 ± 0.91	3.95 ± 0.93

Values are presented as mean ± standard deviation.

3.1.2 Operational efficiency (X_5–X_{11})

- The proportion of service revenue (X_5) remained relatively stable (~33.5%), reflecting consistent reliance on core medical services over drugs or diagnostics.
- The personnel cost ratio (X_6) declined steadily from 50.42% to 39.53%, suggesting improved financial efficiency. However, increasing standard deviation indicates widening disparity in cost control strategies across hospitals.
- The asset-liability ratio (X_7) remained stable with a slight downward trend in 2023, but high dispersion points to unequal debt structures and financial pressure between institutions.
- The growth rates of outpatient costs (X_8) and outpatient drug costs (X_9) surged significantly in 2023, exceeding 40%. Such spikes imply possible lapses in cost regulation or changes in insurance pricing structures.
- Meanwhile, inpatient cost (X_{10}) and drug cost growth (X_{11}) both entered negative territory post-2021. This aligns with national efforts to reduce hospitalization expenditures under DRG and insurance payment reforms.

3.1.3 Sustainability (X_{12}–X_{14})

- The nurse-to-doctor ratio (X_{12}) improved incrementally, reflecting minor adjustments in workforce composition and possibly enhanced nursing investment.
- The average daily inpatient workload per physician (X_{13}) showed a steady decline, suggesting a reduction in individual burden, although at the potential cost of system efficiency.
- The pharmacist-to-bed ratio (X_{14}) continued its downward trend, raising concerns over pharmaceutical care capacity and drug-use governance.

3.2 Comprehensive evaluation via entropy-TOPSIS

3.2.1 Indicator weights and discrimination power

As presented in Table 3, the entropy analysis yielded consistently high values for most indicators ($e_j > 0.95$), suggesting strong uniformity of hospital performance in many dimensions. However, certain variables exhibited greater discriminative potential. Surgical discharge ratio (X_3) showed a relatively low entropy and the highest weight (17.46%), indicating its substantial role in differentiating service complexity and procedural capabilities among hospitals. Pharmacists per 100 beds (X_{14}) ranked second in weight (16.03%), reflecting the importance of pharmaceutical staffing in assessing service comprehensiveness and support quality. Inpatient drug cost growth rate (X_{11}) held the third highest weight (13.06%), highlighting the growing relevance of cost control and insurance adaptability as policy pressure on inpatient costs intensifies. Conversely, outpatient drug cost growth (X_9) and surgical complication rate (X_4), despite high entropy values, received minimal weight due to excessive variance or weak inter-hospital differentiation, suggesting limited evaluation utility under current measurement conditions.

TABLE 3 Entropy values and weights of service capacity evaluation indicators (2019–2023).

Code	Indicator	Entropy value (e_j)	Entropy weight (w_j)
X_1	Average length of stay (days)	0.9574	0.0278
X_2	Mortality rate of low-risk patients (%)	0.9689	0.0198
X_3	Surgical discharge ratio (%)	0.9127	0.1746
X_4	Complication rate among surgical patients (%)	0.9785	0.0142
X_5	Proportion of service revenue (non-drug, non-consumable, %)	0.9564	0.0287
X_6	Personnel cost ratio (%)	0.9511	0.0321
X_7	Asset-liability ratio (%)	0.9623	0.0236
X_8	Outpatient cost growth rate (%)	0.9596	0.0253
X_9	Outpatient drug cost growth rate (%)	0.9796	0.0134
X_{10}	Inpatient cost growth rate (%)	0.9563	0.0288
X_{11}	Inpatient drug cost growth rate (%)	0.9337	0.1306
X_{12}	Nurse-to-doctor ratio (%)	0.9495	0.0335
X_{13}	Inpatient workload per physician (bed-days/day)	0.9649	0.0213
X_{14}	Pharmacists per 100 beds (persons)	0.9183	0.1603

3.2.2 Ranking results and hospital trajectories

As shown in Table 4, the composite TOPSIS scores reveal a dual pattern: overall capacity improved marginally, yet internal divergence intensified. The score range widened from [0.2667, 0.6982] in 2019 to [0.2711, 0.6199] in 2023, indicating slower progress among lagging hospitals and greater gains among leaders. Hospital A8, which fell to the bottom in 2021, surged to 1st place in 2023, implying effective strategic transformation or targeted investment in capacity domains with high weight. Hospital A10, once ranked 2nd in 2019, plummeted to last place by 2023, reflecting long-term stagnation, management inefficiencies, or weakened policy support. Hospitals A4 and A12 remained consistently above average, showing stable and balanced development across all three dimensions. These transitions suggest that secondary public hospitals can rapidly upgrade their service capacity with focused resource reallocation, though without consistent intervention, structural weaknesses persist over time.

3.2.3 Kernel density distribution and polarization trends

To analyze the dynamic evolution of service capacity across institutions, a 3D Kernel Density Estimation (KDE) was constructed using MATLAB, based on composite TOPSIS scores from 2019 to 2023. As shown in Figure 1, the distribution of scores has undergone significant structural changes. In 2019–2020, the KDE surface displays a unimodal and symmetric peak, centered around the 0.4–0.6 interval. This reflects a relatively cohesive system, with most hospitals clustered around a

TABLE 4 Composite service capacity scores and rankings of 12 secondary public hospitals in Guangzhou (2019–2023).

Hospital code	2019 score	2019 rank	2020 score	2020 rank	2021 score	2021 rank	2022 score	2022 rank	2023 score	2023 rank
A1	0.4348	9	0.4682	7	0.5304	6	0.5047	9	0.5486	6
A2	0.4043	10	0.4472	8	0.4424	9	0.4505	11	0.4692	9
A3	0.4776	7	0.4656	9	0.5244	7	0.5352	7	0.4961	8
A4	0.6309	2	0.6359	2	0.5943	2	0.5923	2	0.6176	2
A5	0.5229	5	0.5006	5	0.4743	8	0.5072	8	0.5046	7
A6	0.2667	12	0.3359	11	0.4012	10	0.4329	12	0.4385	11
A7	0.6982	1	0.6185	3	0.5934	3	0.5836	3	0.5982	3
A8	0.4917	6	0.4982	6	0.2932	12	0.5136	6	0.6199	1
A9	0.4138	8	0.4193	10	0.4284	11	0.5396	5	0.5569	5
A10	0.6678	3	0.6636	1	0.6081	1	0.5949	1	0.2711	12
A11	0.6065	4	0.5824	4	0.5882	4	0.5612	4	0.5828	4
A12	0.5193	6	0.5152	5	0.5406	5	0.5503	5	0.5702	5

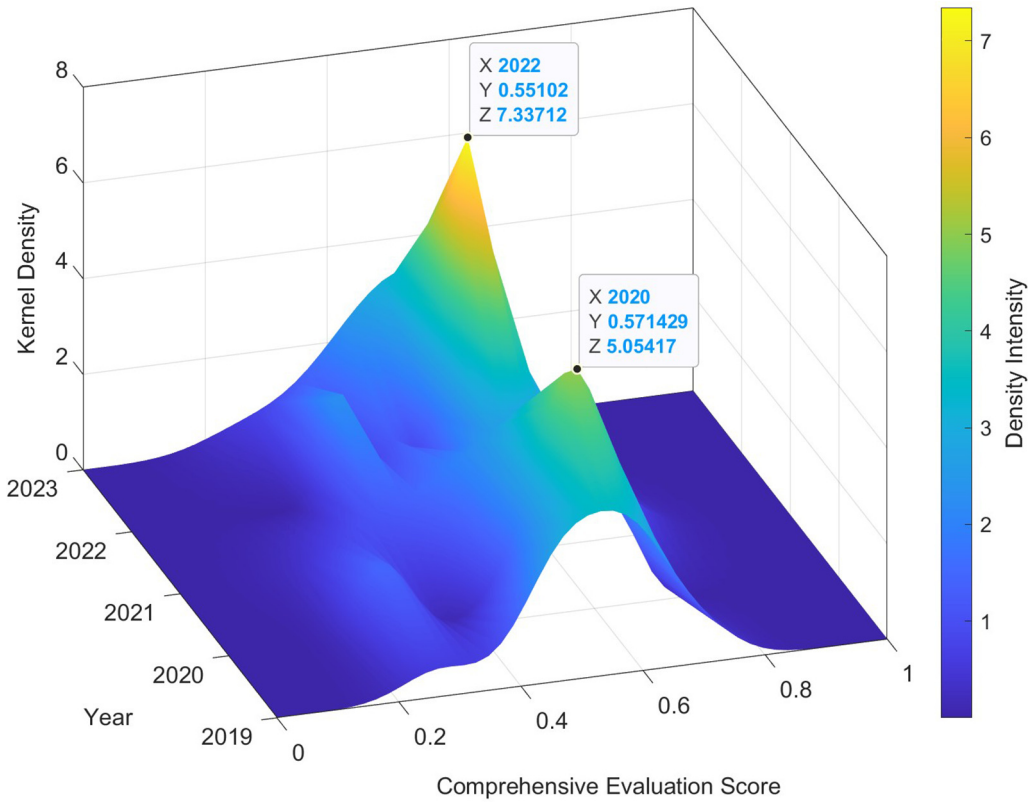


FIGURE 1
3D Kernel Density Estimation of composite service capacity scores for 12 secondary public hospitals in Guangzhou (2019–2023).

moderate level of service capacity. Starting in 2021, under the continued impact of the COVID-19 pandemic, the distribution began to diverge. A portion of hospitals improved significantly—moving above 0.6—while others fell behind. This shift produced a bimodal distribution, signaling the initial onset of performance polarization. By 2022–2023, the divide had further intensified. A new density peak formed in the 0.6–0.8 range, indicating the rise of high-performing institutions. Meanwhile, a persistent group of hospitals remained in the <0.4 score range, suggesting stagnation at the lower end. These changes point to a clear dual structure in institutional performance: top-tier hospitals advanced rapidly, while bottom-tier facilities failed to catch up. The density peaks grew sharper during 2021–2022, suggesting accelerated reordering of institutional capacity. Although the overall curve shifted rightward in 2023, indicating general improvement, the expanded variance suggests growing internal stratification across the hospital system. This pattern underscores the urgency for differentiated policy support: capacity enhancement strategies for

lagging hospitals, and performance stabilization and innovation support for emerging leaders.

3.3 Regional disparity analysis via Dagum Gini decomposition

3.3.1 Regional division principles

To systematically assess spatial differences in healthcare service capacity, the 12 secondary public hospitals in Guangzhou were grouped according to the city's official spatial development strategy into four functional regions, each aligned with distinct policy orientations and urban development priorities:

- C: Central Administrative Core— Includes Yuexiu, Liwan, and Haizhu districts. This area represents Guangzhou's traditional urban center, housing many longstanding hospitals and administrative institutions.
- E: Eastern Innovation Corridor— Includes Tianhe, Huangpu, and Zengcheng districts. This zone serves as a technology and education hub, with growing investment in research-based healthcare facilities.
- S: Southern Bay Area Gateway— Covers Panyu and Nansha districts, representing the interface between Guangzhou and the Guangdong–Hong Kong–Macao Greater Bay Area. It features newly established or upgraded hospitals under port-oriented urban expansion policies.
- N: Northern Ecological Corridor— Includes Baiyun, Huadu, and Conghua districts. This zone focuses on ecological protection and suburban development, where many hospitals serve sparsely distributed populations.

These divisions reflect Guangzhou's "multi-center, polycentric spatial layout", which underpins its urban healthcare planning. Such classification allows for a more accurate analysis of service capacity disparities by spatial typology and functional mandate.

3.3.2 Temporal patterns and inequality dynamics

Using the Dagum Gini coefficient and its subgroup decomposition, Table 5 and Figure 2 provide insight into the spatial structure of inequality in service capacity from 2019 to 2023.The overall inequality index (G) remained relatively stable, with a notable peak in 2021 ($G \approx 0.1241$), reflecting structural shocks during the mid-phase of the COVID-19 pandemic. By 2023, G slightly rebounded after a temporary decline in 2022, indicating partial re-concentration of capacity. The Southern Gateway (S) region consistently displayed the highest intra-regional inequality. This reflects the uneven development between Panyu's mature hospitals and Nansha's emerging but still under-resourced institutions. The area's transitional status—between metropolitan core and new development frontier—has led to fragmented service capability. In contrast, the Central Core (C) experienced a sharp but short-lived surge in internal disparity in 2020, likely due to extreme performance variations in a few large institutions during the pandemic. The Eastern (E) and Northern (N) zones maintained relatively balanced internal distributions, though E-region scores surged in 2022, suggesting successful infrastructure upgrades in one or more hospitals in the science-tech corridor.

3.3.3 Inter-Regional disparity and component contributions

Figure 2B illustrates the inter-regional Gini coefficients between the six pairwise region combinations (e.g., C–S, C–E, E–S).The most pronounced inequality occurred in C–S and C–E during 2020, driven by differences in surge capacity and infection control preparedness between central and peripheral areas. The E–S combination maintained high inequality levels through 2021–2022, suggesting delayed convergence between the innovation belt and southern port corridor. By 2023, all inter-regional gaps showed a decline, indicating improved coordination and policy harmonization under post-pandemic reforms. Figure 2C shows the annual contributions of inequality components. Inter-regional inequality (Gnb) accounted for ~47% in 2020, but decreased steadily to under 30% in 2023, implying that regional gaps are narrowing. Intra-regional inequality (Gw) increased slightly in 2023 (~32%), pointing to emerging fragmentation within zones, especially in S and E regions. Most

TABLE 5 Decomposition of Dagum Gini coefficients and inequality components of hospital service capacity in four functional regions of Guangzhou (2019–2023).

Component	Subcomponent/Region pair	2019	2020	2021	2022	2023
Total Gini soefficient (G)	—	0.1135	0.1208	0.1241	0.0959	0.1098
Within-region inequality (G_w)	Central Administrative Core (C)	0.0023	0.2212	0.1418	0.0145	0.0162
	Eastern Innovation Corridor (E)	0.0088	0.0239	0.0294	0.159	0.1021
	Southern Bay Area Gateway (S)	0.1368	0.1053	0.1103	0.0866	0.122
	Northern Ecological Corridor (N)	0.0516	0.0223	0.0045	0.0326	0.0438
Between-region inequality (G_{nb})	C–E	0.115	0.1925	0.1471	0.1521	0.0962
	C–S	0.134	0.2114	0.1585	0.0635	0.0929
	C–N	0.0513	0.1887	0.1328	0.0437	0.1145
	E–S	0.0935	0.09	0.172	0.1573	0.1292
	E–N	0.12	0.032	0.1004	0.1458	0.1079
	S–N	0.1422	0.1034	0.0971	0.0824	0.1233
Contribution rates (G_z, %)	Within-region	32.38%	26.27%	27.37%	27.70%	31.78%
	Between-region	39.19%	46.61%	37.79%	30.58%	29.45%
	Transvariation (Overlapping Density)	28.43%	27.11%	34.84%	41.73%	38.77%

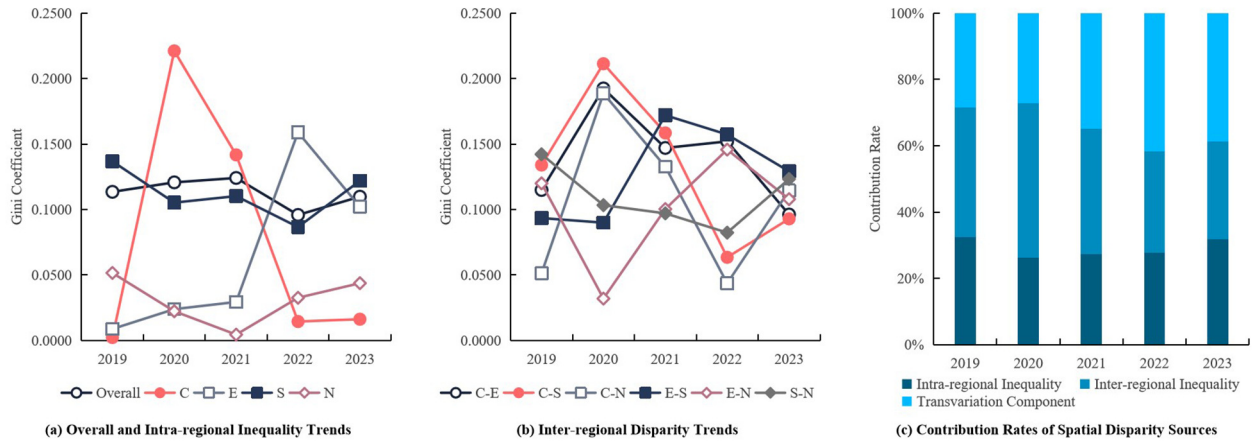


FIGURE 2
Decomposition of regional inequality in service capacity among secondary public hospitals in Guangzhou (2019–2023).

notably, the transvariation component (Gt)—reflecting overlapping capacity differences across hospitals from different zones—rose significantly after 2022, exceeding 40% in 2023, and became the dominant inequality source. This shift reveals that inequality is no longer driven solely by spatial location, but increasingly by individual institutional divergence, regardless of region. It highlights the importance of hospital-specific reforms, such as digital infrastructure, workforce incentives, and clinical specialization, over region-wide structural investment alone.

4 Discussion

Based on panel data from 12 secondary public hospitals in Guangzhou between 2019 and 2023, this study utilized entropy-weighted TOPSIS, Kernel Density Estimation, and Dagum Gini decomposition to comprehensively assess the temporal evolution and spatial disparities in hospital service capacity. Results indicate a general improvement in performance across medical quality, operational efficiency, and sustainability dimensions. However, these gains were accompanied by increasing internal divergence and persistent regional inequality. In light of international evidence and China's ongoing healthcare reforms, this section discusses critical challenges and future policy directions across four domains: problem identification, capacity development strategies, governance pathways, and institutional resilience.

4.1 Key issues and systemic challenges

4.1.1 Medical quality: efficiency–safety trade-offs and functional regression

In the quality dimension, Guangzhou's secondary hospitals exhibited signs of a trade-off between treatment efficiency and patient safety. The prolonged average length of stay (X_1)—particularly in hospitals like A3 and A10—may partially reflect COVID-19 protocols but also indicates poor bed turnover and inefficient case management. The significant decline in surgical case ratios (X_3) suggests a functional hollowing effect due to tertiary hospital siphoning and insufficient technical capabilities within secondary hospitals. This nationwide trend, if unchecked, could lead to the erosion of core competencies in secondary-level care (39). While the improvement in mortality among low-risk patients (X_2) reflects better basic care quality, the fluctuating surgical complication rate (X_4) underscores ongoing weaknesses in perioperative safety and clinical governance.

4.1.2 Operational efficiency: cost-structure imbalances and fiscal stress

Hospitals face mounting tension between cost containment and revenue structure optimization. For instance, A7 and A11 reported over 40% annual growth in outpatient and drug costs (X_8/X_9), highlighting a problematic reliance on pharmaceuticals and diagnostics, contrary to the policy goals of the "restructuring revenue mix" reform agenda. Although declining inpatient costs (X_{10}/ X_{11}) suggest effective insurance payment control, excessive cost-cutting may compromise diagnostic scope and financial sustainability, as seen in A3's declining rankings. Hospitals with high asset–liability ratios (e.g., A7 reaching 75%) face sustainability risks, especially when paired with declining personnel expenditure ratios (X_6), which reflect a dilemma: lower spending does not necessarily yield higher efficiency.

4.1.3 Sustainability: workforce structure and professional burnout

In terms of long-term sustainability, persistent workforce structural weaknesses hinder the development of resilient service capacity. While the nurse-to-doctor ratio (X_{12}) has improved overall (reaching 0.734), understaffed pharmacy units (X_{14}) remain a barrier to pharmaceutical services and rational drug use. Unequal physician inpatient workloads (X_{13})—exceeding two beds per day in hospitals like A6 and A10—may lead to burnout

and undermine care consistency. These personnel imbalances reveal fundamental constraints in human resource planning that could hinder hospitals' adaptive capacity in the face of public health crises.

4.1.4 Spatial disparities: fragmentation and cross-regional competition

The spatial pattern of healthcare service capacity has become increasingly fragmented. The Southern Bay Area Gateway (S) exhibited the highest intra-regional inequality (Gw = 0.1220), driven by gaps between newly established hospitals in Nansha and mature institutions in Panyu. Moreover, the rise in transvariation contribution (Gz = 38.77%) indicates intensified cross-regional overlap in hospital performance. For example, Hospital A8 (Eastern Innovation Corridor) and Hospital A4 (Central Core) now compete in overlapping patient markets, reflecting unbalanced spatial allocation of resources and system-wide coordination challenges. These trends call for a dual focus on regional integration and differentiated policy design, to both strengthen underperforming institutions and foster synergy across urban functional zones. A more equitable and resilient health system requires nuanced governance beyond mere expansion of infrastructure.

4.2 Strategic pathways for capacity optimization

Drawing on the findings of this study, a coherent reform strategy is essential to enhance the capacity, resilience, and coordination of secondary public hospitals in Guangzhou. Key insights suggest that while service quality has generally improved, operational efficiency remains uneven, and structural challenges persist in sustainability.

4.2.1 Quality-led differentiated development

The evaluation results show diverging trends in quality indicators: while low-risk mortality rates declined and complication rates slightly improved, average length of stay increased, and surgical discharge rates declined, especially in hospitals like A3 and A10. These trends suggest a weakening of procedural functionality and the fragmentation of surgical capacity in some institutions—possibly due to case siphoning by tertiary centers or internal capability stagnation. To address these issues, reforms should: Designate clinical specialization tracks for underperforming hospitals—e.g., those with high length of stay, low surgical output, or redundant catchment areas—to evolve into focused hubs in areas like rehabilitation or geriatrics; Define eligibility thresholds using capacity metrics (e.g., surgical discharge rate <20%, stay >9 days, or domain-specific staffing strengths); Align with national zoning and global best practices, such as China's Health Service Plan, NHS trust models, and Mayo's hub-and-spoke frameworks, to enhance service clarity and resource efficiency.

4.2.2 Efficiency-oriented financial and human resource governance

The divergence in outpatient and drug cost growth in 2023 (over 40% in some hospitals) reflects a growing gap in cost control capabilities. Asset-liability ratios also indicate uneven financial health, with some hospitals approaching high-risk thresholds (40). To address this, reforms should: Standardize cost governance mechanisms, including bundled payments and global budgeting pilots; Adjust personnel expenditure structures, rewarding performance while ensuring workforce retention; Build digital financial dashboards to allow real-time monitoring of cost drivers, flagging anomalies in outpatient and pharmaceutical expenses.

4.2.3 Sustainability-focused workforce and institutional resilience

Human resource data reveal a stable yet suboptimal trajectory: the nurse-to-doctor ratio has slightly improved (from 0.713 to 0.734), and physician workload shows minor relief. However, pharmacist staffing has declined, raising concerns about pharmaceutical governance. Therefore: Revise workforce standards to reflect differentiated service needs across specialties; Incentivize pharmacy and public health professionals to counterbalance current personnel imbalances; Embed resilience benchmarks into hospital evaluations—e.g., surge capacity, staffing flexibility, and supply chain autonomy.

These pathways align with the broader goals of China's hierarchical medical system reform and the WHO's call for resilient, integrated health systems. Through differentiated development, refined financial governance, and targeted workforce strategies, secondary hospitals can better fulfill their role as stable, adaptable, and equitable pillars within urban health systems.

4.3 Implementation roadmap

To ensure policy effectiveness, the proposed capacity enhancement strategies should be implemented in a phased manner—short-term, medium-term, and long-term—tailored to institutional readiness and policy capacity. Figure 3 presents a strategic roadmap that outlines the temporal and functional dimensions of reform.

Short-term (1–2 years): Target hospitals with abnormal cost growth for focused remediation. Leverage DRG-based payment reform as an entry point. Joint inspections by the Health Commission and Medical Insurance Bureau should be conducted, with penalties such as budget reductions for non-compliant institutions. These actions will help restore expenditure discipline and enhance accountability.

Medium-term (3–5 years): Establish 3–5 regional specialty alliances to optimize resource allocation and improve professional collaboration. Municipal funding should support equipment upgrades and pharmacist deployment across alliance hospitals. Resource sharing will enhance service integration across zones.

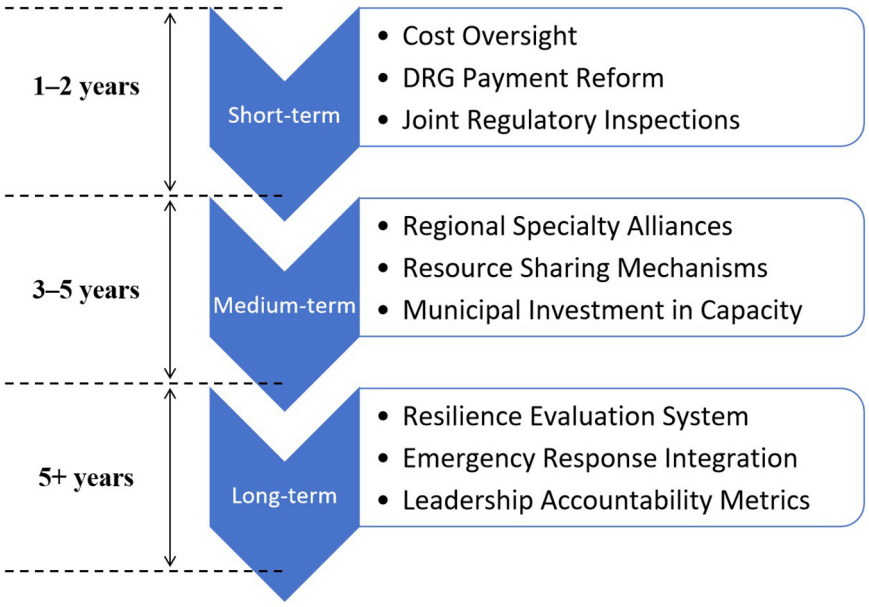


FIGURE 3
Strategic roadmap for implementing capacity enhancement in secondary public hospitals.

Long-term (5+ years): Develop a resilience evaluation framework for hospitals that includes emergency response capacity. Performance in crisis response and service conversion should be incorporated into hospital leadership assessments, enabling hospitals to evolve in both "routine" and "emergency" dimensions. This dual-track capacity model ensures system-wide adaptability and public health readiness (41).

4.4 Potential challenges and strategic countermeasures

While well-designed, the implementation of these strategies may encounter multiple barriers, including fiscal constraints, data silos, and institutional inertia. Given limited public finance, local governments could issue dedicated municipal health bonds, prioritizing investment in high-weight indicators such as surgical capability and pharmacist allocation. This ensures targeted reinforcement of structural bottlenecks. Fragmented information systems across the Medical Insurance Bureau, Health Commission, and Human Resources departments hinder policy synergy. Authorities should develop a real-time data visualization platform based on KDE, enabling dynamic surveillance, early warnings, and resource redeployment. Resistance to role reform among medical staff remains a persistent problem. Reforming promotion and evaluation systems to include indicators such as surgical volume, grassroots service, and technical outreach will help incentivize downward mobility and skill transfer to community settings, thereby improving service equity and accessibility (39).

5 Conclusion

This study investigates the evolution of service capacity across 12 secondary public general hospitals in Guangzhou from 2019 to 2023. A multidimensional evaluation framework was constructed, incorporating four core dimensions: medical quality, operational efficiency, sustainability, and regional coordination. By integrating the entropy-weighted TOPSIS method, Kernel Density Estimation (KDE), and Dagum Gini decomposition, the analysis revealed the spatiotemporal dynamics of institutional performance and inequality.

The results suggest that while overall service capacity has improved, significant inter-hospital and inter-regional disparities persist. Key structural bottlenecks—particularly in surgical capability and pharmacist staffing—remain critical obstacles to realizing the functional positioning and high-quality development of secondary hospitals.

At the methodological level, this research contributes an innovative modeling approach, validating the combined application of entropy-TOPSIS and Dagum Gini decomposition in capturing spatial divergence and performance trends. The proposed strategy emphasizes a dual-pathway approach: precision-targeted capacity enhancement, and adaptive governance, incorporating DRG-based payment reform, KDE-driven real-time monitoring, regional specialty alliance building, and human resource restructuring. These policy recommendations aim to strike a balance between efficiency, equity, and resilience.

In terms of global relevance, the study outlines a potential "Guangzhou Model" that could inform capacity-building in urbanizing middle-tier hospital systems across Southeast Asia and other fast-growing urban regions.

Nonetheless, several limitations remain. First, the current indicator system is primarily structural and does not capture subjective measures such as patient satisfaction or staff experience. Future research should incorporate survey-based metrics to improve sensitivity and completeness. Second, methodological expansion is needed—e.g., introducing machine learning techniques like random forests for predictive modeling and scenario classification. Third, the strategic pathways proposed in this study have not undergone longitudinal validation. Future evaluations should focus on dynamic monitoring of reform implementation, particularly the long-term effects of regional specialty alliances on surgical volume, cost structure, and service quality post-2025.

In conclusion, strengthening the capacity of secondary public hospitals in Guangzhou is not only vital for internal optimization of the healthcare system but also foundational to the efficiency of hierarchical diagnosis and treatment and the realization of equitable, accessible healthcare. Moving forward, a data-driven, problem-oriented, and regionally coordinated strategy is essential to support the long-term development of a modernized Chinese healthcare system.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author.

Author contributions

BW: Conceptualization, Formal analysis, Investigation, Methodology, Supervision, Writing – original draft, Writing – review & editing. WW: Conceptualization, Formal analysis, Investigation, Methodology, Software, Supervision, Writing – original draft, Writing – review & editing. XW: Writing – review & editing, Methodology, Validation, Visualization. WH: Project administration, Writing – original draft. ZL: Methodology, Writing – review & editing. JL: Visualization, Writing – original draft.

Funding

The author(s) declare that financial support was received for the research and/or publication of this article. This work was supported by the Accredited Scientific Research Project (Featured Innovation Project) of Universities in Guangdong Province (Grant no. 2021WTSCX072) and the 2025 Scientific Research Capability Improvement Plan Project of Guangzhou Medical University (Grant no. 2025SRP051).

Acknowledgments

The authors are grateful to the colleagues and experts who provided valuable guidance throughout this study. The views expressed in this paper are solely those of the authors and do not necessarily reflect the opinions of any affiliated organizations.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The author(s) declare that no Generative AI was used in the creation of this manuscript.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

References

1. Wu F, Chen W, Lin L, Ren X, Qu Y. The balanced allocation of medical and health resources in urban areas of China from the perspective of sustainable development: a case study of Nanjing. *Sustainability*. (2022) 14(11):6707. doi: 10.3390/su14116707

2. Nnadi HC, Ossai OG, Nwokocha VC. Urbanization factors and the vagaries of the rural health care industry in Nigeria: an analysis of the accessibility of healthcare services by older adults in the Nsukka local government area. *Human Soc Sci Commun*. (2024) 11(1):1–9. doi: 10.1057/s41599-024-03799-4

3. Iamtrakul P, Chayphong S, Gao W. Assessing spatial disparities and urban facility accessibility in promoting health and well-being. *Trans Res Interdiscip Perspect*. (2024) 25:101126. doi: 10.1016/j.trip.2024.101126

4. World Health Organization. *Integrating Health Services: Brief*. Geneva: World Health Organization (2018). p. 1–16. Report No.: WHO/HIS/SDS/2018.50. Available at: https://www.who.int/publications/i/item/WHO-HIS-SDS-2018.50

5. Veillard J, Champagne F, Klazinga N, Kazandjian V, Arah OA, Guisset AL. A performance assessment framework for hospitals: the WHO regional office for Europe PATH project. *Int J Qual Health Care*. (2005) 17(6):487–96. doi: 10.1093/intqhc/mzi072

6. Veillard JHM, Schiøtz ML, Guisset AL, Brown AD, Klazinga NS. The PATH project in eight European countries: an evaluation. *Int J Health Care Qual Assur*. (2013) 26(8):703–13. doi: 10.1108/IJHCQA-11-2011-0065

7. World Health Organization. *Service Availability and Readiness Assessment (SARA): Reference Manual*. Geneva: World Health Organization (2015). Available at: https://www.who.int/publications/i/item/WHO-HIS-HSI-2014.5-Rev.1

8. World Health Organization. Service Availability and Readiness Assessment (SARA): An Annual Monitoring System for Service Delivery. World Health Organization (2015). Available at: https://www.who.int/publications/i/item/WHO-HIS-HSI-2015.5 (Accessed April 05, 2025).

9. Paromita P, Chowdhury HA, Mayaboti CA, Rakhshanda S, Rahman AKMF, Karim M, et al. Assessing service availability and readiness to manage chronic respiratory diseases (CRDs) in Bangladesh. *PLoS One*. (2021) 16(3):e0247700. doi: 10.1371/journal.pone.0247700

10. Millogo O, Doamba JEO, Sié A, Utzinger J, Vounatsou P. Constructing a malaria-related health service readiness index and assessing its association with child malaria mortality: an analysis of the Burkina Faso 2014 SARA data. *BMC Public Health*. (2021) 21(1):20. doi: 10.1186/s12889-020-09994-7

11. Ayanore M, Asampong R, Akazili J, Awoonor-Williams JK, Akweongo P. Sub-national variations in general service readiness of primary health care facilities in Ghana: health policy and equity implications towards the attainment of universal health coverage. *PLoS One*. (2022) 17(6):e0269546. doi: 10.1371/journal.pone.0269546

12. Cane RM, Sheffel A, Salomão C, Sambo J, Matusse E, Ismail E, et al. Structural readiness of health facilities in Mozambique: how is Mozambique positioned to deliver nutrition-specific interventions to women and children? *J Glob Health Rep*. (2023) 7: e2023074. doi: 10.29392/001c.89000

13. O'Neill K, Takane M, Sheffel A, Abou-Zahr C, Boerma T. Monitoring service delivery for universal health coverage: the service availability and readiness assessment. *Bull W H O*. (2013) 91(12):923–31. doi: 10.2471/BLT.12.116798

14. Chen CH. A novel multi-criteria decision-making model for building material supplier selection based on entropy-AHP weighted TOPSIS. *Entropy*. (2020) 22(2):259. doi: 10.3390/e22020259

15. Chaube S, Pant S, Kumar A, Uniyal S, Singh MK, Kotecha K, et al. An overview of multi-criteria decision analysis and the applications of AHP and TOPSIS methods. *Int J Math Eng Sci*. (2024) 9(3):581–615. doi: 10.33889/IJMEMS.2024.9.3.030

16. Li L, Liu Z. Research on efficiency measurement and spatiotemporal disparity of rural public health services in China. *PLoS One*. (2021) 16(7):e0252871. doi: 10.1371/journal.pone.0252871

17. Song C, Fang L, Xie M, Tang Z, Zhang Y, Tian F, et al. Revealing spatiotemporal inequalities, hotspots, and determinants in healthcare resource distribution: insights from hospital beds panel data in 2308 Chinese counties. *BMC Public Health*. (2024) 24(1):423. doi: 10.1186/s12889-024-17950-y

18. Zhao P, Li S, Liu D. Unequable spatial accessibility to hospitals in developing megacities: new evidence from Beijing. *Health Place*. (2020) 65:102406. doi: 10.1016/j.healthplace.2020.102406

19. Yu Y, Zhou R, Qian L, Yang X, Dong L, Zhang G. Supply-demand balance and spatial distribution optimization of primary care facilities in highland cities from a resilience perspective: a study of Lhasa, China. *Front Public Health*. (2023) 11:1131895. doi: 10.3389/fpubh.2023.1131895

20. Behrens DA, Rauner MS, Sommersguter-Reichmann M. Why resilience in health care systems is more than coping with disasters: implications for health care policy. *Schmalenbachs Zeitschrift Fur Betriebswirtschaftliche Forschung*. (2022) 74(4):465–95. doi: 10.1007/s41471-022-00132-0

21. Ravaghi H, Khalil M, Al-Badri J, Naidoo AV, Ardalan A, Khankeh H. Role of hospitals in recovery from COVID-19: reflections from hospital managers and frontliners in the eastern Mediterranean region on strengthening hospital resilience. *Front Public Health*. (2022) 10:1073809. doi: 10.3389/fpubh.2022.1073809

22. Chen CH. A hybrid multi-criteria decision-making approach based on ANP-entropy TOPSIS for building materials supplier selection. *Entropy*. (2021) 23(12):1597. doi: 10.3390/e23121597

23. Liu L, Wan X, Li J, Wang W, Gao Z. An improved entropy-weighted topsis method for decision-level fusion evaluation system of multi-source data. *Sensors*. (2022) 22(17):6391. doi: 10.3390/s22176391

24. Dai X, Jiang Y, Li Y, Wang X, Wang R, Zhang Y. Evaluation of community basic public health service effect in a city in Inner Mongolia autonomous region——based on entropy weight TOPSIS method and RSR fuzzy set. *Arch Public Health*. (2023) 81(1):149. doi: 10.1186/s13690-023-01151-x

25. Chen P. Effects of the entropy weight on TOPSIS. *Expert Syst Appl*. (2021) 168:114186. doi: 10.1016/j.eswa.2020.114186

26. Lin M, Huang C, Xu Z. TOPSIS Method based on correlation coefficient and entropy measure for linguistic pythagorean fuzzy sets and its application to multiple attribute decision making. *Complexity*. (2019) 2019(1):6967390. doi: 10.1155/2019/6967390

27. Dehdasht G, Ferwati MS, Zin RM, Abidin NZ. A hybrid approach using entropy and TOPSIS to select key drivers for a successful and sustainable lean construction implementation. *PLoS One*. (2020) 15(2):e0228746. doi: 10.1371/journal.pone.0228746

28. Roszkowska E, Wachowicz T. Impact of normalization on entropy-based weights in hellwig's method: a case study on evaluating sustainable development in the education area. *Entropy*. (2024) 26(5):365. doi: 10.3390/e26050365

29. Zambom AZ, Dias R. A review of kernel density estimation with applications to econometrics. *arXiv*. (2012) arXiv:1212.2812. doi: 10.48550/arXiv.1212.2812

30. Węglarczyk S. Kernel density estimation and its application. *ITM Web Conf*. (2018) 23:00037. doi: 10.1051/itmconf/20182300037

31. Wang F, Wang H, An Y, Xue R, Zhang Y, Hao T. From location advantage to innovation: exploring interprovincial co-funding networks in mainland China. *Systems*. (2025) 13(1):58. doi: 10.3390/systems13010058

32. Gong H, Zhang T, Wang X, Chen B, Wu B, Zhao S. Analysis of regional differences, dynamic evolution, and influencing factors of medical service levels in Guangzhou under the health China strategy. *Risk Manag Healthc Policy*. (2024) 17:2811–28. doi: 10.2147/RMHP.S479911

33. Deng J, Song Q, Liu H, Jiang Z, Ge C, Li D. The coupling coordination between health service supply and regional economy in China: spatio-temporal evolution and convergence. *Front Public Health*. (2024) 12:1352141. doi: 10.3389/fpubh.2024.1352141

34. Liang B, Huang L, Chen Z, Hao B, Li C. Regional differences, dynamic evolution, and influencing factors of high-quality medical resources in China's ethnic minority areas. *Front Public Health*. (2024) 12:1436244. doi: 10.3389/fpubh.2024.1436244

35. Dagum C. A new approach to the decomposition of the gini income inequality ratio. In: Slottje DJ, Raj B, editors. *Income Inequality, Poverty, and Economic Welfare*. Heidelberg: Physica-Verlag HD (1998). p. 47–63.

36. Kleiber C. A Guide to the Dagum Distributions. WWZ Working Paper (2007). Report No.: 23/07. Available at: https://www.econstor.eu/handle/10419/123385 (Accessed April 05, 2025).

37. Ma T, Liu Y, Yang M. Spatial-Temporal heterogeneity for commercial building carbon emissions in China: based the Dagum Gini coefficient. *Sustainability*. (2022) 14(9):5243. doi: 10.3390/su14095243

38. Li M, Peng P, Ao Y, Zhou Z, Zuo J, Martek I. Equity in public decision-making: a dynamic comparative study of urban–rural elderly care institution resource allocation in China. *Hum Soc Sci Commun*. (2024) 11(1):1–16. doi: 10.1057/s41599-024-04041-x

39. Chen B, Jin F. Spatial distribution, regional differences, and dynamic evolution of the medical and health services supply in China. *Front Public Health*. (2022) 10:1020402. doi: 10.3389/fpubh.2022.1020402

40. Guan X, Xu J, Huang X. Digital economy and the medical and health service supply in China. *Front Public Health*. (2024) 12:1441513. doi: 10.3389/fpubh.2024.1441513

41. Ji H, Yu Y. Examining coordination and equilibrium: an analysis of supply index and spatial evolution characteristics for older adult services in Zhejiang province. *Front Public Health*. (2023) 11:1222424. doi: 10.3389/fpubh.2023.1222424

frontiers | Frontiers in Health Services

TYPE Original Research
PUBLISHED 29 August 2025
DOI 10.3389/frhs.2025.1650709

Check for updates

OPEN ACCESS

EDITED BY
Kevin Lu,
University of South Carolina, United States

REVIEWED BY
Valentin Marian Antohi,
Dunarea de Jos University, Romania
Fotini Santos Toscas,
University of São Paulo, Brazil

*CORRESPONDENCE
Haixia Ding
✉ dhxnjmu@126.com

RECEIVED 20 June 2025
ACCEPTED 18 August 2025
PUBLISHED 29 August 2025
CORRECTED 19 September 2025

CITATION
Xu Y, Wan J, Wan B and Ding H (2025) A multi-stakeholder multicriteria decision analysis for implantable medical devices assessment in China.
Front. Health Serv. 5:1650709.
doi: 10.3389/frhs.2025.1650709

COPYRIGHT
© 2025 Xu, Wan, Wan and Ding. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

A multi-stakeholder multicriteria decision analysis for implantable medical devices assessment in China

Yizhou Xu[1], Junjie Wan[1], Bin Wan[2] and Haixia Ding[1,3]*

[1]School of Pharmacy, Nanjing Medical University, Nanjing, Jiangsu, China, [2]School of International Pharmaceutical Business, China Pharmaceutical University, Nanjing, Jiangsu, China, [3]Department of Health Insurance Management, The First Affiliated Hospital with Nanjing Medical University, Nanjing, Jiangsu, China

Objectives: This study aims to develop a standardized multicriteria decision analysis (MCDA) framework tailored for implantable medical devices in China, addressing the challenges of inconsistent evaluation processes under China's evolving healthcare financing policies.
Methods: A mixed-methods design combining a discrete choice experiment (DCE) and MCDA was employed. Six criteria (clinical effectiveness, clinical safety, innovation, disease severity, implementation capacity, and cost) were identified through literature reviews and expert consultations. A DCE survey with 540 multi-stakeholder participants (decision-makers, HTA experts, clinicians, hospital administrators, and citizens) was conducted to derive criterion weights using mixed logit models. The framework was validated through a real-world case study assessing endoscopic linear staplers.
Results: Clinical safety (35.45%) and cost (27.94%) emerged as the most critical criteria, followed by implementation capacity (16.56%) and clinical effectiveness (15.07%). Innovation (2.54%) and disease severity (2.44%) received minimal weight. The MCDA application demonstrated high inter-rater consistency (CV < 0.25).
Conclusions: This study proposes a transparent, stakeholder-driven framework for evaluating implantable medical devices, specifically designed to support China's healthcare policies. The framework ensures that healthcare decisions are grounded in clinical effectiveness, safety, and long-term economic viability.

KEYWORDS

medical devices, multicriteria decision analysis, discrete choice experiment, technology assessment, preference, China

1 Introduction

China's basic medical insurance program has achieved broad population coverage [over 95% as of 2023 (1)], significantly improving healthcare accessibility and financial risk protection for citizens. The nationwide rollout of DRG/DIP prospective payment systems (2) has mandated stricter cost containment and value-based resource allocation across healthcare providers. By replacing fee-for-service with bundled payments and retrospective utilization reviews, these reforms align provider incentives with predefined budget frameworks while maintaining clinical quality standards.

Medical devices (MDs), defined by the World Health Organization as "health technologies for disease diagnosis, treatment or rehabilitation," (3) play a pivotal role in China's healthcare delivery system. This study focuses on implantable high-value MDs (e.g., cardiac pacemakers, orthopedic prostheses, vascular stents) that constitute major

expenditure items in national health insurance funds. Within China's universal healthcare coverage framework, the fragmented medical consumables market presents dual challenges: (a) insurance fund sustainability risks from unregulated price-quality variations, and (b) inequitable patient access due to regional procurement disparities.

The National Healthcare Security Administration (NHSA) has implemented strategic purchasing mechanisms through policies like the Volume-Based Procurement Implementation Plan and dynamic adjustment rules for medical insurance payment standards (4). These initiatives mandate value-based assessment of MDs incorporating clinical efficacy, cost-effectiveness, and budget impact analysis (BIA). Nevertheless, the absence of unified Health Technology Assessment (HTA) guidelines has resulted in two systemic issues: (a) Provider-level evaluation criteria disproportionately weighted (60%–70%) (5) on procurement costs rather than long-term clinical outcomes; (b) Insufficient integration of real-world evidence (RWE) from national insurance claim databases (6).

The inclusion of MDs in healthcare reimbursement schemes necessitates comprehensive evaluation given their substantial financial implications and clinical significance, requiring systematic balancing among three core dimensions: clinical effectiveness, safety profile, and cost-effectiveness (7). Previous studies have underscored both the challenges and critical importance of integrating multi-stakeholder perspectives in medical technology assessments (8).

To overcome these methodological challenges, multi-criteria decision analysis (MCDA) has gained prominence as an evidence-based decision support tool (9, 10). The MCDA framework enables structured decision-making through decomposition of complex evaluations into well-defined criteria, followed by systematic weighting and scoring based on their predetermined importance hierarchy. This methodology has been increasingly adopted in health technology assessment (HTA) systems to enhance decision transparency, maintain evaluative consistency, and improve systemic adaptability within evolving healthcare contexts.

Global implementations of MCDA for medical devices vary significantly based on healthcare system structures, policy priorities, and stakeholder landscapes. Queensland Health's MCDA model reflects Australia's universal healthcare goals through its focus on clinical benefit, cost-effectiveness, and equity of access, with the notable inclusion of explicit criteria for "implement capacity" (e.g., workforce training needs)—a dimension less emphasized in market-driven systems (7). Egypt's recent MCDA tool for implantable devices, by contrast, prioritizes technical characteristics and country of origin, which diverges from Western focus on clinical outcomes (9). These international examples highlight that MCDA frameworks are inherently context-specific, requiring adaptation to local policy objectives and healthcare financing models.

This study aims to develop a multi-criteria decision analysis framework to address the following questions: (a) What are the core criteria for evaluating implantable medical devices in China, considering the priorities of diverse stakeholders? (b) How do stakeholder preferences for these criteria differ, and what weights should be assigned to reflect China's policy goals? (c) Can a stakeholder-driven MCDA framework improve the consistency and transparency of device evaluation in China, as validated through real-world application? By integrating evidence-based evaluation criteria for clinical value and economic sustainability, which were preliminarily established through 6 criteria derived from our prior DCE study (8), the proposed system seeks to standardize MDs selection processes and enhance transparency in resource utilization under China's evolving healthcare financing policies.

2 Materials and methods

2.1 MCDA

Multicriteria decision analysis structured decision-making by establishing explicit criteria with systematically assigned scores and weights that reflect their relative importance. We constituted a custom weighted sum model in this study. While methodological variations exist across MCDA implementations, four core components consistently emerge: (a) contextual framing of the decision problem; (b) criterion selection and definition; (c) scoring alternatives based on predefined metrics; and (d) weight determination through systematic prioritization (11, 12). To operationalize these principles, our study employed a discrete choice experiment (DCE), a empirical technique validated for preference quantification in healthcare (13, 14). The process of this MCDA study is shown in Figure 1.

2.2 Criteria identification and definition

The criteria for the MCDA in this study were based on the validated attributes and levels derived from our group's previously published DCE research 8. This approach served to validate and confirm the findings reported in that prior study. Building upon established research foundations, a rapid review of medical devices (MDs) prioritization and assessment literature was conducted to identify supplementary evaluation criteria (7, 15, 16). Comprehensive searches were performed in PubMed, Web of Science, and the Cochrane Library through April 2024, utilizing the following search terms: "medical devices", "decision making", "discrete choice experiment", "Multicriteria decision analysis" and "preference". Identified criteria were systematically collated and critically reviewed to align with foundational DCE principles: completeness, non-redundancy, feasibility and mutual independence. Each criterion underwent rigorous operational definition to ensure conceptual clarity, direct measurability (excluding proxy indicators), and stakeholder interpretability (12).

To finalize the criteria, structured consultations were conducted with five HTA experts, whose selection followed three eligibility criteria: (a) all experts had ≥5 years of experience in health technology assessment; (b) the expert panel included specialists from three key domains (health economics, clinical

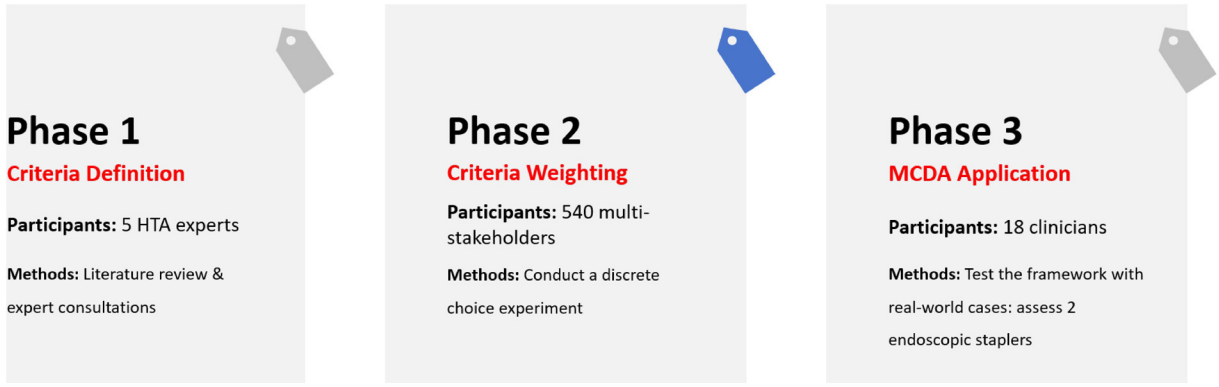


FIGURE 1
Phases of the MCDA study.

medicine and health policy) to ensure multi-dimensional perspectives; (c) experts were affiliated with diverse organizations, including a tertiary teaching hospital, and a provincial healthcare security administration, to avoid institutional bias. Consultations were conducted via semi-structured interviews, where experts reviewed the initial criteria list for completeness, non-redundancy, and feasibility. Revisions were integrated iteratively until consensus was reached. After that, 20 participants were randomly sampled to conduct a pilot test to refine six criteria.

2.3 Criteria weights

A discrete choice experiment (DCE) was implemented to systematically quantify preferences across multi-stakeholder groups. Participants were purposively sampled based on their roles in pharmaceutical pricing and reimbursement governance, encompassing representatives from national health insurance administrations, tertiary care facilities, HTA committees, clinicians, and patient groups. Adhering to Orme's guidelines for DCE sample adequacy, a minimum cohort of 75 respondents was recruited (17). Given the inclusion of five stakeholder groups, we calculated the required sample size to detect significant preference differences between subgroups. Using G*Power 3.1, assuming a medium effect size ($f^2 = 0.15$), $\alpha = 0.05$, and power = 0.80, the minimum sample size per subgroup was estimated at 90. To account for potential invalid responses (e.g., inconsistent answers in the validation set), we oversampled by 10%, resulting in a target sample size of 540 (90 respondents × 5 groups × 1.2). The final valid sample ($n = 540$) exceeded this target, ensuring sufficient power for both overall and subgroup analyses.

Based on the finalized 6 criteria, a D-efficiency design was generated to maximize attribute-level balance while minimizing cognitive burden (18). The design generated 27 different choice tasks, partitioned into three balanced blocks of nine scenarios each. Block assignments were randomized across participants to mitigate order effects. To assess internal consistency, the No.5 choice set within each block was replicated as a verification set (designated set No.10) and integrated into the survey questionnaire. As a result, 48 respondents with inconsistent answers were excluded.

The DCE analysis utilized both Mixed Logit Model and Conditional Logit Model, with final model selection informed by comparative evaluation of Akaike (AIC) and Bayesian (BIC) information criteria (19).

Relative importance (RI) metrics were computed to quantify the maximum marginal contribution of individual criteria to preference formation, normalized to a 100% scale across all evaluated attributes. This metric reflects both stakeholder prioritization patterns and the proportional influence of specific criteria on trade-off decisions (20). For n operationalized criteria, RI values were derived from standardized regression coefficients (β) using the following equation:

$$RI_k = \frac{max\beta_k - min\beta_k}{\sum_{k=1}^{k}(max\beta_k - min\beta_k)}$$

β_k: coefficient.

2.4 Application of the MCDA model

Preference data obtained from multi-stakeholder groups in the primary DCE were integrated into a MCDA framework to estimate (a) which among the approved implantable medical devices multi-stakeholders would choose and (b) the impact of each criteria in driving this decision.

The MCDA framework for MDs was applied to access two different endoscopic linear cutting staplers at Jiangsu Provincial People's Hospital in November 2024. Participating clinicians were from gastrointestinal and thoracic surgery departments with prior experience using endoscopic linear cutting staplers.

The consistency of scoring results for the two staplers was accessed using the coefficient of variation (CV). CV < 0.25 was considered indicative of high agreement among the clinicians.

Given that the clinicians were from two distinct departments (gastrointestinal surgery and thoracic surgery), we perform a two-sample *t*-test to statistically analyze the average scores assigned to each criterion by the two groups. $P > 0.05$ would indicate that the clinicians scored the criteria based on similar standards.

3 Results

3.1 Participant characteristics

From May 11 to June 24, 2024, a total of 588 participants completed the survey questionnaire after excluding 48 individuals who failed to meet the validation set (set No. 10 in all survey versions). Among the valid respondents, 12% held decision-making positions within national, provincial, and municipal healthcare security administrations, overseeing medical device tendering and bidding processes, national drug reimbursement list management, and medical insurance payment systems (Table 1). Hospital administrators comprised personnel from medical insurance, medical affairs, and medical device pricing departments, responsible for overseeing medical device management processes within healthcare institutions. Nationally recognized HTA experts accounted for 12% of respondents. Approximately one-quarter (27%) of respondents held positions equivalent to deputy chief physician or higher in specialized medical fields including orthopedics, general surgery, thoracic surgery, neurosurgery, and cardiovascular medicine. The remaining participants represented diverse occupational backgrounds.

TABLE 1 Demographic characteristics in DCE ($n = 540$).

Characteristics	*N*	%
Stakeholder		
Decision-makers	76	14%
HTA experts	65	12%
Hospital administrators	102	19%
Medical doctors	146	27%
Citizens	151	28%
Gender		
Female	135	25%
Male	405	75%
Average age	43	range 22–67 year

3.2 Criteria identification and definition

Following a comprehensive review of previously published MDs evaluation criteria, we conducted structured consultations with five HTA experts to finalize 6 criteria: clinical effectiveness, clinical safety, innovation, disease severity, implementation capacity, and cost (Table 2 were placed at the end of the file).

Clinical effectiveness was categorized into two categories: low-level, defined as enhancements in short-term outcomes (e.g., reduction of surgery duration, the amount of surgical bleeding and the length of hospitalization), and high-level, encompassing both short-term and long-term treatment outcome (e.g., reduction of recurrence rates, extended survival, and improved quality of life).

Clinical safety was evaluated using a two-category classification (1% vs. 8% adverse event incidence), revised from an original three-level system (1%, 8%, 15%) derived from a network meta-analysis of stent-related adverse events (15). Clinicians indicated during pilot testing that an 8% adverse event rate represented a

TABLE 2 Multicriteria decision analysis criteria and weights.

Criteria	Definition	Criteria weighting (%)	Criteria categories	Category weight (%)
Clinical Effectiveness	The enhancement of patients' health outcome following therapy	15.07%	Enhancements in short-term outcomes	7.45%
			Enhancements in both short-term and long-term treatment outcomes	15.07%
Clinical safety	The occurrence rate of adverse reactions associated with MDs, along with associated procedural risks	35.45%	1%	17.52%
			8%	35.45%
Innovation	The introduction of upgrades to existing technologies or the expansion of their application scope to new indications	2.54%	Without: Alternative options available	1.26%
			With: Involves upgrades or expanded applications	2.54%
Disease severity	The critical nature of the targeted disease condition, specifically whether it poses a threat to survival	2.44%	Non-life-threatening condition	2.44%
			Life-threatening condition	1.21%
Implement Capacity	Assessed based on the Implement Capacity across three domains: the healthcare system, medical institutions, and clinicians' proficiency acquisition	16.56%	Limited assurance in implement capacity across all three domains	0.00%
			Demonstrated implement capacity across any two domains	16.56%
			High assurance in implement capacity across all three domains	11.86%
Cost	The cost of the MDs used in every single treatment	27.94%	2,000 yuan	27.94%
			20,000 yuan	17.77%
			50,000 yuan	0.81%

realistic threshold in real world therapy, while 15% was deemed implausible. We recruited 4 clinicians from thoracic surgery with ≥3 years of experience in using implantable devices. Participants completed a pilot version of the DCE questionnaire (including the original 3-level safety criteria: 1%, 8%, 15%) followed by a semi-structured interview. All 4 participants agreed that "15% exceeds the maximum acceptable rate in clinical practice for implantable devices". Based on this consensus, the 15% level was removed.

The cost of MDs per treatment episode were stratified into three categories (2,000yuan/20,000yuan/50,000yuan), informed by pricing distributions of high-value MDs in Nanjing medical insurance list and experts consultation, consistent with the cost category defined in published studies (16).

Disease Severity and Innovation were defined using two categories adapted from a previously published Queensland study (7). Implementation capacity were assessed across three domains: the healthcare system, medical institutions, and clinicians' proficiency acquisition.

A pilot study involving 14 participants was subsequently implemented to examine data quality, assess respondents' ability to differentiate criteria categories and make trade-offs between them.

3.3 Criteria weights

Methodologically, the mixed logit model outperformed the conditional logit model (AIC: 2,342.17 vs. 2,433.34), attributable to its capacity to account for unobserved preference heterogeneity across stakeholders (e.g., decision-makers prioritized cost containment while clinicians emphasized clinical safety).

The mixed logit model revealed that clinical safety (35.45%, 95% CI: 31.28–39.62%) and cost (27.94%, 95% CI: 24.15–31.73%) emerged as the two most critical criteria for evaluating MDs in China, collectively accounting for over 63% of the total weight (Table 2 were placed at the end of the file). This consistency with the published findings of Wan et al. These findings also align with the priorities of China's ongoing DRG/DIP payment reforms, which emphasize cost containment and risk mitigation in healthcare delivery.

Secondary criteria included implementation capacity (16.56%, 95% CI: 13.82%–19.30%) and clinical effectiveness (15.07%, 95% CI: 12.64%–17.50%), with long-term outcomes weighted higher than short-term gains (7.45%). In contrast, innovation (2.54%, 95% CI: 1.89%–3.19%) and disease severity (2.44%, 95% CI: 1.76%–3.12%) received minimal weight, consistent with industry data indicating that 88% of China's Class III medical devices in 2022 were incremental modifications rather than breakthrough technologies (21).

Subgroup preferences across the six criteria (Supplementary Table S2) revealed both convergence and divergence. There was a clear consensus on clinical safety, with all subgroups showing strong and significant preference for high safety levels (all $P < 0.001$), with hospital administrators (RI = 2.714) and medical doctors (RI = 2.147) placing the highest emphasis, while cost was also consistently prioritized across all subgroups (all $P < 0.001$). Notable divergences included: HTA experts valuing disease severity (RI = 0.379, $P < 0.000$) in contrast to hospital administrators who showed a negative association (RI = −0.578, $P < 0.000$); hospital administrators and medical doctors prioritizing moderate implementation capacity (RI = 1.140, 1.150, all $P < 0.000$) while decision-makers devalued high capacity (RI = −0.923, $P < 0.000$), which may suggest that excessively high implementation thresholds (including technical complexity, training costs, etc.) reduce its practical application value; and medical doctors, citizens, and hospital administrators preferring innovation (RI = 0.546, 0.427, 0.528, all $P < 0.05$) unlike HTA experts (RI = 0.106, $P = 0.293$).

3.4 MCDA results

In November 2024, a MCDA was conducted at Jiangsu Provincial People's Hospital for two endoscopic linear cutting staplers: a leading imported brand and a domestic brand. Clinicians independently assessed each device across all predefined criteria using a standardized scoring sheet (Supplementary Figure S1). For each stapler, a composite score was generated via the weighted sum method, a validated MCDA framework (22), by multiplying each criterion score by the weight and summing the weighted criterion scores to produce one total score, as demonstrated in Supplementary Figure S1. Individual total scores were then collated to calculate a mean score for each stapler.

The assessment involved 12 thoracic surgeons and 6 gastrointestinal surgeons, all with prior experience using the evaluated products (Table 3). The overall MCDA scores assigned by clinicians were 86.5% for stapler A and 82.4% for stapler B (see Figure 2). The 4.1% score difference between stapler A and B was significant, as stapler A showed lower adverse event rates and lower long-term cost in real-world use.

The consistency of scores across the 18 participating clinicians was evaluated using the coefficient of variation (CV). With CV < 0.25 for two staplers (0.0914 and 0.0909), indicating a high level of agreement among clinicians. An independent two-sample

TABLE 3 The clinicians' characteristics in MCDA ($n = 18$).

Characteristics	*N*	%
Gender		
Male	18	100%
Education experience		
Ph.D. or above	13	72%
Master	4	22%
Undergraduate	1	6%
Department		
Thoracic surgery	12	67%
Gastrointestinal surgery	6	33%
Year of service	11.6	Range 2–27 year
Average age	38.7	Range 28–51 year

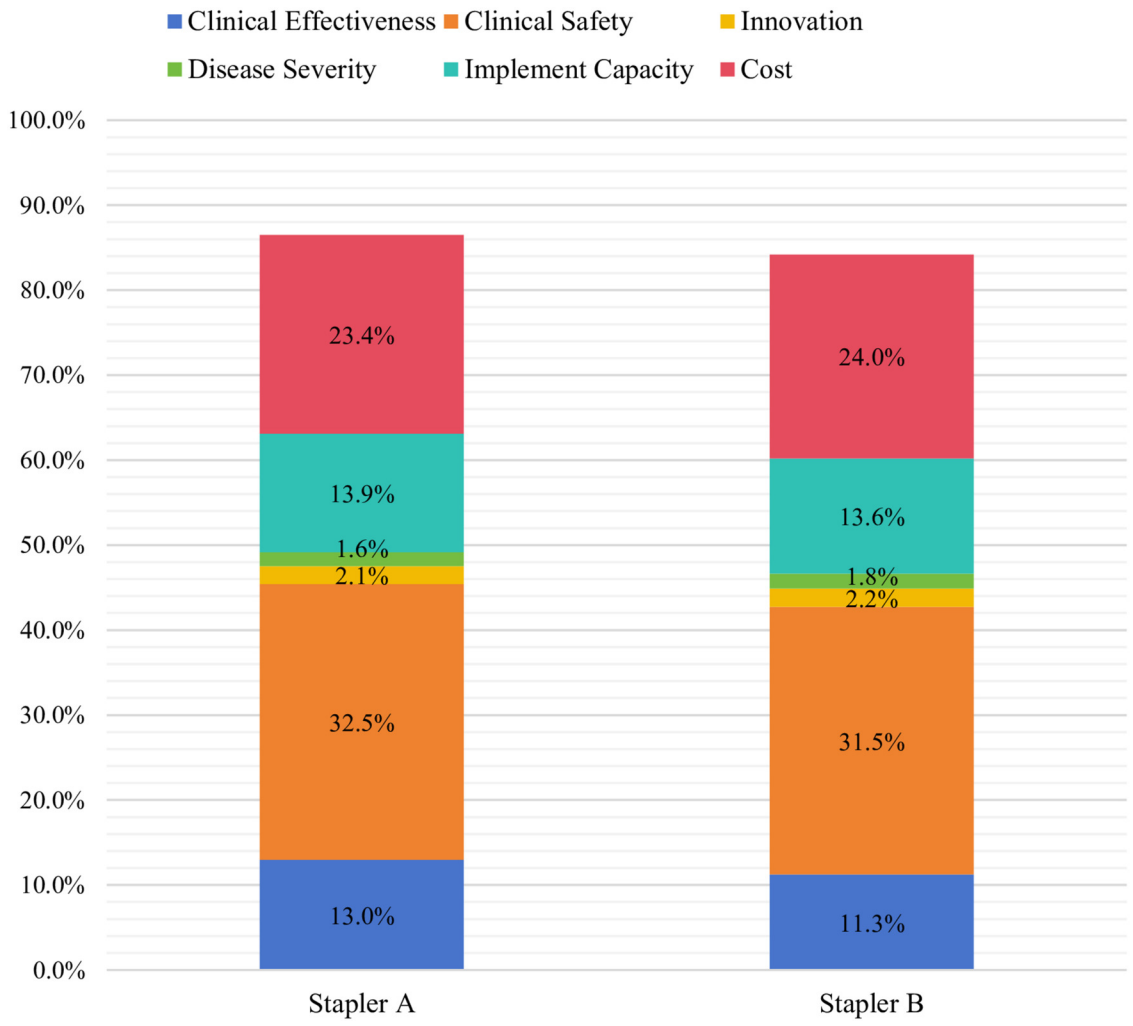


FIGURE 2
Overall MCDA scores for endoscopic linear cutting staplers. *Stapler A: 95%CI (83.1%, 89.9%); Stapler B: 95%CI (80.9%, 87.5%).

t-test was conducted to compare the average scores for each criterion between the thoracic and gastrointestinal surgeons, assuming unequal variances. The results showed no significant differences ($p > 0.05$) across the six criteria, suggesting that the clinicians scored the staplers based on consistent standards.

4 Discussion

This study integrates multicriteria decision analysis (MCDA) and discrete choice experiments (DCEs) to establish a stakeholder-driven evaluation framework for implantable medical devices (MDs) within the context of China's healthcare reform. Under China's current policy landscape, two initiatives dominate medical device procurement and reimbursement: (a) Volume-Based Procurement (VBP), which leverages bulk purchasing to negotiate price reductions for high-value MDs while ensuring quality standards, and (b) medical insurance coverage policies and evidence-driven payment adjustments, which dynamically link reimbursement rates to clinical value and budget impact analyses through evidence-based formulary updates. By establishing an MCDA framework to delineate value parameters of medical devices, this methodological approach systematically addresses multidimensional evaluation criteria through structured value assessment.

By explicitly weighting criteria such as clinical safety (35.45%) and cost (27.94%), our model addresses systemic challenges in China's healthcare system, including fragmented procurement practices and overreliance on short-term cost considerations. The framework's emphasis on safety aligns with regulatory mandates from the National Healthcare Security Administration (NHSA) to prioritize risk mitigation in high-value device reimbursement. Meanwhile, the prominence of cost mirrors DRG/DIP's bundled payment structure, which compels hospitals to balance clinical outcomes with stringent budget constraints—a tension less pronounced in systems like Australia's Queensland framework, where clinical benefit alone accounted for 27.2% of weights 7. While Egypt's tool isolates financial evaluation as a separate

post-technical phase, prioritizing technical characteristics (29.4%) and country of origin (19.5%) to emphasize manufacturing quality over immediate cost considerations (9).

Notably, innovation received minimal weight (2.54%). The lower weight of innovation in our study does not indicate that innovation is unimportant. This discrepancy stems from China's current innovation landscape: a significant portion of domestically developed medical MDs approved in recent years have been categorized as incremental modifications (e.g., material upgrades in orthopedic implants), with fewer examples of transformative technological breakthroughs. Such trends reduce perceived value in HTA processes, as minor iterations seldom justify premium pricing under DRG/DIP's fixed reimbursement rates. However, this does not negate innovation's importance; rather, it underscores the need for manufacturers to align R&D with China's policy priorities-specifically, devices that demonstrably lower long-term costs (e.g., reducing revision surgeries) or address unmet clinical needs (e.g., pediatric-specific implants).

The proposed MCDA framework could further optimize decision-making processes across two critical dimensions. First, at the macro-policy level, it supports the design and implementation of value-driven procurement strategies, such as VBP and dynamic adjustments to medical insurance payment standards. By explicitly quantifying trade-offs between cost and clinical outcomes, the framework enables policymakers to prioritize devices that align with population health goals while containing systemic expenditures-a key challenge under China's centralized procurement reforms. Second, the framework enhances transparency in hospital-level decision-making. By incorporating standardized criteria, it provides a replicable protocol for device selection and procurement committees, reducing institutional biases and fostering accountability in MDs adoption.

For health policymakers, this study provides a transparent and evidence-based tool that supports budget planning and equitable resource allocation. The alignment with DRG/DIP payment systems ensures that high-value MDs are reimbursed based on clear, standardized criteria, improving efficiency in medical expenditure.

For healthcare institutions, the MCDA framework offers a structured approach to balance clinical priorities with operational constraints. Hospitals, particularly under DRG/DIP payment models, face dual pressures to optimize clinical outcomes while adhering to strict reimbursement caps. By integrating criteria such as implementation capacity and safety, the framework enables procurement committees to standardize device selection processes, reducing subjective biases in MDs adoption.

For medical device manufacturers, the findings highlight the need for a strategic shift toward developing devices that not only demonstrate clinical superiority but also align with cost-effectiveness and implementation feasibility. The lower priority assigned to incremental innovation indicates that small, non-impactful modifications of existing products are insufficient to gain market access. Instead, companies should focus on substantial advancements that lead to significant clinical and economic improvements.

For emerging technologies, where cost may initially be higher but potential long-term gains are substantial. The framework could be adapted by adjusting cost weights to include long-term economic gains like reducing revision surgeries. For example, a disruptive stent with higher upfront cost but 25% lower 5-year complication rates could be re-evaluated using time-dependent cost metrics.

While our model is tailored to China's institutional context, its core criteria—clinical effectiveness, safety, cost, and implementation capacity—align with global HTA priorities (12). Adapting the framework for cross-country use would require adjusting weights to reflect regional priorities: for instance, high-income countries might assign greater weight to innovation, while low- and middle-income countries could emphasize implementation capacity and cost (9). Aligning with ISPOR's MCDA good practices could facilitate such harmonization.

Despite its strengths, the study has some limitations. The sample size, while substantial, is limited to specific stakeholder groups. Its generalizability may be constrained by the overrepresentation of tertiary hospitals (64% of participants), which face different cost pressures than rural facilities. Stakeholder preferences in our study may also be shaped by cultural and institutional biases inherent to China's healthcare system. Institutionally, VBP and DRG/DIP reforms create strong incentives for cost containment, explaining why decision-makers and hospital administrators prioritized cost more heavily than clinicians. Culturally, the emphasis on collective healthcare sustainability may influence citizens' willingness to trade off marginal innovation for lower costs, as reflected in their moderate preference for innovation (Supplementary Table S2). These biases highlight the need for context-specific calibration when applying the framework across diverse healthcare settings.

Additionally, a multicenter validation study across various hospital settings would strengthen the generalizability of the findings. Incorporating real-world evidence (RWE) into periodic weight updates could enhance the framework's responsiveness to real-world performance, particularly for devices with long-term safety profiles. For example, RWE on post-implantation complication rates could refine the clinical safety weight, while data on long-term healthcare utilization could adjust cost weights to reflect lifetime economic impact. Future studies should explore incorporating real-world clinical data to refine the weighting of criteria further.

The framework's applicability beyond implantable MDs should also be tested in other high-value consumables, such as diagnostic technologies, ensuring broader utility in healthcare decision-making.

5 Conclusion

This study presents a novel MCDA-based framework for implantable MD evaluation, tailored to China's healthcare reforms. By incorporating structured criteria weighting, stakeholder preferences, and real-world validation, the model offers a transparent, replicable, and adaptable assessment tool for procurement and reimbursement decisions.

For national-level implementation of the framework, it is advisable to collaborate with the National Healthcare Security Administration to embed the framework into dynamic medical insurance payment adjustment mechanisms, linking reimbursement rates to the weighted scores of core criteria (such as clinical safety and cost) to align with DRG/DIP reforms. A periodic review mechanism should also be established to incorporate real-world evidence from national insurance databases, refining criterion weights and enhancing the framework's responsiveness to evolving clinical needs and policy priorities.

The proposed framework exhibits strong versatility beyond MDs. Its core criteria—clinical effectiveness, safety, cost, and implementation capacity—are adaptable to diverse high-value medical technologies like diagnostic imaging systems and cell/gene therapies. With minor adjustments, such as tailoring "implementation capacity" to fit laboratory needs for diagnostics, the framework can effectively evaluate these technologies, enhancing its utility in healthcare decision-making.

Future refinements integrating multicenter data and real-world evidence will further enhance the framework's robustness and scalability, contributing to evidence-based policymaking and sustainable healthcare financing.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author.

Author contributions

YX: Methodology, Writing – original draft, Investigation. JW: Methodology, Investigation, Formal analysis, Writing – original draft. BW: Writing – review & editing, Methodology, Resources. HD: Funding acquisition, Resources, Supervision, Writing – review & editing.

Funding

The author(s) declare that financial support was received for the research and/or publication of this article. This study was supported by Research on Improving the Online Procurement Rate of High-value Medical Devices in Public Medical Institutions funded by the First Affliated Hospital with Nanjing Medical University (No. 202431).

Acknowledgments

This article has been developed in the context of the activities of the Jiangsu Province Hospital. The views expressed are purely those of the authors and may not in any circumstances be regarded as stating an official position of the government of People's Republic of China.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Correction note

A correction has been made to this article. Details can be found at: 10.3389/frhs.2025.1695328.

Generative AI statement

The author(s) declare that no Generative AI was used in the creation of this manuscript.

Any alternative text (alt text) provided alongside figures in this article has been generated by Frontiers with the support of artificial intelligence and reasonable efforts have been made to ensure accuracy, including review by the authors wherever possible. If you identify any issues, please contact us.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/frhs.2025.1650709/full#supplementary-material

References

1. National healthcare security administration. Statistical bulletin of the national healthcare security administration. (2023). Available online at: https://www.nhsa.gov.cn/art/2024/7/25/art_7_13340.html (Accessed July 25, 2024).

2. National Healthcare Security Administration. The national medical insurance bureau officially launched the three-year action plan for DRG/DIP payment reform. (2021). Available online at: http://www.nhsa.gov.cn/art/2021/11/26/art_104_7413.html (Accessed August 10, 2023).

3. World Health Organization. Health-topic medical-devices. (2023). Available online at: https://www.emro.who.int/health-topics/medical-devices/index.html (Accessed August 10, 2023).

4. National Healthcare Security Administration. Pilot plan for centralized procurement and use of drugs. (2019). Available online at: https://www.gov.cn/gongbao/content/2019/content_5361793.htm (Accessed January 1, 2019).

5. National Healthcare Security Administration. Regulations on medical equipment procurement management. (2019). Available online at: https://www.gov.cn/gongbao/content/2019/content_5442286.htm (Accessed June 6, 2019).

6. Chuanchao L, Xin G. International experience and implications of real-world evidence supporting drug medical insurance access. *China Health Insur*. (2024) 2024(7):24–32. doi: 10.19546/j.issn.1674-3830.2024.7.003

7. Howard S, Scott IA, Ju H, McQueen L, Scuffham PA. Multicriteria decision analysis (MCDA) for health technology assessment: the Queensland health experience. *Aust Health Rev*. (2019) 43(5):591–9. doi: 10.1071/AH18042

8. Wan B, Shen J, Chen J, Weng L, Zhao P, Deng Y, et al. Quantifying stakeholders' preference for implantable medical devices in China: a discrete choice experiment. *Int J Technol Assess Health Care*. (2024) 40(1):e8. doi: 10.1017/S0266462323002799

9. Elezbawy B, Fasseeh AN, Németh B, Gamal M, Eldebeiky M, Refaat R, et al. A multicriteria decision analysis (MCDA) tool to purchase implantable medical devices in Egypt. *BMC Med Inform Decis Mak*. (2022) 22(1):289. doi: 10.1186/s12911-022-02025-y

10. Khan I, Pintelon L, Martin H. The application of multicriteria decision analysis methods in health care: a literature review. *Med Decis Mak*. (2022) 42(2):262–74. doi: 10.1177/0272989X211019040

11. Devlin N, Sussex J. *Incorporating Multiple Criteria in HTA: Methods and Processes*. London: Office of Health Economics (2011).

12. Marsh K, IJzerman M, Thokala P, Baltussen R, Boysen M, Kaló Z, et al. Multiple criteria decision analysis for health care decision making–emerging good practices: report 2 of the ISPOR MCDA emerging good practices task force. *Value Health*. (2016) 19(2):125–37. doi: 10.1016/j.jval.2015.12.016

13. Clark MD, Determann D, Petrou S, Moro D, de Bekker-Grob EW. Discrete choice experiments in health economics: a review of the literature. *PharmacoEconomics*. (2014) 32(9):883–902. doi: 10.1007/s40273-014-0170-x

14. Soekhai V, de Bekker-Grob EW, Ellis AR, Vass CM. Discrete choice experiments in health economics: past, present and future. *PharmacoEconomics*. (2019) 37(2):201–26. doi: 10.1007/s40273-018-0734-2

15. Madhavan MV, Kirtane AJ, Redfors B, Généreux P, Ben-Yehuda O, Palmerini T, et al. Stent-related adverse events >1 year after percutaneous coronary intervention. *J Am Coll Cardiol*. (2020) 75(6):590–604. doi: 10.1016/j.jacc.2019.11.058

16. Lee HJ, Bae EY. Eliciting preferences for medical devices in South Korea: a discrete choice experiment. *Health Policy*. (2017) 121(3):243–9. doi: 10.1016/j.healthpol.2017.01.002

17. Orme BK. *Getting Started with Conjoint Analysis: Strategies for Product Design and Pricing Research. 4*. Manhattan Beach, CA: Research Publishers LLC (2020).

18. Reed Johnson F, Lancsar E, Marshall D, Kilambi V, Mühlbacher A, Regier DA, et al. Constructing experimental designs for discrete-choice experiments: report of the ISPOR conjoint analysis experimental design good research practices task force. *Value Health*. (2013) 16(1):3–13. doi: 10.1016/j.jval.2012.08.2223

19. Dziak JJ, Coffman DL, Lanza ST, Li R, Jermiin LS. Sensitivity and specificity of information criteria. *Brief Bioinform*. (2020) 21(2):553–65. doi: 10.1093/bib/bbz016

20. Hauber AB, González JM, Groothuis-Oudshoorn CG, Prior T, Marshall DA, Cunningham C, et al. Statistical methods for the analysis of discrete choice experiments: a report of the ISPOR conjoint analysis good research practices task force. *Value in Health*. (2016) 19(4):300–15. doi: 10.1016/j.jval.2016.04.004

21. Dong J, Yujun C, Xiaoping C. *Annual Report on the Data of Medical Device Industry in China (2023)*. Peking: Social Sciences Academic Press (China) (2023).

22. Thokala P, Duenas A. Multiple criteria decision analysis for health technology assessment. *Value in Health*. (2012) 15(8):1172–81. doi: 10.1016/j.jval.2012.06.015

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 05 September 2025
DOI 10.3389/fpubh.2025.1596676

Check for updates

OPEN ACCESS

EDITED BY
Kevin Lu,
University of South Carolina, United States

REVIEWED BY
Davi Rumel,
Retired, São Paulo, Brazil
Di Cui,
Agency for Science, Technology and Research (A*STAR), Singapore

*CORRESPONDENCE
Ruxu You
✉ youruxu2008@163.com

RECEIVED 20 March 2025
ACCEPTED 18 August 2025
PUBLISHED 05 September 2025

CITATION
Wang C, Lin X, Liu J, Zhang Y and You R (2025) Cost-effectiveness analysis of Chinese patent medicines for the treatment of postmenopausal osteoporosis in China. *Front. Public Health* 13:1596676. doi: 10.3389/fpubh.2025.1596676

COPYRIGHT
© 2025 Wang, Lin, Liu, Zhang and You. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

Cost-effectiveness analysis of Chinese patent medicines for the treatment of postmenopausal osteoporosis in China

Cong Wang[1], Xihan Lin[1], Jinyu Liu[2], Yu Zhang[1] and Ruxu You[1]*

[1]Department of Pharmacy, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, China, [2]Department of Pharmacy, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, China

Introduction: Evidence indicates that Chinese patent medicines can significantly increase bone mass in patients with osteoporosis and alleviate symptoms associated with low bone density. Although the therapeutic effects of these two drugs have been compared both directly and indirectly, no economic-related studies currently exist. Therefore, this study aims to assess the cost-effectiveness of Xianling Gubao Capsules compared to Jintiange Capsules and non-treatment for postmenopausal osteoporosis from the perspective of Chinese healthcare providers.

Methods: A Markov microsimulation model was employed to estimate the cost-effectiveness of the Xianling Gubao capsule and the Jintiange capsule in a hypothetical cohort of postmenopausal osteoporotic women aged 55 to 74 years with no prior history of fractures, over a treatment period of 6 months. Model parameters, including transition probabilities and costs, were derived from Chinese sources. Efficacy data for the treatments were obtained from two network meta-analyses. Outcomes were expressed as incremental costs per quality-adjusted life-year (QALY) gained. Sensitivity analyses were performed to ensure the robustness of the findings, with a cost-effectiveness threshold established at three times the Gross Domestic Product (GDP) per capita in China ($38,223) per QALY.

Result: Compared to the control group that did not receive drug treatment, the preventive therapy using Chinese patent medicine significantly increased bone mineral density and reduced the probability of fractures across all age groups in the intervention group. The incremental cost-effectiveness ratios (ICERs) for the Jintiange capsule compared to the Xianling Gubao capsule ranged from $11,955 per QALY at age 55 to $9,711 per QALY at age 74, indicating that the cost-effectiveness of the Jintiange capsule improved consistently with age. Sensitivity analyses confirmed the robustness of the results across all parameter variations, with the annual cost of the Jintiange capsule identified as the most sensitive factor.

Conclusion: From the perspective of Chinese healthcare providers, preventive therapy using Chinese patent medicine, when compared to a control group that did not receive drug treatment, resulted in increased bone mineral density and a reduced probability of fractures across all age levels in the intervention group. Additionally, the Jintiange capsule appears to be a cost-effective treatment option for postmenopausal women with osteoporosis.

10.3389/fpubh.2025.1596676

KEYWORDS

osteoporosis, Chinese patent medicines, postmenopausal, cost-effectiveness, Xianling Gubao capsules, Jintiange capsules

Introduction

Osteoporosis is a chronic, progressive skeletal disorder characterized by reduced bone mass, deterioration of bone microstructure, and increased fragility, which collectively elevate the risk of fragility fractures that can severely compromise patients' quality of life (1). Projections indicate that by 2040, nearly 319 million individuals worldwide will be at risk of osteoporotic fractures, with 55% of these cases expected to occur in Asia (2). According to the national census data from the National Bureau of Statistics of China at the end of 2021, the population aged 60 and above in China was 267.36 million, accounting for 18.9% of the total population. Among this group, the population aged 65 and above was 200.56 million, representing 14.2% (3). The Diagnosis and Treatment Guidelines for Primary Osteoporosis (2022) in China indicate that the prevalence of osteoporosis among women aged 50 and above is 32.1%, which is six times higher than that of men in the same age group (4). Furthermore, the prevalence of osteoporosis significantly increases among females aged 60 and above (1). Osteoporosis can lead to various types of fractures. A study conducted in 2015 estimated that the medical expenses for major osteoporotic fractures in China would reach as high as 11 billion, 20 billion, and 25 billion USD in 2015, 2035, and 2050, respectively (5). Therefore, it is essential to identify safe, effective, and economical treatment options.

Traditional osteoporosis medications include bisphosphonates, parathyroid hormone, selective estrogen receptor modulators, calcium supplements, estrogen replacement therapy, and calcilytics (6–8). While these drugs have demonstrated varying degrees of efficacy in the treatment of osteoporosis, patient compliance remains unsatisfactory due to the occurrence of adverse reactions (9–11). Hormone replacement therapy (HRT), a common treatment for osteoporosis, has been associated with an increased risk of cardiovascular disease and breast cancer (12). Additionally, long-term calcium intake, a routine preventive measure for osteoporosis, has also been linked to a heightened risk of myocardial infarction (13). Given the chronic nature of osteoporosis, it is crucial to balance the associated risks and benefits (14). In China, Chinese patent medicines (CPMs) are ready-made medications formulated in specific dosage forms based on prescriptions or standards guided by the principles of traditional Chinese medicine (15, 16). These medicines are widely utilized in the treatment of osteoporosis (15, 17). Evidence indicates that CPMs can significantly enhance bone mass in patients with osteoporosis and alleviate symptoms associated with low bone mass. The Xianling Gubao Capsule and Jintiange Capsule are two CPMs primarily recommended by various treatment guidelines (1, 18). Although there have been both direct and indirect comparisons of the therapeutic effects of these two medications, no economic evaluations have been conducted (19). Therefore, this study aims to compare the cost-effectiveness of Xianling Gubao Capsules and Jintiange Capsules, as well as non-treatment options for postmenopausal osteoporosis, from the perspective of Chinese healthcare providers, thereby addressing a significant gap in the existing literature.

Methods

Study design

This study utilized a 100,000 hypothetical individuals Markov microsimulation model to estimate the cost-effectiveness of Xianling Gubao Capsules and Jintiange Capsules in Chinese postmenopausal women, compared to no intervention. Each cycle lasts 1 year, during which each participant may experience a hip fracture, clinical vertebral fracture, or other types of fractures. Adopting the perspective of Chinese healthcare providers and extending the analysis to a lifetime horizon, the states are continuously updated until the patient's death. A consistent discount rate of 3% was applied to both costs and health outcomes to account for time preference. The analysis was conducted using TreeAge Pro (Healthcare Version) 2022, in accordance with the Consolidated Health Economic Reporting Standards (CHEERS), as detailed in Supplementary Table 1 (20).

The model meticulously simulated a cohort of Chinese postmenopausal women with no prior history of fragility fractures across various age groups: 55–59, 60–64, 65–69, and 70–74 years. The base case focused on individuals aged 55–59 years. In our model construction and parameterization, age-specific mean and standard deviation (SD) data of BMD shown in Table 1 were derived from Wang et al. (21). The simulation incorporated a normal distribution derived from the mean and standard deviation (SD) values reported by Wang et al., based on the statistical assumption of a large-sample distribution. An initial BMD value was sampled from this normal distribution at the commencement of the Markov microsimulation and subsequently assigned randomly to individual participants. In accordance with established guidelines (1, 18), patients in all groups were administered calcium and activated vitamin D. The cohort was then assigned to receive either Xianling Gubao treatment (Xianling Gubao capsules 1.5 g b.i.d. for 6 months) or Jintiange treatment (Jintiange capsules 1.2 g t.i.d. for 6 months), while the no-intervention group was designated as the status quo.

Model structure

Figure 1 illustrates the structure of the Markov model, which includes the states of no fracture, simple fracture, complex

TABLE 1 Mean BMDs, SDs of the femoral neck in different initial medicated ages of female (g/cm^2).

Age (years)	Number	Mean	SD	95%CI
55–59	3,152	0.73	0.13	(0.72, 0.73)
60–64	3,155	0.66	0.12	(0.65, 0.66)
65–69	925	0.58	0.11	(0.58, 0.59)
70–74	137	0.55	0.13	(0.53, 0.58)

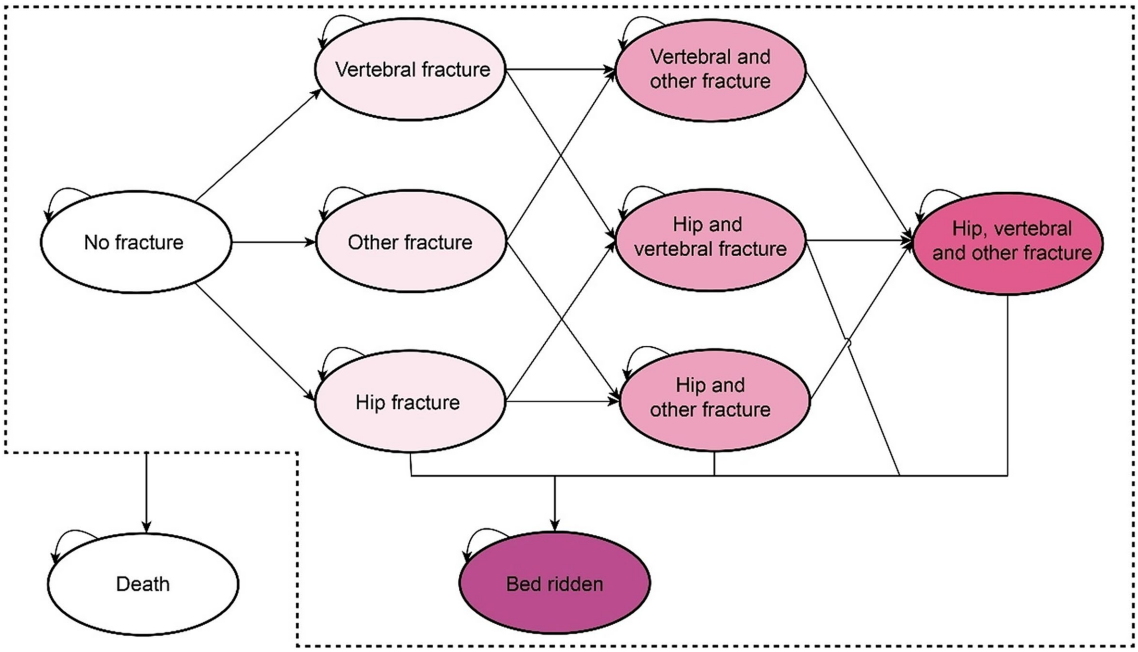


FIGURE 1
The Markov model structure for the disease progression of postmenopausal women with osteoporosis (omitting the arrow pointing to the death state).

fracture, bedridden due to hip fracture, and death from fracture or other causes. The simple fracture state indicates that individuals had experienced any hip, vertebral, or other types of fractures. The complex fracture state was defined as the occurrence of multiple simple fracture events. It was assumed that a certain proportion of individuals diagnosed with hip fractures may transition to the bedridden state without experiencing any additional fractures.

All patients entered the model in a "no fracture" healthy state. During each cycle, patients could experience a fracture, remain healthy, or die. Patients in the "fracture" state could either remain in the same fracture state if a refracture occurred, transition to another fracture state if a new fracture occurred, or move to the corresponding "post-fracture" state. Among these states, only patients with hip fractures may enter a bedridden state. For instance, patients who have experienced a vertebral fracture might subsequently experience another vertebral fracture or a hip fracture. Fractured patients could not return to the "no fracture" healthy state and would remain in the "post vertebral fracture" or "post hip fracture" state unless another fracture occurs or they entered the bedridden state. Ultimately, all patients were subject to the risk of death, and upon decease, they were transferred to the terminal death state.

Model parameters

All model parameters were sourced from China whenever possible to ensure their relevance to the local healthcare environment. In the absence of local data, information was synthesized from published literature through systematic literature searches. The input data utilized in the model is presented in the following section (Table 2).

Transition probabilities

Fracture risks

The transition probability of the fracture state was calculated based on age-specific and BMD-specific incidence rates of fragility fractures (Supplementary Table 2). Equations for the incidence of hip, vertebral, and other fractures associated with age and BMD were derived from published epidemiological data on the Chinese population (22–27). The fitted algorithms were evaluated using the R-squared statistic and adjusted for clinical plausibility. The probability of fracture was further modified based on the relative risk associated with a history of previous fractures, as individuals who have experienced any osteoporotic fracture are at an increased risk of subsequent fracture events. These values were obtained from a meta-analysis (28). Additionally, the probability of a bedridden state resulting from a hip fracture was extracted from a prior study conducted in Japan (29).

Mortality

Baseline age-specific mortality rates in the general population were extracted by sex and age from the seventh national population census in China (30). Excess mortality rates attributed to hip fractures were derived from published literature on Chinese women by multiplying the age-dependent risk ratio of mortality following a hip fracture (31).

Treatment

The efficacy data for Xianling Gubao capsules and Jintiange capsules were derived from a network meta-analysis of 22 randomized controlled trials that compared the effectiveness of various anti-osteoporotic agents (32). This study represents the largest analysis to date concerning the two aforementioned drugs and included a total of 2,016 postmenopausal women diagnosed with primary osteoporosis. Compared to placebo, Xianling Gubao capsules significantly enhanced

10.3389/fpubh.2025.1596676

TABLE 2 Estimates of parameters used in the model.

Parameter	Base-case value	Range	Distribution	Source
Relative risk of fracture in individuals with osteoporosis				
RR of hip fractures with complications				
History of previous fractures	1.97	1.12–3.48	Log-normal	(29)
RR of vertebral fractures with complications				
History of previous fractures	1.91	1.50–2.43	Log-normal	(29)
RR of other fractures with complications				
History of previous fractures	1.91	1.50–2.43	Log-normal	(29)
Probability of bedridden after hip fracture	0.136	0.095–0.177	Fixed	(32)
The therapeutic effect of drugs				
Xianling Gubao capsule				(59)
Increase in bone density (g/cm^2)	0.05	0.01–0.08	Beta	
Treatment time (year)	0.5		Fixed	
Jintiange capsule				(59)
Increase in bone density (g/cm^2)	0.11	0.03–0.19	Beta	
Treatment time (year)	0.5		Fixed	
Cost (in 2022 China)				
Annual Cost of Medication (US $)				
Xianling Gubao capsule	$93.24	±20%	Triangular	(36)
Jintiange capsule	$574.82	±20%	Triangular	
Annual medical expenses (US $)	$439.78	±20%	Triangular	
Cost of fracture treatment (US$)				
Hip fracture	$7,379.82	±20%	Triangular	(60)
Vertebral fracture	$1,361.12	±20%	Triangular	
Other fracture	$1,758.30	±20%	Triangular	
Annual bedridden care expenses (US$)	$4,948.90	±20%	Triangular	
Health utility (QALY)				
Age-Related Baseline Utility				(41)
55–59	0.88	0.862–0.897	Beta	
60–65	0.869	0.852–0.885	Beta	
66–70	0.827	0.802–0.851	Beta	
71–74	0.808	0.770–0.846	Beta	
Disutility resulting from hip fractures				(42)
First year	×0.776	0.720–0.844	Beta	
subsequent years	×0.855	0.800–0.909	Beta	
Disutility resulting from vertebral fracture				
First year	×0.724	0.667–0.779	Beta	
subsequent years	×0.868	0.827–0.922	Beta	
Disutility resulting from other fracture				(39)
First year	×0.910	0.880–0.940	Beta	
subsequent years	×1			
Utility of Bedridden State	0.192		Fixed	(41)
Discount rate				
Cost	0.03	0–0.05		(35)
QALYs	0.03	0–0.05		(35)

lumbar and femoral neck BMD (Mean Difference, MD = 0.13, 95% CI [0.03, 0.22], MD = 0.17, 95% CI [0.06, 0.29]). In contrast, Jintiange capsules significantly improved femoral BMD compared to placebo (MD = 0.11, 95% CI [0.03–0.19]).

In addition, treatment-related adverse events were excluded from the model because previous studies did not find any statistically significant differences between patients treated with Xianling Gubao capsules and those treated with Jintiange capsules (33, 34). Therefore, we assumed that treatment-related adverse events had a negligible impact on the costs and outcomes for patients receiving either Xianling Gubao capsules or Jintiange capsules.

Health resource use and costs

According to the Chinese Pharmacoeconomic Guidelines (35), the cost evaluation was conducted from the perspective of Chinese healthcare providers. Direct medical costs encompass the expenses associated with treatment regimens resulting from fracture events, direct medical expenses for each health state, and other medical expenditures. The cost data for this section were primarily obtained from a multi-center survey in China (36). The costs of Xianling Gubao capsules and Jintiange capsules were calculated based on the market share of generic drugs and their branded counterparts in China, utilizing official databases from China's National Medical Products Administration (NMPA) (37). The estimated annual cost of Xianling Gubao capsules was USD 93.24 (3 capsules, twice a day), while the cost for Jintiange capsules was USD 574.82 (3 capsules, three times a day). All related costs were adjusted to 2022 Chinese Yuan (CNY) using the Consumer Price Index (CPI). For reference, the average exchange rate in 2022 was USD 1 = CNY 6.7321.

Utilities

Baseline utility data were extracted from published literature to provide reference value for the decision analysis model (38). The utility values were derived from a Chinese large population using EQ-5D. The disutility multiplier associated with post-fracture in the first and subsequent years was derived from meta-analysis (39, 40). Utility for bed-ridden state was collected from a study of Chinese patients provided with nursing care (41).

Statistical analysis

In base case analysis, using first-order Monte Carlo simulation, total costs and QALYs for each treatment with Xianling Gubao capsules, Jintiange capsules, and no treatment were estimated at different starting ages of 55, 60, 65, and 70 years. To estimate the cost-effectiveness of Xianling Gubao capsules and Jintiange capsules, an incremental cost-effectiveness ratio (ICER) was calculated by dividing an incremental cost by an incremental quality-adjusted life-year (QALY) to obtain the cost per QALY gained. To explore key drivers of parameters, deterministic sensitivity analyses were conducted, and parameters assessed and their ranges are shown in Table 2. Probabilistic sensitivity analyses were conducted by a second-order Monte Carlo simulation with 1,000 iterations and selecting the assigned parameters distributed randomly (shown in Table 2). Following the analyses, cost-effectiveness acceptability curves were illustrated to determine the probability of being cost-effective for each strategy based on an assumed willingness-to-pay (WTP) threshold of three-time GDP per capita in China ($38,223) per QALY gained.

Results

Model validation

This model was validated by comparing the age-specific incidence of hip fractures and clinical vertebral fractures per year with estimates from published epidemiological surveys (shown in Figure 2) (23, 42).

Base-case analyses

Table 3 presents the costs, QALYs, and ICERs for Xianling Gubao or Jintiange compared with no treatment at the starting ages of 55, 60, 65, and 70 years. Compared with the control group without drug treatment, the preventive treatment with Chinese patent medicine increased bone mineral density and reduced fracture probability at all age levels in the intervention group. Model simulation results based on females aged 55–59 showed that the use of Xianling Gubao capsules reduced hip fracture incidence by 8.20% and vertebral fracture incidence by 12.03%, with an increase in total per capita cost of $119.21 and an increase in quality-adjusted life years (QALYs) by 0.0379. The use of Jintiane capsule reduced hip fracture rates by 18.33% and vertebral fracture rates by 30.05%, with an increase in total per capita cost of $956.38 and an increase in QALYs by 0.08. Under the willingness-to-pay (WTP) threshold of three times China's per capita GDP, the use of traditional Chinese medicine for preventive treatment had a cost-effective advantage. Moreover, compared with the Xianling Gubao capsule, the Jintiange capsule was cost-effective (ICER: $11,955/QALY).

For the population aged 60–74, the use of traditional Chinese medicine for preventive treatment still had a cost-effective advantage. Compared with the Xianling Gubao capsule, the Jintiange capsule was cost-effective (ICER: $9858-10731/QALY) under the condition of WTP being 3 times China's per capita GDP.

One-way sensitivity analyses

One-way sensitivity analyses comparing the Xianling Gubao capsule with the Jintiange capsule or no treatment indicated that the ICERs were most sensitive to the discount rate, the loss of utility due to fractures, the first-year BMD of the study population, and drug acquisition costs (Figure 3). The graph demonstrates that the cost-effectiveness results of CPM treatment are relatively stable and unaffected by changes in these parameters. It is cost-effective to initiate preventive treatment with CPMs for individuals with below-average BMD who experience a significant impact on their quality of life due to fractures.

Probabilistic sensitivity analyses

At a WTP threshold of $3,000 (approximately 0.24 times GDP per capita), the use of CPMs for preventive treatment in the female population aged 55–59 was deemed cost-effective. When the WTP exceeded $24,000 (about 1.88 times per capita GDP), the economic benefits of using the Jintiange capsule became more pronounced compared to the Xianling Gubao capsule. Under the WTP conditions established in the study, the probabilities of the Xianling Gubao capsule and the Jintiange capsule being cost-effective were 31 and 49%, respectively (Figure 4).

Discussion

Previous systematic reviews had indicated a relative scarcity of cost-effectiveness research concerning CPMs (43). In this study, we constructed a Markov model based on life status to simulate the

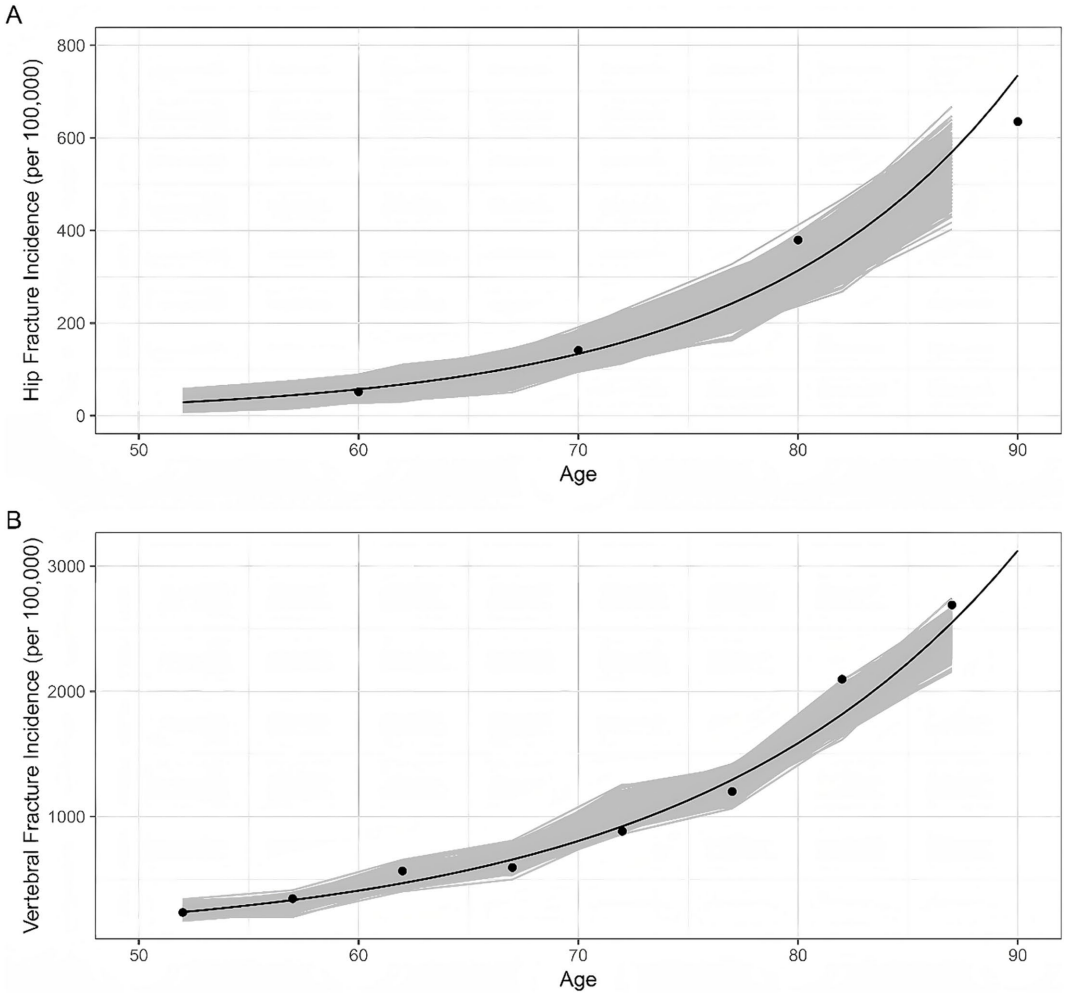


FIGURE 2
Model validation results. Dots represent the data reported by epidemiological surveys in China. Lines represent the trend curves fitted by the data above-mentioned. Shaded areas represent the model outputs of 1,000 simulations. **(A)** Hip fracture incidence; **(B)** Vertebral fracture incidence.

long-term effects of CPMs on the treatment outcomes of menopausal women with osteoporosis. Our base analysis suggests that, at a WTP threshold of $3,000 per QALY, the use of CPMs for preventive treatment in postmenopausal women aged 55 to 59 was cost-effective. Furthermore, at a WTP threshold equivalent to three times China's per capita GDP, the combined use of Jintiange capsules was cost-effective across all age groups. This study provided reference values for future long-term economic evaluations of CPMs for osteoporosis in postmenopausal women.

The primary treatment approaches for bone loss diseases such as osteoporosis are HRT and bisphosphonates. Continuous HRT was associated with a high risk of breast cancer and endometrial cancer, as well as coronary artery issues and other cardiac disorders, while bisphosphonates could lead to osteonecrosis of the jawbone and skeletal system (44–46). Due to these adverse effects, the clinical use of HRT and bisphosphonates is limited. Therefore, new treatment strategies were needed to develop osteoporosis treatments that are less likely to cause adverse reactions to some extent (47). CPMs had gained popularity due to their minimal adverse effects while effectively treating various ailments. Traditional Chinese Medicine (TCM) had been utilized to address a range of orthopedic conditions, particularly osteoporosis, fractures, and rheumatism, with notable success (48, 49). Xianling Gubao and Jintiange treatments played significant roles in managing osteoporosis with CPMs, making them the preferred choice for treating postmenopausal osteoporosis according to clinical application guidelines for Chinese patent medicines. Xianling Gubao capsules consist entirely of CPMs (50), which help regulate the balance of serum calcium and phosphorus deposition, enhance levels of vitamin D3 and alkaline phosphatase (ALP), and improve bone mineral density through the synergistic effects of various natural herbs targeting multiple pathways (51, 52). The primary component of Jintiange capsules was artificial tiger bone powder. The physical and chemical properties, as well as the pharmacological effects were consistent. Researchers studying the serum of patients with osteoporosis found that Jintiange capsules inhibited the κB inhibitor signaling pathway by downregulating the overexpression of osteopontin, ultimately reducing MMP-3 expression. This action may strengthen the kidneys and bones, alleviate inflammation and pain, and combat osteoporosis (53). Furthermore, recent studies have identified Jintiange capsules as the first CPM that could effectively improve primary osteoporosis and enhance muscle strength (54). While the therapeutic potential of

10.3389/fpubh.2025.1596676

TABLE 3 Cost-effectiveness of Xianling Gubao compared with Jintiange or no treatment at the starting ages of 55, 60, 65, and 70 years.

Treatment Strategy	Probability of patients experiencing a fracture within the study period		Cost, $	QALYs	ICER, $/QALY
	Hip fracture	Vertebral fracture			
55–59 years					
No Treatment	6.71%	21.03%	7174.94	13.0513	Ref
Xianling Gubao Treatment	6.16%	18.50%	7294.16	13.0892	3,147
Jintiange Treatment	5.48%	15.47%	8131.32	13.1313	11,955
60–64 years					
No Treatment	7.30%	23.58%	6791.35	11.4976	Ref
Xianling Gubao Treatment	6.90%	20.81%	6883.21	11.5373	2,313
Jintiange Treatment	5.94%	17.40%	7681.96	11.5879	9,858
65–69 years					
No Treatment	6.60%	20.40%	6075.22	9.9942	Ref
Xianling Gubao Treatment	6.09%	18.04%	6184.11	10.052	1886
Jintiange Treatment	5.29%	14.91%	6978.64	10.0784	10,731
70–74 years					
No Treatment	7.46%	23.00%	5572.26	8.0271	Ref
Xianling Gubao Treatment	6.49%	20.63%	5646.1	8.0875	1,221
Jintiange Treatment	5.86%	17.16%	6393.42	8.1116	9,711

CPMs in managing osteoporosis is evident, there is a lack of economic studies to support their widespread adoption. Therefore, further economic evaluations are necessary to inform clinical and policy decisions regarding the integration of CPMs into standard osteoporosis treatment protocols.

The choice of research perspective in economic evaluation determines the measurement range of cost. Our results demonstrated that the use of CPMs preventive treatment appears to be a cost-effective treatment option for postmenopausal osteoporotic women at the starting age of 55 from the perspective of Chinese healthcare providers. Our results also revealed that the cost-effectiveness of Jintiange Treatment improved with an increase in the starting age. Our findings were consistent with previous economic evaluations in which the Jintiange treatment was generally cost-effective compared with the Xianling Gubao treatment (19, 32, 55). We did not find any studies that were different from this conclusion, which may be caused by the lack of relevant economic studies. However, pharmacoeconomic assessments were based on data from clinical trials or real-world data, and further CPMs clinical trials and real-world studies were recommended.

Currently, the pharmacoeconomic studies on the treatment of osteoporosis in menopausal women published both at home and abroad mainly concentrate on RANKL inhibitors, bisphosphonates, and other Western medicine preparations. There have been relatively few studies on CPMs for treating osteoporosis in menopausal women. Only Lai Fuchong et al. (34) carried out an economic analysis of Xianling Gubao capsules and Jintiange capsules in the treatment of type-I osteoporosis. The results indicated that the cost-effectiveness ratio of alendronate combined with Xianling Gubao capsule was the lowest, followed by alendronate combined with Jintiange capsule. Nevertheless, the limitations of this study include the lack of ICERs, which are essential for definitively determining the most cost-effective treatment strategy. Furthermore, the data were gathered from a restricted patient sample across two hospitals, without taking into account potential confounding factors. This may have an impact on the generalizability of the results. The current study aims to fill this gap by presenting a comparative economic assessment of Xianling Gubao Capsules and Jintiange Capsules in postmenopausal women of various age groups at the start of treatment. Such an analysis is crucial for promoting the rational clinical use of CPMs in osteoporosis management, providing valuable perspectives for healthcare providers and policymakers when considering the incorporation of these treatments into standard care guidelines.

Although there were studies on the synergistic effect of CPM combined with conventional Western medicine in the treatment of osteoporosis (56), unfortunately, we had not found any direct comparative studies on the treatment of osteoporosis in postmenopausal women with CPM and Western medicine, including safety, efficacy and economy. Although no direct research evidence comparing CPM and Western medicine in the treatment of osteoporosis in postmenopausal women has been found so far, our team had fully realized the importance of this research gap for clinical practice and health policy-making. Currently, we were actively promoting the preparatory work for subsequent observational and real-world studies to provide solid methodological support for future research design. We were confident that through standardized research implementation and rigorous data analysis, we will gradually fill this research gap and provide more comprehensive evidence-based basis for the optimization of treatment decisions for osteoporosis in postmenopausal women.

As with any modeling research, our analyses had certain limitations. First, due to the absence of epidemiological data fully consistent with the study population, the efficacy parameter of the model transition probability involved a series of assumptions and corrections. This might deviate to some extent from the actual disease outcomes. Second, owing to the lack of relevant research, our data on the efficacy of drug treatment were solely obtained from a network meta-analysis. Although this was the largest study related to both drugs, the data dated back to 2016, and the study endpoint was bone mineral density (BMD), which

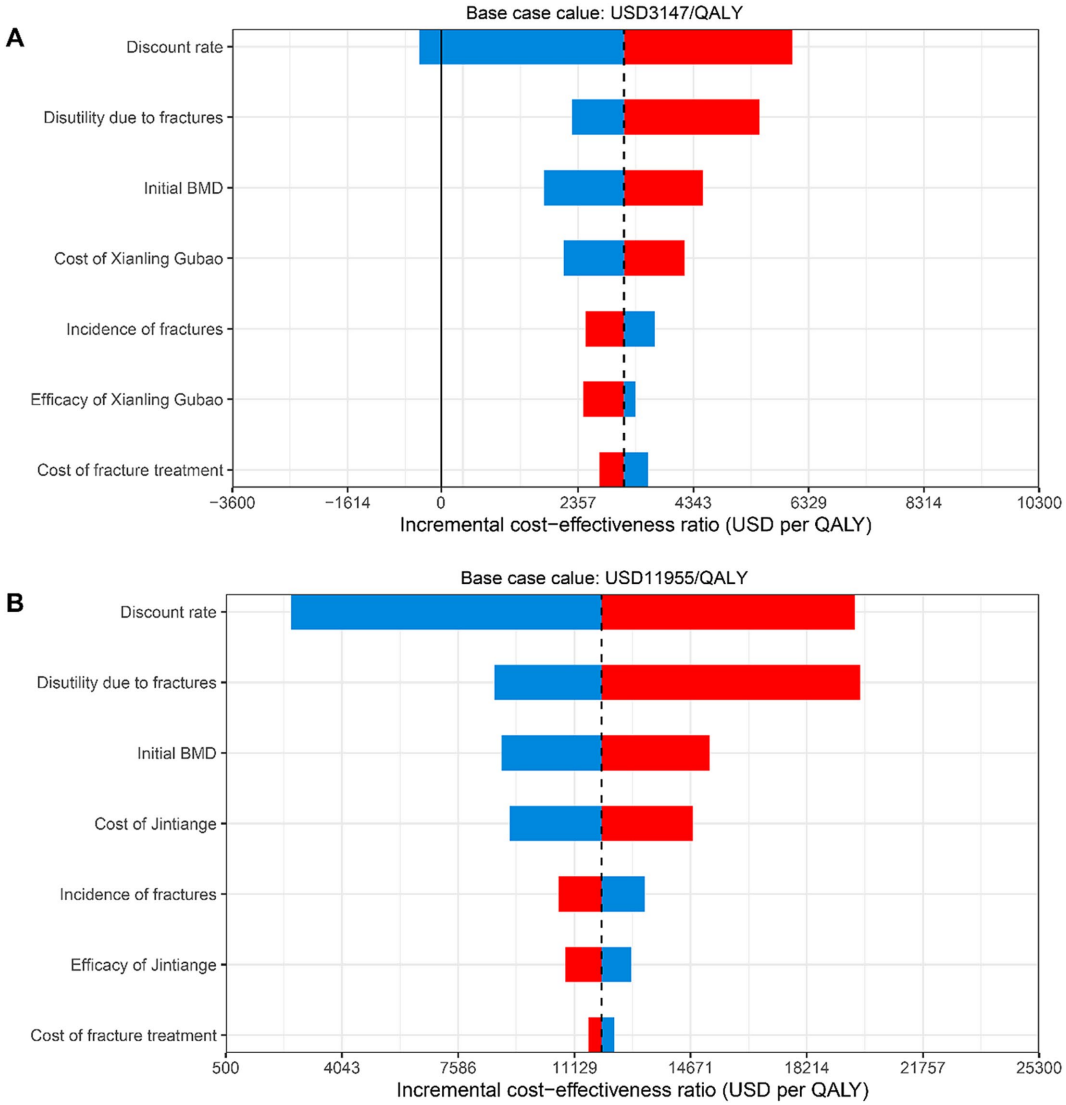


FIGURE 3
Tornado diagrams for one-way sensitivity analyses on the incremental cost-effectiveness ratio of Xianling Gubao capsule compared with Jintiange capsule or no treatment. Blue and red represent the ICER results in lower limit and upper limit values of parameters used, respectively. **(A)** Xianling Gubao; **(B)** Jintiang.

was used to predict the incidence of fractures subsequently. This could introduce bias to our results. Third, to maintain model parsimony, we did not incorporate adverse events. However, serious adverse events caused by Xianling Gubao capsules and Jin Tiange in the treatment of osteoporosis are considered rare (33, 34). Thus, they were unlikely to affect the results of our cost-effectiveness analyses. Similarly, this was a commonly adopted assumption in previous economic evaluations (57, 58). The impact of treatment-related adverse events on costs and outcomes can be regarded as minimal. Nevertheless, if data on adverse events become available, they should be integrated into the model.

Conclusion

From the perspective of the Chinese healthcare providers, compared with the control group without drug therapy, the preventive treatment with Chinese patent medicine increased bone mineral density and reduced fracture probability at all age levels in the intervention group, and Jintiange capsule appears to be a cost-effective treatment choice for postmenopausal osteoporotic women. This study provides valuable information to both clinical practitioners and decision-makers in ensuring the rational use of Chinese patent medicine, especially in the face of the growing clinical and economic burden of osteoporotic fractures in China.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

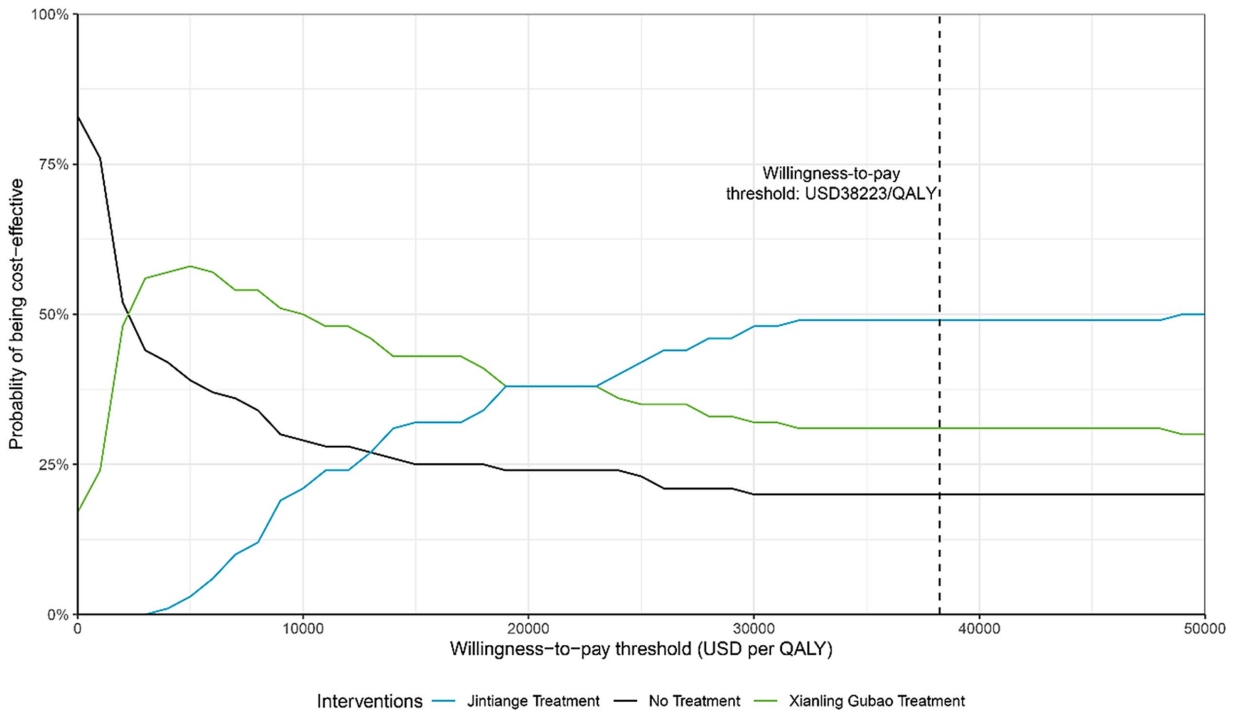


FIGURE 4
Cost-effectiveness acceptability curve of Xianling Gubao capsules compared with Jintiange capsules or no treatment.

Author contributions

CW: Writing – original draft, Writing – review & editing. XL: Data curation, Writing – original draft. JL: Investigation, Writing – review & editing. YZ: Methodology, Writing – review & editing. RY: Writing – review & editing, Conceptualization, Supervision.

Funding

The author(s) declare that financial support was received for the research and/or publication of this article. This work was funded by Administration of Traditional Chinese Medicine of Hubei Province (2Y2023Q012); Development Center for Medical Science & Technology, National Health Commission of People's Republic of China (WKZX2023CX200001); National Institute of Hospital Administration, National Health Commission of People's Republic of China (NIHAYS2324); Chinese Pharmaceutical Association (XH20231205). All the fundings had no influence over the study design, execution, or decision to publish.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The authors declare that no Gen AI was used in the creation of this manuscript.

Any alternative text (alt text) provided alongside figures in this article has been generated by Frontiers with the support of artificial intelligence and reasonable efforts have been made to ensure accuracy, including review by the authors wherever possible. If you identify any issues, please contact us.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Supplementary material

The Supplementary material for this article can be found online at:https://www.frontiersin.org/articles/10.3389/fpubh.2025.1596676/full#supplementary-material

References

1. Chinese Society of Osteoporosis and Bone Mineral Research. Guidelines for the diagnosis and treatment of primary osteoporosis (2022). *Chin Gen Pract*. (2023) 26:1671–91. doi: 10.12114/j.issn.1007-9572.2023.0121

2. Oden A, McCloskey EV, Kanis JA, Harvey NC, Johansson H. Burden of high fracture probability worldwide: secular increases 2010-2040. *Osteoporos Int*. (2015) 26:2243–8. doi: 10.1007/s00198-015-3154-6

3. National Bureau of Statistics. (2021). Bulletin of the seventh national population census. Available online: https://www.stats.gov.cn/zt_18555/zdtjgz/zgrkpc/dqcrkpc/ggl/202302/t20230215_1903997. (accessed on 2024-11-20).

4. Ruihua D, Xiaoming X, Jixiang Z, Ning L. Best evidence summary of the exercise management in women with postmenopausal osteoporosis. *Chin Nurs Res*. (2022) 36:640–4. doi: 10.12102/j.issn.1009-6493.2022.04.013

5. Si L, Winzenberg TM, Jiang Q, Chen M, Palmer AJ. Projection of osteoporosis-related fractures and costs in China: 2010-2050. *Osteoporos Int*. (2015) 26:1929–37. doi: 10.1007/s00198-015-3093-2

6. Burns RB, Rosen H, Berry S, Smetana GW. How would you manage this patient with osteoporosis? Grand rounds discussion from Beth Israel Deaconess Medical Center. *Ann Intern Med*. (2018) 168:801–8. doi: 10.7326/M18-0950

7. Chang B, Quan Q, Li Y, Qiu H, Peng J, Gu Y. Treatment of osteoporosis, with a focus on 2 monoclonal antibodies. *Med Sci Monit*. (2018) 24:8758–66. doi: 10.12659/MSM.912309

8. Vidal M, Thibodaux RJ, Neira LFV, Messina OD. Osteoporosis: a clinical and pharmacological update. *Clin Rheumatol*. (2019) 38:385–95. doi: 10.1007/s10067-018-4370-1

9. Netelenbos JC, Geusens PP, Ypma G, Buijs SJ. Adherence and profile of non-persistence in patients treated for osteoporosis--a large-scale, long-term retrospective study in the Netherlands. *Osteoporos Int*. (2011) 22:1537–46. doi: 10.1007/s00198-010-1372-5

10. Hiligsmann M, Bours SP, Boonen A. A review of patient preferences for osteoporosis drug treatment. *Curr Rheumatol Rep*. (2015) 17:61. doi: 10.1007/s11926-015-0533-0

11. Tadrous M, Mamdani MM, Juurlink DN, Krahn MD, Lévesque LE, Cadarette SM. Comparative gastrointestinal safety of bisphosphonates in primary osteoporosis: a network meta-analysis-reply to Pazianas and Abrahamsen. *Osteoporos Int*. (2014) 25:2671–2. doi: 10.1007/s00198-014-2789-z

12. Rossouw JE, Anderson GL, Prentice RL, LaCroix AZ, Kooperberg C, Stefanick ML, et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial. *JAMA*. (2002) 288:321–33. doi: 10.1001/jama.288.3.321

13. Cipriani C, Pepe J, Minisola S, Lewiecki EM. Adverse effects of media reports on the treatment of osteoporosis. *J Endocrinol Investig*. (2018) 41:1359–64. doi: 10.1007/s40618-018-0898-9

14. Reginster JY, Pelousse F, Bruyere O. Safety concerns with the long-term management of osteoporosis. *Expert Opin Drug Saf*. (2013) 12:507–22. doi: 10.1517/14740338.2013.793669

15. Cui X, Wang S, Cao H, Guo H, Li Y, Xu F, et al. A review: the bioactivities and pharmacological applications of Polygonatum sibiricum polysaccharides. *Molecules*. (2018) 23:23. doi: 10.3390/molecules23051170

16. Zhang ND, Han T, Huang BK, Rahman K, Jiang YP, Xu HT, et al. Traditional Chinese medicine formulas for the treatment of osteoporosis: implication for antiosteoporotic drug discovery. *J Ethnopharmacol*. (2016) 189:61–80. doi: 10.1016/j.jep.2016.05.025

17. Zhao H, Zhao N, Zheng P, Xu X, Liu M, Luo D, et al. Prevention and treatment of osteoporosis using Chinese medicinal plants: special emphasis on mechanisms of immune modulation. *J Immunol Res*. (2018) 2018:1–11. doi: 10.1155/2018/6345857

18. National Administration of Traditional Chinese Medicine (NATCM). Clinical application guidance for treating osteoporosis by Chinese patent medicine(2021). *Chin J Integr Tradit West Med*. (2022) 42:393–404. doi: 10.7661/j.cjim.20220204.063

19. Zhao J, Zeng L, Wu M, Huang H, Liang G, Yang W, et al. Efficacy of Chinese patent medicine for primary osteoporosis: a network meta-analysis. *Complement Ther Clin Pract*. (2021) 44:101419. doi: 10.1016/j.ctcp.2021.101419

20. Husereau D, Drummond M, Petrou S, Carswell C, Moher D, Greenberg D, et al. Consolidated health economic evaluation reporting standards (CHEERS) statement. *Int J Technol Assess Health Care*. (2013) 29:117–22. doi: 10.1017/S0266462313000160

21. Wang L, Yu W, Yin X, Cui L, Tang S, Jiang N, et al. Prevalence of osteoporosis and fracture in China: the China osteoporosis prevalence study. *JAMA Netw Open*. (2021) 4:e2121106. doi: 10.1001/jamanetworkopen.2021.21106

22. Zhang CG, Feng JN, Wang SF, Gao P, Xu L, Zhu JX, et al. Incidence of and trends in hip fracture among adults in urban China: a nationwide retrospective cohort study. *PLoS Med*. (2020) 17:e1003180. doi: 10.1371/journal.pmed.1003180

23. Bow CH, Cheung E, Cheung CL, Xiao SM, Loong C, Soong C, et al. Ethnic difference of clinical vertebral fracture risk. *Osteoporos Int*. (2012) 23:879–85. doi: 10.1007/s00198-011-1627-9

24. Lau EM, Woo J, Leung PC, Swaminthan R. Low bone mineral density, grip strength and skinfold thickness are important risk factors for hip fracture in Hong Kong Chinese. *Osteoporos Int*. (1993) 3:66–70. doi: 10.1007/BF01623375

25. Kwok AW, Gong JS, Wang YX, Leung JC, Kwok T, Griffith JF, et al. Prevalence and risk factors of radiographic vertebral fractures in elderly Chinese men and women: results of Mr. OS (Hong Kong) and Ms. OS (Hong Kong) studies. *Osteoporos Int*. (2013) 24:877–85. doi: 10.1007/s00198-012-2040-8

26. Tsang SW, Kung AW, Kanis JA, Johansson H, Oden A. Ten-year fracture probability in Hong Kong southern Chinese according to age and BMD femoral neck T-scores. *Osteoporos Int*. (2009) 20:1939–45. doi: 10.1007/s00198-009-0906-1

27. Kwok TCY, Su Y, Khoo CC, Leung J, Kwok A, Orwoll E, et al. Predictors of non-vertebral fracture in older Chinese males and females: Mr. OS and Ms. OS (Hong Kong). *J Bone Miner Metab*. (2017) 35:330–7. doi: 10.1007/s00774-016-0761-z

28. Kanis JA, Johnell O, De Laet C, Johansson H, Oden A, Delmas P, et al. A meta-analysis of previous fracture and subsequent fracture risk. *Bone*. (2004) 35:375–82. doi: 10.1016/j.bone.2004.03.024

29. Yoshimura M, Moriwaki K, Noto S, Takiguchi T. A model-based cost-effectiveness analysis of osteoporosis screening and treatment strategy for postmenopausal Japanese women. *Osteoporos Int*. (2017) 28:643–52. doi: 10.1007/s00198-016-3782-5

30. Office of the Leading Group of the State Council for the Seventh National Population Census. China population census yearbook (2020). Available online at:http://www.stats.gov.cn/sj/pcsj/rkpc/7rp/zk/indexch.htm (accessed on 2024-11-5).

31. Koh GCH, Tai BC, Ang LW, Heng D, Yuan JM, Koh WP. All-cause and cause-specific mortality after hip fracture among Chinese women and men the Singapore Chinese health study. *Osteoporos Int*. (2013) 24:1981–9. doi: 10.1007/s00198-012-2183-7

32. Luo MH, Zhao JL, Xu NJ, Xiao X, Feng WX, Li ZP, et al. Comparative efficacy of Xianling Gubao capsules in improving bone mineral density in postmenopausal osteoporosis: a network meta-analysis. *Front Endocrinol*. (2022) 13:839885. doi: 10.3389/fendo.2022.839885

33. Zhongzhou Z, Dongsheng X, Xiujun J, Yongsheng S. Network meta-analysis of six Chinese patent medicines in treatment of knee osteoarthritis. *Pharm Clin Res*. (2024) 32:338–42. doi: 10.13664/j.cnki.pcr.2024.04.023

34. Fuchong L. Clinical study of Xianlinggubao and Jintiange capsules in treating type I Osteoporosischinese abstract. *Master*. (2020). doi: 10.27460/d.cnki.gyzyc.2020.000079

35. Guoen L, Shanlian H, Jiuhong W. China guidelines for pharmacoeconomic evaluations. *China J Pharm Econ*. (2020) 3–9. https://www.cpa.org.cn/cpadmn/attached/file/20201203/1606977380634185.pdf

36. Qu B, Ma Y, Yan M, Wu HH, Fan L, Liao DF, et al. The economic burden of fracture patients with osteoporosis in western China. *Osteoporos Int*. (2014) 25:1853–60. doi: 10.1007/s00198-014-2699-0

37. National Medical Products Administration. Available online at:https://www.nmpa.gov.cn/yaopin/index.html (accessed on 2024-10-30).

38. Si L, Shi L, Chen MS, Palmer AJ. Establishing benchmark EQ-5D-3L population health state utilities and identifying their correlates in Gansu Province, China. *Qual Life Res*. (2017) 26:3049–58. doi: 10.1007/s11136-017-1614-5

39. Hiligsmann M, Ethgen O, Richy F, Reginster JY. Utility values associated with osteoporotic fracture: a systematic review of the literature. *Calcif Tissue Int*. (2008) 82:288–92. doi: 10.1007/s00223-008-9117-6

40. Si L, Winzenberg TM, de Graaff B, Palmer AJ. A systematic review and meta-analysis of utility-based quality of life for osteoporosis-related conditions. *Osteoporos Int*. (2014) 25:1987–97. doi: 10.1007/s00198-014-2636-2

41. Liu N, Zeng LX, Li Z, Wang JE. Health-related quality of life and long-term care needs among elderly individuals living alone: a cross-sectional study in rural areas of Shaanxi Province, China. Bmc. *Public Health*. (2013) 13:13. doi: 10.1186/1471-2458-13-313

42. Zheng XQ, Xu L, Huang J, Zhang CG, Yuan WQ, Sun CG, et al. Incidence and cost of vertebral fracture in urban China: a 5-year population-based cohort study. *Int J Surg*. (2023) 109:1910–8. doi: 10.1097/JS9.0000000000000411

43. Zhang F, Kong LL, Zhang YY, Li SC. Evaluation of impact on health-related quality of life and cost effectiveness of traditional Chinese medicine: a systematic review of randomized clinical trials. *J Altern Complement Med*. (2012) 18:1108–20. doi: 10.1089/acm.2011.0315

44. Dinger J, Bardenheuer K, Heinemann K. Drospirenone plus estradiol and the risk of serious cardiovascular events in postmenopausal women. *Climacteric*. (2016) 19:349–56. doi: 10.1080/13697137.2016.1183624

45. He JB, Chen MH, Lin DK. New insights into the tonifying kidney-yin herbs and formulas for the treatment of osteoporosis. *Arch Osteoporos*. (2017) 12:2–13. doi: 10.1007/s11657-016-0301-4

46. Spivakovsky S. Treatment for bisphosphonate-related osteonecrosis of the jaw. *Evid Based Dent*. (2017) 18:56. doi: 10.1038/sj.ebd.6401243

47. Lungu AE, Lazar MA, Tonea A, Rotaru H, Roman RC, Badea ME. Observational study of the bisphosphonate-related osteonecrosis of jaws. *Clujul Med*. (2018) 91:209–15. doi: 10.15386/cjmed-838

48. Mukwaya E, Xu F, Wong MS, Zhang Y. Chinese herbal medicine for bone health. *Pharm Biol*. (2014) 52:1223–8. doi: 10.3109/13880209.2014.884606

49. Suvarna V, Sarkar M, Chaubey P, Khan T, Sherje A, Patel K, et al. Bone health and natural products- an insight. *Front Pharmacol*. (2018) 9:981. doi: 10.3389/fphar.2018.00981

50. Wang X, He Y, Guo B, Tsang MC, Tu F, Dai Y, et al. In vivo screening for anti-osteoporotic fraction from extract of herbal formula Xianlinggubao in ovariectomized mice. *PLoS One*. (2015) 10:e0118184. doi: 10.1371/journal.pone.0118184

51. Zihui Z, Qiong L, Wenying L, Baige Z, Lin M, Zinan Z. Systematic review of efficacy of Xianling Gubao capsules combined with Methorexatein the treatment of rheumatoid arthritis with Osteoporisis. *Evaluation Anal Drug-Use in Hospitals China*. (2021) 21:329–32. doi: 10.14009/j.issn.1672-2124.2021.03.017

52. Yuan L, Wu R, Liang Z, Wang H. Meta-analysis of xianling gubao capsule in the treatment of osteoporotic vertebral compression fracture. *Chin J Mod Appl Pharm*. (2023) 40:830–838. doi: 10.13748/j.cnki.issn1007-7693.20214277

53. Z Y, Xu W, J J, Z Y, W S, X Y. Systemic review of Jintiange capsules in treatment of postmenopausal osteoporosis. *Zhongguo Zhong Yao Za Zhi*. (2019) 44:186–92. doi: 10.19540/j.cnki.cjcmm.20180709.007

54. Liang H, Wang O, Cheng Z, Xia P, Wang L, Shen J, et al. Jintiange combined with alfacalcidol improves muscle strength and balance in primary osteoporosis: a randomized, double-blind, double-dummy, positive-controlled, multicenter clinical trial. *J Orthopaedic Translation*. (2022) 35:53–61. doi: 10.1016/j.jot.2022.05.002

55. Nan P, Shanshan L, Jiangxia y, Haijing G. Economic evaluation of Jintiange capsule in the treatment of postmenopausal osteoporosis. *Chin J New Drugs*. (2024) 33:1403–8. doi: 10.3969/j.issn.1003-3734.2024.13.015

56. Jin H, Huang C, Zhang Y, Dong Y, Xiong Q, Wang D, et al. Meta-analysis of the synergistic effect of traditional Chinese medicine compounds combined with conventional Western medicine in the treatment of osteoporosis. *Front Endocrinol (Lausanne)*. (2025) 16:1606753. doi: 10.3389/fendo.2025.1606753

57. Darba J, Kaskens L, Sorio Vilela F, Lothgren M. Cost-utility of denosumab for the treatment of postmenopausal osteoporosis in Spain. *Clinicoecon Outcomes Res*. (2015) 7:105–17. doi: 10.2147/CEOR.S78349

58. Hiligsmann M, Reginster JY. Cost effectiveness of denosumab compared with oral bisphosphonates in the treatment of post-menopausal osteoporotic women in Belgium. *PharmacoEconomics*. (2011) 29:895–911. doi: 10.2165/11539980-000000000-00000

59. You R, Mori T, Ke L, Wan Y, Zhang Y, Luo F, et al. Which injected antiosteoporotic medication is worth paying for? A cost-effectiveness analysis of teriparatide, zoledronate, ibandronate, and denosumab for postmenopausal osteoporotic women in China. *Menopause (New York, NY)*. (2021) 29:210–8. doi: 10.1097/gme.0000000000001911

60. Chinese National Bureau of Statistics. (2023). Consumer Price Index 2022(2023-01-09). Available online at: https://www.sg.gov.cn/sgtjjdcd/gkmlpt/content/2/2354/mpost_2354542.html#7996 (Accessed on 2024-10-09).

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 08 September 2025
DOI 10.3389/fpubh.2025.1659721

Check for updates

OPEN ACCESS

EDITED BY
Jing Yuan,
Fudan University, China

REVIEWED BY
Jay Pan,
Sichuan University, China
Lanting Lyu,
Renmin University of China, China
Hai Lin,
Shanghai Health Development Research Center, China
Jie Song,
Shanghai Health Development Research Center, China

*CORRESPONDENCE
Feng Chang
✉ cpucf@163.com

RECEIVED 04 July 2025
ACCEPTED 19 August 2025
PUBLISHED 08 September 2025

CITATION
Jiang C, Nie M, Lu Y, Jiang T, Guo D, Qi P, Li N and Chang F (2025) Impact of China's National Volume-Based Procurement policy exclusively for insulin on the volume, expenditure and price: an interrupted time series analysis in Guangdong Province. *Front. Public Health* 13:1659721. doi: 10.3389/fpubh.2025.1659721

COPYRIGHT
© 2025 Jiang, Nie, Lu, Jiang, Guo, Qi, Li and Chang. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

Impact of China's National Volume-Based Procurement policy exclusively for insulin on the volume, expenditure and price: an interrupted time series analysis in Guangdong Province

Changsong Jiang[1,2], Manling Nie[3], Yun Lu[1], Ting Jiang[2], Dan Guo[2], Peng Qi[2], Na Li[2] and Feng Chang[1]*

[1]School of International Pharmaceutical Business, China Pharmaceutical University, Nanjing, China, [2]National Institute of Healthcare Security, Capital Medical University, Beijing, China, [3]HEOA Group, West China School of Public Health and West China Fourth Hospital, Sichuan University, Chengdu, China

Objective: This study aims to evaluate the effect of China's National Volume-Based Procurement (NVBP) policy exclusively for insulin by analyzing the trend in volume, expenditure, and price before and after NVBP policy.

Methods: Taking Guangdong Province, China as an example, descriptive statistics and interrupted time series analysis were used to quantitatively measure the immediate and long-term effect of the NVBP policy on insulin volume, expenditure and price. In terms of volume, subgroup analysis is further conducted based on different generations and enterprise ownership to examine the impact of NVBP on the insulin utilization pattern.

Results: Following the implementation of the NVBP policy, monthly insulin procurement volume increased significantly from 7.69 million to 9.37 million defined daily doses (DDDs), while monthly expenditure decreased from CNY 86.64 million to CNY 52.55 million, accompanied by a reduction in defined daily dose cost (DDDc) from CNY 11.24 to CNY 5.57. Interrupted time series analysis (ITSA) confirmed these trends, showing an immediate post-intervention increase of 1.547 million DDDs ($p < 0.001$), expenditure reduction of CNY 42.57 million ($p < 0.001$), and DDDc decrease of CNY 5.427 ($p < 0.001$) in instantaneous level. Subgroup analysis demonstrated divergent trends between insulin generations, with non-significant decrease in second-generation insulin and increase in third-generation insulin procurement in long-term trend. Notably, domestic insulin showed a significant increase in procurement volume ($p < 0.05$), while imported insulin exhibited a non-significant declining trend.

Conclusion: These findings demonstrate that the NVBP policy significantly reduced insulin expenditure while improving treatment accessibility and affordability for insulin. The policy effectively promoted therapeutic upgrading from human insulin to insulin analogue and optimized medication regimen. Notably, it stimulated domestic insulin market development through substitution effect. This multi-dimensional improvement exemplifies the principles of value-based healthcare delivery.

KEYWORDS

National Volume-Based Procurement, insulin, value-based medicine, availability, utilization pattern, interrupted time series analysis

1 Introduction

According to the International Diabetes Federation (IDF) *Global Diabetes Atlas* (11th edition, 2025), there are 148 million adults aged 20–79 with diabetes in China (1), the highest number globally, accounting for approximately a quarter of the world's diabetic patients. Diabetes often refers to the "non-lethal cancer," and is the fundamental progenitor of multi-organ complications (2–4). Patients with diabetes need to inject insulin lifelong or take other glucose-lowering drugs, contributing to substantial economic costs. The inability to access affordable insulin remains a critical barrier to effective treatment, leading to unnecessary complications and premature mortality (5).

To alleviate the financial burden on patients, the National Healthcare Security Administration (NHSA) launched a nationwide centralized volume-based procurement policy for insulin in November 2021, which is the only procurement for biologics in China at the national level. The procurement involves second-generation human insulin and third-generation insulin analogue. Insulin analogue as upgraded product of human insulin, is generally more expensive but more stable in controlling blood glucose and significantly reducing the risk of hypoglycemia (6). The centralized procurement targeted commonly used insulin types in clinical practice to maintain stability in clinical medication use. The insulin was categorized into six bidding groups in process of procurement, including mealtime human insulin, basal human insulin, premixed human insulin, rapid-acting analogue (aspart, lispro, glulisine), long-acting basal analogue (glargine, detemir, degludec) and premixed analogue (protamine lispro and lispro, protamine aspart and aspart). Different from chemical drugs, insulin production is more complex, with longer production cycle, higher cost, and limited capacity expansion in the short term (7). Therefore, centralized procurement for insulin differs from that of chemical drugs in terms of rule design, competition mechanism, and supply of bid-winning companies. Medical institutions can report their demand of insulin by brand name before procurement, whereas chemical drugs are reported by their generic name. In order to narrow the price gap, the unit price of insulin must not exceed 1.3 times the lowest unit price within the same bidding group to be selected, whereas for chemical drugs, this threshold is 1.8 times. Insulin bids can be selected if the price is below 60% of the highest valid bid, while chemical drugs require a bid below 50%. In summary, insulin competition is milder, and price reduction is smaller. In terms of supply, multiple selected enterprises provide insulin, allowing medical institutions to choose freely, ensuring market supply and respecting clinical choice to better guarantee patient accessibility. In contrast, for chemical drugs, a single selected enterprise supplies most of the volume within a province.

The NVBP for insulin involved 14,000 medical institutions nationwide, with a total demand volume of 215 million shots in the first year (8). Of this, human insulin accounted for 42%, while insulin analogue accounted for 58%. Domestic insulin made up 32% of the demand, and imported insulin represented 68%. Major insulin manufacturers such as Novo Nordisk, Eli Lilly, Sanofi, and seven domestic companies were winning bidders, the average price reduction was 48% (9). The procurement result was implemented starting in May 2022 across provinces, with a two-year procurement cycle.

The NVBP policy is of great significance for reducing patient financial burden, saving medical expenditure, and optimizing the allocation of medical resource (10–12). It is also a key driver for achieving value-based medicine, which focuses on patient health outcome, aiming to achieve healthcare system sustainability by optimizing resource allocation, controlling costs, and improving service quality (13). The NVBP policy leverages volume-based bargaining and market access to synergy government and market forces, promoting efficient allocation of medical resource. And it helps to improve health outcome of some patients by enhancing patients' accessibility to drugs after price reduction. While some academic studies have empirically analyzed the impact of NVBP for chemical drugs (14–18), there are few research on the effect of NVBP for biologics, only Yuan et al.'s study has introduced the procurement mechanism of the NVBP for insulin and the impact on affordability of patients (7).

This study aims to evaluate the impact of the NVBP policy exclusively in three key aspects: (1) Whether the policy effectively improves the accessibility and affordability of insulin, saves insulin expenditure, and enhances the sustainability of medical expenditure. (2) Under the context of value-based medicine, whether the policy helps to optimize the drug utilization pattern by increasing the share of insulin analogue and promoting the use of high-quality insulin analogue among more patients. (3) Whether the policy reduces the dependence on imported insulin, encourages the substitution of domestic insulin, and mitigates supply chain risks.

Guangdong Province, located in southern China, with a total population of 127 million, representing 10% of China's population, had a per capita GDP of CNY 106,985 and a per capita disposable income of CNY 49,327 in 2023 (19). Guangdong ranks among the top regions in China in terms of economic development level, healthcare coverage, and proportion of young people, playing a significant role nationally. However, there is a significant income disparity across different regions of the province, with the Pearl River Delta (PRD) region far surpassing the northwestern part. In 2023, the province had 62,819 medical institutions, with 4.95 hospital beds and 92.02 healthcare personnel per 1,000 people (19). Despite the overall abundance of healthcare resources, the distribution is uneven—nearly 70% of medical institutions are concentrated in the PRD, making it a microcosm of healthcare inequality in China properly. There are over 8 million diagnosed diabetes cases in Guangdong (20), ranking among the highest prevalence regions nationally. This study used insulin procurement data from Guangdong Province for quantitative descriptive analysis and policy intervention modeling. The findings provide evidence for evaluating the impact of the NVBP policy on insulin accessibility and affordability.

2 Methods

2.1 Data sources

The data were obtained from the Guangdong provincial centralized drug procurement and trading platform (21), through which all pharmaceutical procurement and transactions by medical institutions and pharmaceutical enterprises across the province are conducted. Monthly insulin procurement transaction records from May 2020 to June 2024 were adopted in this study, and the procurement transaction records including key variables such as procurement time, drug name, brand name, dosage form, package specification, manufacturer, procurement volume, and procurement expenditure. The implementation time of the NVBP policy for insulin in Guangdong Province was May 31, 2022, with a procurement cycle of 2 years. This study designates June 2022 as the policy intervention point and conducts analysis using procurement data from the 25 months preceding (from May 2020 to May 2022) and the 25 months following the intervention (from June 2022 to June 2024).

2.2 Statistical analysis

Descriptive statistics were conducted on the procurement volume, expenditure, and defined daily dose cost of insulin before and after the NVBP policy, as well as for different subgroups. The volume was measured as Defined Daily Doses (DDDs), which is the ratio of the total consumption of the drug to its Defined Daily Dose (DDD).

$$\text{DDDs} = \frac{\text{unit strength} \times \text{pack size} \times \text{procurement amount}}{\text{DDD}}$$

The DDD, representing the average daily dose used in the principal indication for adults, was set at 40 IU for all insulin based on the WHO ATC/DDD index (22). Expenditure was represented by procurement costs, while the price was measured by the Defined Daily Dose cost (DDDc), calculated as the ratio of procurement costs to DDDs.

$$\text{DDDc} = \frac{\text{procurement costs}}{\text{DDDs}}$$

Interrupted time series analysis is considered one of the most robust quasi-experimental methods for evaluating the longitudinal impact of policy interventions (23). The ITS was employed using volume, expenditure, and DDDc as outcome variables to assess the immediate and long-term effect of the NVBP on insulin usage and costs. A single-group ITS model was constructed as follows (24, 25):

$$Y_t = \beta_0 + \beta_1 T_t + \beta_2 X_t + \beta_3 P_t X_t + \beta_4 D_t + \in_t$$

Where, Y_t indicates the measured outcome variable in month t. T_t denotes the time series number, which corresponds to each observation point. The number "1" is assigned to April 2020, and "50" is assigned to June 2024. X_t is a dummy variable indicating the intervention, where "0" represents the period before NVBP and "1" represents the period after the implementation of NVBP. P_t is the time series after intervention, which value is "0" before intervention and is denoted in sequence according to the monthly order after intervention. Besides, a dummy variable D_t is introduced to control the influence of the Chinese Spring Festival holiday on the transaction between medical institutions and pharmaceutical enterprises (14, 26). During the Spring Festival holiday, which lasts for about one-third of the month in February, insulin transactions between medical institutions and pharmaceutical enterprises tend to decrease significantly. Both the procurement volume and the expenditure show a marked decline in February. Therefore, D_t is set to 1 for February and set to 0 for other months.

In this model, β_0 represents the initial level of the outcome variables at the start of the study. β_1 represents the slope before the intervention. β_2 represents the level change of outcome variables at the intervention moment. β_3 represents the slope change after the intervention. β_4 represents the level change of outcome variable in abnormal months.

The Durbin-Watson test was employed to assess autocorrelation (27). Residual plots were visually inspected to identify heteroscedasticity (28, 29). Models were weighted using the inverse of squared residuals when heteroscedasticity occurred. The R4.4.1 software was used to perform statistical analysis for the study.

3 Results

3.1 Changes in insulin procurement volume, expenditure, and DDDc following NVBP implementation

The volumes of insulins in Guangdong Province increased after NVBP, while the expenditure and DDDc significantly decreased compared with those before volume-based procurement. The results are shown in Table 1.

(1) The average monthly volume of insulins was 7.69 million DDDs before NVBP, which increased to 9.37 million DDDs after centralized procurement. The total procurement volume of insulins rose from 192.40 million DDDs to 235.80 million DDDs. (2) The average monthly expenditure of insulins was CNY 86.64 million before centralized procurement, decreasing to CNY 52.55 million after centralized procurement. The total procurement expenditure decreased from CNY 2165.90 million to CNY 1313.66 million, which reduced by 39.35%. (3) The DDDc of insulins decreased from CNY 11.24 to CNY 5.57 after centralized procurement, representing a year-on-year decrease of approximately 50%.

Subgroup analyses further differentiated these effects across insulin generations (human insulins vs. insulin analogues), manufacturer types (domestic insulins vs. imported insulins) and bidding groups, with detailed results presented in Table 1.

3.2 Insulin procurement volume, expenditure, and DDDc across different generations

The average monthly volume of human insulins increased from 2.10 million DDDs to 2.34 million DDDs after the implementation of NVBP, while the average monthly volume of insulin analogues rose from 5.60 million DDDs to 7.10 million DDDs. Besides, the

TABLE 1 Insulin volume and expenditure in Guangdong Province, from May 2020 to June 2024.

Categories	Before the NVBP (2020.05–2022.05)			After the NVBP (2022.06–2024.06)		
	Volume/ million DDDs	Expenditure/ million CNY	DDDc/CNY	Volume/ million DDDs	Expenditure/ million CNY	DDDc/ CNY
Generations						
Human insulin	52.47	267.95	5.11	58.41	191.91	3.29
Insulin analogue	139.92	1897.95	13.53	177.39	1121.75	6.32
Enterprises						
Domestic insulin	61.27	487.76	7.94	91.67	387.12	4.23
Imported insulin	131.13	1678.14	12.76	144.13	926.55	6.42
Bidding groups						
Basal human	0.83	4.81	5.85	1.34	5.20	3.88
Mealtime human	21.00	75.78	3.61	27.48	76.39	2.78
Premixed human	30.65	187.36	6.12	29.60	110.32	3.73
Long-acting basal analogue	46.10	1027.74	22.29	66.48	596.93	8.98
Rapid-acting analogue	37.72	355.94	9.44	52.75	260.83	4.95
Premixed analogue	56.10	514.27	9.16	58.15	263.98	4.53
Total	192.40	2165.90	11.24	235.80	1313.66	5.57

The volume and expenditure refer to the cumulative procurement volume and expenditure of various insulin categories, respectively. DDDc represents the arithmetic mean of monthly DDDc for various insulin categories. NVBP, national volume-based procurement; DDDs, defined daily doses; DDDc, defined daily dose cost.

proportion of human insulins procurement decreased from 27.27% before the procurement to 24.77%, while the proportion of insulin analogues increased from 72.73 to 75.23%. The average monthly expenditure for human insulins decreased from CNY 10.71 million to CNY 7.68 million, and the total expenditure decreased from CNY 267.95 million to CNY 191.91 million; The average monthly expenditure for insulin analogues decreased from CNY 75.92 million to CNY 44.87 million, and the total procurement expenditure decreased from CNY 1,897.95 million to CNY 1,121.75 million. The DDDc difference between the two generations of insulin before and after the NVBP were CNY 8.42 and CNY 3.03, respectively, which have been narrowing following the NVBP policy.

3.3 Insulin procurement volume, expenditure, and DDDc across different enterprises

The volume for both domestic insulins and imported insulins increased following the NVBP policy. The average monthly volume of domestic insulins rose from 2.45 million DDDs to 3.67 million DDDs (a 49.62% increase), while the average monthly volumes of imported insulin increased from 5.24 million DDDs to 5.76 million DDDs (a 9.92% increase). The market share of domestic insulin grew from 31.84 to 38.88%.

Procurement expenditure declined for both insulins, with a sharper reduction for imported insulins (44.79% decline) than for domestic insulins (20.63% decline). Expenditure for domestic insulins decreased from average monthly CNY 19.51 million to average monthly CNY 15.48 million, while imported insulins expenditure fell from average monthly CNY 67.12 million to average monthly CNY 37.06 million.

The DDDc difference between the two market share distribution insulins narrowed significantly, decreasing from CNY 4.82 to CNY 2.19.

3.4 Insulin procurement volume, expenditure, and DDDc across different bidding groups

Overall, except for the premixed human insulin, procurement volume increased for the remaining groups, with the basal human insulin showing the highest growth at 61.04%. The procurement expenditure of basal and mealtime human insulin increased post-policy, while other groups decreased. The DDDc of six bidding groups decreased, with the long-acting basal insulin analogue experiencing the most substantial reduction—from 22.29 CNY to 8.98 CNY.

The volume of basal human insulin surged from 0.83 million DDDs to 1.34 million DDDs (a 61.4% increase), while its expenditure increased by 8.1%. The volume of mealtime human insulin rose by 30.9%, with a small increase in its expenditure. However, premixed human insulin was the only group to experience a decrease in volume, with expenditure reducing from CNY 187.36 million to CNY 110.32 million. Among insulin analogues, the most notable divergence was observed in the long-acting basal analogue, whose volume increased by 44.2%, expenditure decreased by 41.9%, and DDDc dropped by 59.7%. The reduction in DDDc of long-acting basal analogues is the most significant, but the DDDc post-policy of long-acting basal analogue still exceeds that of other groups. The volume of rapid-acting analogue increased from 37.72 million DDDs to 52.75 million DDDs (a 39.8% increase), with a 26.7% reduction in expenditure. The price of premixed analogue halved (DDDc dropped by 50.5%), with the volume stagnated with a modest 3.7% increase.

3.5 ITS analysis for insulin procurement volume, expenditure, and DDDc

The results of the ITS analysis for all insulin categories are presented in Table 2. A statistically significant instantaneous level increase of 1.547 million DDDs ($p < 0.001$) was observed in volume. Following the intervention, the procurement volume showed an upward trend change, but this change was not statistically significant (see Figure 1A).

A statistically significant instantaneous level decrease of CNY 42.57 million occurred in expenditure in June 2022. However, the effect on the long-term trend change in expenditure was not statistically significant ($p = 0.175$) (see Figure 1B).

The baseline level of DDDc at start was CNY 11.172. The policy intervention resulted in a statistically significant instantaneous level decrease of CNY 5.427 ($p < 0.001$). Following the intervention, the DDDc exhibited a statistically significant downward trend change of CNY 0.028 per month ($p < 0.05$) (see Figure 1C).

In conclusion, the instantaneous level changes for all different outcome variables were statistically significant upon policy implementation. However, the long-term effect of the NVBP policy was not consistently significant in this study.

3.6 ITS analysis of insulin procurement volume for different subgroups

The results of the ITS analysis on insulin volume across different generations are presented in Table 2. In the month of NVBP implementation, the volume of human insulins increased by 0.439 million DDDs ($p < 0.001$), while that of insulin analogues rose by 1.13 million DDDs ($p < 0.001$). A declining trend in the volume of human insulins and an increasing trend for insulin analogues were observed after NVBP; however, neither trend reached statistical significance (Figure 2A).

ITS analysis of volume by manufacturers is also shown in Table 2. The procurement volume of domestic and imported insulins increased significantly by 0.978 million DDDs ($p < 0.05$) and 0.579 million DDDs ($p < 0.001$) at an instantaneous monthly level, respectively, with a larger increase observed in domestic insulins. A significant upward trend in the volume of domestic insulins was observed following the NVBP policy ($p = 0.016$), whereas imported insulins showed a non-significant downward trend ($p = 0.342$) (Figure 2B).

4 Discussion

The present study examined the impact of the NVBP policy on the use of insulin through interrupted time series analysis using the procurement data from Guangdong. Overall, we found that after the implementation of the NVBP policy, the procurement volume of insulin increased in an instantaneous level, while the procurement expenditure and DDDc decreased. And there is a rise in the proportion of high-quality insulin analogue and domestic insulin, which improving overall medication quality level and promoting domestic substitution.

The NVBP policy for insulin has effectively saved expenditure. Compared with the 2 years prior to the procurement, the expenditure on insulin in Guangdong Province decreased by CNY 852.24 million in the 2 years following the procurement. According to the National Health Service Development Statistical Bulletin (30), the total national health expenditure in China surpassed CNY 9 trillion in 2023, accounting for 7.2% of GDP. The growth rate of total health expenditure not only exceeded the GDP growth rate in China but also surpassed the level of OECD countries (31, 32), posing a certain challenge to healthcare insurance fund. The reduction in pharmaceutical expenditure after NVBP has properly played a substantial role in controlling the rapid increase in health expenditure and improved the sustainability of healthcare insurance fund. However, the saving expenditure from the NVBP policy are primarily used to support the development of innovative drugs and the clinical application of new technologies, which may dilute the overall impact on healthcare system costs.

Patients' accessibility and affordability to insulin significantly improved after NVBP. Insulin procurement volume increased substantially after NVBP, enhancing availability for patients to access affordable insulin, which aligns with findings from Wang et al. (33), Zhao and Wu (26), and Yuan et al. (15, 34), as well as Chen et al. (35) that focused on centralized procurement for chemical drugs. However, long-term analysis revealed no sustained upward trend in volume, which

TABLE 2 Results of ITS analysis for insulin volume, expenditure, and DDDc.

Insulin categories	Baseline level	Baseline trend	Level change	Trend change
Volume/million DDDs				
Overall	7.32***	0.007 (0.612)	1.547***	0.008 (0.629)
Human insulin	2.039***	−0.002 (0.616)	0.439***	−0.009 (0.080)
Insulin analogue	5.299***	0.009 (0.292)	1.13***	0.017 (0.149)
Domestic insulin	2.296***	0.003 (0.392)	0.978***	0.016**
Imported insulin	5.04***	0.006 (0.477)	0.579***	−0.009(0.346)
Expenditures/million CNY				
Overall	81.18***	0.71(0.078)	−42.57***	−0.722(0.175)
DDDc/CNY				
Overall	11.172***	0.014(0.333)	−5.427***	−0.042*

All models exhibited statistically significant results ($p < 0.05$) with no evidence of autocorrelation. p values corresponding to coefficients are reported in parentheses; *$p < 0.05$, **$p < 0.01$, and ***$p < 0.001$. ITS, interrupted time series; DDDs, defined daily doses; DDDc, defined daily dose cost.

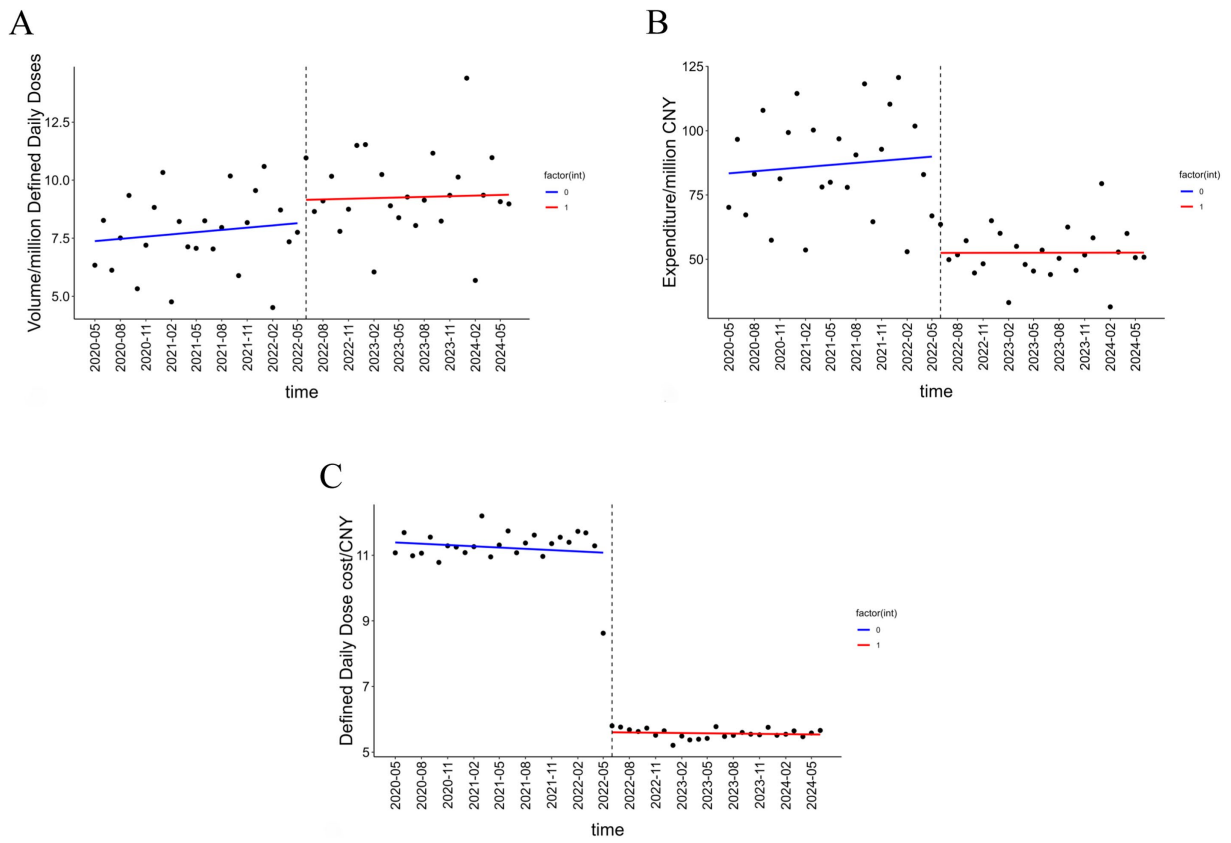


FIGURE 1
Trends in insulin volume, procurement expenditure, and DDDc. **(A)** The volume trend of insulin before and after the NVBP policy. **(B)** The expenditure trend of insulin before and after the NVBP policy. **(C)** The price trend of insulin before and after the NVBP policy.

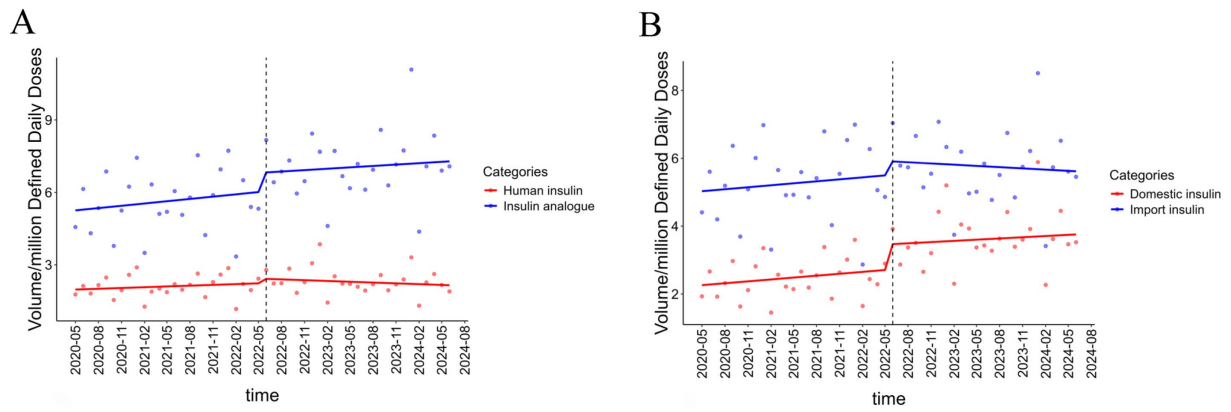


FIGURE 2
Results of ITSA on insulin procurement volume in different subgroups. **(A)** The result of ITS on volume in human insulin and insulin analogue. **(B)** The result of ITS on volume in domestic insulin and imported insulin.

may be attributed to the biphasic insulin (e.g., insulin degludec and insulin aspart) included in medical insurance (33), exerting a alternative effect on winning insulin in NVBP. The research by Chen et al. (36) and Zhang et al. (37) pointed out that there was a negative correlation between economic indicators and insulin use. Due to the high per capita GDP in southern China, the proportion of new hypoglycemic drugs is higher. Therefore, the long-term trend of insulin volume not showing a significant increase may also be related to the rapid increase in the clinical use of new hypoglycemic drugs, such as SGLT-2 inhibitors, GLP-1 receptor agonists, and DPP-4 inhibitors. The result indicates that the impact of NVBP policy is more accurately described as a one-time structural 'shock' that reshaped price and market dynamics, exploring a new equilibrium. The market initially responded to the shock, but the absence of a clear, continuous long term trend. Therefore, while the

NVBP policy may have delivered short-term benefit in terms of price reduction and efficiency gains, its long term influence on healthcare accessibility and system sustainability remains uncertain (7). This calls for ongoing monitoring and flexible policy adaptation to ensure that any negative longer-term consequences are addressed promptly.

The DDDc of insulin decreased from CNY 11.24 to CNY 5.57 after the policy implementation—a reduction exceeding 50%. The observed reduction in DDDc provides substantial financial relief to many insulin-dependent patients, particularly those who were previously struggling to afford this life-sustaining medication. However, a nearly 50% decrease in DDDc of insulin does not directly indicate that patients with diabetes have reduced the same expenditure, since insulin expenditure is only a part of the expenditure of patients with diabetes, and there may even be a compensatory cost shift phenomenon that other diabetes-related treatment or examination expenses increased after the decrease in insulin price. Therefore, future research can comprehensively evaluate the impact of the NVBP policy on patient expenditure from the perspective of diabetes management.

The NVBP policy has facilitated the upgrading of insulin usage, thereby optimizing the insulin utilization pattern in China. Compared with human insulins, insulin analogues exhibit superior pharmacokinetic properties, more closely mimicking the natural secretion pattern of insulin in human body, which associating with a lower risk of treatment-related hypoglycemic events, improving glycemic control, offering greater flexibility and convenience in injection timing, and effectively enhancing patient medication adherence and treatment outcome (38, 39). The volume of insulin analogues increased more significantly than that of human insulins, with an increased market share after NVBP. This may highlight a difference between the effect of the NVBP policy for biologics and chemical drugs. Centralized procurement of biologics may enhance patient access to upgraded products by narrowing the price gap between normal and upgraded products, thereby promoting the innovation and upgrading of biologics. In Guangdong Province, the average usage proportion of insulin analogues increased from 72.73 to 75.23%, indicating an upgrading of patient medication structure. The volume proportion of insulin analogues exceeded that of some developed countries (40). According to the NHSA, the proportion of insulin analogues use has increased to 70% at the national level following the implementation of centralized procurement, bringing it closer to the medication structure seen in European countries. Following the completion of the insulin procurement agreement in 2024 and subsequent renewal procurement, the national reported volume for human insulin was approximately 76 million shots, while that for insulin analogue insulin was about 165 million shots (41). The proportion of insulin analogue increased from 58% at the initial reporting to 69%, reflecting the optimization of insulin utilization pattern in China. Furthermore, we found a significant portion of the overall reduction in insulin procurement expenditure (91.08%) can be attributed to the reduction in insulin analogues expenditure, consistent with the findings of Yuan et al. (7). After the NVBP, the DDDc difference between human insulins and insulin analugues narrowed, promoting the availability for patients with diabetes to acquire more high-quality insulin analogues.

The reliance on imported insulin has been reduced after NVBP, mitigating supply chain risks. Following NVBP, the proportion of domestic insulin in volume increased from 31.8 to 38.9%, expanding its market share. The procurement volume of domestic insulin has shown a significant upward trend after NVBP, while imported insulin has exhibited a non-significant decline, promoting the substitution of domestic insulin for imported insulin to some extent. Domestic insulin manufacturers get the opportunity for rapid hospital adoption attributing to the NVBP policy, accelerating the domestic substitution process, which is beneficial for reducing supply chain risks and enhancing supply stability under the global tariff uncertainty. Similar findings were reported by Wang et al. (42), who, using a difference-in-differences approach, demonstrated that the NVBP Policy effectively promoted the substitution of original drug by generic drug.

This quantitative analysis of insulin procurement demonstrates that China's volume-based procurement policy has effectively reduced healthcare expenditure while improving medication accessibility and affordability. The policy has successfully facilitated therapeutic upgrading of insulin products, enhanced supply chain resilience, and embodied the principles of value-based healthcare, offering valuable insights for medical reforms in other countries.

5 Limitation

Firstly, this study used data only from Guangdong due to data availability. While Guangdong is a major province economically and demographically in China, with a per capita GDP is equivalent to that of some European and South American countries. The utilization pattern of insulin may be different from that of some economically underdeveloped provinces in China, so it is not suitable for direct extrapolation to the national situation.

Secondly, although this study utilized data from 25 observations both before and after the policy intervention, meeting the requirement for fitting an interrupted time series model, the 25-month post-policy period may still be insufficient to fully assess the long-term effect of the policy. Future research should extend the observation period to further validate the findings of this study.

Finally, the study focused on the impact of the NVBP policy on insulin utilization, without accounting for other potential influencing factors—such as per capita GDP, education levels, or the utilization of new hypoglycemic agents —that could affect observed outcomes. Additionally, the constitution of healthcare costs is a highly complex and interconnected systemic issue, reductions in insulin price do not be consistent to decreased expenditures for patients with diabetes or lower overall healthcare costs. Future research should further investigate potential spillover effects of insulin expenditure saving on other medical expenditure.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

CJ: Conceptualization, Formal analysis, Methodology, Project administration, Supervision, Writing – original draft, Writing – review

& editing. MN: Data curation, Methodology, Software, Visualization, Writing – original draft, Writing – review & editing. YL: Conceptualization, Supervision, Writing – review & editing. TJ: Conceptualization, Project administration, Writing – review & editing. DG: Conceptualization, Project administration, Writing – review & editing. PQ: Conceptualization, Project administration, Writing – review & editing. NL: Conceptualization, Project administration, Writing – review & editing. FC: Conceptualization, Supervision, Writing – review & editing.

Funding

The author(s) declare that no financial support was received for the research and/or publication of this article.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

The reviewer JP declared a shared affiliation with the author MN, to the handling editor at time of review.

Generative AI statement

The authors declare that no Gen AI was used in the creation of this manuscript.

Any alternative text (alt text) provided alongside figures in this article has been generated by Frontiers with the support of artificial intelligence and reasonable efforts have been made to ensure accuracy, including review by the authors wherever possible. If you identify any issues, please contact us.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2025.1659721/full#supplementary-material

References

1. International diabetes federation. IDF Diabetes Atlas (2025). Available online at: https://diabetesatlas.org/resources/idf-diabetes-atlas-2025/ [Accessed June 30, 2025]

2. Tomic D, Shaw JE, Magliano DJ. The burden and risks of emerging complications of diabetes mellitus. *Nat Rev Endocrinol*. (2022) 18:525–39. doi: 10.1038/s41574-022-00690-7

3. Antar SA, Ashour NA, Sharaky M, Khattab M, Ashour NA, Zaid RT, et al. Diabetes mellitus: classification, mediators, and complications; a gate to identify potential targets for the development of new effective treatments. *Biomed Pharmacother*. (2023) 168:115734. doi: 10.1016/j.biopha.2023.115734

4. Tseng Y, Tsan Y, Chen P. Association between severity of diabetic complications and risk of cancer in middle-aged patients with type 2 diabetes. *J Diabetes Invest*. (2025) 16:16–24. doi: 10.1111/jdi.14364

5. World Health Organization. Global report on diabetes. Geneva: World Health Organization. (2016). 83 Available online at: https://iris.who.int/handle/10665/204871 [Accessed July 2, 2025]

6. Freeman JS. Are analogue insulins superior to human insulin in clinical practice? *Curr Diab Rep*. (2010) 10:176–83. doi: 10.1007/s11892-010-0104-8

7. Yuan J, Li M, Jiang X, Lu ZK. National volume-based procurement (NVBP) exclusively for insulin: towards affordable access in China and beyond. *BMJ Glob Health*. (2024) 9:e014489. doi: 10.1136/bmjgh-2023-014489

8. The Joint Procurement Office. Announcement of the joint procurement office on the release of the national drug centralized procurement exclusively for insulin (GYYD-2021-3). (2021). Available online at: https://www.smpaa.cn/gjsdcg/2021/11/05/10361.shtml [Accessed June 30, 2025]

9. The Joint Procurement Office. Announcement on the insulin products procured for the sixth round of national drug centralized procurement exclusively for insulin. (2021). Available online at: https://www.smpaa.cn/gjsdcg/2021/11/30/10435.shtml [Accessed June 30, 2025]

10. Lu S, Liu X, Huang Z, Zhou Z, Feng Z. Administrative regulation-informed analysis of the developmental path of national volume-based procurement to improve drug accessibility in China. *Front Public Health*. (2024) 12:1342632. doi: 10.3389/fpubh.2024.1342632

11. Li X, Tao R, Jin Y, Li N. National centralized drug procurement and health care expenditure of households—micro-evidence from CFPS. *Front Public Health*. (2024) 12:1405197. doi: 10.3389/fpubh.2024.1405197

12. Wang Z, Wang K, Hua Y, Dong X, Zhang L. Impact and implications of national centralized drug procurement in China. *Int J Clin Pharm*. (2024) 46:1557–62. doi: 10.1007/s11096-024-01767-1

13. Porter ME. A strategy for health care reform — toward a value-based system. *N Engl J Med*. (2009) 361:109–12. doi: 10.1056/nejmp0904131

14. Yang Y, Chen L, Ke X, Mao Z, Zheng B. The impacts of Chinese drug volume-based procurement policy on the use of policy-related antibiotic drugs in Shenzhen, 2018–2019: an interrupted time-series analysis. *BMC Health Serv Res*. (2021) 21:668. doi: 10.1186/s12913-021-06698-5

15. Yuan J, Lu ZK, Xiong X, Lee T-Y, Huang H, Jiang B. Impact of National Volume-Based Procurement on the procurement volumes and spending for antiviral medications of hepatitis B virus. *Front Pharmacol*. (2022) 13:842944. doi: 10.3389/fphar.2022.842944

16. Song J, Guo W, Jin C, Xu Y, Hu X, Zhang Z, et al. Analysing the effects of National Centralised Drug Procurement and Price negotiation policies on novel hypoglycaemic drug usage and costs in Shanghai, China: an interrupted time series analysis. *BMJ Open*. (2024) 14:e088318. doi: 10.1136/bmjopen-2024-088318

17. Yang Z, Han X, Liang P, Zhao X, Zhu Q, Ye H, et al. Study on the effects of National Volume-Based Procurement of chemical drugs on Chinese patent medicines: lipid-lowering drugs as an example. *Health Care Sci*. (2025) 4:14–24. doi: 10.1002/hcs2.70003

18. Xue A, Xue Q, Fu J, Fan K, Zhang J, Cai P, et al. Quantifying the impacts of volume-based procurement policy on spatial accessibility of antidepressants via generic substitution: a four-city cohort study using drug sales data. *PLoS One*. (2025) 20:e0318509. doi: 10.1371/journal.pone.0318509

19. National Health Commission of the People's Republic of China. China health statistics yearbook (2024). Available online at: https://www.stats.gov.cn/sj/ndsj/2024/indexch.htm [Accessed June 30, 2025]

20. Li Y, Teng D, Shi X, Qin G, Qin Y, Quan H, et al. Prevalence of diabetes recorded in mainland China using 2018 diagnostic criteria from the American Diabetes Association: national cross sectional study. *BMJ*. (2020) 369:m997. doi: 10.1136/bmj.m997

21. Centralized Drug Procurement Platform in Guangdong. Available online at: https://gpo.gzggzy.cn/webPortal/home.html [Accessed July 2, 2025]

22. World Health Organization. ATCDDD - ATC/DDD Index. Available online at: https://atcddd.fhi.no/atc_ddd_index/ [Accessed July 1, 2025]

23. Wagner AK, Soumerai SB, Zhang F, Ross-Degnan D. Segmented regression analysis of interrupted time series studies in medication use research. *J Clin Pharm Ther*. (2002) 27:299–309. doi: 10.1046/j.1365-2710.2002.00430.x

24. Linden A. Conducting interrupted time-series analysis for single- and multiple-group comparisons. *Stata J*. (2015) 15:480–500. doi: 10.1177/1536867X1501500208

25. Bernal JL, Cummins S, Gasparrini A. Corrigendum to: interrupted time series regression for the evaluation of public health interventions: a tutorial. *Int J Epidemiol*. (2021) 50:1045–5. doi: 10.1093/ije/dyaa118

26. Zhao B, Wu J. Impact of China's National Volume-Based Procurement on drug procurement Price, volume, and expenditure: an interrupted time series analysis in Tianjin. *Int J Health Policy Manag*. (2023) 12:7724. doi: 10.34172/ijhpm.2023.7724

27. Huitema BE, McKean JW. A simple and powerful test for autocorrelated errors in OLS intervention models. *Psychol Rep*. (2000) 87:3–20. doi: 10.2466/PR0.87.5.3-20

28. Cheng T-C. On simultaneously identifying outliers and heteroscedasticity without specific form. *Computational Statis Data Analysis*. (2012) 56:2258–72. doi: 10.1016/j.csda.2012.01.004

29. Su L, Zhao Y, Yan T, Li F. Local polynomial estimation of heteroscedasticity in a multivariate linear regression model and its applications in economics. *PLoS One*. (2012) 7:e43719. doi: 10.1371/journal.pone.0043719

30. National Health Commission of the People's republic of China. National Health Service Development Statistical Bulletin. (2023). Available online at: https://www.nhc.gov.cn/wjw/c100178/202408/1de460738f81464280e9ed3277630e33.shtml [Accessed July 1, 2025]

31. Zhai T, Goss J, Li J. Main drivers of health expenditure growth in China: a decomposition analysis. *BMC Health Serv Res*. (2017) 17:185. doi: 10.1186/s12913-017-2119-1

32. Zeng X, Chen L, Chen L. Analysis of health expenditures in China from 2000 to 2019 compared with the world and upper-middle-income countries. *Front Public Health*. (2025) 12:1464214. doi: 10.3389/fpubh.2024.1464214

33. Wang X, Huang H, Sun Y, Zhu Z, Jiang B, Yang L. Effects of volume-based procurement policy on the usage and expenditure of first-generation targeted drugs for non-small cell lung cancer with EGFR mutation in China: an interrupted time series study. *BMJ Open*. (2023) 13:e064199. doi: 10.1136/bmjopen-2022-064199

34. Yuan J, Lu ZK, Xiong X, Jiang B. Lowering drug prices and enhancing pharmaceutical affordability: an analysis of the national volume-based procurement (NVBP) effect in China. *BMJ Glob Health*. (2021) 6:e005519. doi: 10.1136/bmjgh-2021-005519

35. Chen L, Yang Y, Luo M, Hu B, Yin S, Mao Z. The impacts of National Centralized Drug Procurement Policy on drug utilization and drug expenditures: the case of Shenzhen, China. *IJERPH*. (2020) 17:9415. doi: 10.3390/ijerph17249415

36. Chen C, Liu X, Zhang J, Hu S, Zhang J, Liu X, et al. Changes in insulin utilization in China from 2020 to 2022. *Diabetes Obesity Metabol*. (2024) 26:5681–9. doi: 10.1111/dom.15936

37. Zhang J, Xu S, Liu X, Zhang J, Hu S, Liu X, et al. Time trends and regional variation in utilization of antidiabetic medicines in China, 2015–2022. *Diabetes Obesity Metabol*. (2024) 26:2752–60. doi: 10.1111/dom.15594

38. Jarosinski MA, Chen Y-S, Varas N, Dhayalan B, Chatterjee D, Weiss MA. New horizons: next-generation insulin analogues: structural principles and clinical goals. *J Clin Endocrinol Metabol*. (2022) 107:909–28. doi: 10.1210/clinem/dgab849

39. Danne T, Heinemann L, Pieber TR. New insulins, Biosimilars, and insulin therapy. *Diabetes Technol Ther*. (2024) 26:S-45–67. doi: 10.1089/dia.2024.2504

40. Godman B, Wladysiuk M, McTaggart S, Kurdi A, Allocati E, Jakovljevic M, et al. Utilisation trend of long-acting insulin analogues including Biosimilars across Europe: findings and implications. *Biomed Res Int*. (2021) 2021:9996193. doi: 10.1155/2021/9996193

41. The Joint Procurement Office. Announcement of the joint procurement office on the release of the national drug centralized procurement exclusively for insulin (GYYD-2024-1). (2024). Available online at: https://www.smpaa.cn/gjsdcg/2024/03/29/13375.shtml [Accessed July 2, 2025]

42. Wang J, Yang Y, Xu L, Shen Y, Wen X, Mao L, et al. Impact of '4+7' volume-based drug procurement on the use of policy-related original and generic drugs: a natural experimental study in China. *BMJ Open*. (2022) 12:e054346. doi: 10.1136/bmjopen-2021-054346

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 15 September 2025
DOI 10.3389/fpubh.2025.1610722

Check for updates

OPEN ACCESS

EDITED BY
Kevin Lu,
University of South Carolina, United States

REVIEWED BY
Fengshi Jing,
City University of Macau, Macao SAR, China
Pingping Gu,
Nantong University, China

*CORRESPONDENCE
Jiachun Li
2965140787@qq.com

RECEIVED 14 April 2025
ACCEPTED 25 August 2025
PUBLISHED 15 September 2025

CITATION
Zhang X, Meng Y and Li J (2025) A queuing game theory approach to strategies for supplementing medical alliances with internet hospitals. *Front. Public Health* 13:1610722. doi: 10.3389/fpubh.2025.1610722

COPYRIGHT
© 2025 Zhang, Meng and Li. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

A queuing game theory approach to strategies for supplementing medical alliances with internet hospitals

Xin Zhang, Yue Meng and Jiachun Li*

Management School, Tianjin Normal University, Tianjin, China

With large hospitals actively establishing Internet-based healthcare initiatives to facilitate the downward referral of discharged patients, it is essential to examine the conditions under which such implementations are truly beneficial. This study categorizes medical alliances (MAs) into two types: tightly integrated and loosely integrated. Utilizing queuing-game theory, we constructed a two-stage model to evaluate referral efficiency, measured by the volume of downward referrals from tertiary hospitals and the effort levels exerted by community hospitals. By comparing MAs with and without supplementary internet hospitals, we identify the circumstances in which hospital-established internet hospitals enhance patient referrals. The findings indicate that within tightly integrated MAs, the referral volume increases with the potential patient arrival rate. When the cost coefficient of internet hospitals is low, MAs that incorporate internet hospitals demonstrate both higher referral volumes and increased effort, with profits favored by Internet-based healthcare under low arrival rates. In loosely integrated MAs, effort levels exhibit a similar pattern while referral volume depends heavily on the revenue-sharing ratio of the internet hospital. Specifically, referral volume increases when the ratio is low, arrival rates are high, and cost coefficients remain low. Conversely, at high revenue-sharing ratios, referral volumes rise regardless of the cost coefficient, provided arrival rates are either low or high. For tertiary hospitals, profits are higher with Internet-based healthcare only under low arrival rates when the revenue-sharing ratio is low; this threshold declines as the cost coefficient increases. When the ratio is high, digital healthcare consistently yields higher profits. For community hospitals, a low ratio leads to higher profits only within a moderate range of arrival rates—a range that narrows with rising cost coefficients. Under high ratios, profitability improves only at low arrival rates and increases alongside the cost coefficient.

KEYWORDS

downward referral efficiency, Internet-based healthcare, referral optimization, medical alliance, two-stage queuing game

1 Introduction

With rapid socioeconomic development and continuous improvement in living standards, the demand for healthcare services is rising. Although the overall supply of medical resources increases each year, challenges such as high costs, limited access, uneven distribution, and underutilization of services persist. Consequently, the government has promoted a hierarchical healthcare system, encouraging collaboration and division of labor among medical institutions at different levels and shifting general diagnoses and treatments

to primary care settings. However, factors such as conflicting hospital interests and limited service capacity of primary care facilities impede the effective implementation of two-way referrals. To refine and popularize the hierarchical diagnosis and treatment system, promote downward patient referrals, and alleviate the imbalance between healthcare supply and demand, China has actively encouraged the development of medical alliances (MAs) since 2009. By the end of 2023, over 18,000 MAs have been established nationwide, enabling 14.722 million downward patient referrals—a 29.9% increase over the previous year. The issue of MA referral efficiency is crucial for the implementation of hierarchical treatment policies, yet it has received limited scholarly attention to date.

At the same time, ongoing advancements in information technology have given rise to new models of healthcare delivery. Among them, Internet-based healthcare has rapidly expanded—especially under normalized epidemic prevention and control—easing the burden on central hospitals. This model provides robust technological support for initial consultations within MA community clinics, chronic disease management, prescription renewals, and two-way referrals. As such, innovative collaborations incorporating Internet-based healthcare contribute meaningfully to the development of a hierarchical treatment system. While some scholars have explored the integration of Internet-based healthcare and MAs, critical questions remain—particularly whether such integration genuinely benefits hierarchical healthcare delivery. Therefore, examining the complementary role and operational mechanisms of Internet-based healthcare within MAs is essential for advancing the implementation of hierarchical treatment and enhancing downward referral effectiveness.

Building upon this, this study aims to identify the optimal strategies for supplementing MAs with Internet-based healthcare. Initially, existing literature on the collaboration between internet hospitals and MAs, patient referrals, and MA queuing service systems will be reviewed and synthesized. Drawing from this body of research, we develop a two-stage queuing-game model to capture the dynamic interactions among tertiary A-level hospitals, community hospitals, internet hospitals, and patients. Referral efficiency is quantified by the volume of downward referrals from tertiary hospitals and the effort level of community hospitals. By optimizing the model and analyzing objective functions and equilibrium solutions under varying conditions, we compare the referral efficiency of MAs with and without internet hospital support. This comparison allows us to identify the conditions under which hospital-established internet hospitals effectively facilitate patient referrals.

2 Literature review

The relevant literature for this study spans four key domains: Internet-based healthcare, medical alliances (MAs), hierarchical diagnosis and treatment, and queuing service systems.

In recent years, research on internet hospitals has primarily centered on innovations in telemedicine and remote monitoring technologies, exploring how these tools can enhance healthcare efficiency and improve patient management and disease monitoring. Davis et al. noted that remote medical services have entered a phase of stable growth, with Internet-based healthcare effectively facilitating remote diagnosis, monitoring, and doctor–patient communication through technologies such as video conferencing, sensors, and wearable devices (1). Ahmad et al. explored the potential opportunities and adaptive challenges of blockchain technology in telemedicine and remote healthcare fields. Blockchain plays a critical role in strengthening information security and privacy protection, while also enhancing the transparency of business operations. By ensuring the immutability and traceability of data, it enables effective monitoring of fraudulent activities such as false patient insurance claims and physician credential verification (2). As research into the behavior of Internet healthcare users deepens, the significance of satisfaction evaluation has become increasingly apparent. Singh et al. conducted empirical studies to examine the differing expectations of patients and doctors within the emerging Internet healthcare device ecosystem. Their findings revealed that device usability significantly boosted patient satisfaction, whereas the increase in doctor satisfaction was comparatively modest (3). Wang et al. employed Python crawlers to extract text content from Internet healthcare platforms and applied natural language processing (NLP) techniques to develop an information quality evaluation index system (4). Some scholars focus on the regulatory issues of Internet-based healthcare. Marelli et al. pointed out that the rapid advancement of digital healthcare has outpaced the adaptability of existing data governance systems, necessitating the construction of more flexible and rapidly responsive regulatory policies (5). Xanthidou et al. conducted an in-depth study on the application of electronic health records, identifying several challenges related to data access rights, security regulations, and authorization protocols. In summary, existing research on Internet-based healthcare predominantly addresses its service benefits, user adoption, and regulatory challenges. However, studies examining the collaboration between Internet healthcare and MAs remain limited. This study bridges that gap by integrating Internet-based healthcare with MAs, investigating the effectiveness of Internet healthcare as a supplementary channel to enhance downward patient referrals within MAs, thereby expanding the research landscape of Internet-based healthcare (6).

Another stream of literature pertains to MAs. Due to differences in social structures and healthcare systems worldwide, no universally consistent concept functionally or structurally equivalent to the "Medical Alliance" has yet emerged. The closest international counterpart is integrated healthcare services, which emphasize collaborative operations and comprehensive integration among medical institutions. This approach aims to optimize the allocation of medical resources while simultaneously improving service fairness and accessibility. Some scholars have explored the development of integrated healthcare services. For example, Bernard argued that rapid advances in Internet technology have positioned telemedicine services as a vital tool for optimizing medical resource allocation and management, thereby significantly enhancing healthcare efficiency and accessibility (7). Baxter et al. developed an integrated healthcare service model grounded in evidence-based policy and assessed its effectiveness in improving patient service quality, optimizing labor structure, streamlining

work processes, maintaining financial stability, and strengthening management integration (8). Some researchers concentrate on model innovation and practical application. Li et al. examined the development of a tightly integrated medical alliance at the Second People's Hospital of Guangdong Province, identifying innovative approaches and categorizing the construction of tightly integrated MAs into three distinct models: business-led, participatory advisory, and menu-customized (9). Some scholars focus on the effectiveness evaluation of MAs. He et al., using urban MAs as their research subject and employing the difference-in-differences method, found that MAs significantly enhance the medical service capacity, clinical standards, and administrative efficiency of secondary and lower-level hospitals within the alliance. These improvements are driven by strengthened technology spillover and management coordination effects, which also contribute to more harmonious doctor–patient relationships (10). Currently, research on the collaboration between MAs and Internet-based healthcare is limited. Most studies concentrate on the application of MA and Internet healthcare collaboration in promoting the hierarchical diagnosis and treatment system (reviewed in the section on hierarchical diagnosis and treatment). A smaller subset of research examines the informatization of MAs. For example, Xu et al., in addressing the uneven distribution of medical resources among hospitals, emphasized the construction and application of information platforms. Their work actively explores the role of "Internet+" in advancing MA development, with the goal of achieving vertical integration of medical resources and strengthening primary healthcare service capacity (11). Wang et al. pointed out that insufficient interoperability of information systems within MAs is a major obstacle, highlighting the urgent need to strengthen and optimize Internet platform infrastructure while also improving public awareness and acceptance (12). In summary, both domestic and international scholars have examined the construction and practical application of MAs, yet research on their collaboration with Internet hospitals remains limited, primarily focusing on the informatization of MAs. Few scholars have explored the selection problem of Internet hospitals within MAs, but the research assumes hospital scale as the premise. This paper uses the downward referral efficiency of MAs promoted by Internet-based healthcare as the basis to explore the selection of hospital-owned Internet hospitals by MAs.

Due to differences in healthcare system structures and policy environments across countries, the concept of hierarchical diagnosis and treatment has not been formally established abroad. Its closest counterpart is the three-tier healthcare service system. Nonetheless, there is broad consensus within the medical community on the necessity of implementing hierarchical diagnosis and treatment systems. Greenfield et al. found that primary healthcare services are highly effective in controlling medical costs and play a key role in easing the burden on medical resources. However, the practical implementation of a hierarchical diagnosis and treatment system remains complex, requiring large-scale system coordination and being influenced by a wide range of factors (13). Zhao evaluated the impact of MA policies on hierarchical diagnosis and treatment from the perspective of medical staff, finding that the institutional level significantly influences evaluation outcomes. Primary medical institutions, in particular, tend to focus on policy formulation and implementation to secure associated benefits (14). Some scholars have examined the optimization of MA resource allocation. Liu et al. and Wang et al. investigated the problem of determining optimal referral rates in a two-tier service system—comprising tertiary hospitals and community hospitals—by constructing sequential game models under both centralized and decentralized decision-making scenarios (15, 16). Other scholars focus on research concerning the hierarchical diagnosis and treatment system under the MA framework. Ma et al. believe that MAs are important carriers of the hierarchical diagnosis and treatment system. Based on practical observations, they identified several challenges, including weak incentives for downward referrals, limited primary care capacity, and difficulties in coordinating the interests of MA member institutions. To address these issues, they proposed measures such as improving referral procedures, strengthening triage guidance, leveraging the strengths of primary care, and enhancing the overall service capabilities of lower level institutions (17). Some scholars have explored the construction of hierarchical diagnosis and treatment systems and the development of new models from the perspective of "Internet+". Heng et al. proposed that "Internet+" hierarchical diagnosis and treatment utilizes informatization and intelligent means to assist MAs in efficiently integrating regional medical resources. Leveraging localized advantages, it can maximally integrate medical resources and improve diagnostic efficiency (18). In recent years, many scholars have realized the important role of the hierarchical diagnosis and treatment system in alleviating the problem of unreasonable medical resource allocation and have studied patient downward referrals. Wang et al. using simulation optimization techniques, verified that implementing downward referral strategies can effectively alleviate resource constraints in higher-level hospitals and improve resource utilization in lower-level hospitals (19). In addition to constructing queuing optimization models to find optimal referral strategies, some scholars consider the non-cooperative competitive relationship between general hospitals and primary care hospitals, analyzing the game interactions among multiple participants. Yao et al. constructed a three-party evolutionary game model involving medical insurance departments, hospitals, and critically ill patients in tertiary hospitals. They explored the evolutionary paths and influencing factors of hospital and patient strategies under different government coordination strategies, concluding that the government holds a coordinating C-level position in advancing hierarchical diagnosis and treatment (20). Most of the literature reviewed examines Internet-based healthcare as a supplementary pathway for MAs, highlighting its potential and effectiveness in advancing the hierarchical diagnosis and treatment system. However, its actual impact remains contested, and diverse "Internet+MA" models have been proposed and studied. Some scholars conduct quantitative research on optimizing medical resource allocation in the hierarchical diagnosis and treatment system, but their studies do not incorporate Internet-based healthcare. This paper integrates Internet-based healthcare with MAs, employing quantitative mathematical modeling to examine the effectiveness of Internet healthcare as a supplementary channel for promoting patient downward referrals, thereby expanding the research frontier on their collaboration.

Furthermore, queuing theory provides a solid methodological foundation for optimizing resource allocation and utilization, facilitating rigorous and precise analysis of complex real-world queuing challenges. International scholars have applied queuing theory principles and methods to develop scientific optimization solutions for hospital operations. Tyagi et al. aiming to reduce patient waiting times and improve medical resource utilization, applied queuing theory to optimize the number of servers in a healthcare service system (21). Ala et al., through case studies applying queuing theory, utilized mixed-integer linear programming (MILP) and approximate solution algorithms (ASA) to tackle supply chain network design and patient scheduling problems in healthcare (22). Wang Wenjuan et al. established an integrated queuing and game model for a referral system, exploring how the government can incline patients toward initial community consultations by configuring hospital scales and adjusting medical service prices (23). Yu used queuing theory to construct a game model involving patients, tertiary A-level hospitals, and community hospitals, investigating effective subsidy strategies to guide the downward allocation of medical resources (24). This study similarly employs queuing theory to analyze the downward referral efficiency of MAs. However, unlike previous studies, it incorporates Internet-based healthcare into the model, examining its impact on stakeholders, decision-making stages, and processes within MAs under various cooperation modes following the integration of Internet hospitals, thereby expanding the scope of existing research.

In summary, while existing literature offers valuable insights, a comprehensive review reveals notable gaps. Building on prior research, this paper develops a queuing-game model to evaluate the effectiveness of hospital-owned Internet hospitals in supplementing MAs and facilitating patient downward referrals. Furthermore, it advances the analysis by categorizing MAs by type and exploring optimal strategies for integrating Internet hospitals across different MA models.

3 Model development

This study considers a two-tier healthcare service system comprising one tertiary A-level hospital (hereinafter referred to as the tertiary hospital) and one community hospital. Patients initially visit the tertiary hospital, which refers those with milder conditions to the community hospital, while retaining severe cases for further treatment. The tertiary hospital offers more specialized services at higher costs, whereas the community hospital treats only minor cases at lower costs. With the introduction of Internet-based healthcare, the tertiary hospital can enhance the community hospital's service capacity through online support. This not only helps free up its own resources and accommodate more patients but also promotes more efficient use of community hospital resources, thereby improving the overall performance of the healthcare system.

Patients arrive at the tertiary hospital according to a Poisson distribution with a potential arrival rate of Λ. Based on their perceived utility U, patients decide whether to enter the system. Those who ultimately receive treatment are termed the effective arrival rate, denoted by λ_e. For instance, if 25 patients seek treatment (indicating a potential arrival rate of 25), but 5 patients opt out due to factors like long wait times, the remaining 20 constitute the effective arrival rate. Patient conditions are heterogeneous and represented by φ, where a higher φ, indicates a more severe condition and increased likelihood of remaining in the tertiary hospital for follow-up care. The community hospital can only provide follow-up services for patients with $\varphi \in [0, \varphi_0]$, Thus, the downward referral quantity to the community hospital is $q = \int_0^{\varphi_0} f(\varphi)d\varphi$. That is, the clinical transfer criteria established by tertiary hospitals.

Assume the service capacity of the tertiary hospital is constant at v_H. If a patient receives complete treatment at the tertiary hospital, the total service time follows an exponential distribution with mean $\frac{1}{v_H}$, Let $\frac{\theta}{v_H}$ and $\frac{1-\theta}{v_H}$ represent the time for surgery and subsequent recovery, respectively. θ denotes the proportion of time allocated to preliminary surgical treatment at tertiary hospitals relative to total treatment time. When $\theta = 0.4$, this indicates that surgical procedures constitute 40% of the total treatment duration. After completing surgical treatment at the tertiary hospital, a patient has a probability $\frac{q}{\lambda_e}$ of being referred to the community hospital and a probability $1 - \frac{q}{\lambda_e}$ of remaining in the tertiary hospital. Assume the cost of treatment is fully covered by the Medical Insurance Bureau. Under the DRG-based payment system, the tertiary hospital earns a revenue of g_1 and incurs a cost of C_{1H} for providing initial surgical treatment services per patient. For providing subsequent recovery services, the revenue is g_2 and the cost is C_{2H}.

Assume the community hospital's service capacity is constant at v_L, and it serves referred patients. Referred patients arrive at the community hospital following a Poisson distribution with rate q. Drawing lessons from Shenzhen's capitation-based payment model for primary care clinics, the community hospital earns a revenue of g_L and incurs a cost of C_L for providing subsequent recovery services per patient. Community hospital require corresponding manpower, technology and other inputs to provide services, that is the effort level e. The effort-related cost required for the community hospital to enhance its service level is $C_E = C_e e^2$, which increases with the effort level e. When Internet-based healthcare is introduced, the community hospital's effort-related cost becomes $C_E = \frac{C_e e^2}{\gamma}$, where γ represents the service level provided by the Internet hospital; the unit effort-related cost decreases as γ increases. When the community hospital fails to treat a patient due to insufficient capacity, it incurs a penalty cost $M = \frac{mq^2}{e}$. This penalty cost increases with the referral quantity q and decreases with the effort level e. In a tightly integrated MA, the entire MA bears the penalty cost. In a loosely integrated MA, the cost is shared proportionally, with the tertiary hospital bearing $\alpha M$and the community hospital bearing $(1 - \alpha)M$, where α is an exogenous parameter.

Assume the Internet hospital has sufficient service capacity. Based on the current operations of the Bohe Doctor Platform, the initial establishment phase requires investment in development costs, with technical and operational expenditures increasing as more personalized services are offered. The construction and operation of the Internet hospital incur a corresponding technological cost $C_p = d\gamma^2$, where $d$is the marginal cost.

10.3389/fpubh.2025.1610722

Drawing on the revenue-sharing mechanism implemented by Shanghai Putuo District Central Hospital, community hospitals receive reimbursements from health insurance funds for accepting rehabilitative patients, while the internet platform retains 10% as a technical support fee. The Internet hospital adopts a revenue-sharing model to distribute the revenue obtained from treating referred patients at the community hospital, $g_s = \beta g_L$.

This study examines tightly integrated and loosely integrated MAs before and after the introduction of hospital-owned Internet hospitals.

Scenario 1: Tightly integrated MA without the Internet hospital. The MA determines the optimal referral quantity q (from the tertiary hospital) and effort level e (of the community hospital) based on maximizing overall profit. Patients then decide whether to seek treatment based on their individual utility.

Scenario 2: Loosely integrated MA without the Internet hospital. The tertiary hospital first decides the referral quantity q based on maximizing its own profit. Then, the community hospital determines its effort level e. Finally, patients decide whether to enter the system.

Scenario 3: Tightly integrated MA with the hospital-owned Internet hospital. The MA determines the optimal referral quantity q, community hospital effort level e, and Internet hospital service level γ based on maximizing overall profit. Patients then decide whether to seek treatment.

Scenario 4: Loosely integrated MA with the hospital-owned Internet hospital. The tertiary hospital first determines the referral quantity q and Internet hospital service level γ based on maximizing its own profit. Then, the community hospital determines its effort level e. Finally, patients decide whether to enter the system.

3.1 Patient treatment choice decision model

Let U represent the net utility for a patient entering the healthcare system. Assuming treatment costs are fully covered by medical insurance, if a patient enters the tertiary hospital, their expected waiting time is $E(\varepsilon)$. The net utility can be expressed as:

$$U = R - bE(\varepsilon) \tag{3.1}$$

where $E(\varepsilon) = \frac{\lambda_e\theta^2+(1-\theta)(\lambda_e-q)}{v_H(v_H-\lambda_e+q(1-\theta))}$, is the patient's perceived value of treatment, and b is the cost per unit of waiting time. Patients choose to enter the tertiary hospital if $U \geq 0$.

Theorem 3.1:The patient's equilibrium arrival rate λ_e depends on the potential arrival rate Λ and the tertiary hospital's referral quantity q.

The equilibrium arrival rate is:

$$\lambda_e = \begin{cases} \lambda_0, 0 < q < \dfrac{(b+b(1-\theta)\theta+Rv_H)\Lambda - Rv_H^2}{(1-\theta)(b+Rv_H)} \\ \Lambda, \dfrac{(b+b(1-\theta)\theta+Rv_H)\Lambda - Rv_H^2}{(1-\theta)(b+Rv_H)} \leq q \leq \Lambda \end{cases} \tag{3.2}$$

$$\lambda_0 = \frac{Rv_H^2 + q(1-\theta)(b+Rv_H)}{b\theta^2 + b(1-\theta) + Rv_H}$$

Given a constant potential arrival rate Λ, when the tertiary hospital's referral quantity is small, more patients utilize the tertiary hospital's resources for subsequent recovery, leading to longer waiting times due to insufficient capacity. Thus, the equilibrium arrival rate λ_e increases with the referral quantity q. Once q exceeds a certain threshold, the tertiary hospital's capacity is sufficient to handle all incoming patients' initial treatment services, so all potential patients enter the system, and λ_e no longer changes, becoming equal to Λ.

3.2 MA revenue model without internet hospital introduction

Tightly integrated MA: The MA obtains revenue from services provided by both hospitals but bears the penalty cost and the community hospital's effort-related cost collectively. The MA determines the optimal referral quantity q and effort level e to maximize overall profit.

Total profit function:

$$\pi_T = (g_1 - C_{1H})\lambda_e + (g_2 - C_{2H})(\lambda_e - q) + (g_L - C_L) q - C_E(e)q - M(q,e) \tag{3.3}$$

Theorem 3.2: In a tightly integrated MA, there exist optimal q and e that maximize profit. The optimal effort level for the community hospital is $e_1 = 3\sqrt{\frac{mq}{2C_e}}$. The optimal referral quantity q depends on the potential arrival rate Λ :

$$q^C = \begin{cases} \Lambda,\ 0 < \Lambda \leq q_2 \\ q_2, q_2 < \Lambda \leq \frac{Rv_H^2+q_2(1-\theta)(b+Rv_H)}{b\theta^2+b(1-\theta)+Rv_H} \\ q_0, \frac{Rv_H^2+q_2(1-\theta)(b+Rv_H)}{b\theta^2+b(1-\theta)+Rv_H} < \Lambda \leq \frac{Rv_H^2+q_1(1-\theta)(b+Rv_H)}{b\theta^2+b(1-\theta)+Rv_H} \\ q_1, \Lambda > \frac{Rv_H^2+q_1(1-\theta)(b+Rv_H)}{b\theta^2+b(1-\theta)+Rv_H} \end{cases}$$

Loosely integrated MA: Hospitals make decisions separately. The tertiary hospital maximizes its profit to determine q, and the community hospital maximizes its profit to determine e, considering their respective shares of the penalty cost.

Tertiary Hospital Profit:

$$\pi_H = (g_1 - C_{1H})\lambda_e + (g_2 - C_{2H})(\lambda_e - q) - \alpha M(q,e) \tag{3.4}$$

Community Hospital Profit:

$$\pi_L = (g_L - C_L)q - C_E(e)q - (1-\alpha)M(q,e) \tag{3.5}$$

Theorem 3.3: In a loosely integrated MA, optimal q and e exist. The optimal effort level is $e_2 = \sqrt[3]{\frac{(1-\alpha)mq}{2C_e}}$. The optimal referral quantity q D depends on Λ :

$$q^D = \begin{cases} q_0, \Lambda \leq \dfrac{Rv_H^2 + q_3(1-\theta)(b+Rv_H)}{b\theta^2 + b(1-\theta) + Rv_H} \\ q_3, \Lambda > \dfrac{Rv_H^2 + q_3(1-\theta)(b+Rv_H)}{b\theta^2 + b(1-\theta) + Rv_H} \end{cases}$$

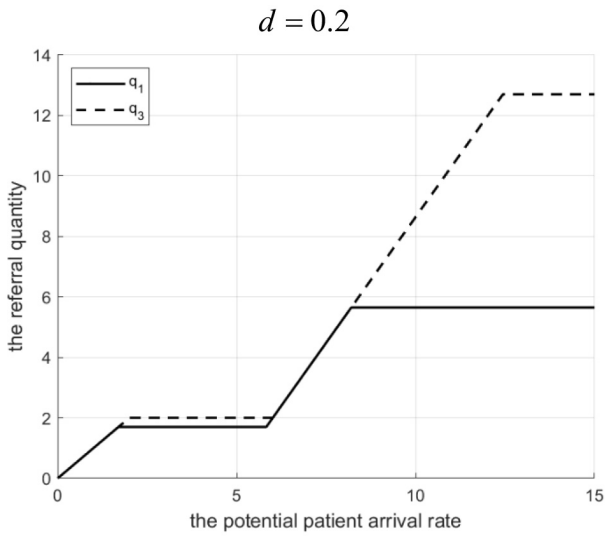


FIGURE 1
Referral quantity in a tightly integrated MA before and after the introduction of internet medical care ($d = 0.2$).

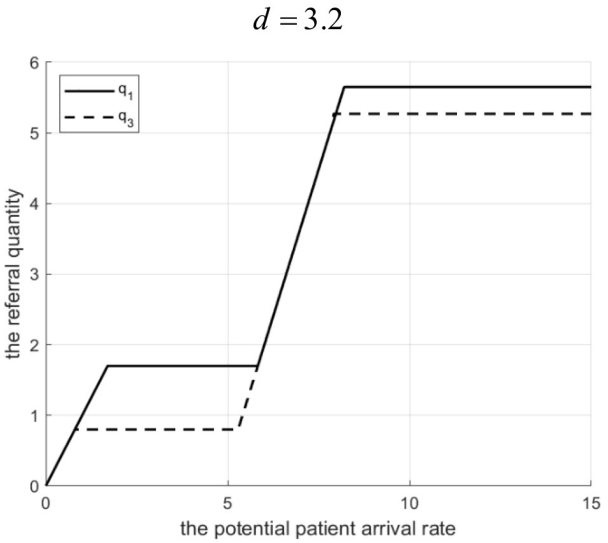


FIGURE 2
Referral quantity in a tightly integrated MA before and after the introduction of internet medical care ($d = 3.2$).

3.3 MA revenue model with internet hospital introduction

Tightly integrated MA: The MA earns revenue, facilitates referrals via the Internet hospital, and helps the community hospital improve its service level. The MA bears the penalty cost, effort-related cost, and Internet hospital cost. It determines optimal q, e, and γ.

Total Profit Function:

$$\pi_T = (g_1 - C_{1H})\lambda_e + (g_2 - C_{2H})(\lambda_e - q) + (g_L - C_L)q - C_E q - M - C_p \quad (3.6)$$

Theorem 3.4: In a tightly integrated MA with an Internet hospital, optimal q, e, and γ exist. The optimal effort level is $e_3 = \sqrt[3]{\frac{\gamma m q}{2C_e}}$. The optimal referral quantity q^C depends on Λ. The maximum profit:

$$q^C = \begin{cases} \Lambda,\ 0 < \Lambda \le q_6 \\ q_6, q_6 < \Lambda \le \frac{Rv_H^2 + q_6(1-\theta)(b+Rv_H)}{b\theta^2 + b(1-\theta) + Rv_H} \\ q_0, \frac{Rv_H^2 + q_6(1-\theta)(b+Rv_H)}{b\theta^2 + b(1-\theta) + Rv_H} < \Lambda \le \frac{Rv_H^2 + q_5(1-\theta)(b+Rv_H)}{b\theta^2 + b(1-\theta) + Rv_H} \\ q_5, \Lambda > \frac{Rv_H^2 + q_5(1-\theta)(b+Rv_H)}{b\theta^2 + b(1-\theta) + Rv_H} \end{cases}$$

Loosely integrated MA: Hospitals decide separately. The tertiary hospital determines q and γ. The community hospital determines e. The tertiary hospital shares β of the community hospital's revenue g_L and both share the penalty cost $\alpha M$and $(1 - \alpha)M$, respectively.

Tertiary Hospital Profit:

$$\pi_H = (g_1 - C_{1H})\lambda_e + (g_2 - C_{2H})(\lambda_e - q) + \beta g_L q - \alpha M(q, e) - C_p(\gamma) \quad (3.7)$$

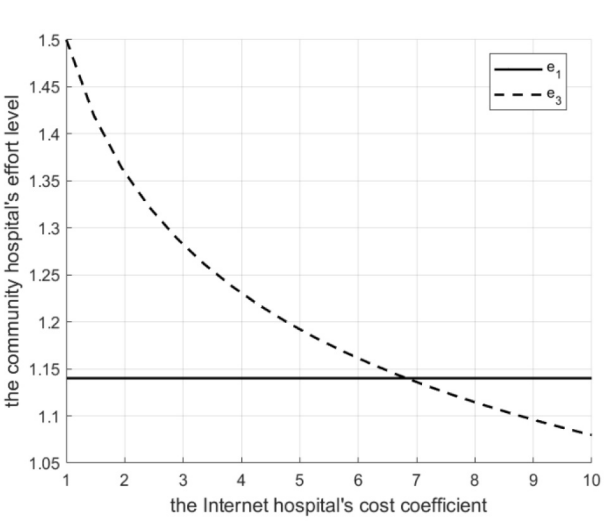


FIGURE 3
The Degree of effort to introduce a tightly integrated MA before and after the introduction of internet medical care.

Community Hospital Profit:

$$\pi_L = ((1-\beta)g_L - C_L)q - C_E(e) \quad q - (1-\alpha)M(q, e) \quad (3.8)$$

Theorem 3.5: In a loosely integrated MA with an Internet hospital, optimal q, e, and γ exist. The optimal effort level is $e_4 = \sqrt[3]{\frac{(1-\alpha)\gamma m q}{2C_e}}$. The optimal referral quantity q^D, depends on Λ and the revenue sharing factor β :

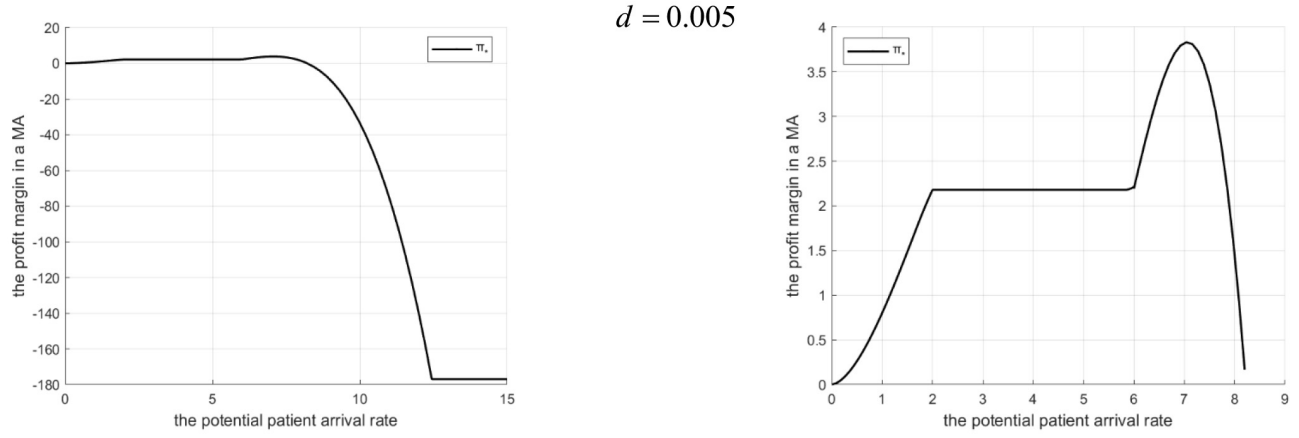


FIGURE 4
Profits of a tightly integrated MA before and after the introduction of internet medical care ($d = 0.005$).

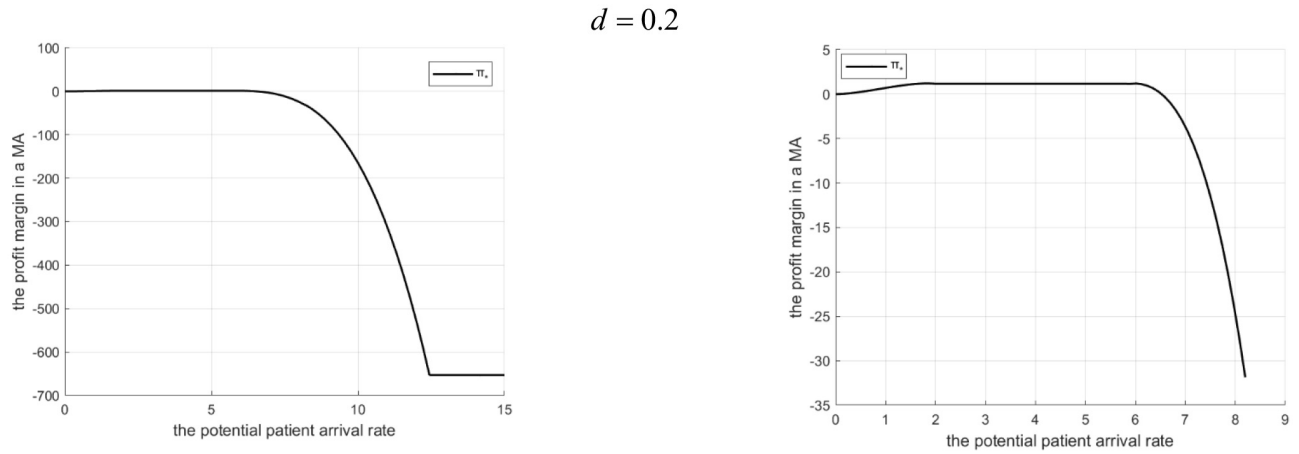


FIGURE 5
Profits of a tightly-integrated MA before and after the introduction of internet medical care ($d = 0.2$).

If $\beta \geq \frac{g_2 - C_{2H}}{g_L}$:

$$q^D = \begin{cases} \Lambda,\ 0 < \Lambda \leq q_8 \\ q_8, q_8 < \Lambda \leq \frac{Rv_H^2 + q_8(1-\theta)(b+Rv_H)}{b\theta^2 + b(1-\theta) + Rv_H} \\ q_0, \frac{Rv_H^2 + q_8(1-\theta)(b+Rv_H)}{b\theta^2 + b(1-\theta) + Rv_H} < \Lambda \leq \frac{Rv_H^2 + q_7(1-\theta)(b+Rv_H)}{b\theta^2 + b(1-\theta) + Rv_H} \\ q_7, \Lambda > \frac{Rv_H^2 + q_7(1-\theta)(b+Rv_H)}{b\theta^2 + b(1-\theta) + Rv_H} \end{cases}$$

If $0 < \beta < \frac{g_2 - C_{2H}}{g_L}$:

$$q^D = \begin{cases} q_0, \Lambda \leq \frac{Rv_H^2 + q_7(1-\theta)(b+Rv_H)}{b\theta^2 + b(1-\theta) + Rv_H} \\ q_7, \Lambda > \frac{Rv_H^2 + q_7(1-\theta)(b+Rv_H)}{b\theta^2 + b(1-\theta) + Rv_H} \end{cases}$$

4 Comparative analysis and numerical simulation

(Using MATLAB simulation with parameters: $g_1 = 8, C_{1H} = 6, g_2 = 6, C_{2H}, g_L = 5, C_L = 1, C_e = 1, m = 0.3, R = 10, b = 2, v_H = 5, \theta = 0.4.\alpha$=0.5 for loosely integrated cases).

4.1 Comparative analysis of optimal decisions in tightly integrated MA

Proposition 1: The referral quantity in a tightly integrated MA is influenced by the Internet hospital's cost coefficient d and the potential patient arrival rate λ.

(1) Referral quantity increases withΛ. When Λ is very small or very large (such that some potential patients do not enter), the Internet hospital cannot increase referrals.
(2) There exists a threshold d^*. If $0 < d < d^*$, introducing a hospital-owned Internet hospital leads to a referral quantity not lower than without it. If $d > d^*$, the referral quantity is higher without the Internet hospital.

Rationale and Simulation (Figure 1 $d = 0.2$, Figure 2 $d = 3.2$): When Λ is small, MA resources are ample, minimizing penalty cost dictates low referrals. When Λ is large but some don't enter, raising referrals increases penalty > benefit, so referrals aren't increased. As Λ grows in the mid-range, treatment benefits exceed penalty costs, encouraging higher referrals. The Internet hospital enhances community capacity, raising the referral threshold. Low-cost d means referral benefits cover Internet costs, encouraging higher service levels (γ) and thus higher referrals ($q_3 > q_1$ in Figure 1). High-cost d makes Internet operation costly, leading to lower γ, reduced community effort, and lower referrals to minimize penalties ($q_3 < q_1$ in Figure 2 where q_1 and q_3 denote the downward referral volumes before and after implementing Internet-based healthcare in tightly integrated MA, respectively).

Proposition 2: For a given referral quantity, the service effort of the community hospital in a tightly integrated MA is influenced by the Internet hospital's cost coefficient d. There exists d_1. If, effort is higher with the Internet hospital. If $0 < d \leq d_1$, effort is higher without it.

Rationale and Simulation (Figure 3 q=10): When d is low, the Internet hospital operates at a lower cost and provides a high service level (γ), thereby reducing the community hospital's unit effort-related cost. To maximize profit (and reduce penalty costs which decrease with effort), the MA chooses a higher effort level ($e_3 > e_1$). When d is high, the Internet hospital's cost is high, the MA reduces γ to save costs, which increases the community hospital's unit effort-related cost, leading to lower optimal effort ($e_3 < e_1$) (Figure 3 shows $e_3 > e_1$ when $d \leq 6.8$, where e_1 and e_3 represent the effort levels before and after implementing Internet-based healthcare in tightly integrated MA, respectively.).

4.2 Comparative profitability analysis in tightly integrated MA

Proposition 3: The profit margin in a tightly integrated MA (with vs. without Internet hospital) depends on Λ and d.

(1) There exists Λ_1. If $0 < \Lambda \leq \Lambda_1$, profit is higher with the Internet hospital. If $\Lambda > \Lambda_1$, profit is higher without it.
(2) Λ_1 decreases d as increases.

Rationale and Simulation (Figure 4 $d = 0.005$, Figure 5 $d = 0.2$): When Λ is low, introducing the Internet hospital increases referrals, boosting community hospital revenue. Scale effects cover Internet costs, and higher effort reduces penalties, increasing overall profit. When Λ is high, the increased referral threshold exceeds community capacity, leading to high penalty costs that damage MA profit, making the non-Internet scenario better. Λ_1 (the threshold Λ where profits equalize) decreases with increasing d because higher Internet costs reduce the profitability range for the Internet hospital scenario (smaller referral increase, lower effort, higher potential penalty).

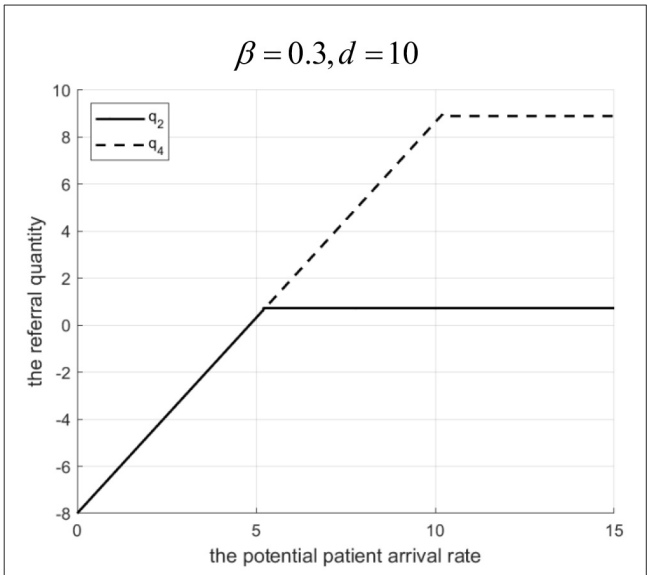


FIGURE 6
Referral quantity in a loosely integrated MA before and after the introduction of internet medical care ($\beta = 0.3$, $d = 10$).

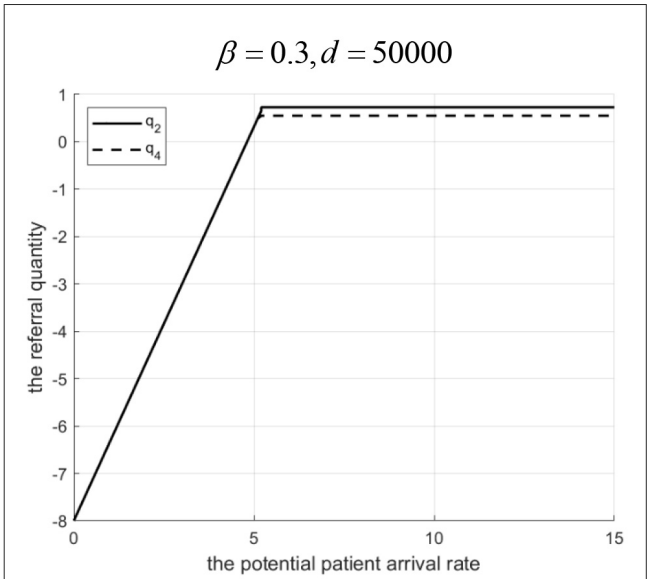


FIGURE 7
Referral quantity in a loosely integrated MA before and after the introduction of internet medical care ($\beta = 0.3$, $d = 50,000$).

4.3 Comparative analysis of optimal decisions in loosely-integrated MA

Proposition 4: Referral quantity in a loosely-integrated MA depends on d, revenue sharing ratio β, and Λ.

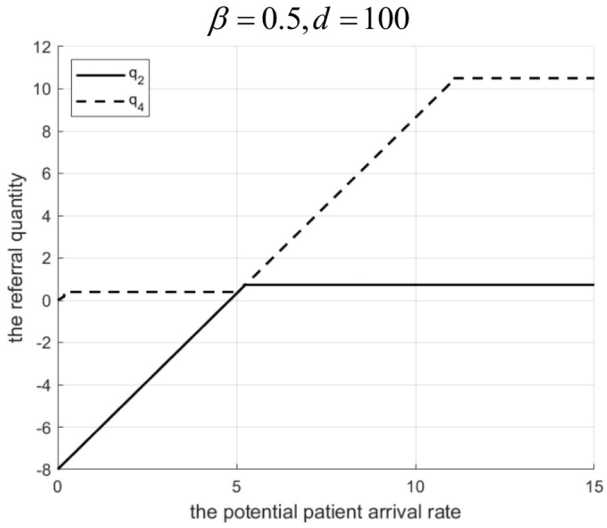


FIGURE 8
Referral quantity in a loosely integrated MA before and after the introduction of internet medical care ($\beta = 0.5, d = 100$).

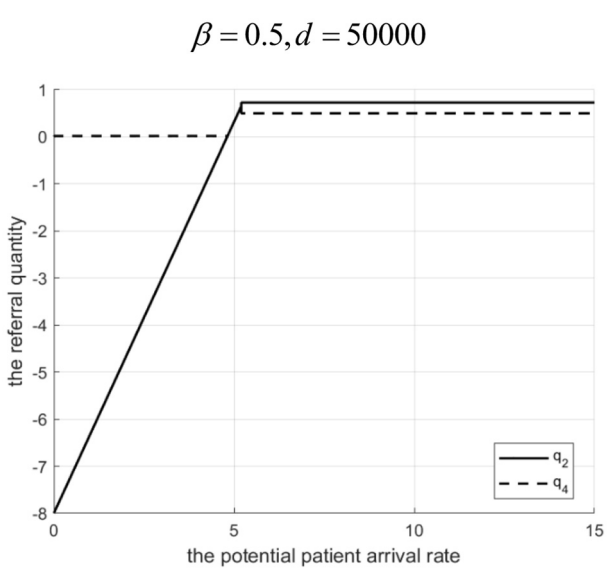


FIGURE 9
Referral quantity in a loosely integrated MA before and after the introduction of internet medical care ($\beta = 0.5, d = 50,000$).

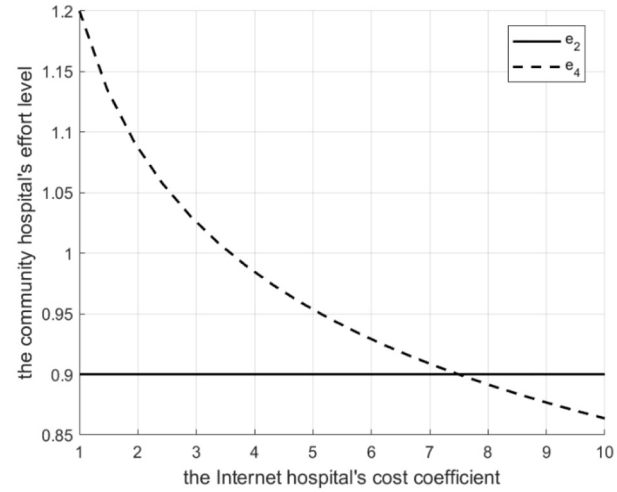


FIGURE 10
Degree of effort of loosely integrated MA before and after the introduction of internet medical care.

(1) If $0 < \beta < \frac{g_2 - C_{2H}}{g_L}$ (low sharing): For low Λ, Internet hospital cannot increase referrals. For high Λ, there exists d_1. If $0 < d < d_1$, referrals are higher with the Internet hospital. If $d \geq d_1$, referrals are higher without it.

(2) If $\beta \geq \frac{g_2 - C_{2H}}{g_L}$ (high sharing): For low Λ, Internet hospital can increase referrals. For high Λ, there exists d_2. If $0 < d < d_2$, referrals are higher with the Internet hospital. If $d \geq d_2$, referrals are higher without it.

Rationale and Simulation (Figure 6 β =0.3, d =10; Figure 7 β = 0.3, d = 50,000; Figure 8 β = 0.5, d = 100; Figure 9 β = 0.5, d = 50,000):

Low β, low Λ: Tertiary hospital lacks incentive to refer as it gets a little share of community revenue.

Low β, high Λ: Tertiary hospital refers more. If d is low, Internet costs are covered by increased tertiary revenue (from reduced penalty share αM& βg_L), supporting higher γ and referrals. If d is high, Internet cost > benefit, tertiary reduces γ and referrals.

High β, low Λ: Tertiary incentive exists ($\beta g_L > g_2$). Even with low Λ, some referrals occur. Internet hospital (even if costly) can be used moderately to improve community services without high cost, facilitating referrals.

High β, high Λ: Tertiary wants high referrals. If d is low, Internet is cost-effective. If d is high, high γ is too costly, so tertiary reduces γ and referrals to balance costs. Let q_2 and q_4 denote the downward referral volumes before and after implementing Internet-based healthcare in loosely-integrated MA, respectively.

Proposition 5: For a given referral quantity, community hospital effort in a loosely integrated MA depends on d. There exists d_1. If d_1, effort is higher with the Internet hospital. If $d > d_1$, effort is higher without it.

Rationale and Simulation (Figure 10 $q = 10$): Similar logic to Proposition 2, but driven by the tertiary hospital's decision on γ (to maximize its own profit by influencing penalty cost γM) and the community hospital's response (balancing its revenue $(1 - \beta)g_L$ against effort-related cost $\frac{C_e e^2}{\gamma}$ and penalty $((1 - \alpha)M)$. Low d > high γ chosen by tertiary > lower unit effort-related cost for community > higher e chosen by community. High d > low > higher unit effort-related cost> lower e. e_2 and e_4 represent the effort levels before and after implementing Internet-based healthcare in loosely integrated medical MA, respectively.

4.4 Comparative profitability analysis in loosely integrated MA

Proposition 6: The tertiary hospital's profit margin depends on Λ, d, and β.

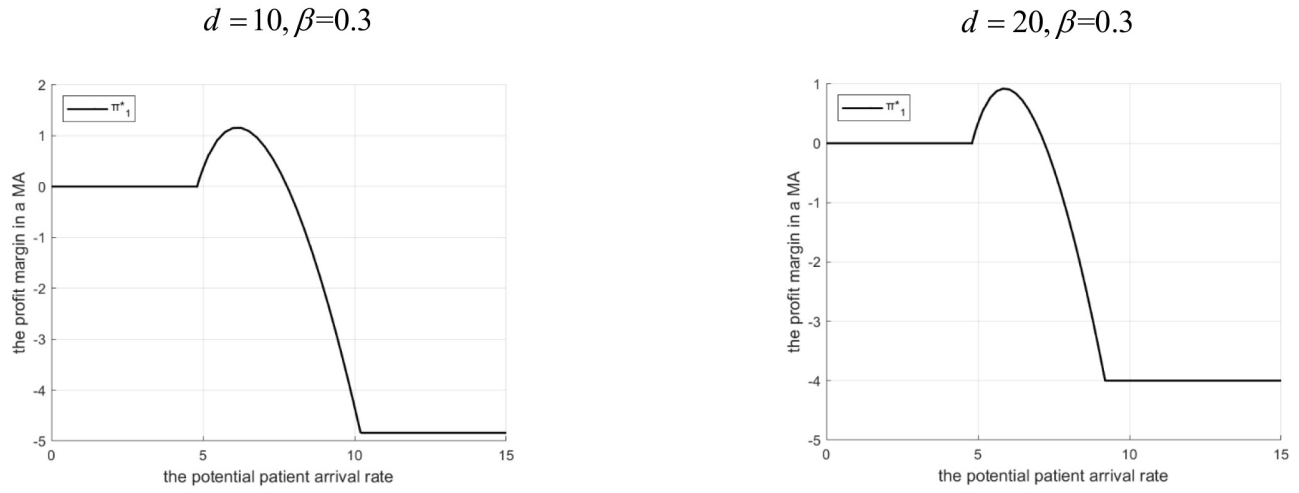


FIGURE 11
Profits of tertiary A-level hospitals before and after the introduction of internet medical care (β = 0.3).

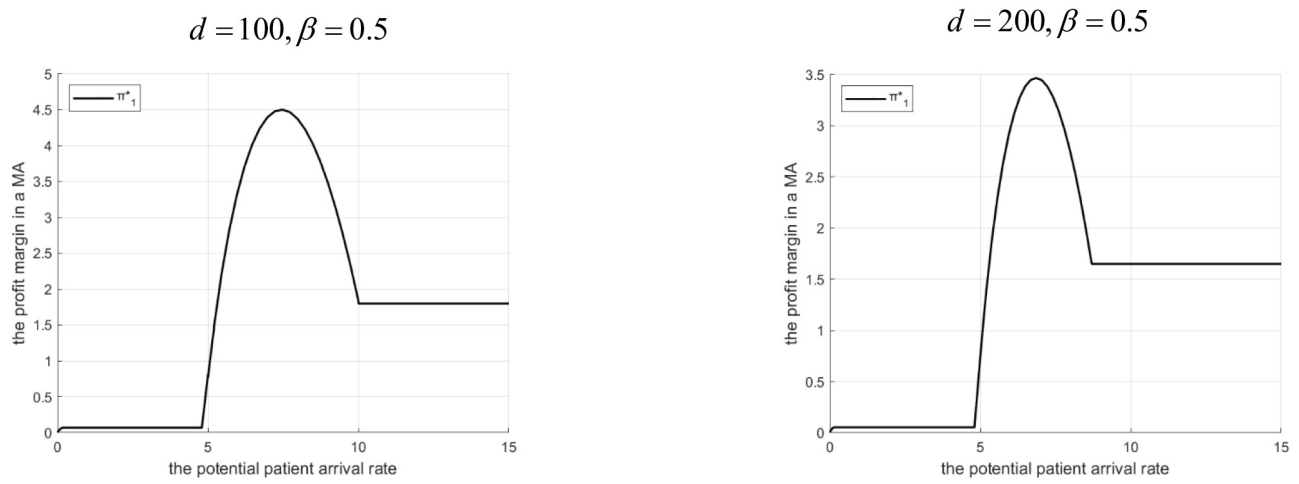


FIGURE 12
Profits of tertiary A-level hospitals before and after the introduction of internet medical care (β = 0.5).

(1) If $0 < \beta < \frac{g_2 - C_{2H}}{g_L}$: There exists Λ_2. If $0 < \Lambda \leq \Lambda_2$, profit is higher with the Internet hospital. If $\Lambda > \Lambda_2$, profit is higher without it. Λ_2 decreases as d increases.

(2) If $\beta \geq \frac{g_2 - C_{2H}}{g_L}$: Profit is always higher with the Internet hospital. The profit advantage decreases as d increases.

Rationale and Simulation (Figure 11 β =0.3, d=10, d =20; Figure 12 β =0.5, d =100, d=200):

Low β, low Λ : Tertiary lacks referral incentive, Internet offers little benefit.

Low β, mid Λ : Internet helps increase referrals, brings revenue (βg_L), reduces penalty share (αM)> profit increases.

Low β, high Λ : High referrals> high penalty cost share > profit erodes. Threshold Λ_2 exists. Higher d> lower γ, smaller referral increase, less benefit > Λ_2 decreases.

High β : The tertiary A-grade hospital always benefits from referrals. Internet facilitates this, adds revenue (βg_L), and reduces penalty share. Even when d is high, it merely reduces the advantage rather than eliminating it—provided that the Internet hospital's cost remains lower than the benefit gained from increased or more efficient referrals.

Proposition 7: The community hospital's profit margin depends on Λ, d, and β.

(1) If $0 < \beta < \frac{g_2 - C_{2H}}{g_L}$: There exist Λ_3 and Λ_4 ($\Lambda_3 < \Lambda_4$). If $0 < \Lambda \leq \Lambda_3$ or $\Lambda \geq \Lambda_4$, profit is not higher with the Internet hospital. If $\Lambda_3 < \Lambda\Lambda_4$, profit is higher with it. The interval$[\Lambda_3, \Lambda_4]$ shrinks as d increases.

(2) If $\beta \geq \frac{g_2 - C_{2H}}{g_L}$: There exists Λ_5. If $0 < \Lambda \leq \Lambda_5$, profit is higher with the Internet hospital. If $\Lambda \geq \Lambda_5$, profit is higher without it. The profit advantage (when with the Internet) increases with d.

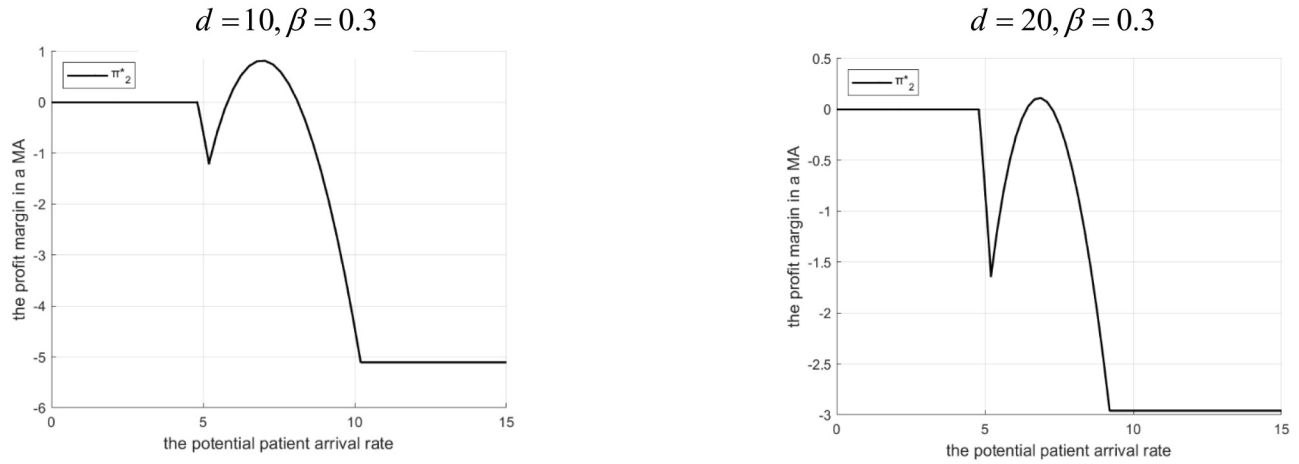


FIGURE 13
Profits of community hospitals before and after the introduction of internet medical care (β = 0.3).

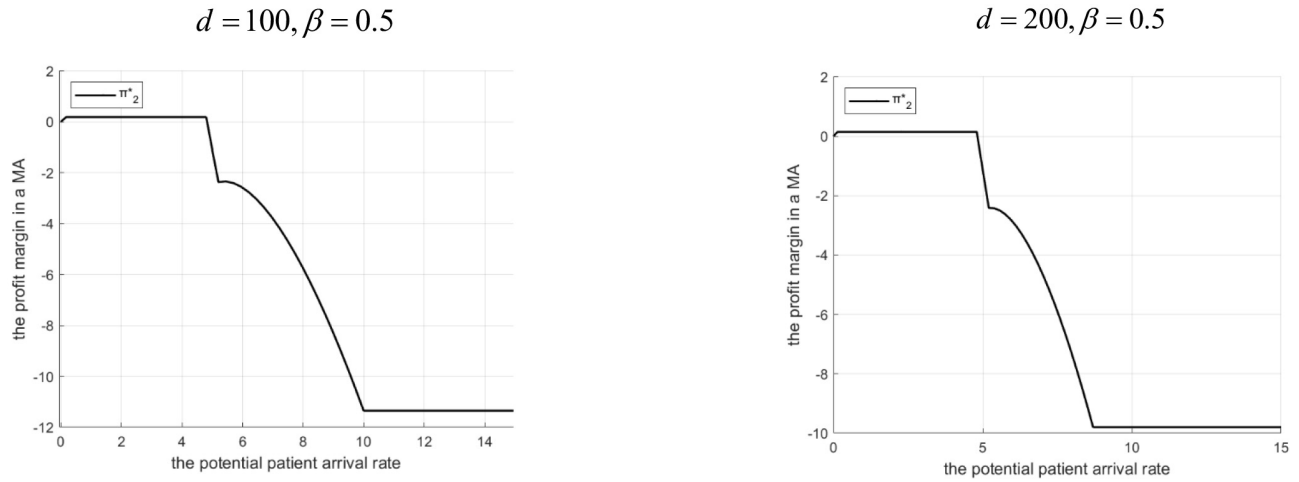


FIGURE 14
Profits of community hospitals before and after the introduction of internet medical care (β = 0.5).

Rationale & Simulation (Figure 13 β =0.3, d=10, d=20; Figure 14 β =0.5, d =100, d=200):
Low β: Community gets small share $(1-\beta)g_L$.
Low Λ: Tertiary doesn't refer much, Internet changes little for community profit.
Mid Λ ($\Lambda_3 < \Lambda \leq \Lambda_4$): Tertiary refers more with Internet. Community gains revenue $((1-\beta)g_L)$ + benefits from higher γ (lower effort-related cost $\frac{C_e e^2}{\gamma}$) potentially offsetting penalty share $(1-\alpha)M>$ profit increases.
High Λ ($> \Lambda_4$): High referrals exceed capacity, high penalty share $(1-\alpha)M >$ profit decreases. Higher $d >$ smaller referral increase, less benefit, higher effort-related cost > interval $[\Lambda_3, \Lambda_4]$shrinks.
High β: Community gets large share $(1-\beta)g_L$.
Low Λ ($\leq \Lambda_5$): Tertiary has an incentive to refer (due to its own high β). The Internet facilitates this. The community hospital benefits from increased revenue and reduced unit effort-related costs, resulting in higher overall profit.
High Λ ($> \Lambda_5$): Tertiary refers heavily. Internet introduction leads to even higher referrals. However, the resulting rise in effort and penalty costs for the community hospital outweighs the additional revenue, leading to a decline in overall profit. Counterintuitively, profit advantage with Internet increases with d within the $\Lambda \leq$ range because higher d forces tertiary to use lower γ, reducing referrals slightly, which lessens the burden (effort/penalty) on the community hospital compared to a scenario with very low d and extremely high referrals.

5 Conclusion and outlook

This study addresses the suboptimal implementation of patient downward referrals within MAs, often driven by conflicting

interests between tertiary A-grade hospitals and community hospitals as well as the latter's limited service capacity. It highlights the potential of Internet hospitals to promote referrals and enhance community hospital capabilities. By constructing queuing game models for tightly integrated and loosely integrated MAs, both before and after the introduction of hospital-owned Internet hospitals, this research investigates the conditions under which such supplementation is effectively promotes patient referrals across different MA types.

Key findings include:

Tightly integrated MAs: Referral quantity and effort levels increase with potential patient arrival rates (Λ). When the Internet hospital cost coefficient (d) is low, its introduction leads to higher (or equal) referral quantity and effort compared to scenarios without it; the opposite holds when $d$is high. Profitability is higher with the Internet hospital at lowerΛ, but higher without it at higher Λ, with the threshold arrival rate decreasing as d increases.

Loosely integrated MAs: Effort level changes follow a similar pattern to tightly integrated MAs based on d. Referral quantity and tertiary hospital profitability are highly sensitive to the revenue sharing ratio (β). Low β: Internet hospitals increase referrals only at high Λ and low d. Tertiary profit is higher with Internet hospitals only below a certain Λ threshold (Λ_2), which decreases with d. High β : Internet hospitals can increase referrals even at low Λ. Tertiary profit is consistently higher with Internet hospitals, though the advantage diminishes with increasing d. Community hospital profit (Low β): Profitability is higher with Internet hospitals only within a specific intermediate range of Λ ($[\Lambda_3, \Lambda_4]$), which shrinks with increasing d. Community hospital profit (High β): Profitability is higher with Internet hospitals only below a certain Λ threshold (Λ_5). The profit advantage increases with d within this range.

Based on these findings, several management implications emerge:

Strategic Introduction: Tightly integrated and loosely integrated MAs are advised to adopt hospital-owned Internet hospitals primarily under conditions of high potential patient inflow and low operational costs associated with Internet hospital implementation. Capacity Consideration: When implementing patient referrals, it is essential to account for the service capacity of community hospitals to avoid excessive referrals that may incur substantial penalty costs and compromise service quality. Revenue Sharing Design: Loosely integrated MAs should carefully calibrate the Internet healthcare revenue sharing ratio (β) to balance incentives for tertiary hospital referrals while safeguarding the financial sustainability of community hospitals. Policy Support: Governments may consider introducing supportive policies—such as providing technological subsidies to tertiary hospitals for establishing Internet hospitals—to encourage the adoption of digital health solutions and advance the implementation of the hierarchical diagnosis and treatment system.

This study assumes that the payment strategies and standards of the Medical Insurance Bureau remain static over time. Future research could incorporate the Medical Insurance Bureau into the game model to analyze the interplay among the bureau, MAs, and Internet hospitals, exploring how MA referral efficiency and Internet healthcare strategy choices might change under dynamic payment policies. Furthermore, this study focuses exclusively on hospital-owned Internet hospitals; Future work could broaden the scope to include third-party Internet hospitals by developing models that capture the interactions among MAs, Internet hospitals, and patients, thereby identifying the optimal choice of Internet hospital provider based on referral efficiency. Additionally, the current analysis assumes that tertiary hospitals maintain sole authority over downward referrals. Subsequent research could explore how patient transfer preferences affect Internet-based healthcare strategy decisions.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

XZ: Writing – original draft, Writing – review & editing. YM: Writing – original draft, Writing – review & editing. JL: Writing – original draft, Writing – review & editing.

Funding

The author(s) declare that financial support was received for the research and/or publication of this article. This work was supported by the MOE Humanities and Social Sciences Research Planning Fund (Grant No. 24YJA630128).

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The author(s) declare that Gen AI was used in the creation of this manuscript. Optimizing English writing with generative AI.

Any alternative text (alt text) provided alongside figures in this article has been generated by Frontiers with the support of artificial intelligence and reasonable efforts have been made to ensure accuracy, including review by the authors wherever possible. If you identify any issues, please contact us.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

References

1. Davis CB, Lorentzen AK, Patel H, Cheung D, Wright A, Lemery J, et al. The intersection of telemedicine and wilderness care: past, present, and future. *Wilderness Environ Med.* (2022) 33:224–31. doi: 10.1016/j.wem.2022.02.012

2. Ahmad RW, Salah K, Jayaraman R, Yaqoob I, Ellahham S, Omar M. The role of blockchain technology in telehealth and telemedicine. *Int J Med Inform.* (2021) 148:104399. doi: 10.1016/j.ijmedinf.2021.104399

3. Singh M, Tandon U, Mittal A. Modeling users' and practitioners' intention for continued usage of the Internet of Medical Devices (IoMD): an empirical investigation. *Inf Discov Deliv.* (2023) 51:306–21. doi: 10.1108/IDD-02-2022-0016

4. Wang J, Yao T, Wang Y. The research on information quality evaluation of internet medical platform based on text content analysis. *J Med Inform.* (2023) 44:7–12+29. doi: 10.3969/j.issn.1673-6036.2023.11.002

5. Marelli L, Lievevrouw E, Hoyweghen IV. Fit for purpose? The GDPR and the governance of European digital health. *Policy Studes.* (2020) 41:447–67. doi: 10.1080/01442872.2020.1724929

6. Xanthidou OK, Xanthidis D, Manolas C, Wang H-I. Security and privacy consideration for the deployment of electronic health records: a qualitative study covering Greece and Oman. *Inform Security J Glob Perspect.* (2023) 32:266–82. doi: 10.1080/19393555.2021.2003914

7. Bernard K, Clovis F. Telemedicine and mobile health with integrative medicine in developing countries. *Health Policy Technol.* (2014) 3:264–71. doi: 10.1016/j.hlpt.2014.08.008

8. Baxter S, Johnson M, Chambers D, Sutton A, Goyder E, Booth A. Understanding new models of integrated care in developed countries: a systematic review. *Health Serv Deliv Res.* (2018) 6:1–132. doi: 10.3310/hsdr06290

9. Li WH, Chen SH. Practice and exploration of the construction model of close medical alliance. *Chin Hosp Manag.* (2025) 45:94–6.

10. He QH, Zhu FM, Wang Z. Medical resource sharing and improvement of doctor-patient relationship: Investigation based on the construction of urban medical alliance. *Soc Policy Res.* (2024) 4:105–18+135–136. doi: 10.19506/j.cnki.cn10-1428/d.2024.04.007

11. Xu L, Gong KB, Chen Y, Qu YY, Liu YX, Meng XC, et al. Practice and exploration of "Internet+" children's specialized medical alliance in Shandong Province. *Chin Hosp Manag.* (2022) 42:88–90.

12. Wang SF, Chen SH, Zhou QR, and Li CH. Investigation and research on county "Internet+ medical alliance" using Colaizzi analysis method. *Chin Hosp.* (2024) 28:44–6. doi: 10.19660/j.issn.1671-0592.2024.8.11

13. Greenfield G, Foley K, Majeed A. Rethinking primary care's gatekeeper role. *BMJ.* (2016) 354:i4803. doi: 10.1136/bmj.i4803

14. Zhao Z, Xie X, Wu Q. Medical staff evaluation on 'the effect of medical alliance policy on hierarchical diagnosis and treatment'. *Front Public Health.* (2024) 12:1366100. doi: 10.3389/fpubh.2024.1366100

15. Liu X Y, Cai X Q, Zhao R Q, Lan Y F. Mutual referral policy for coordinating health care systems of different scales. *Int J Prod Res.* (2015) 53:7411–33. doi: 10.1080/00207543.2015.1082039

16. Wang J, Li Z, Shi J, Chang A. Hospital referral and capacity strategies in the two-tier healthcare systems. *Omega.* (2021) 100:102229. doi: 10.1016/j.omega.2020.102229

17. Ma Q, Xu J, Shi Y, Liu GB, Wang Y, Zhai XW, et al. Difficulties and countermeasures of hierarchical diagnosis and treatment under the background of medical consortium. *Med Philos.* (2024) 45:22–4. doi: 10.12014/j.issn.1002-0772.2024.12.05

18. Heng J, Xu Z. New development of hierarchical diagnosis and treatment model under the background of "Internet+". *Mod Hosp Manage.* (2019) 17:5–8+12. doi: 10.3969/j.issn.1672-4232.2019.03.002

19. Wang Q, Wang Y, Yin D. Simulation and optimization research on two-way referral service for surgical patients in medical consortium. *Ind Eng Manage.* (2022) 27:1–7. doi: 10.19495/j.cnki.1007-5429.2022.04.001

20. Yao X, Wen Z, Lu Y. Evolutionary game analysis of referral of rehabilitation patients in tertiary hospitals under hierarchical diagnosis and treatment. *Chin J Med Manag Sci.* (2023) 13:21–6. doi: 10.3969/j.issn.2095-7432.2023.01.004

21. Tyagi M, Tyagi P K, Singh S, Sathpathy S, Kant S, Gupta SK, et al. Impact of application of queuing theory on operational efficiency of patient registration. *Med J Armed Forces India.* (2023) 79:300–8. doi: 10.1016/j.mjafi.2021.06.028

22. Ala A, Yazdani M, Ahmadi M, Poorianasab A, Attari, MYN. An efficient healthcare chain design for resolving the patient scheduling problem: queuing theory and MILP-ASA optimization approach. *Ann Operat Res.* (2023) 328:3–33. doi: 10.1007/s10479-023-05287-5

23. Wang WJ, Wang JD. Overmedicalization and referral system: a game model under queuing theory. *J Manag Sci China.* (2019) 22:63–76. doi: 10.3969/j.issn.1007-9807.2019.02.005

24. Yu TJ. *Research on Subsidy Strategies to Incentivize the Sinking of High-Quality Medical Resources Under Hierarchical Diagnosis and Treatment*. Southeast University (2023).

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 19 September 2025
DOI 10.3389/fpubh.2025.1631872

Check for updates

OPEN ACCESS

EDITED BY
Jing Yuan,
Fudan University, China

REVIEWED BY
Yuehui Zhang,
Shanghai Jiao Tong University, China
Zhongcheng An,
Zhejiang Chinese Medical University, China

*CORRESPONDENCE
Zhi-wei Wang
✉ wzw9902@126.com

RECEIVED 27 May 2025
ACCEPTED 04 September 2025
PUBLISHED 19 September 2025

CITATION
Chen M-e, Wang Y-h, Yu J, Xia S-j, Zhang X-x, Wang Y, Yuan Y-s, Jia X, Sun H-n, Wu G-p, Wang J-y, Cong T-z, Kong F-x, Hou H-j, Yang J-y and Wang Z-w (2025) Unpacking the cost implications of diagnosis-related groups reform for lumbar disc herniation patients in Chinese medicine: a closer look at evidence from China.
Front. Public Health 13:1631872.
doi: 10.3389/fpubh.2025.1631872

COPYRIGHT
© 2025 Chen, Wang, Yu, Xia, Zhang, Wang, Yuan, Jia, Sun, Wu, Wang, Cong, Kong, Hou, Yang and Wang. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

Unpacking the cost implications of diagnosis-related groups reform for lumbar disc herniation patients in Chinese medicine: a closer look at evidence from China

Meng-en Chen[1,2], Yu-han Wang[2], Jing Yu[2], Shi-ji Xia[2], Xiao-xi Zhang[1,2,3], Yan Wang[1,2], You-shu Yuan[1,2], Xuan Jia[2], He-nong Sun[2], Guo-ping Wu[2], Jia-yi Wang[4], Tian-zhen Cong[4], Fan-xin Kong[5], Hao-jia Hou[4], Jing-yu Yang[4,6] and Zhi-wei Wang[2,7]*

[1]School of Traditional Chinese Medicine, Beijing University of Chinese Medicine, Beijing, China, [2]School of Management, Beijing University of Chinese Medicine, Beijing, China, [3]Guang'anmen Hospital, China Academy of Chinese Medicine Sciences, Beijing, China, [4]School of Health Management, Gansu University of Chinese Medicine, Lanzhou, China, [5]Gansu Health and Population Development Research Center, Gansu Provincial Health and Wellness Commission, Lanzhou, China, [6]School of Public Health, Lanzhou University, Lanzhou, China, [7]National Institute of Chinese Medicine Development and Strategy, Beijing University of Chinese Medicine, Beijing, China

Objectives: Lumbar disc herniation (LDH) presents a significant economic burden globally, worsening in China due to an aging population. Traditional Chinese Medicine (TCM) offers effective treatment options for LDH, making its integration with Diagnosis-Related Groups (DRG) payment reform crucial for reducing medical costs and enhancing healthcare quality.

Methods: We analyzed data from hospitalized patients at Qingyang City Hospital of Chinese Medicine, Gansu Province, from 2017 to 2022. Univariate analysis was conducted to examine changes in patient demographics before and after the DRG reform. A single group interrupted-time series analysis (ITSA) model was used to compare key indicators of medical costs and length of stay pre- and post-reform.

Results: A total of 2,857 LDH patients were included in the study. Pre-DRG reform, 1,294 patients were recorded, with males comprising 46.06% and a mean age (SD) of 58.29 (14.22) years. Post-DRG reform, 1,563 patients were observed, with males accounting for 40.88% and a mean age (SD) of 60.64 (14.25) years. No significant differences were found in nationality, marital status, use of Chinese medicine diagnostic and therapeutic equipment, use of Chinese medicine diagnostic and treatment techniques or diagnosis and treatment based on Chinese medicine evidence ($p > 0.05$). However, significant differences were noted in sex, age, visit times, admission pathways, admission disease status, complications and comorbidities, and surgeries and operations ($p < 0.05$). Healthcare-related costs and length of stay are associated with sex, age,visit times, and other factors, showing a positive correlation among different costs and length of stay ($p < 0.05$). Post-reform, average monthly hospitalization cost decreased by CNY 36.78 ($\beta_1 + \beta_3 = -36.78, p < 0.05$), Chinese medicine cost fell by CNY 8.87 ($\beta_1 + \beta_3 = -8.87, p < 0.05$), and Western medicine cost dropped

by CNY 31.68 ($\beta_1 + \beta_3 = -31.68$, $p < 0.05$). While the rising trend in diagnosis cost was curtailed, both medical services cost and TCM treatment cost increased, with the length of stay remaining stable.

Conclusion: The DRG reform is associated with lower hospitalization cost and reduced costs for both Chinese medicine and Western medicine. However, its impact on overall medical services cost, diagnosis cost, TCM treatment cost, and length of stay is limited. Future DRG reform should leverage the distinctive advantages of TCM, enhance the payment system, improve treatment outcomes, and further reduce healthcare costs while shortening hospitalization times.

KEYWORDS

LDH, DRG, TCM, hospitalization cost, Chinese medicine hospitals

1 Introduction

Low back pain is one of modern society's most common orthopedic conditions (1). Currently, over 600 million people suffer from low back pain worldwide, and this number is projected to exceed 800 million by 2050 (2–4). Low back pain attributable solely to occupational ergonomic factors contributed to global economic losses of US$216.1 billion. Recent Chinese healthcare statistics revealed an average hospitalization cost of ¥11,085.9 (US$1,604) per low back pain episode. Both China and the global community face substantial economic burdens from low back pain, with China experiencing particularly accelerated growth in this burden due to its rapidly aging population (5, 6). Low back pain ranks among the top causes of disability globally, with long recovery times that impose a significant economic burden on patients and their families. LDH has emerged as a primary contributor to low back pain, leg pain, and mobility impairments (7, 8), with its incidence climbing each year due to an aging population, evolving work patterns, lifestyle shifts, and increasingly sedentary behavior (9). Research from countries such as the United States (10, 11), the United Kingdom (12), Brazil (13), New Zealand (14), and Spain underscores the substantial healthcare burden posed by LDH (15, 16). Given China's large population and accelerating aging process, healthcare costs associated with LDH are expected to continue rising soon.

TCM demonstrates unique advantages in treating LDH. It utilizes various modalities, including acupuncture, tuina (Chinese massage), herbal medicine, and moxibustion. By adopting a holistic approach and differential diagnosis, TCM effectively alleviates pain and enhances the body's self-repair capabilities (17, 18). Furthermore, exercises such as Tai Chi and Wuqinxi have demonstrated significant effectiveness in preventing low back pain, as highlighted in several studies (19, 20). In contrast, conventional treatments like medication and surgery often carry numerous complications and side effects (21–23). TCM's conservative, non-surgical methods typically result in fewer complications and better recovery outcomes (24–27). Reforming the DRG payment system in Chinese medicine hospitals to harness TCM strengths can significantly reduce hospitalization cost and length of stay for LDH patients, making this an important practical consideration.

DRG introduced by Fetter et al. in the 1980s, classify cases based on similarities in clinical processes and resource consumption (28). DRG has been adopted by various countries (29–33) for its benefits in hospital management and healthcare costs, achieving notable results (30, 34–36). Through decades of practice-oriented research and development, China has established several regional pilot DRG systems, including BJ-DRG, CN-DRG, CR-DRG, and C-DRG. These initiatives aim to address China's rapidly growing healthcare expenditures while positively impacting the quality of medical services. On June 18, 2020, the China National Healthcare Security Administration officially promulgated the "China Healthcare Security Diagnosis Related Groups (CHS-DRG) Fine Classification Scheme (Version 1.0)," initiating nationwide pilot implementation and subsequent progressive rollout. The CHS-DRG framework adopts China's national health insurance versions of ICD-10 (comprising 2,048 diagnostic categories, 10,172 subcategories, and 33,324 specific entries) and ICD-9-CM-3 (including 890 surgical procedure subcategories, 3,666 detailed items, and 12,995 entries). Following the grouping principles of "clinical process similarity" and "resource consumption similarity," the system established 376 Adjacent Diagnosis-Related Groups (ADRGs), consisting of 167 surgical procedure groups, 22 non-operating room procedure groups, and 187 medical diagnosis groups, comprehensively covering all acute and severe short-term hospitalization cases (37, 38). While traditional Chinese medicine hospitals are required to implement the unified CHS-DRG standards alongside other medical institutions, a gradual transition period is permitted. For certain TCM-dominant disease categories with demonstrated treatment efficacy and stable cost structures, specially designated reimbursement standards may be alternatively applied. As a vital part of healthcare in China, the reform of DRG payment systems in Chinese medicine hospitals is important, particularly for LDH, a condition where TCM shows distinct advantages.

This study focuses on LDH patients at Qingyang City Hospital of Chinese Medicine, Gansu Province, examining the impact of DRG payment reform on healthcare-related costs and length of stay. The findings aim to provide insights for Chinese health policymakers to advance DRG reforms, leveraging TCM's strengths to alleviate the economic burden of diseases like LDH in China.

2 Materials and methods

2.1 Data sources

Data were sourced from the Gansu Provincial Health and Health Commission, covering case records from January 2017 to June 2022 for Qingyang City Hospital of Chinese Medicine. Inclusion criteria included TCM diagnosis code International Classification of Disease

(ICD)-10 M51.202 and TCM coding BNS150 (1995 version) or A03.06.04.06.01 (2021 version). Exclusion criteria involved length of stay less than 1 day or greater than 90 days, zero hospitalization cost, and logically inconsistent visit information, resulting in a final dataset of 2,857 valid cases.

The data were regularly validated and cleaned by qualified personnel, ensuring reliable quality for analysis. The dataset encompasses patient demographics, including sex, age, and marital status, alongside medical information including visit times, surgeries and operations, complications and comorbidities, medical costs, and length of stay.

To evaluate the impact of DRG reform on medical costs and length of stay for LDH patients in Chinese medicine hospitals, our study employed a quasi-experimental model for data analysis. As one of the pioneering tertiary Chinese medicine hospitals in Northwest China to implement DRG payment reform, this research is instrumental in advancing DRG reimbursement systems in the TCM sector.

2.2 Statistical analysis

To address healthcare economic costs, we used 2016 as the base year and adjusted relevant costs based on the Consumer Price Index (CPI) for healthcare in Gansu Province from 2017 to 2022, minimizing potential biases in the study. It is worth highlighting that Qingyang City in Gansu Province, began trial implementation of the DRG reimbursement system in October 1, 2019. Accordingly, the period from January 1, 2017 to September 30, 2019 is designated as the pre-reform phase, during which the medical insurance payment was implemented under the fee-for-service (FFS) model. In contrast, the period from October 1, 2019 to June 30, 2022 is defined as the post-reform phase, with the implementation of the DRG-based medical insurance payment method.

Next, we compared the basic characteristics of patient visits before and after the DRG reform. For normally distributed numerical variables, paired sample *t*-tests were used, reporting data as means and standard deviations. For non-normally distributed numerical variables, we applied the Wilcoxon rank-sum test, expressing results in median and quartiles. Categorical variables were analyzed using chi-square tests, with frequencies and percentages reported. Moreover, multiple linear regression and Spearman correlation analyses were performed to investigate determinants of hospitalization expenditures and length of stay, as well as inter-variable relationships.

Finally, we employed an interrupted time-series analysis (ITSA) model - a quasi-experimental method specifically designed to assess causal effects of interventions (e.g., policy changes, clinical practice implementations) on longitudinal data. This approach compares pre- versus post-intervention trends while controlling for underlying temporal patterns, thereby providing robust effect estimation (39–41). We applied ITSA to evaluate key healthcare cost indicators for LDH patients in Chinese medicine hospitals. The analysis included hospitalization cost, medical service cost, diagnostic cost, TCM treatment cost, Chinese medicine cost, Western medicine cost, and length of stay. This methodology facilitated a comprehensive investigation of the changes in these indicators before and after the DRG reform, with the model equation expressed as follows:

$$Y_t = \beta_0 + \beta_1 T_t + \beta_2 X_t + \beta_3 X_t T_t + \varepsilon_t$$

In this equation, Y_t is the dependent variable (the primary outcome), β_0 is the intercept, β_1 reflects the pre-reform trend, β_2 indicates the level change at the reform, and β_3 represents the difference in slopes between the post-reform and pre-reform periods, with the post-reform slope being the sum of β_1 and β_3. T_t denotes the time series spanning January 2017 to June 2022, with T ranging from 1 to 66. Interaction terms include X_tT_t, ZT_t, ZX_t, and ZX_tT_t, while ε_t denotes random error. To address the skewed distributions of healthcare costs and length of stay, we selected the median values for each month as the data for the interrupted time series analysis, ensuring the rigor of the analysis. A schematic of the model is shown in Figure 1.

We used the Cumby-Huizinga tests to assess the autocorrelation of the dependent variable and adjusted calculations using the 'lag (#)' command along with the Newey-West method (39, 40, 42). All statistical analyses were conducted using Excel 2019, SPSS 26.0, and Stata 15.0, with a significance level set at $\alpha = 0.05$.

3 Results

3.1 General information of LDH hospitalized patients in Qingyang City Hospital of Chinese medicine in pre- and post-DRG reform

We included a total of 2,857 LDH patients in our analysis. Before the implementation of the DRG reform, there were 1,294 cases, with 46.06% of the patients being male and an average age (SD) of 58.29 (14.22) years. Following the DRG reform, the sample comprised 1,563 cases, with a male proportion of 40.88% and an average age (SD) of 60.64 (14.25) years. Further demographic details are provided in Table 1.

As shown in Table 1 and Figure 2, there were no statistical differences in nationality, marital status, use of Chinese medicine diagnostic and treatment techniques, use of Chinese medicine diagnostic and treatment techniques, diagnosis and treatment based on Chinese medicine evidence, and hospitalization cost among LDH patients pre- and post-DRG reforms ($p > 0.05$), but there were significant differences in sex, age, visit times, admission pathways, admission disease status, complications and comorbidities, surgeries

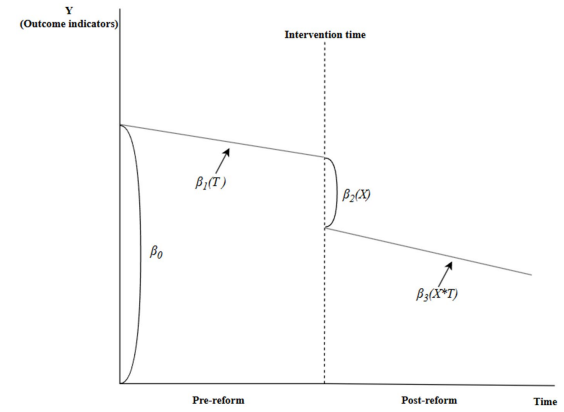


FIGURE 1
Schematic diagram of interrupted time-series model.

TABLE 1 General information on LDH patients pre- and post-DRG reform.

Items	DRG[1] reform		$\chi^2/t/Z$-value	*p*-value
	Pre-reform (*n* = 1,294)	Post-reform (*n* = 1,563)		
Sex (Male/n, %)[a,j]	596(46.06)	639(40.88)	7.728	0.005
Age(years)[b]	58.29 ± 14.22	60.64 ± 14.25	−4.257	<0.001
Nationality (Han/n, %)[c,j]	1,292(99.85)	1,559(99.74)	0.032	0.858
Visit times (One time /n, %)[d,j]	1,277(98.69)	1,400(89.57)	99.629	<0.001
Marital status (Married/n, %)[e,j]	1,147(88.64)	1,401(89.64)	0.727	0.394
Admission pathways (Outpatient or emergency/n, %)[f,j]	255(19.71)	35(2.24)	236.820	<0.001
Admission disease status (Determination/n, %)[g,j]	1,252(96.75)	1,539(98.46)	9.175	0.002
Complications and comorbidities (Yes/n, %)[h,j]	50(3.86)	684(43.76)	590.282	<0.001
Use of Chinese medicine diagnostic and therapeutic equipment (Yes/n, %)[h,j]	1,047(80.91)	1,246(79.72)	0.636	0.425
Use of Chinese medicine diagnostic and treatment techniques (Yes/n, %)[h,j]	1,045(80.76)	1,239(79.27)	0.976	0.323
Diagnosis and treatment based on Chinese medicine evidence (Yes/n, %)[h,j]	1,101(85.09)	1,320(84.45)	0.219	0.640
Surgeries and operations (Yes/n, %)[h,j]	98(7.57)	776(49.65)	590.216	<0.001
Hospitalization cost (CNY)[2,i]	5712.74(4273.84,7428.76)	5361.70(4051.83,7425.91)	−0.957	0.339
Medical services cost (CNY)[2,i]	691.36(429.18,1085.52)	1023.30(720.79,1409.90)	−13.195	<0.001
Diagnosis cost (CNY)[2,i]	1375.20(955.61,1925.81)	1454.59(1151.55,1961.62)	−2.522	0.012
TCM[3] treatment cost (CNY)[2,i]	1222.40(698.67,2149.66)	2089.49(1106.24,4027.23)	−15.377	<0.001
Chinese medicine cost (CNY)[2,i]	494.80(233.01,869.84)	436.22(239.01,738.85)	−2.794	0.005
Western medicine cost (CNY)[2,i]	1355.00(873.14,2004.53)	602.36(278.47,1210.06)	−16.392	<0.001
Length of stay (days)[2,i]	11.00(8.00,15.00)	10.00(8.00,14.00)	−3.550	<0.001

[1]DRG, diagnosis-related group.
[2]CNY, Chinese Yuan.
[3]TCM, traditional Chinese medicine.
[a]Sex: male vs. female.
[b]The normal distribution continuous data were presented as "mean ± standard deviation," the data were compared using paired-samples t-test (t).
[c]Nationality: Han vs. other nationalities.
[d]Visit times: one time vs. two or more times.
[e]Marital status: married vs. unmarried and others.
[f]Admission pathways: outpatient or emergency vs. other pathways.
[g]Admission disease status: determination vs. indetermination or none.
[h]Categorization outcome includes yes and no.
[i]The non-normal distribution continuous data were presented as "median (the first quartile, the third quartile)," the data were compared using the Wilcoxon rank sum test (Z).
[j]The categorical data were presented as numbers (frequencies, %), and the chi-square test was used for categorical data (χ^2).

and operations, medical services cost, diagnosis cost, TCM treatment cost, Chinese medicine cost, Western medicine cost and length of stay among LDH patients pre- and post-DRG reforms ($p < 0.05$).

3.2 Results of factors affecting LDH patients' healthcare-related costs and length of stay in Qingyang City Hospital of Chinese medicine

To further investigate the factors influencing healthcare-related costs and length of stay in LDH patients, we constructed multiple linear regression models using hospitalization cost, medical service cost, diagnostic cost, TCM treatment cost, Chinese medicine cost, and Western medicine cost, and length of stay as dependent variables, with sex, age, nationality, and other general information as independent variables. Stepwise regression was employed for the analysis.

The regression results (Table 2) revealed that: hospitalization cost was significantly lower in patients using Chinese medicine diagnostic and therapeutic equipment ($p < 0.05$); medical service cost increased with complications, two or more times hospitalizations, use of Chinese medicine diagnostic and treatment technique, and post-DRG reform ($p < 0.05$); diagnostic cost decreased for patients with complications, younger patients, outpatient or emergency admissions, use of Chinese medicine diagnostic and therapeutic equipment, and no diagnosis and treatment based on Chinese medicine evidence ($p < 0.05$); TCM treatment cost was higher for complicated cases, females, two or more times hospitalizations, other pathways, determination disease status, use of Chinese medicine diagnostic and treatment techniques, and pre-DRG reform ($p < 0.05$); Chinese medicine cost decreased for uncomplicated

cases, males, younger patients, no use of Chinese medicine diagnostic and treatment techniques, and post-DRG reform ($p < 0.05$); Western medicine cost increased for uncomplicated cases, older adults patients, one time hospitalizations, outpatient or emergency admissions, indetermination or none disease status, no use of Chinese medicine diagnostic and therapeutic equipment, and pre-DRG reform ($p < 0.05$); and length of stay was shorter for uncomplicated cases, older adults patients, one time hospitalizations, use of Chinese medicine diagnostic and therapeutic equipment, no use of Chinese medicine diagnostic and treatment techniques, and post-DRG reform ($p < 0.05$).

To further elucidate the correlations between hospitalization-related costs and length of stay, we conducted Spearman correlation

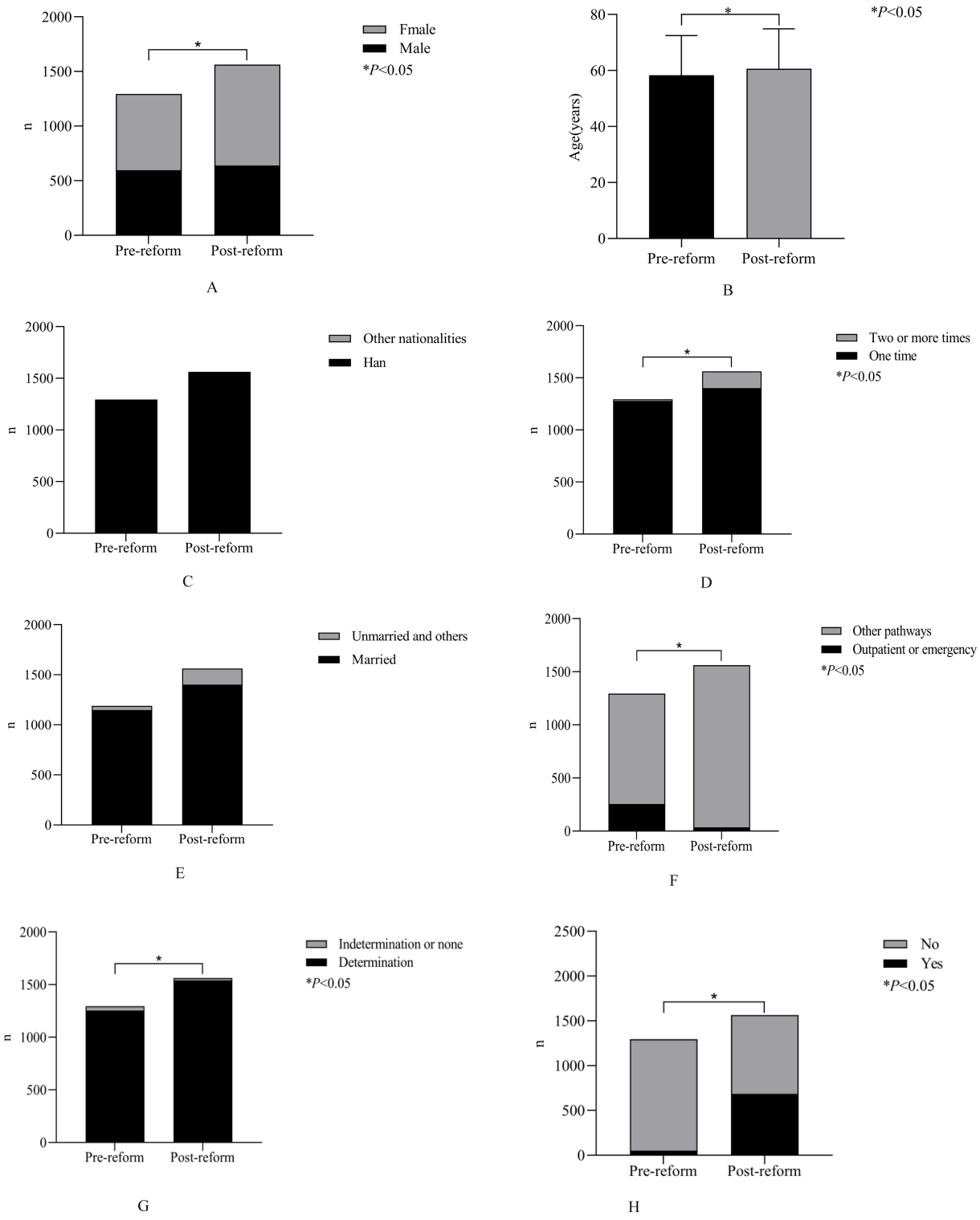


FIGURE 2 (Continued)

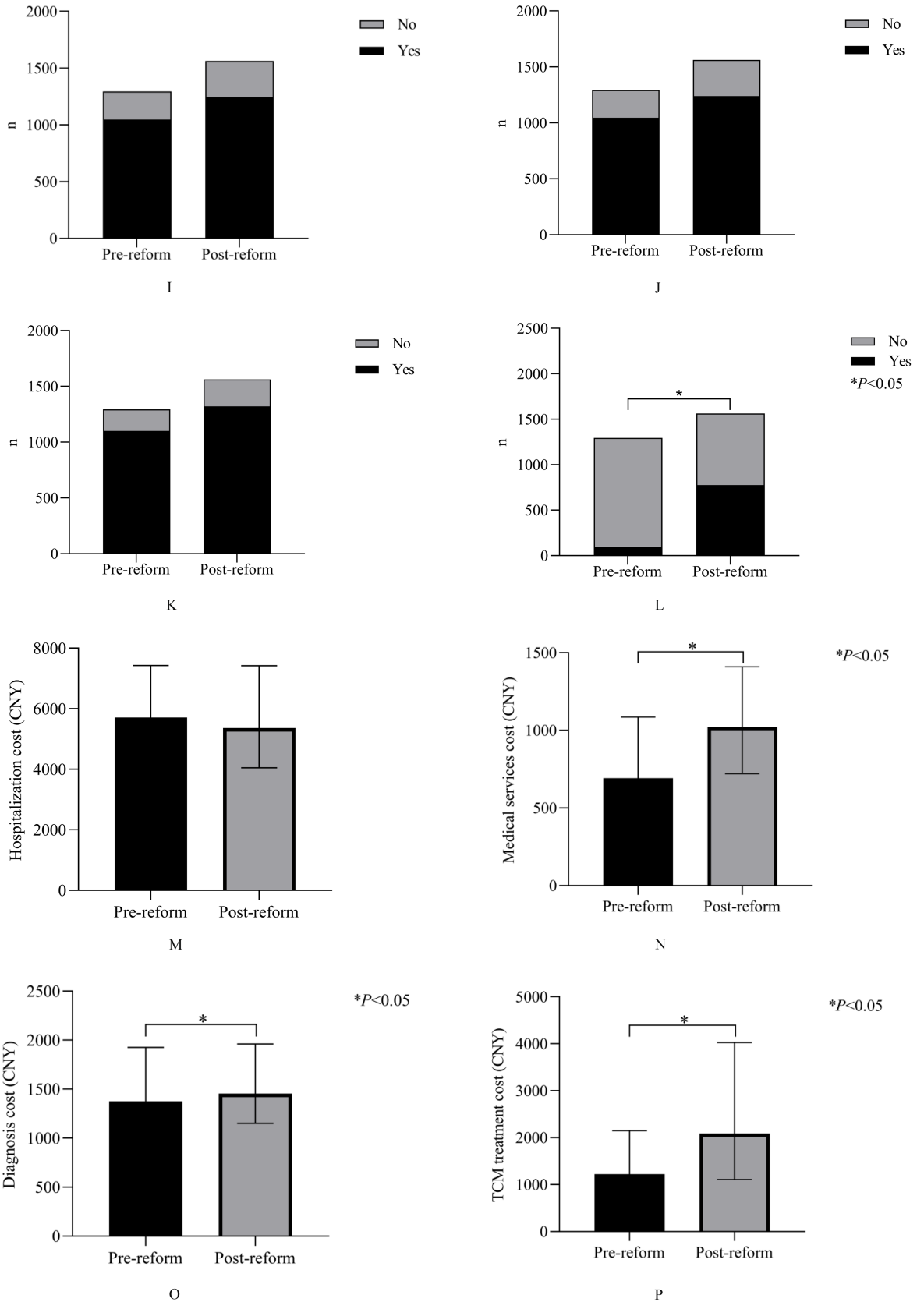
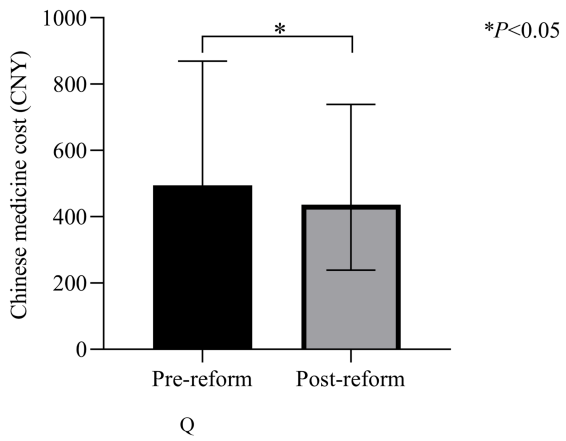
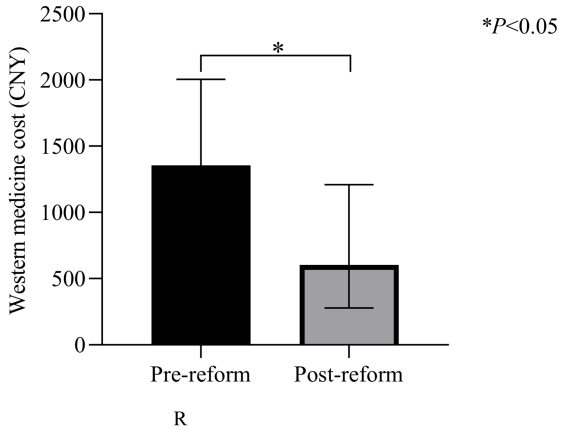


FIGURE 2 (Continued)





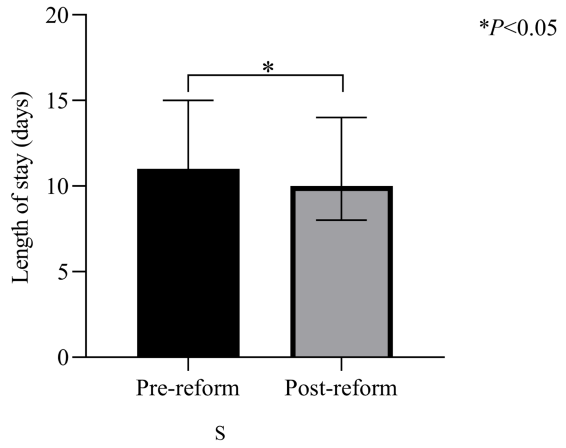


FIGURE 2
Comparative analysis of LDH patients characteristics pre- and post-DRG reform.

analyses. The results demonstrated statistically significant positive correlations ($p < 0.05$) among all measured variables, including hospitalization cost, medical service cost, TCM treatment cost, Chinese medicine cost, Western medicine cost, and length of stay, indicating consistent directional trends across these parameters. Complete results are presented in Table 3.

3.3 Results of ITSA of DRG reform on LDH patients' healthcare-related costs in Qingyang City Hospital of Chinese medicine

We performed Cumby-Huizinga autocorrelation tests on hospitalization cost, medical service cost, diagnostic cost, TCM treatment cost, Chinese medicine cost, and Western medicine cost. The results indicated that hospitalization cost, TCM treatment cost, and Chinese medicine cost exhibited no autocorrelation. However, diagnostic cost and Western medicine cost may demonstrate first-order autocorrelation, while medical service cost could indicate second-order autocorrelation, as summarized in Table 4. To ensure the robustness of our interrupted time-series analysis, we employed the 'lag (1)'or 'lag (2)' command to adjust for autocorrelation effects in the medical costs analysis.

Before the DRG reform at Qingyang City Hospital of Chinese Medicine, hospitalization cost exhibited a significant upward trajectory, with an average monthly increase of CNY 43.49 ($\beta_1 = 43.49$, $p < 0.05$). Conversely, during the reform, fluctuations in hospitalization cost were not statistically significant ($\beta_2 = -333.52$, $p > 0.05$). Following the reform, however, cost demonstrated a pronounced downward trend, decreasing by an average of CNY 36.78 per month ($\beta_1 + \beta_3 = -36.78$, $p < 0.05$). Comprehensive results are presented in Table 5, and the corresponding trend changes are illustrated in Figure 3.

In terms of medical services cost, the pre-reform trend was not significant ($\beta_1 = -2.76$, $p > 0.05$). Nevertheless, during the reform, there was a substantial increase of CNY 361.98 ($\beta_2 = 361.98$, $p < 0.05$), while post-reform changes remained insignificant ($\beta_1 + \beta_3 = -3.26$, $p > 0.05$), as detailed in Table 5 and depicted in Figure 4.

Regarding diagnosis cost, a clear upward trend was evident before the reform, with an average monthly increase of CNY 26.16 ($\beta_1 = 26.16$, $p < 0.05$). During the reform, diagnosis cost significantly decreased by CNY 307.11 ($\beta_2 = -307.11$, $p < 0.05$), yet the post-reform trend was again not significant ($\beta_1 + \beta_3 = -3.66$, $p > 0.05$), as outlined in Table 5 and shown in Figure 5.

Concerning TCM treatment cost, there was a notable increase before the reform, averaging CNY 39.04 per month ($\beta_1 = 39.04$, $p < 0.05$). Following a significant decrease of CNY 466.54 during the reform ($\beta_2 = -466.54$, $p < 0.05$), the cost rebounded, displaying a

10.3389/fpubh.2025.1631872

TABLE 2 Results of multiple linear regression analysis for healthcare-related costs and length of stay in LDH patients.

Variables	Hospitalization cost	Medical services cost	Diagnosis cost	TCM treatment cost	Chinese medicine cost	Western medicine cost	Length of stay
Constant	5001.91 (9.52)*	866.43 (11.42)*	422.92 (3.65)*	238.83 (1.10)	380.84 (6.98)*	1361.79 (5.26)*	12.65 (14.70)*
Complications and comorbidities (ref = No)		181.18 (4.918)*	−87.30 (−2.46)*	788.68 (14.66)*	65.99 (2.77)*	−159.83 (−2.52)*	2.04 (5.99)*
Sex(ref = Male)				92.07 (2.22)*	37.83 (2.04)*		
Age			3.31 (3.10)*		4.88 (7.53)*	4.53 (2.63)*	−0.02 (−2.29)*
Visit times (ref = One time)		131.37 (2.21)*		537.66 (6.21)*		−215.83 (−2.11)*	2.19 (3.98)*
Admission pathways (ref = Outpatient or emergency)			363.56 (7.07)*	659.69 (9.17)*		−323.04 (−3.81)*	
Admission disease status (ref = Determination)				−279.92 (−2.00)*		407.79 (2.47)*	
Use of Chinese medicine diagnostic and therapeutic equipment (ref = Yes)	2281.12 (5.48)*		431.27 (6.70)*			414.30 (6.50)*	2.34 (2.36)*
Use of Chinese medicine diagnostic and treatment techniques (ref = Yes)		−113.43 (−3.18)*		−403.90 (−7.52)*	−82.39 (−3.55)*		−3.15 (−3.19)*
Diagnosis and treatment based on Chinese medicine evidence (ref = Yes)			−179.56 (−2.53)*				
DRG reform (ref = Pre-reform)		206.52 (6.42)*		−398.25 (−8.25)*	−107.65 (−5.18)*	−663.61 (−11.65)*	−1.86 (−6.26)*

t-values are shown in parentheses. *$p < 0.05$.

TABLE 3 Results of correlation analysis for healthcare-related costs and length of stay in LDH patients.

Variables	Hospitalization cost	Medical services cost	Diagnosis cost	TCM treatment cost	Chinese medicine cost	Western medicine cost	Length of stay
Hospitalization cost	1						
Medical services cost	0.687*	1					
Diagnosis cost	0.387*	0.075*	1				
TCM treatment cost	0.591*	0.363*	−0.034	1			
Chinese medicine cost	0.514*	0.464*	−0.058*	0.350*	1		
Western medicine cost	0.627*	0.274*	0.267*	0.107*	0.235*	1	
Length of stay	0.821*	0.724*	0.156*	0.583*	0.483*	0.495*	1

*$p < 0.05$.

clear upward trend post-reform, with an average increase of CNY 50.08 ($\beta_1 + \beta_3 = 50.08$, $p < 0.05$), as detailed in Table 5 and represented in Figure 6.

Chinese medicine cost exhibited no significant trend before the reform ($\beta_1 = -3.96$, $p > 0.05$). However, during the reform, the cost rose significantly by CNY 142.27 ($\beta_2 = 142.27$, $p < 0.05$), while post-reform expenses revealed a significant downward trend, decreasing by an average monthly of CNY 8.87 ($\beta_1 + \beta_3 = -8.87$, $p < 0.05$), as presented in Table 5 and illustrated in Figure 7.

Finally, Western medicine cost showed a significant downward trend before the reform, decreasing by an average of CNY 9.93 ($\beta_1 = -9.93$, $p < 0.05$). Changes during the reform were not statistically significant ($\beta_2 = -41.39$, $p > 0.05$). However, the cost exhibited a marked downward trend, with an average monthly decrease of CNY 31.68 ($\beta_1 + \beta_3 = -31.68$, $p < 0.05$) post-reform, which was notably more pronounced than the pre-reform trend. Detailed results can be found in Table 5, with trend changes depicted in Figure 8.

TABLE 4 Autocorrelation test results of healthcare-related costs for LDH patients.

Items	H_0: q = 0 (serially uncorrelated)				H_0: q = lag-1				Items	H_0: q = 0 (serially uncorrelated)				H_0: q = lag-1			
	H_1: s.c. present at range specified				H_1: s.c. present at lag specified					H_1: s.c. present at range specified				H_1: s.c. present at lag specified			
	lags	chi2	df	*p*-value	lags	chi2	df	*p*-value		lags	chi2	df	*p*-value	lags	chi2	df	*p*-value
Hospitalization cost	1–1	0.521	1	0.471	1	0.521	1	0.471	Medical services cost	1–1	9.548	1	0.002	1	9.548	1	0.002
	1–2	1.212	2	0.545	2	0.548	1	0.459		1–2	11.001	2	0.004	2	4.081	1	0.043
	1–3	2.381	3	0.497	3	0.762	1	0.383		1–3	11.044	3	0.012	3	1.324	1	0.250
	1–4	3.927	4	0.416	4	0.741	1	0.390		1–4	11.183	4	0.025	4	0.163	1	0.686
	1–5	4.044	5	0.543	5	0.753	1	0.386		1–5	11.200	5	0.048	5	0.006	1	0.938
	1–6	5.550	6	0.475	6	0.809	1	0.369		1–6	12.200	6	0.058	6	0.900	1	0.343
Diagnosis cost	1–1	7.124	1	0.008	1	7.124	1	0.008	TCM[1] treatment cost	1–1	0.006	1	0.939	1	0.006	1	0.939
	1–2	7.201	2	0.027	2	0.964	1	0.326		1–2	1.578	2	0.454	2	1.576	1	0.209
	1–3	8.017	3	0.046	3	1.153	1	0.283		1–3	1.585	3	0.663	3	0.021	1	0.886
	1–4	8.069	4	0.089	4	0.438	1	0.508		1–4	4.990	4	0.288	4	2.536	1	0.111
	1–5	8.089	5	0.151	5	0.087	1	0.768		1–5	5.025	5	0.413	5	0.021	1	0.884
	1–6	8.090	6	0.232	6	<0.001	1	0.993		1–6	5.044	6	0.538	6	0.149	1	0.699
Chinese medicine cost	1–1	1.161	1	0.281	1	1.161	1	0.281	Western medicine cost	1–1	8.915	1	0.003	1	8.915	1	0.003
	1–2	2.047	2	0.359	2	0.610	1	0.435		1–2	9.248	2	0.010	2	2.103	1	0.147
	1–3	2.220	3	0.528	3	0.026	1	0.873		1–3	11.531	3	0.009	3	0.294	1	0.588
	1–4	2.464	4	0.651	4	0.086	1	0.769		1–4	11.976	4	0.018	4	1.050	1	0.305
	1–5	3.616	5	0.606	5	0.697	1	0.404		1–5	11.980	5	0.035	5	0.859	1	0.354
	1–6	4.259	6	0.642	6	0.119	1	0.730		1–6	20.100	6	0.003	6	7.127	1	0.008

[1]TCM, traditional Chinese medicine.

10.3389/fpubh.2025.1631872

10.3389/fpubh.2025.1631872

TABLE 5 Results of ITS analysis on healthcare-related costs for LDH patients.

Items	Value	Std. Err.	*t*-value	*p*-value	95% Conf. interval
Hospitalization cost (CNY[2])					
Baseline level, β_0	5024.90	211.29	23.78	<0.001	4602.53 to 5447.27
Baseline trend, β_1	43.49	10.97	3.97	<0.001	21.56 to 65.41
Level change, β_2	−333.52	367.83	−0.91	0.368	−1068.81 to 401.77
Trend change, β_3	−80.27	17.31	−4.64	<0.001	−114.87 to −45.67
Late trend, $\beta_1 + \beta_3$	−36.78	13.39	−2.75	0.008	−63.56 to −10.01
Medical services cost (CNY[2])					
Baseline level, β_0	833.54	127.17	6.55	<0.001	579.32 to 1087.76
Baseline trend, β_1	−2.76	7.24	−0.38	0.704	−17.25 to 11.72
Level change, β_2	361.98	160.06	2.26	0.027	42.02 to 681.95
Trend change, β_3	−0.50	7.90	−0.06	0.950	−16.28 to 15.28
Late trend, $\beta_1 + \beta_3$	−3.26	2.83	−1.15	0.254	−8.93 to 2.40
Diagnosis cost (CNY[2])					
Baseline level, β_0	989.30	61.10	16.19	<0.001	867.15 to 1111.44
Baseline trend, β_1	26.16	3.49	7.49	<0.001	19.18 to 33.13
Level change, β_2	−307.11	87.34	−3.52	0.001	−481.70 to −132.52
Trend change, β_3	−29.82	4.91	−6.07	<0.001	−39.64 to −19.99
Late trend, $\beta_1 + \beta_3$	−3.66	3.18	−1.15	0.254	−10.02 to 2.70
TCM[1] treatment cost (CNY[2])					
Baseline level, β_0	709.14	93.72	7.57	<0.001	521.78 to 896.49
Baseline trend, β_1	39.04	4.68	8.35	<0.001	29.70 to 48.39
Level change, β_2	−466.54	196.34	−2.38	0.021	−859.01 to −74.07
Trend change, β_3	11.03	11.89	0.93	0.357	−12.74 to 34.81
Late trend, $\beta_1 + \beta_3$	50.08	10.94	4.58	<0.001	28.21 to 71.94
Chinese medicine cost (CNY[2])					
Baseline level, β_0	587.73	59.24	9.92	<0.001	469.32 to 706.14
Baseline trend, β_1	−3.96	2.59	−1.53	0.132	−9.15 to 1.22
Level change, β_2	142.27	62.41	2.28	0.026	17.51 to 267.04
Trend change, β_3	−4.91	3.36	−1.46	0.148	−11.63 to 1.80
Late trend, $\beta_1 + \beta_3$	−8.87	2.13	−4.16	<0.001	−13.14 to −4.61
Western medicine cost (CNY[2])					
Baseline level, β_0	1531.37	104.52	14.65	<0.001	1322.44 to 1740.29
Baseline trend, β_1	−9.93	4.74	−2.10	0.040	−19.40 to −0.46
Level change, β_2	−41.39	119.89	−0.35	0.731	−281.05 to 198.27
Trend change, β_3	−21.75	6.32	−3.44	0.001	−34.38 to −9.12
Late trend, $\beta_1 + \beta_3$	−31.68	4.17	−7.59	<0.001	−40.02 to −23.34

[1]TCM, traditional Chinese medicine.
[2]CNY, Chinese Yuan.

3.4 Results of ITSA of DRG reform on length of stay in Qingyang City Hospital of Chinese medicine

We conducted a Cumby-Huizinga autocorrelation test on the length of stay, which revealed no evidence of autocorrelation, as presented in Table 6. This finding underscores the stability of the data regarding length of stay.

Pre-DRG reform, the trend in length of stay was not statistically significant, with a coefficient of $\beta_1$is −0.03 ($p > 0.05$). This lack of significance indicates that there were no noteworthy changes in the average length of stay during this period.

Similarly, the analysis of length of stay during the reform period also yielded insignificant results ($\beta_2 = 0.27$, $p > 0.05$), and post-reform trends remained unremarkable, as reflected in the combined coefficient ($\beta_1 + \beta_3 = -0.02$, $p > 0.05$). Detailed results are provided in Table 7,

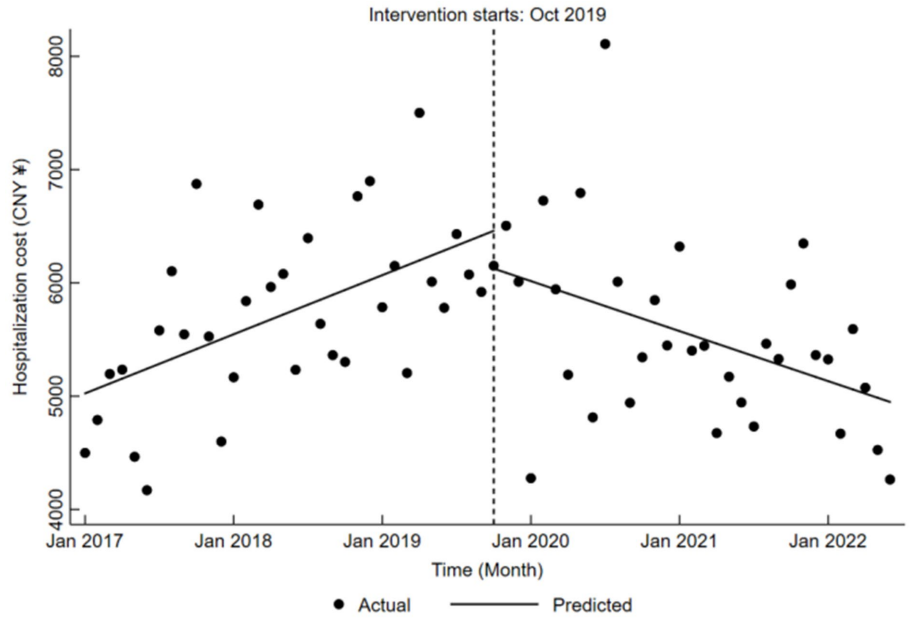


FIGURE 3
Trends in hospitalization cost for LDH patients pre- and post-DRG reform.

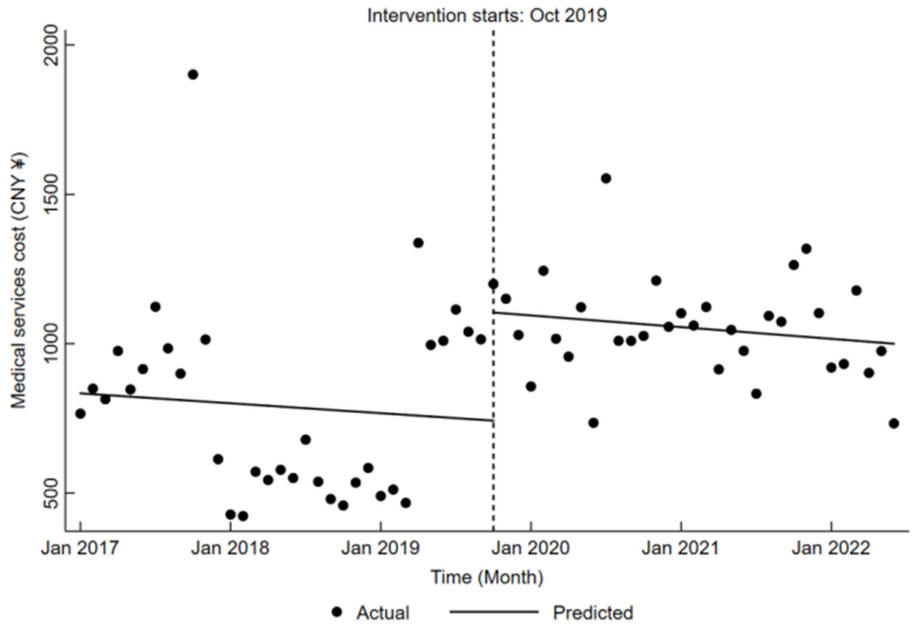


FIGURE 4
Trends in medical services cost for LDH patients pre- and post-DRG reform.

and the corresponding trend changes are illustrated in Figure 9, further emphasizing the consistency of length of stay across the study periods.

4 Discussion

We are the first to investigate the effects of the DRG reform on medical costs and length of stay for LDH patients in Chinese medicine hospitals. This study provides valuable insights into the ongoing reforms of DRG payment systems in TCM. Our univariate analysis revealed differences in patient characteristics before and after the reform, including sex, age, visit times, admission pathways, admission disease status, complications and comorbidities, and surgeries and operations. Post-reform, there was an increase in female patients, older patients, those admitted through other pathways, and patients with defined disease status, complications and comorbidities, and

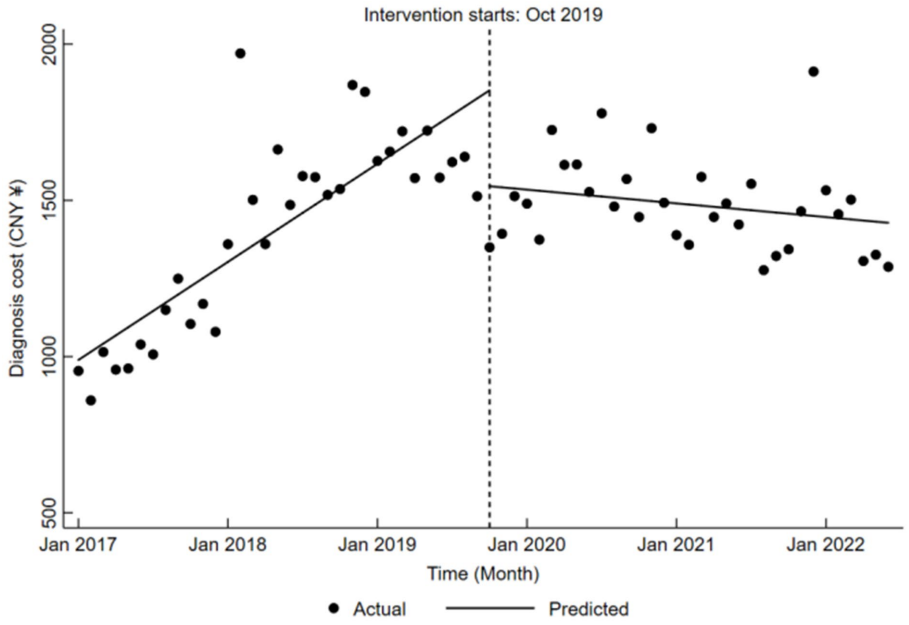


FIGURE 5
Trends in diagnosis cost for LDH patients pre- and post-DRG reform.

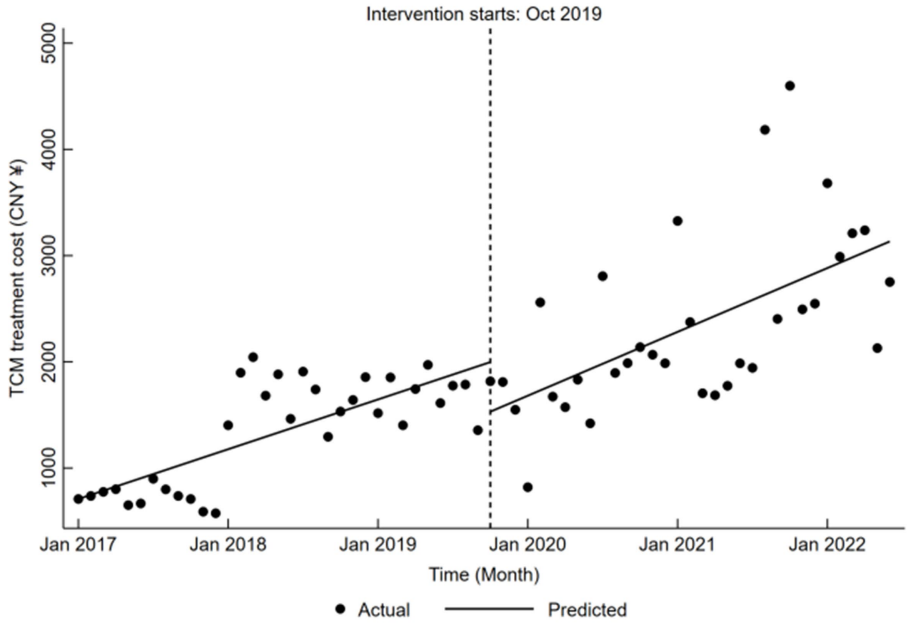


FIGURE 6
Trends in TCM treatment cost for LDH patients pre- and post-DRG reform.

surgical needs. Notably, the proportion of patients admitted through other pathways and those with repeated hospitalizations also increased, suggesting that the reform measures have successfully attracted more patients and fostered repeat admissions to the hospital. The higher number of patients with defined disease status aligns with the reform's objective of improving diagnostic precision. Additionally, the increase in patients with complications and operations needs suggests a rise in case complexity, potentially leading to higher reimbursement standards, which benefits the hospital departments during cost settlement.

Integrating the results of multiple linear regression and correlation analyses, we identified significant associations between healthcare-related costs and multiple factors including patient age, sex, complications and comorbidities, visit times, admission pathways, admission disease status, use of Chinese medicine diagnostic and therapeutic equipment, use of Chinese medicine diagnostic and treatment techniques, diagnosis

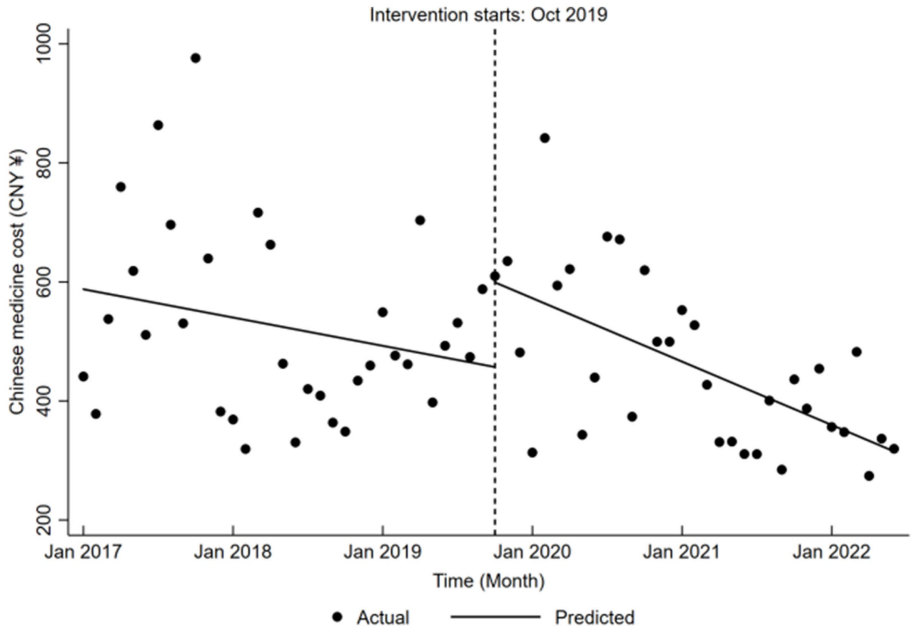


FIGURE 7
Trends in Chinese medicine cost for LDH patients pre- and post-DRG reform.

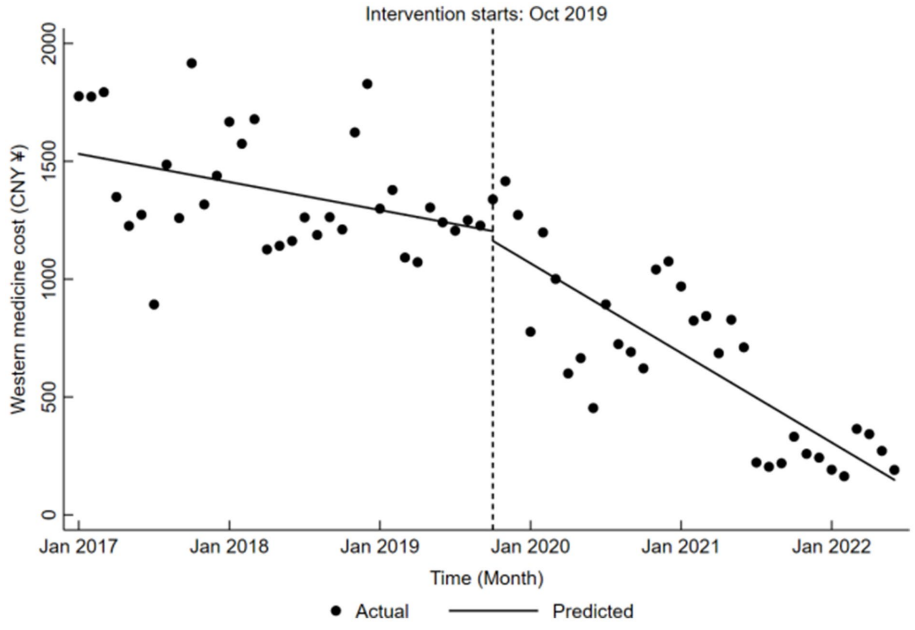


FIGURE 8
Trends in Western medicine cost for LDH patients pre- and post-DRG reform.

and treatment based on Chinese medicine evidence, and DRG reform. Comprehensive analysis revealed that advanced age, presence of complications and comorbidities, and no use of Chinese medicine diagnostic and therapeutic equipment and use of Chinese medicine diagnostic and treatment techniques were associated with higher hospitalization costs, while DRG reform demonstrated cost-containment effects. Furthermore, a positive correlation was observed among healthcare-related costs and length of stay, suggesting that effective cost control for LDH patients requires comprehensive medication cost management coupled with appropriate reduction of length of stay.

The results from our interrupted time-series analysis indicate a significant downward trend in hospitalization cost, Chinese medicine cost, and Western medicine cost following the DRG reform. While the rising trend in diagnostic cost before the reform was curtailed, overall medical service cost increased post-reform, alongside a marked rise in TCM treatment cost. It is noteworthy that hospitalization cost for LDH

TABLE 6 Autocorrelation test results of length of stay for LDH patients.

H_0: q = 0 (serially uncorrelated)				H_0: q = lag-1			
H_1: s.c. present at range specified				H_1: s.c. present at lag specified			
lags	chi2	df	*p*-value	lags	chi2	df	*p*-value
1–1	0.159	1	0.690	1	0.159	1	0.690
1–2	0.250	2	0.882	2	0.072	1	0.789
1–3	0.649	3	0.885	3	0.338	1	0.561
1–4	0.986	4	0.912	4	0.245	1	0.621
1–5	0.988	5	0.964	5	0.025	1	0.874
1–6	8.317	6	0.216	6	6.733	1	0.010

TABLE 7 Results of ITS analysis on length of stay for LDH patients.

Item	Value	Std. Err.	*t*-value	*p*-value	95% Conf. interval
Baseline level, β_0	11.99	0.54	22.21	<0.001	10.91 to 13.06
Baseline trend, β_1	−0.03	0.02	−1.41	0.163	−0.08 to 0.01
Level change, β_2	0.27	0.80	0.34	0.737	−1.33 to 1.87
Trend change, β_3	0.01	0.04	0.30	0.767	−0.07 to 0.10
Late trend, $\beta_1 + \beta_3$	−0.02	0.03	−0.63	0.533	−0.09 to 0.05

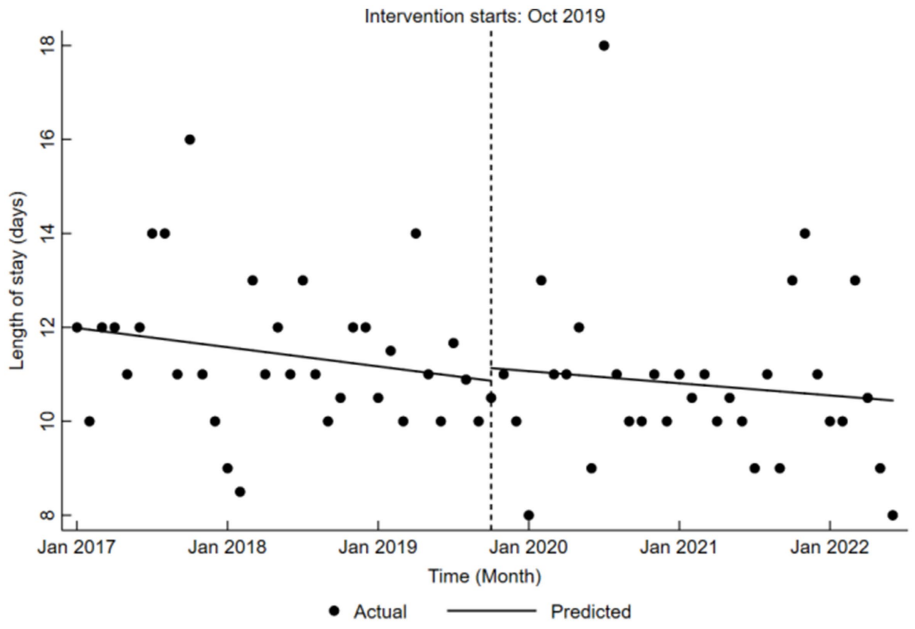


FIGURE 9
Trends in length of stay for LDH patients pre- and post-DRG reform.

patients changed significantly after the DRG reform, demonstrating a marked decrease that aligns with findings from various other studies (41, 43, 44). Certainly, the component costs of hospitalization, including those for Chinese and Western medicine, have concurrently declined alongside the overall reduction in hospitalization cost. However, diagnostic cost and medical service cost were higher post-reform than before, indicating that Chinese hospitals are leveraging their unique strengths by providing more specialized services to address patient needs. This aligns with the Chinese government's objectives for DRG reform in TCM.

Interestingly, the length of stay for LDH patients did not decrease following the DRG reform, which stands in contrast to findings from several other studies (32, 45–47). What's more, previous studies suggest that length of stay is a critical factor influencing hospitalization cost, implying that a significant cost reduction should typically accompany shorter stay (48–50). The absence of a reduction in length of stay, despite the cost reduction, may be related to the unique characteristics of TCM treatment, which often has a slower onset of effects and fewer side effects. The relatively prolonged treatment duration for LDH in TCM is

inherently difficult to substantially reduce, which is fundamentally associated with TCM's diagnostic and therapeutic paradigm. First, this stems from TCM's holistic therapeutic philosophy that necessitates simultaneous management of both pain symptoms and underlying pathological mechanisms (e.g., kidney deficiency, qi-blood stagnation). Second, it reflects the characteristic therapeutic modalities of TCM: acupuncture requires cumulative sessions to activate the endogenous analgesic system, while Chinese herbal compounds need time for multi-target regulation of inflammation and tissue repair. Third, TCM manual therapies follow the natural tissue repair cycle requirements. Although TCM demonstrates a relatively slower onset of therapeutic effects, clinical evidence confirms its superior medium-to-long-term efficacy for LDH management. The majority of TCM treatment occurs in the initial days of hospitalization, suggesting that later cost may be lower, making it challenging to significantly reduce recovery times through DRG payment reforms alone. However, integrating and standardizing TCM treatment methods, along with reducing medication usage, could help achieve the goal of lowering hospitalization cost.

In conclusion, the reform of DRG payment system in TCM has a substantial impact on controlling overall medical costs for LDH patients, although its effectiveness in reducing the length of stay remains limited. Future refinements of the DRG payment system should account for the distinctive characteristics of TCM, optimizing treatment methods and enhancing the quality of healthcare. Establishing a unique and effective reimbursement framework for TCM will further reduce patient treatment cost and length of stay, ultimately benefiting a greater number of patients.

5 Conclusion

DRG reform is associated with lower hospitalization cost, as well as reduced costs for both Chinese and Western medicine among LDH patients in Chinese medicine hospitals. However, it does not correlate with reductions in medical services cost, diagnostic cost, TCM treatment cost, or length of stay. While the reform effectively leverages the unique strengths of TCM to alleviate the economic burden of illness, there is a need to deepen institutional reforms and enhance the quality and content of medical services, with the goal of further reducing healthcare costs and shortening hospitalization durations.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

M-eC: Conceptualization, Data curation, Writing – original draft, Writing – review & editing. Y-hW: Data curation, Writing – original draft, Formal analysis. JY: Data curation, Writing – original draft, Formal analysis. S-jX: Project administration, Writing – review & editing, Investigation, Methodology. X-xZ: Writing – original draft, Methodology, Data curation. YW: Data curation, Methodology, Writing – original draft, Project administration. Y-sY: Writing – original draft, Resources, Software. XJ: Writing – original draft, Software, Methodology. H-nS: Software, Resources, Writing – original draft. G-pW: Writing – review & editing, Data curation, Formal analysis. J-yW: Writing – original draft, Formal analysis, Data curation, Validation. T-zC: Investigation, Project administration, Writing – original draft. F-xK: Software, Writing – original draft, Supervision, Project administration. H-jH: Formal analysis, Data curation, Writing – original draft, Visualization. J-yY: Resources, Supervision, Writing – review & editing, Software. Z-wW: Software, Writing – review & editing, Conceptualization, Resources, Validation, Supervision.

Funding

The author(s) declare that financial support was received for the research and/or publication of this article. This study was supported by the State Administration of Traditional Chinese Medicine (SACM), China (grant no. ZYZB-2023-435 and no. GZY-FJS-2022-045).

Acknowledgments

We thank the Gansu Provincial Health and Wellness Commission for data support for our study.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The author(s) declare that no Gen AI was used in the creation of this manuscript.

Any alternative text (alt text) provided alongside figures in this article has been generated by Frontiers with the support of artificial intelligence and reasonable efforts have been made to ensure accuracy, including review by the authors wherever possible. If you identify any issues, please contact us.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2025.1631872/full#supplementary-material

References

1. Hartvigsen J, Hancock MJ, Kongsted A, Louw Q, Ferreira ML, Genevay S, et al. What low back pain is and why we need to pay attention. *Lancet*. (2018) 391:2356–67. doi: 10.1016/s0140-6736(18)30480-x

2. Manuela LF, Katie DL, Lydia MH, Jaimie DS, Garland TC, Marita C, et al. Global, regional, and national burden of low back pain, 1990-2020, its attributable risk factors, and projections to 2050: a systematic analysis of the global burden of disease study 2021. *Lancet Rheumatol*. (2023) 5:e316–29. doi: 10.1016/s2665-9913(23)00098-x

3. Theo V, Christine A, Megha A, Ryan MB, Zulfiqar AB, Alexandria B, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990-2015: a systematic analysis for the global burden of disease study 2015. *Lancet*. (2016) 388:1545–602. doi: 10.1016/s0140-6736(16)31678-6

4. Chen S, Chen M, Wu X, Lin S, Tao C, Cao H, et al. Global, regional and national burden of low back pain 1990-2019: a systematic analysis of the global burden of disease study 2019. *J Orthop Translat*. (2022) 32:49–58. doi: 10.1016/j.jot.2021.07.005

5. Chen N, Fong DYT, Wong JYH. The global health and economic impact of low-back pain attributable to occupational ergonomic factors in the working-age population by age, sex, and geography in 2019. *Scand J Work Environ Health*. (2023) 49:487–95. doi: 10.5271/sjweh.4116

6. China National Health Commission. China health statistics yearbook 2023. Beijing: Peking Union Medical College Press (2023).

7. Buchbinder R, van Tulder M, Öberg B, Costa LM, Woolf A, Schoene M, et al. Low back pain: a call for action. *Lancet*. (2018) 391:2384–8. doi: 10.1016/s0140-6736(18)30488-4

8. Hoy D, March L, Brooks P, Blyth F, Woolf A, Bain C, et al. The global burden of low back pain: estimates from the global burden of disease 2010 study. *Ann Rheum Dis*. (2014) 73:968–74. doi: 10.1136/annrheumdis-2013-204428

9. Zhou M, Theologis AA, O'Connell GD. Understanding the etiopathogenesis of lumbar intervertebral disc herniation: from clinical evidence to basic scientific research. *JOR Spine*. (2024) 7:e1289. doi: 10.1002/jsp2.1289

10. Yang H, Liu H, Li Z, Zhang K, Wang J, Wang H, et al. Low back pain associated with lumbar disc herniation: role of moderately degenerative disc and annulus fibrous tears. *Int J Clin Exp Med*. (2015) 8:1634–44.

11. Dieleman JL, Cao J, Chapin A, Chen C, Li Z, Liu A, et al. US health care spending by payer and health condition, 1996-2016. *JAMA*. (2020) 323:863–84. doi: 10.1001/jama.2020.0734

12. Katz JN. Lumbar disc disorders and low-back pain: socioeconomic factors and consequences. *J Bone Joint Surg Am*. (2006) 88:21–4. doi: 10.2106/jbjs.E.01273

13. Hong J, Reed C, Novick D, Happich M. Costs associated with treatment of chronic low back pain: an analysis of the UK general practice research database. *Spine (Phila Pa 1976)*. (2013) 38:75–82. doi: 10.1097/BRS.0b013e318276450f

14. Carregaro RL, Tottoli CR, Rodrigues DDS, Bosmans JE, da Silva EN, van Tulder M. Low back pain should be considered a health and research priority in Brazil: lost productivity and healthcare costs between 2012 to 2016. *PLoS One*. (2020) 15:e0230902. doi: 10.1371/journal.pone.0230902

15. Lambeek LC, van Tulder MW, Swinkels IC, Koppes LL, Anema JR, van Mechelen W. The trend in total cost of back pain in the Netherlands in the period 2002 to 2007. *Spine (Phila Pa 1976)*. (2011) 36:1050–8. doi: 10.1097/BRS.0b013e3181e70488

16. Alonso-García M, Sarría-Santamera A. The economic and social burden of low Back pain in Spain: a National Assessment of the economic and social impact of low Back pain in Spain. *Spine (Phila Pa 1976)*. (2020) 45:E1026–e1032. doi: 10.1097/brs.0000000000003476

17. Yang Y, Lai X, Li C, Yang Y, Gu S, Hou W, et al. Focus on the impact of social factors and lifestyle on the disease burden of low back pain: findings from the global burden of disease study 2019. *BMC Musculoskelet Disord*. (2023) 24:679. doi: 10.1186/s12891-023-06772-5

18. Liang H, Huang J. Case report: spontaneous regression of extruded lumbar disc herniation with acupuncture therapy. *Front Neurol*. (2024) 15:1381292. doi: 10.3389/fneur.2024.1381292

19. Chou R, Côté P, Randhawa K, Torres P, Yu H, Nordin M, et al. The global spine care initiative: applying evidence-based guidelines on the non-invasive management of back and neck pain to low- and middle-income communities. *Eur Spine J*. (2018) 27:851–60. doi: 10.1007/s00586-017-5433-8

20. Chou R. Low back pain. *Ann Intern Med*. (2021) 174:Itc113–28. doi: 10.7326/aitc202108170

21. Knezevic NN, Candido KD, Vlaeyen JWS, Van Zundert J, Cohen SP. Low back pain. *Lancet*. (2021) 398:78–92. doi: 10.1016/s0140-6736(21)00733-9

22. Skljarevski V, Ossanna M, Liu-Seifert H, Zhang Q, Chappell A, Iyengar S, et al. A double-blind, randomized trial of duloxetine versus placebo in the management of chronic low back pain. *Eur J Neurol*. (2009) 16:1041–8. doi: 10.1111/j.1468-1331.2009.02648.x

23. Chaparro LE, Furlan AD, Deshpande A, Mailis-Gagnon A, Atlas S, Turk DC. Opioids compared to placebo or other treatments for chronic low-back pain. *Cochrane Database Syst Rev*. (2013) 2013:Cd004959. doi: 10.1002/14651858

24. Deyo RA, Von Korff M, Duhrkoop D. Opioids for low back pain. *BMJ*. (2015) 350:g6380. doi: 10.1136/bmj.g6380

25. Zhang B, Xu H, Wang J, Liu B, Sun G. A narrative review of non-operative treatment, especially traditional Chinese medicine therapy, for lumbar intervertebral disc herniation. *Biosci Trends*. (2017) 11:406–17. doi: 10.5582/bst.2017.01199

26. Wang CA, Zhao HF, Ju J, Kong L, Sun CJ, Zheng YK, et al. Reabsorption of intervertebral disc prolapse after conservative treatment with traditional Chinese medicine: a case report. *World J Clin Cases*. (2023) 11:2308–14. doi: 10.12998/wjcc.v11.i10.2308

27. Huang SR, Pan LD, Ma YW, Wang ZJ, Chen YY, Yu ZX. Research on community promotion and application of single acupoint electroacupuncture therapy for lumbar intervertebral disc herniation. *Zhongguo Zhen Jiu*. (2021) 41:391–4. doi: 10.13703/j.0255-2930.20200409-k0001

28. Sun C, Sun K, Wang S, Wang Y, Yuan P, Li Z, et al. Effect of Baimai ointment on lumbar disc herniation: a multicentre, prospective, randomised, double-blind, placebo-controlled trial. *Phytomedicine*. (2024) 122:155138. doi: 10.1016/j.phymed.2023.155138

29. Fetter RB, Shin Y, Freeman JL, Averill RF, Thompson JD. Case mix definition by diagnosis-related groups. *Med Care*. (1980) 18:1–53.

30. Chok L, Bachli EB, Steiger P, Bettex D, Cottini SR, Keller E, et al. Effect of diagnosis related groups implementation on the intensive care unit of a Swiss tertiary hospital: a cohort study. *BMC Health Serv Res*. (2018) 18:84. doi: 10.1186/s12913-018-2869-4

31. Messerle R, Schreyögg J. Country-level effects of diagnosis-related groups: evidence from Germany's comprehensive reform of hospital payments. *Eur J Health Econ*. (2024) 25:1013–30. doi: 10.1007/s10198-023-01645-z

32. Cid C, Dawson N, Medina C, Espinoza A, Bastías G. Using diagnosis-related groups in Chile: lessons and challengesLições e desafios do uso de grupos de diagnósticos relacionados no Chile. *Rev Panam Salud Publica*. (2024) 48:e67. doi: 10.26633/rpsp.2024.67

33. Choi JW, Kim SJ, Park HK, Jang SI, Kim TH, Park EC. Effects of a mandatory DRG payment system in South Korea: analysis of multi-year nationwide hospital claims data. *BMC Health Serv Res*. (2019) 19:776. doi: 10.1186/s12913-019-4650-8

34. Milstein R, Schreyögg J. The end of an era? Activity-based funding based on diagnosis-related groups: a review of payment reforms in the inpatient sector in 10 high-income countries. *Health Policy*. (2024) 141:104990. doi: 10.1016/j.healthpol.2023.104990

35. Meng Z, Hui W, Cai Y, Liu J, Wu H. The effects of DRGs-based payment compared with cost-based payment on inpatient healthcare utilization: a systematic review and meta-analysis. *Health Policy*. (2020) 124:359–67. doi: 10.1016/j.healthpol.2020.01.007

36. Kahn KL, Keeler EB, Sherwood MJ, Rogers WH, Draper D, Bentow SS, et al. Comparing outcomes of care before and after implementation of the DRG-based prospective payment system. *JAMA*. (1990) 264:1984–8.

37. Busse R, Geissler A, Aaviksoo A, Cots F, Häkkinen U, Kobel C, et al. Diagnosis related groups in Europe: moving towards transparency, efficiency, and quality in hospitals? *BMJ*. (2013) 346:f3197. doi: 10.1136/bmj.f3197

38. China National Healthcare Security Administration. Notice regarding the publication of the list of national pilot cities for DRG payment. (2019). Available online at: https://www.nhsa.gov.cn/art/2019/6/5/art_37_1362.html. Accessed Oct 25, 2024.

39. Baum C, Schaffer M. ACTEST: Stata module to perform Cumby-Huizinga general test for autocorrelation in time series. Boston: Mark Schaffer (2015).

40. Linden A. A comprehensive set of postestimation measures to enrich interrupted time-series analysis. *Stata J*. (2017) 17:73–88. doi: 10.1177/1536867x1701700105

41. Lin K, Li Y, Yao Y, Xiong Y, Xiang L. The impact of an innovative payment method on medical expenditure, efficiency, and quality for inpatients with different types of medical insurance: evidence from a pilot city, China. *Int J Equity Health*. (2024) 23:115. doi: 10.1186/s12939-024-02196-2

42. China National Healthcare Security Administration. Notice on the issuance of the three-year action plan for DRG/DIP payment reform. (2019). Available online at: https://www.gov.cn/zhengce/zhengceku/2021-11/28/content_5653858.htm#:~:text=DRG/DI. Accessed Oct 25, 2024.

43. Wang S, Wu N, Wang H, Zhang X, Li F, Wang X, et al. Impacts of a new diagnosis-related group point payment system on children's medical services in China: length of stay and costs. *Int J Health Plann Manag*. (2024) 39:432–46. doi: 10.1002/hpm.3739

44. Liu Y, Du S, Cao J, Niu H, Jiang F, Gong L. Effects of a diagnosis-related group payment reform on length and costs of hospitalization in Sichuan, China: a synthetic control study. *Risk Manag Healthc Policy*. (2024) 17:1623–37. doi: 10.2147/rmhp.S463276

45. Chen YJ, Zhang XY, Yan JQ, Xue T, Qian MC, Ying XH. Impact of diagnosis-related groups on inpatient quality of health care: a systematic review and meta-analysis. *Inquiry*. (2023) 60:469580231167011. doi: 10.1177/00469580231167011

46. Hamada H, Sekimoto M, Imanaka Y. Effects of the per diem prospective payment system with DRG-like grouping system (DPC/PDPS) on resource usage and healthcare quality in Japan. *Health Policy*. (2012) 107:194–201. doi: 10.1016/j.healthpol.2012.01.002

47. Wu Y, Fung H, Shum HM, Zhao S, Wong EL, Chong KC, et al. Evaluation of length of stay, care volume, in-hospital mortality, and emergency readmission rate associated with use of diagnosis-related groups for internal resource allocation in public hospitals in Hong Kong. *JAMA Netw Open*. (2022) 5:e2145685. doi: 10.1001/jamanetworkopen.2021.45685

48. Chen M, Kong F, Su B, Wei X, Yang J. Factors influencing hospitalization cost for diabetic patients in traditional Chinese medicine hospitals in Qingyang City, China. *Int J Environ Res Public Health*. (2022) 19:13859. doi: 10.3390/ijerph192113859

49. Hou HJ, Cong TZ, Cai Y, Ba YH, Chen ME, Yang JY, et al. Influencing factors of hospitalization cost of hypertension patients in traditional Chinese medicine hospitals. *Front Public Health*. (2024) 12:1329768. doi: 10.3389/fpubh.2024.1329768

50. Chen M, Yang J, Hou H, Zheng B, Xia S, Wang Y, et al. Analysis of factors influencing hospitalization cost of patients with distal radius fractures: an empirical study based on public traditional Chinese medicine hospitals in two cities, China. *BMC Health Serv Res*. (2024) 24:605. doi: 10.1186/s12913-024-10953-w

frontiers | Frontiers in Oncology

TYPE Review
PUBLISHED 05 November 2025
DOI 10.3389/fonc.2025.1643022

Check for updates

OPEN ACCESS

EDITED BY
Jing Yuan,
Fudan University, China

REVIEWED BY
Stefano Vagge,
Ente Ospedaliero Ospedali Galliera, Italy
Mei Zhan,
Sichuan University, China

*CORRESPONDENCE
Bikun Cai
695278308@qq.com
Yuhang Liu
19826531981@139.com

RECEIVED 13 June 2025
ACCEPTED 21 October 2025
PUBLISHED 05 November 2025

CITATION
Zhang H, Liu Y, Cai B, Wang M, Li H and Wang H (2025) Durvalumab consolidation therapy in patients with stage III small cell lung cancer after concurrent chemoradiation: a China-based cost-effectiveness analysis. *Front. Oncol.* 15:1643022. doi: 10.3389/fonc.2025.1643022

COPYRIGHT
© 2025 Zhang, Liu, Cai, Wang, Li and Wang. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

Durvalumab consolidation therapy in patients with stage III small cell lung cancer after concurrent chemoradiation: a China-based cost-effectiveness analysis

Hui Zhang[1,2,3], Yuhang Liu[1,2,3]*, Bikun Cai[1,2,3]*, Mengyi Wang[1,2,3], Haonan Li[4,5] and Hong Wang[1]

[1]School of Medical Business, Guangdong Pharmaceutical University, Guangzhou, Guangdong, China, [2]Guangdong Health Economics and Promotion Research Centre, Guangdong Pharmaceutical University, Guangzhou, Guangdong, China, [3]Guangdong Health Economics and Health Promotion Research Centre, Guangdong Pharmaceutical University, Guangzhou, Guangdong, China, [4]School of Pharmaceutical Sciences, Peking University, Beijing, China, [5]International Research Centre for Medicinal Administration, Peking University, Beijing, China

Background: Limited-stage small-cell lung cancer (LS-SCLC) has suboptimal long-term survival despite standard chemoradiotherapy. Durvalumab, an anti-PD-L1 antibody, demonstrated survival benefits in the ADRIATIC Phase III trial, but its cost-effectiveness in China remains uncertain. This study evaluates the economic value of durvalumab as consolidation therapy for LS-SCLC post-chemoradiotherapy.

Methods: A Markov model was constructed using data from the ADRIATIC trial (NCT03703297), simulating three health states: progression-free survival (PFS), progressive disease (PD), and death state, transition probabilities were derived from trial outcomes. A 10-year horizon, 5.0% discount rate, and willingness-to-pay (WTP) thresholds (1-3×per capita gross domestic product (GDP): $12,569.82-$37,709.46/QALY) were applied. All costs were converted to unified currency using the average exchange rate of 1 USD = 7.11 CNY, based on exchange rates from 1 January 2024, to 31 October 2024.

Results: The study results demonstrated that while durvalumab provided clinical benefits by extending quality-adjusted life years (QALYs) by 0.44 compared to placebo (2.24 vs. 1.80), its high cost resulted in poor cost-effectiveness within China's healthcare system. The incremental cost reached $108,609.45, yielding an ICER of $245,591.59 per QALY, exceeding China's standard willingness-to-pay thresholds. Sensitivity analyses revealed drug pricing as the most influential factor, where a 30% price reduction could improve the ICER by 30.3%. The negative incremental net monetary benefit (-$107,394.34) further confirmed the economic challenges. These findings suggest that despite its clinical advantages, durvalumab's current pricing makes it economically unviable for routine use in China's LS-SCLC treatment without substantial cost reductions or alternative reimbursement strategies.

Conclusion: Durvalumab improves survival in LS-SCLC but lacks cost-effectiveness under current pricing in China. Drug costs and health utilities are

critical determinants. Policy measures, such as price negotiation, risk-sharing agreements, or subgroup targeting, may enhance affordability. Balancing clinical benefits with economic burden is essential for optimizing durvalumab's role in LS-SCLC management.

KEYWORDS

durvalumab, limited-stage small-cell lung cancer, Markov model, placebo, cost-effectiveness

1 Introduction

Small cell lung Cancer (SCLC) is a highly aggressive neuroendocrine tumor, accounting for approximately 14.0% of all lung cancer cases, and is closely associated with smoking (with about 95.0% of patients having a history of smoking) (1, 2). SCLC is characterized by early metastasis, rapid proliferation, and susceptibility to drug resistance, with a 5-year survival rate of only 6.4% (3). Based on the extent of disease, SCLC is divided into limited-stage (LS-SCLC) and extensive-stage (ES-SCLC), with the latter accounting for 60%-70% of diagnosed patients (1). In traditional treatment, patients with limited-stage disease primarily receive concurrent chemoradiotherapy, while those with extensive-stage disease are treated with platinum-based chemotherapy combined with etoposide. However, the median overall survival (OS) is only about 10 months, and most patients relapse within 6 months after treatment (4).

In recent years, the introduction of immune checkpoint inhibitors has significantly transformed the treatment landscape for ES-SCLC. Based on the results of the CASPIAN and IMpower133 trials, PD-L1 inhibitors such as durvalumab and atezolizumab, in combination with chemotherapy, have been established as a new standard of first-line treatment (5–7). The CASPIAN trial demonstrated that the median OS in the durvalumab plus chemotherapy group was 13.0 months (compared to 10.3 months in the chemotherapy-alone group, HR = 0.73), with a 3-year OS rate increased to 17.6% (compared to 5.8% in the chemotherapy-alone group) (6, 7). Despite these improvements, the absolute survival benefit of immunotherapy remains relatively limited (an extension of 2–3 months), and some patients require treatment adjustments due to immune-related adverse reactions (such as pneumonia and autoimmune diseases) (5, 7).

Durvalumab is a selective, high-affinity humanized IgG1 monoclonal antibody that exerts anti-tumor effects by blocking the interaction between PD-L1 and PD-1 as well as CD80. In recent years, durvalumab has demonstrated significant efficacy and controllable safety in the treatment of various types of lung cancer. In the CASPIAN trial, durvalumab in combination with platinum–etoposide chemotherapy as first-line treatment for ES-SCLC significantly prolonged OS and progression-free survival (PFS) (8). The POSEIDON study further confirmed the efficacy of durvalumab combined with chemotherapy in metastatic non-small cell lung cancer (mNSCLC). Compared with chemotherapy alone, it significantly improved PFS and showed a trend toward prolonged OS (9). Additionally, the PACIFIC study evaluated the effect of durvalumab as consolidation therapy in patients with stage III unresectable NSCLC. The results showed that it significantly prolonged PFS and OS (10). The AEGEAN trial explored the application of durvalumab in the perioperative period for patients with resectable NSCLC. The results indicated that durvalumab combined with neoadjuvant chemotherapy significantly prolonged event-free survival (EFS) and increased the pathological complete response rate (pCR) (11). Most recently, the ADRIATIC trial investigated the efficacy of durvalumab as adjuvant therapy in LS-SCLC. The results showed that the durvalumab treatment group significantly prolonged OS and PFS compared with the placebo group (12).

These study results indicate that durvalumab has potential application value in the treatment of lung cancer at different stages and types, especially in improving patient survival prognosis. In recent years, China has been continuously advancing policy reforms to improve the accessibility of innovative drugs. The National Medical Products Administration (NMPA) has established breakthrough treatment drug and priority review procedures to accelerate the market entry of drugs with outstanding clinical value. The National Healthcare Security Administration (NHSA) has included several innovative immunotherapy drugs, including durvalumab, in the national medical insurance list through medical insurance negotiation mechanisms (13). However, as a high-value innovative drug with a relatively long treatment cycle, durvalumab has sparked widespread attention regarding its economic affordability and cost-effectiveness.

Pharmacoeconomic studies can systematically model the cost-effectiveness relationship of drugs in real clinical applications, helping clinicians, medical insurance providers, and policymakers make scientific decisions with limited health resources. Especially in the group of patients with LS-SCLC, who need intensive treatment and face a high risk of recurrence, clarifying the cost-effectiveness characteristics of durvalumab as consolidation therapy is of great significance for maximizing its clinical value and optimizing resource allocation.

To ensure scientific rigor, the analysis utilizes data derived from a registered clinical study (NCT03703297) that was first posted on ClinicalTrials.gov on September 27, 2018.

2 Materials and methods

2.1 Target population

The target population of this study consists of patients with limited-stage small-cell lung cancer (LS-SCLC) who have completed radical chemo-radiotherapy without disease progression. These patients still face a high risk of recurrence after standard treatment and require further consolidation therapy to prolong PFS and overall survival (OS). The characteristics of the target population include being in a mild disease state with no progression after radical chemoradiotherapy, and the need for a consolidation treatment that can significantly extend PFS and OS, while also considering the safety and economic affordability of the treatment.

The enrolled patients were derived from a multicenter, randomized, double-blind, phase 3 clinical trial comparing durvalumab (1,500 mg) with or without tremelimumab (75 mg for four doses only) to placebo, administered every 4 weeks for up to 24 months in limited-stage small-cell lung cancer patients who had not experienced disease progression after standard concurrent platinum-based chemoradiotherapy. The study enrolled 730 patients who were randomly assigned in a 1:1:1 ratio, with 264 patients allocated to the durvalumab group, 200 to the durvalumab-tremelimumab group, and 266 to the placebo group. Randomization was stratified according to disease stage (I or II vs. III) and receipt of prophylactic cranial irradiation (yes vs. no). All participants had completed concurrent chemoradiotherapy prior to enrollment. The trial was conducted across multiple centers, representing diverse populations.

All study procedures were rigorously performed in compliance with applicable ethical guidelines and regulatory requirements. The current analysis utilized data from the ADRIATIC phase III clinical trial (Cheng et al.) (13). Prior to study enrollment, written informed consent was obtained from all participating individuals or their legally authorized representatives. The phase 3 trial was conducted across multiple centers in Asia, Europe, and North and South America, representing diverse urban medical centers under various healthcare systems. For the purpose of this analysis, we established standardized baseline patient characteristics, including a median age of 62 years, with most patients being former or current smokers. Adverse events (AEs) were graded according to the Common Terminology Criteria for Adverse Events, version 4.03, and included in the analysis if they reached grade 3 or higher (G3+) in either treatment group (durvalumab or placebo). This study was carried out based on the phase 3 trial and did not involve other human participants, hence, there is no need for the approval of the independent ethics committee.

2.2 Model construction

Based on the ADRIATIC Phase III trial (NCT03703297), this study developed a Markov model to evaluate the cost-effectiveness of adjuvant durvalumab versus placebo in patients with LS-SCLC without progression after chemoradiotherapy (14), from the Chinese healthcare system perspective. The model employed a monthly cycle length and a 10-year time horizon, simulating 95% of clinical events. Health outcomes included life years (LYs), QALYs, and ICERs, with cost-effectiveness thresholds defined as 1–3 times China's 2024 per capita GDP 12,569.82 CNY (89,371.42 USD)-37,709.46 CNY (268114.26 USD). Microsoft Excel 2019 was used for model implementation, and all costs were adjusted to 2024 US dollars (exchange rate: 1 USD = 7.11 CNY) using healthcare-specific inflation indices (10).

The model comprised three mutually exclusive health states: PFS, PD, and Death as shown in Figure 1. All patients initiated treatment in the PFS state, receiving durvalumab (1,500 mg IV every 4 weeks) or placebo until disease progression or unacceptable toxicity. Upon progression to PD, patients received second-line platinum-etoposide rechallenge (administered to 66.2% of progressed patients) or topotecan, followed by best supportive care (BSC).

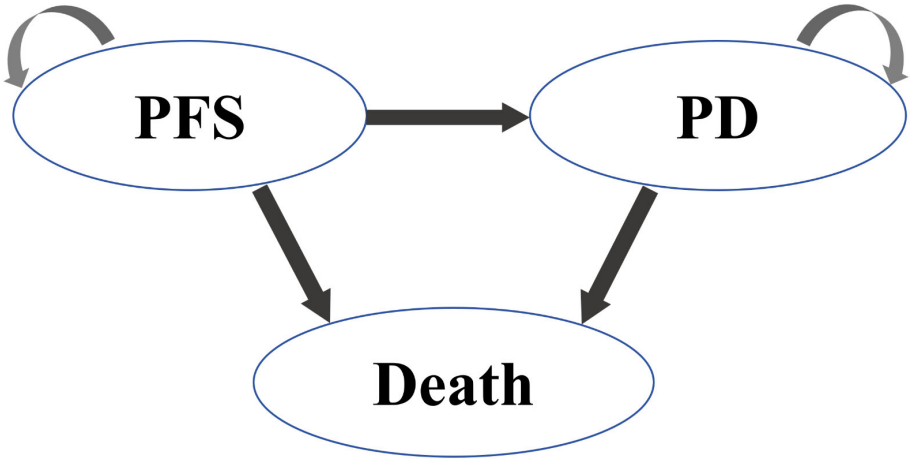


FIGURE 1
Markov model.

2.3 Cost and utility data

The model incorporates the following direct medical costs: drug costs, including durvalumab (1500 mg per infusion at $7,631.74), simulated costs for the placebo group, and chemotherapy drugs such as topotecan ($72.17 per cycle), carboplatin ($87.94 per cycle), and etoposide ($266.67 per cycle). Treatment management-related costs cover durvalumab infusion procedures, laboratory tests ($134.36 per cycle), and imaging examinations ($140.65 per cycle) for monitoring treatment efficacy and safety. Adverse effects were only considered for those graded above 3 and with a probability of >5%, because the impact of milder adverse effects was relatively small. Post-progression treatment is divided into first-line therapy (a platinum-etoposide rechallenge regimen used by 66.2% of patients) and second-line therapy (standard regimens such as topotecan), along with best supportive care in the terminal phase ($327.46 per cycle). Palliative care costs ($2,549.63 per cycle) are used for symptom relief in the advanced stages, with end-of-life care costs included therein. In this study, in accordance with the recommendations of the Chinese Guidelines for Pharmacoeconomic Evaluation 2020, this study applied a 5% annual discount rate was applied for future health utility and cost, with a discount rate variation range of 0% to 8% (15). And all costs were converted to a unified currency using the average exchange rate of 1 USD = 7.11 CNY, based on exchange rates from 1 January 2024 to 31 October 2024 (16) (Table 1).

This period was chosen because it represents the most recent stable interval prior to model construction, consistent with the 2024 per capita GDP data used for willingness-to-pay thresholds, and

TABLE 1 Cost and model parameters.

Parameters	Base value	Lower limit	Upper limit	Distribution	Reference
Cost					
Durvalumab	7,631.74	6,105.39	9,158.09	Gama	NRDL (17).
Topotecan	72.17	57.74	86.61	Gama	NRDL (17).
Carboplatin	87.94	70.35	105.53	Gama	NRDL (17).
Etoposide	266.67	213.33	320.00	Gama	NRDL (17).
Best supportive care	327.46	261.97	392.95	Gama	DRG tariffs (18).
Laboratory test	134.36	107.49	161.23	Gama	DRG tariffs (18).
Imaging examination	140.65	112.52	168.78	Gama	DRG tariffs (18).
Palliative care	2,549.63	2,039.71	3,059.56	Gama	DRG tariffs (18).
Cost of AEs					
Rash	400.00	320.00	480.00	Gama	Yue et al. (19)
Pulmonary embolism	992.26	793.81	1,190.72	Gama	Zhang et al. (20)
Anemia	497.41	397.93	596.89	Gama	Qi et al. (21)
Fatigue	188.20	150.56	225.84	Gama	Georfieva et al. (22)
Diarrhea	5.18	4.14	6.22	Gama	Zhang et al. (23)
Hypertension	14.73	11.78	17.67	Gama	Guan et al. (24)
Utility					
PFS	0.673	0.528	0.808	Beta	Kang et al. (25–28)
PD	0.473	0.378	0.568	Beta	Kang et al. (25–28)
Disutility of AEs					
Rash	0.03	0.02	0.04	Beta	Ward et al. (29)
Pulmonary embolism	0.20	0.16	0.24	Beta	Zhang et al. (20)
Anemia	0.04	0.03	0.05	Beta	Liu et al. (30)
Fatigue	0.01	0.008	0.012	Beta	Georfieva et al. (22)
Diarrhea	0.39	0.27	0.76	Beta	Zhang et al. (23)
Hypertension	0.04	0.03	0.05	Beta	NADEES et al. (31)
Discount rate					
Discount rate	5.00%	0	8.00%	Beta	(15)

reflects the official average central parity rates published by SAFE, thereby minimizing the impact of short-term exchange rate fluctuations."

2.4 Model survival and transition probabilities

The OS and PFS data for both durvalumab and placebo groups were digitally extracted using GetData Graph Digitizer software (version 2.26). These survival curves were subsequently reconstructed and analyzed using R statistical software. To model the time-to-event data, we evaluated multiple parametric survival distributions, including expotional, gamma, gengamma, gompertz, weibull, weibull-PH, log-logistic, and log-normal distributions. Model selection was based on optimal goodness-of-fit criteria, with the final survival function chosen according to the lowest Akaike information criterion (AIC) and Bayesian information criterion (BIC) values (32, 33). Comprehensive model diagnostics are provided in Supplementary Tables 1, 2. The fitted survival curves are presented in Supplementary Figures S1, S2 for visual comparison between the two treatment strategies. The shape (λ) and scale (γ) parameters for the selected survival function were derived directly from the R software (version 4.3.3) output.

2.5 Uncertainty analysis

2.5.1 Sensitivity analysis

To evaluate the robustness of the model outcomes, we conducted both one-way sensitivity analysis and probabilistic sensitivity analysis. The one-way sensitivity analysis identified the most influential parameters, and results were presented in a tornado diagram. Probabilistic sensitivity analysis was then performed by assigning predefined distributions to all parameters and running 1,000 Monte Carlo simulations. The outcomes were illustrated using scatter plots and cost-effectiveness acceptability curves. Together, these analyses revealed that drug price and utility values were the dominant drivers of cost-effectiveness uncertainty, highlighting the importance of these parameters for future policy evaluation.

2.5.2 Scenario analysis

We established three distinct scenarios to simulate changes in benefits under different circumstances. Affected by factors such as medical insurance negotiations and policy support, the prices of innovative drugs included in the medical insurance catalog typically decrease by 10% to 50% through renewal negotiations and dynamic adjustments. This study is based on the average of this reduction range, meaning a further 30% reduction from the original price of durvalumab. Since utility values may vary across different studies and have a significant impact on cost-utility analysis results, this study refers to other relevant literature to modify the utility values for PFS and PD states, thereby further validating the robustness of the model. The adjusted parameters and distributions after changing the utility values are presented in the Table 2. Additionally, to align with the ADRIATIC trial protocol and ensure the accuracy of our cost calculations, we have capped the treatment duration of durvalumab at 24 months. This means that in our cost calculations, we only account for the costs of durvalumab treatment for up to 24 months, as per the trial's specified maximum duration. This approach prevents the overestimation of costs that could arise from assuming treatment beyond the clinically validated timeframe.

Given the suboptimal cost-effectiveness of durvalumab observed in our analysis, we also conducted a threshold price analysis to explore the price at which durvalumab would become cost-effective under different willingness-to-pay (WTP) thresholds. Specifically, we evaluated the cost-effectiveness of durvalumab at both one times (1x) and three times (3x) the WTP threshold. Our analysis aimed to determine the price points at which durvalumab would fall within the commonly accepted cost-effectiveness ratios, thereby providing valuable insights for policymakers and healthcare decision-makers.

2.5.3 Subgroup analysis

The results of the subgroup analysis are presented in Table 3. At a WTP threshold of $12,569.82 per QALY, the subgroup with the highest probability of being cost-effective was the carboplatin-etoposide subgroup in the Previous chemotherapy category, with a cost of $186,589.57 and an ICER of $167,476.98 per QALY. This was followed by the Europe subgroup in the Geographic region category, with a cost of $175,107.56 and an ICER of $181,930.53 per QALY. A similar trend was observed at a WTP threshold of three times the per capita GDP of China.

3 Results

3.1 Base case results

The Table 4 presents the basic case evaluation results of the cost-effectiveness of the two treatment regimens. The total cost for the placebo group is $63,274.61, with a total of 1.80 QALYs; whereas for durvalumab, the total cost amounts to $171,884.05, and the total QALYs reach 2.24. By calculating the ICER, it is determined that an additional expenditure of approximately $245,591.59 is required to gain one extra QALY. Additionally, the NMB was calculated, resulting in -$46,249.06 for the placebo group and -$153,643.40 for the durvalumab group. This indicates that the placebo group yields a higher net benefit compared to durvalumab, as a larger NMB is more favorable. The INMB for durvalumab

TABLE 2 Parameters and distribution of changed utility value.

Utility value	Basis value	Range		Source
		Min	Max	
PFS value	0.86	0.65	0.97	Shen Y et al. (34)
PD value	0.77	0.54	0.80	Shen Y et al. (34)

TABLE 3 CEA results of base-case.

Treatment	Total costs	Total QALYs	Incre costs	Incre QALYs	ICER	NMB	INMB
Placebo group	63,274.61	1.80				-46,249.06	
Durvalumab group	171,884.05	2.24	108,609.45	0.44	245,591.59	-153,643.40	-107,394.34

versus placebo is -$107,394.34, which further demonstrates that the durvalumab group provides a negative incremental net benefit and is not economically advantageous relative to the placebo group. Based on these findings-including the high ICER value, the superior NMB of the placebo group, and the negative INMB-the placebo group is the more cost-effective option at the given WTP threshold implicit in the analysis.

3.2 Results of sensitivity analysis

This deterministic sensitivity analysis, as presented in the results table, demonstrated that among all evaluated parameters, variations in the utility for PFS exerted the most profound influence on model outcomes, with a fluctuation magnitude of $119,119.58 per QALY units between its lower bound ($201,614.41 per QALY) and upper bound ($320,733.99 per QALY), establishing it as the primary sensitivity driver (Figure 2). The cost of durvalumab constituted the second most critical factor, exhibiting a substantial variation of $99,066.78 per QALY units across its tested range ($196,058.29 per QALY - $295,125.06 per QALY), underscoring its pivotal role in cost-effectiveness conclusions. The discount rate ranked third in sensitivity impact, generating a variation of 46,617.70 units ($216,653.60 per QALY - $263,271.29 per QALY), indicating significant temporal effects on economic evaluations. Other parameters-including drug costs, healthcare service costs, progressive disease utility-collectively and etc. induced smaller-scale fluctuations in model outputs.

3.3 Probabilistic sensitivity analysis

In Supplementary Files S3, S4, we have provided the detailed PSA parameter settings and partial results of the Monte Carlo simulations. As shown by the cost-effectiveness scatter plot (Figure 3), all the scatter points are located in the fourth quadrant, indicating that in the treatment of LS-SCLC, the durvalumab treatment regimen, compared with the placebo regimen, can achieve better health outcomes at a higher cost in all simulated scenarios.

Figure 4 showed that when the willingness-to-pay (WTP) threshold was below $37,709.46, the cost-effectiveness probability of placebo was constantly 100%, indicating that it had a significant economic advantage in this range. When the WTP threshold reached or exceeded $130,000.00, the probability of placebo gradually decreased, while the probability of durvalumab increased.

3.4 Expected value of perfect information analysis

Figure 5 demonstrates that the Expected Value of Perfect Information (EVPI) is relatively low at lower WTP thresholds but increases significantly as the WTP approaches $200,000 per QALY, peaking at $6,826.58. This indicates that under high WTP scenarios, the uncertainty in model parameters becomes more critical, highlighting the increased decision risk associated with higher payment thresholds.

TABLE 4 Results of the analysis under different scenarios.

Treatment	Total costs (qalys)	Incre costs (qalys)	ICER	NMB	INMB
Scenario analysis 1: cost value sensitivity results					
Placebo group	63,274.61			-46,512.36	
Durvalumab group	139,025.89	75,751.28	171,291.54	-118,974.78	-72,462.41
Scenario analysis 2: utility value sensitivity results					
Placebo group	(2.47)			-37,184.27	
Durvalumab group	(3.04)	(0.57)	191,017.07	-142,516.19	-105,331.92
Scenario analysis 3: 24 months sensitivity results					
Placebo group	30,143.57			-20,462.27	
Durvalumab group	136,768.70	106,625.13	1,337,187.91	-130,712.35	-110,250.07
Scenario analysis 4: results of value-based pricing analysis					
Durvalumab ($451.28/cycle) group	68,833.41	5,558.81	12,295.73	-46,211.25	156.03
Durvalumab ($1,225.95/cycle) group	79,951.12	16,676.51	36,886.98	-183,759.06	-37,715.96

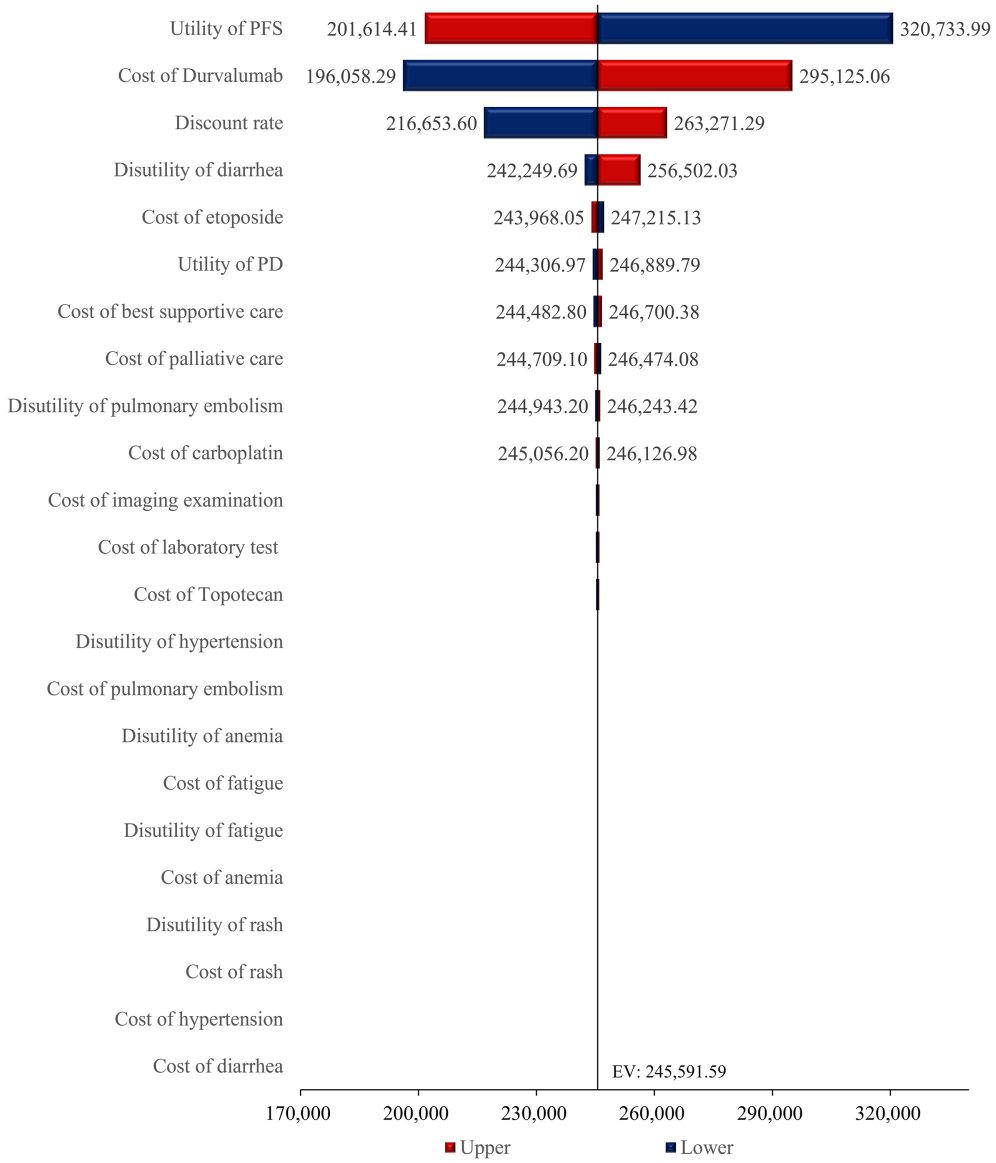


FIGURE 2
Tornado diagram.

3.5 Results of scenario analysis

The results of scenario analysis 1 indicate that under conditions of changing cost values, the cost-effectiveness of the treatment with durvalumab does not change. The durvalumab group also shows improvement in health outcomes compared to the placebo group at a different utility value (lower than 3 times WTP) (Table 4). Scenario analysis 3 indicates that this adjustment does not significantly alter the cost-effectiveness profile of durvalumab, supporting the robustness of our base-case analysis.

Scenario analysis 4: The value-based pricing analysis presented in Table 4 shows that when the ICER of durvalumab is $12,295.73 per QALY, the price of durvalumab per cycle needs to be reduced to $451.28. When the ICER is adjusted to three times the threshold, the price of durvalumab per cycle needs to be reduced to $1,225.95 (Table 4).

3.6 Subgroup analysis

The results of the subgroup analysis are presented in Table 4. At a WTP threshold of $12,569.82 per QALY, the subgroup with the highest probability of being cost-effective was the carboplatin-etoposide subgroup in the Previous chemotherapy category, with a cost of $187,637.23 and an ICER of $175,714.96 per QALY. This was followed by the Europe subgroup in the Geographic region

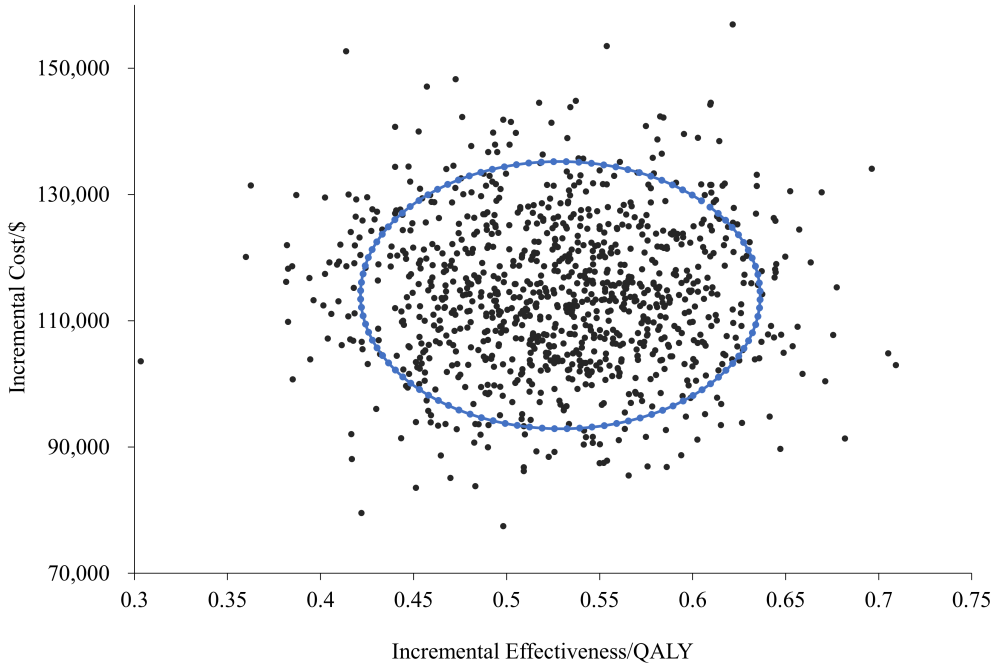


FIGURE 3
Probabilistic sensitivity analysis results of the different treatments.

category, with a cost of $176,166.22 and an ICER of $192,813.78 per QALY. A similar trend was observed at a WTP threshold of three times the per capita GDP of China.

4 Discussion

This study, based on the data from the ADRIATIC Phase III clinical trial, constructed a Markov model adapted to the Chinese health economic context to systematically evaluate the cost-effectiveness of durvalumab as consolidation therapy for LS-SCL following concurrent chemoradiotherapy. The results indicate that although durvalumab significantly prolonged patients' PFS and OS, and increased QALYs, its ICER is much higher than the widely accepted willingness-to-pay threshold, suggesting poor cost-effectiveness under the current pricing strategy and potentially limiting its widespread clinical application in China.

Further sensitivity analysis revealed that drug costs, health utility values, and discount rates are the key parameters affecting the model outcomes. Among them, fluctuations in the price of durvalumab were most sensitive to changes in ICER, demonstrating that drug pricing remains the core factor constraining its cost-effectiveness. Additionally, variations in the upper and lower limits of PFS utility values also had a significant impact on the results, indicating that improvements in quality of life are equally important for enhancing cost-effectiveness.

Notably, the probabilistic sensitivity analysis results showed that the cost-effectiveness advantage of durvalumab is significantly dependent on a higher WTP threshold. When the willingness-to-pay is below $150,000 per QALY, the probability of its cost-effectiveness is close to zero; even with a high payment threshold, although there is some improvement, it remains significantly lower than that of the placebo group. This trend suggests that durvalumab is more suitable for healthcare systems with stronger payment capabilities or for specific high-value patient groups who are extremely sensitive to survival benefits. In contrast, the placebo maintains a strong cost-effectiveness advantage under conventional payment standards.

Moreover, the EVPI analysis indicated that model uncertainty sharply increases in the high willingness-to-pay range, implying that if payment standards are further raised in the future, there will be a greater risk of resource allocation. Therefore, it is necessary to conduct more in-depth research on the sensitivity parameters under high willingness-to-pay scenarios (such as long-term survival data and drug cost structure) to reduce potential losses caused by uncertainty and provide more robust evidence for health insurance policy formulation.

Our study has the following limitation. Although the comparator we selected is consistent with the ADRIATIC trial, differences in real-world practice, such as the use of PCI and follow-up imaging, may affect the generalizability of our study results. To better assess the impact of these differences on cost-effectiveness, future studies could consider incorporating these real-world practices into the analysis to more comprehensively reflect the actual effects in clinical practice.

In summary, although the overall cost-effectiveness is currently insufficient, it may still be possible to improve the cost-effectiveness and accessibility of durvalumab under certain conditions through

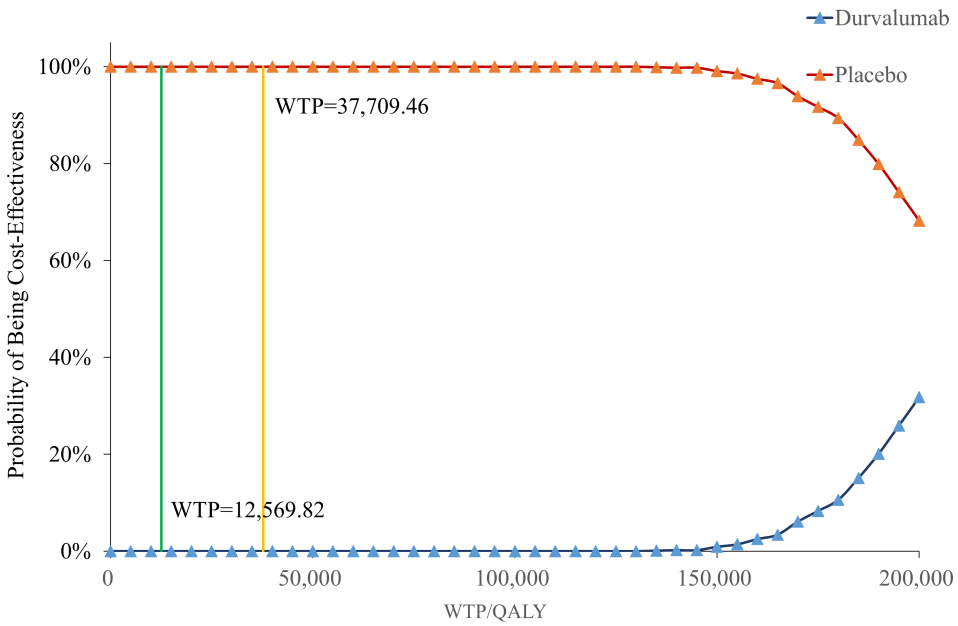


FIGURE 4
Cost-effectiveness acceptability curve.

subgroup strategies targeting high-risk patients or the introduction of price optimization mechanisms (such as risk-sharing agreements).

5 Conclusion

This study demonstrates that durvalumab, as consolidation therapy for limited-stage small cell lung cancer following concurrent chemoradiotherapy, has clear survival benefits and improvements in health-related quality of life. However, its cost-effectiveness remains inadequate under the current pricing system and payment capacity. The core influencing factors include drug pricing, health utility, and uncertainty in long-term efficacy data.

Future policies could consider optimizing the cost structure through differentiated health insurance payment strategies, price negotiation mechanisms, and risk-sharing models, while also strengthening the collection and assessment of real-world efficacy and cost data to further clarify its applicable scenarios within the Chinese healthcare system. Only by achieving a balance between

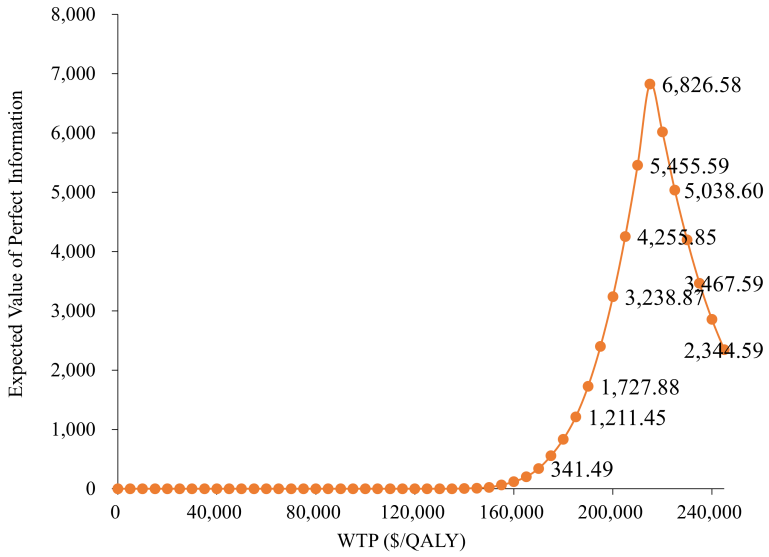


FIGURE 5
Expected value of perfect information.

clinical value and economic burden can durvalumab truly realize its widespread application in the treatment of limited-stage small cell lung cancer.

Author contributions

HZ: Writing – review & editing, Funding acquisition. BC: Methodology, Writing – review & editing, Formal Analysis, Writing – original draft, Investigation, Supervision, Software, Visualization, Funding acquisition, Validation, Resources, Project administration, Conceptualization, Data curation. YL: Methodology, Validation, Supervision, Data curation, Writing – review & editing, Project administration, Formal Analysis, Software. MW: Validation, Writing – review & editing, Supervision. HL: Writing – review & editing, Methodology. HW: Validation, Supervision, Writing – review & editing.

Funding

The author(s) declare financial support was received for the research and/or publication of this article. General Project of Humanities and Social Science Research for the Ministry of Education in 2022 (No.22YJAZH147); Research team of Pharmacoeconomics and Health Technology Evaluation, Guangdong Pharmaceutical University (2024ZZ13); The 2023 General Project for the Development of Philosophy and Social Sciences during the 14th Five-Year Plan in Guangzhou (No. 2023GZYB68); General Project for Planning Philosophy and Social Sciences in Guangdong Province in 2024 (No.GD24CGL29); Guangdong University Innovation Team Project (No.2022WCXTD011).

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The author(s) declare that no Generative AI was used in the creation of this manuscript.

Any alternative text (alt text) provided alongside figures in this article has been generated by Frontiers with the support of artificial intelligence and reasonable efforts have been made to ensure accuracy, including review by the authors wherever possible. If you identify any issues, please contact us.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fonc.2025.1643022/full#supplementary-material

References

1. Segal BH, Freifeld AG, Baden LR, Brown AE, The AS. Prevention and treatment of cancer-related infections. *J Natl Compr Cancer Network Jnccn*. (2008) 6:122–74. doi: 10.1002/jso.23193

2. Vuko M, Segerer F, Xie M, Azqueta Gavaldon M, Spitzmüller A, Hessel H, et al. 1505Spatial profiling of the SCLC tumor microenvironment defined by high MHC-I expression reveals association with functionally relevant antigen presentation. *J Immunotherapy Cancer*. (2023) 11:1. doi: 10.1136/jitc-2023-SITC2023.1505

3. Lee JH, Saxena A, Giaccone G. Advancements in small cell lung cancer. *Semin Cancer Biol*. (2023) 93:123–8. doi: 10.1016/j.semcancer.2023.05.008

4. Tempero MA, Malafa MP, Al-Hawary M, Behrman SW, Benson AB, Cardin DB, et al. Pancreatic adenocarcinoma, version 2.2021, NCCN clinical practice guidelines in oncology. *J Natl Compr Canc Netw*. (2021) 19:439–57. doi: 10.6004/jnccn.2021.0017

5. Horn L, Mansfield AS, Szczęsna A, Havel L, Krzakowski M, Hochmair MJ, et al. First-line atezolizumab plus chemotherapy in extensive-stage small-cell lung cancer. *N Engl J Med*. (2018) 379:2220–9. doi: 10.1056/NEJMoa1809064

6. Paz-Ares L, Dvorkin M, Chen Y, Reinmuth N, Hotta K, Trukhin D, et al. Durvalumab plus platinum-etoposide versus platinum-etoposide in first-line treatment of extensive-stage small-cell lung cancer (CASPIAN): a randomised, controlled, open-label, phase 3 trial. *Lancet*. (2019) 394:1929–39. doi: 10.1016/S0140-6736(19)32222-6

7. Bellmunt J, Paz-Ares L, Cuello M, Cecere FL, Albiol S, Guillem V, et al. Gene expression of ERCC1 as a novel prognostic marker in advanced bladder cancer patients receiving cisplatin-based chemotherapy. *Ann Oncol*. (2007) 18:522–8. doi: 10.1093/annonc/mdl435

8. Paz-Ares L, Dvorkin M, Chen Y, Reinmuth N, Hotta K, Trukhin D. Durvalumab plus platinum–etoposide versus platinum–etoposide in first-line treatment of extensive-stage small-cell lung cancer (CASPIAN): a randomised, controlled, open-label, phase 3 trial. *Lancet*. (2019) 394:1929–39. doi: 10.1016/S0140-6736(19)32222-6

9. Johnson ML, Cho BC, Luft A, Alatorre-Alexander J, Geater SL, Laktionov K, et al. Durvalumab with or without tremelimumab in combination with chemotherapy as first-line therapy for metastatic non-small-cell lung cancer: the phase III POSEIDON study. *J Clin Oncol*. (2023) 41:1213–27. doi: 10.1200/JCO.22.00975

10. Antonia SJ, Villegas A, Daniel D, Vicente D, Murakami S, Hui R, et al. Durvalumab after chemoradiotherapy in stage III non-small-cell lung cancer. *N Engl J Med*. (2017) 377:1919–29. doi: 10.1056/NEJMoa1709937

11. Heymach JV, Harpole D, Mitsudomi T, Taube JM, Galffy G, Hochmair M, et al. Perioperative Durvalumab for Resectable Non-Small-Cell Lung Cancer. *N Engl J Med*. (2023) 389(18):1672–84. doi: 10.1056/NEJMoa2304875

12. Heymach JV, Harpole D, Reck M. Perioperative durvalumab for resectable non-small-cell lung cancer. *N Engl J Med*. (2024) 390:287–8. doi: 10.1056/NEJMc2313778

13. Cheng Y, Spigel DR, Cho BC, Laktionov KK, Fang J, Chen Y, et al. Durvalumab after chemoradiotherapy in limited-stage small-cell lung cancer. *N Engl J Med*. (2024) 391:1313–27. doi: 10.1056/NEJMoa2404873

14. National Healthcare Security Administration (NHSA) Official Website. *Release and Interpretation of the National Reimbursement Drug List* . Available online at: http://www.nhsa.gov.cn (Accessed June 1, 2025).

15. Liu G. China guidelines for pharmacoeconomic evaluations 2020: T/CPHARMA 003-2020. *Introduction to the Guidelines for Pharmacoeconomic Evaluation in China*. Beijing: China Market Press (2022) 2022:25–27

16. State Administration of Foreign Exchange. RMB central exchange rate(2024). Available online at: https://www.safe.gov.cn/safe/rmbhlzjj/index.html (Accessed November 7, 2024).

17. National Healthcare Security Administration. *National Reimbursement Drug List* . NRDL. Available online at: http://www.nhsa.gov.cn (Accessed June 1, 2025).

18. National Health Commission. Diagnosis-related groups (DRG) tariffs. (2023).

19. Yue P, Zhang M, Feng Y, Gao Y, Sun C, Chen P. Cost-effectivenessanalysis of amivantamab plus chemotherapy versus chemotherapy alone in NSCLwith EGFR Exon 20 insertions. *Front Oncol*. (2024) 14:1368804. doi: 10.3389/fonc.2024.1368804

20. Zhang H, Li Y, Liu Y, Li H, Wang H. Cost-effectiveness analyses of amivantamab plus lazertinib and lazertinib versus osimertinib in non-small cell lung cancer with EGFR mutations. *Front Pharmacol*. (2025) 16:1527614. doi: 10.3389/fphar.2025.1527614

21. Qi R, Nie XY, Liu XT, Gao S, Liu. Pharmacoeconomic evaluation of serplulimab combined with chemotherapy regimens for the first-line treatment of extensive-stage small-cell lung cancer. *China Pharm*. (2023) 34:1368–73. doi: 10.6039/j.issn.1001-0408.2023.11.16

22. Georgieva M, Lima JPN, Aguiar P Jr, Lopes GL Jr, Haaland B. Cost-effectiveness of pembrolizumab as first-line therapy for advanced non-small cell lung cancer. *Lung Cancer*. (2018) 124:248–54. doi: 10.1016/j.lungcan.2018.08.018

23. Zhang C, Zhang H, Shi J, Wang D, Zhang X, Yang J, et al. Trial-based cost-utility analysis of icotinib versus gefitinib as second-line therapy for advanced non-small cell lung cancer in China. *PLoS One*. (2016) 11:e0151846. doi: 10.1371/journal.pone.0151846

24. Guan HJ, Liu G, Xie F, Sheng Y, Shi L. Cost-effectiveness of osimertinib as a second-line treatment in patients with EGFR-mutated advanced non-small cell lung cancer in China. *Clin Ther*. (2019) 41:2308–20. doi: 10.1016/j.clinthera.2019.09.008

25. Kang S, Wang X, Zhang Y, Zhang B, Shang F, Guo W. First-line treatments for extensive-stage small-cell lung cancer with immune checkpoint inhibitors plus chemotherapy: A network meta-analysis and cost-effectiveness analysis. *Front Oncol*. (2022) 11:740091. doi: 10.3389/fonc.2021.740091

26. Zhou K, Wen F, Zhang P, Zhou J, Zheng H, Sun L, et al. Cost-effectiveness analysis of sensitive relapsed small-cell lung cancer based on JCOG0605 trial. *Clin Transl Oncol*. (2018) 20:768–74. doi: 10.1007/s12094-017-1787-y

27. Nafees B, Stafford M, Gavriel S, Bhalla S, Watkins J. Health state utilities for non small cell lung cancer. *Health Qual Life Outcomes*. (2008) 6:84. doi: 10.1186/1477-7525-6-84

28. Zhang X. Pharmacoeconomic evaluation of adebrelimab combined with chemotherapy as first-line treatment for extensive-stage small cell lung cancer. *Anhui Univ Traditional Chin Med*. (2025) 2025. doi: 10.26922/d.cnki.ganzc.2025.000383

29. Ward MC, Shah C, Adelstein DJ, Geiger JL, Miller JA, Koyfman SA, et al. Costeffectiveness of nivolumab for recurrent or metastatic head and neckcancer. *Oral Oncol*. (2017) 74:49–55. doi: 10.1016/j.oraloncology.2017.09.017

30. Liu W, Huo G, Chen P. First-line tremelimumab plus durvalumab and chemotherapy versus chemotherapy alone for metastatic non-small cell lung cancer:a cost effectiveness analysis in the United States. *Front Pharmacol*. (2023) 14:1163381. doi: 10.3389/fphar.2023.1163381

31. Nafees B, Lloyd AJ, Dewilde S, Rajan N, Lorenzo M. Health state utilities in non-small cell lung cancer:an international study. *Asia Pac J Clin Oncol*. (2017) 13:e195–203. doi: 10.1111/ajco.12477

32. Hoyle MW, Henley W. Improved curve fits to summary survival data: application to economic evaluation of health technologies. *BMC Med Res Method*. (2011) 11:1–14. doi: 10.1186/1471-2288-11-139

33. Guyot P, Ades AE, Ouwens MJNM, Welton NJ. Enhanced secondary analysis of survival data: reconstructing the data from published Kaplan-Meier survival curves. *BMC Med Res Method*. (2012) 12:9. doi: 10.1186/1471-2288-12-9

34. Shen Y, Wu B, Wang X, Zhu J. Health state utilities in patients with advanced non-small-cell lung cancer in China. *J Comp Eff Res*. (2018) 7:443–52. doi: 10.2217/cer-2017-0069

Glossary

SCLC	Small cell lung cancer	NMPA	The National Medical Products Administration
LS-SCLC	Limited-stage small cell lung cancer	NHSA	The National Healthcare Security Administration
ES-SCLC	Extensive-stage small cell lung cancer	PD	Progressive disease
OS	Overall survival	ICER	Incremental cost-effectiveness ratio
PFS	Progression-free survival	QALYs	Quality-adjusted life-years
mNSCLC	Non-small cell lung cancer	EVPI	Expected value of perfect information
EFS	Event-free survival	Lys	Life years
pCR	Pathological complete response rate	BSC	Best supportive care

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 06 November 2025
DOI 10.3389/fpubh.2025.1674081

Check for updates

OPEN ACCESS

EDITED BY
Jing Yuan,
Fudan University, China

REVIEWED BY
Chun Xia,
Anhui Normal University, China
Chunyang Wang,
Ludong University, China

*CORRESPONDENCE
Fan Yang
6020050038@jsnu.edu.cn
Zhiqing Hu
huzhiqing@njmu.edu.cn
Yuan He
heyuan@njmu.edu.cn

RECEIVED 27 July 2025
ACCEPTED 20 October 2025
PUBLISHED 06 November 2025

CITATION
Zhao Y, Zhang Z, He Y, Gu Z, Yang F, Hu Z and He Y (2025) Determinants of primary care physicians' intention to provide breast cancer screening services for rural women: a structural equation model based on the theory of planned behavior.
Front. Public Health 13:1674081.
doi: 10.3389/fpubh.2025.1674081

COPYRIGHT
© 2025 Zhao, Zhang, He, Gu, Yang, Hu and He. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

Determinants of primary care physicians' intention to provide breast cancer screening services for rural women: a structural equation model based on the theory of planned behavior

Yinren Zhao[1], Zixuan Zhang[2,3], Yubai He[4], Zixin Gu[2,3], Fan Yang[5]*, Zhiqing Hu[2,3,6]* and Yuan He[2,3,6,7]*

[1]School of Law and Public Administration, Nanjing University of Information Science & Technology, Nanjing, China, [2]Institute of Medical Humanities, Nanjing Medical University, Nanjing, China, [3]School of Marxism, Nanjing Medical University, Nanjing, China, [4]School of Health Policy & Management, Nanjing Medical University, Nanjing, China, [5]School of Education Science, Jiangsu Normal University, Xuzhou, China, [6]School of Public Health, Nanjing Medical University, Nanjing, China, [7]Laboratory for Digital Intelligence & Health Governance, Nanjing Medical University, Nanjing, China

Background: Breast cancer has been a serious health problem worldwide. Early detection is undoubtedly effective in combating severe public health problems in developing countries. Meanwhile, primary care physicians play an important role in implementing screening programs. The objective of our study was to evaluate the determinants of primary care physicians' intention to provide the breast cancer screening services (BCSs) for rural women.
Methods: We conducted a cross-sectional survey in 24 towns in Jiangsu Province. A total of 1,101 primary care physicians participated in and completed the study. The data collection tool was developed based on the theory of planned behavior (TPB), which includes attitude, subjective norms, and perceived behavioral control, as well as extended components including knowledge of BCSs and past providing-BCSs behavior.
Results: The results of our study showed that subjective norms (β = 0.352, $p < 0.001$) had the strongest influence on primary care physicians' intention to engage in breast cancer screening, followed by attitudes and perceived behavioral control. Both screening knowledge and past screening provision behavior had an indirect effect on behavioral intentions.
Conclusion: The present study demonstrated that extended TPB is an effective model for explaining primary care physicians' intention to engage in breast cancer screening programs. Meanwhile, our findings provide a reference for governments, hospitals and policies aiming to increase primary care physicians' intention to provide rural women with BCSs.

KEYWORDS

breast cancer, primary care physicians, theory of planned behavior (TPB), intention, structural equation modeling

Introduction

Cancer is a major public health, societal, and economic problem in the 21st century, responsible for almost one in six deaths (16.8%) worldwide (1). Breast cancer is the most common and leading cause of death among women (2). According to recent global cancer burden data, breast cancer accounted for 2.3 million new cases in 2022. In China, the largest developing nation, the increase in breast cancer incidence has outpaced the global average since the 1990s, growing at more than twice the global average rate (3). Data from the National Cancer Center (NCC) of China indicate that in 2022, the number of new breast cancer cases among women reached 357,200, making breast cancer the second most common cancer among women (4). The situation is particularly alarming in rural areas, where the age-standardized incidence rate (ASIR) is rising at an annual rate of approximately 6.9%, and the age-standardized mortality rate (ASMR) at about 2.7%, both significantly higher than rates in urban areas (5). These disparities underscore the urgent need for enhanced breast cancer early, diagnosis, and treatment efforts, particularly in rural areas, to address the growing burden and challenges.

Early screening plays a vital role in improving treatment outcomes and prognosis. It not only reduces the incidence and mortality of breast cancer but also enhances the quality of care for women (6). Population-based screening programs have been implemented in many developed countries over the last few decades, leading to significant reductions in mortality and advanced cancer rates (7–9). In China, a national breast cancer screening (BCS) program was launched in 2009 to provide screening services for women aged 35–64. However, despite these efforts, many rural women remain inadequately screened. Chinese epidemiological data indicate that, as of 2019, only 22.3% of women aged 20 years and older and 30.9% of women aged 35–64 had ever undergone breast cancer screening, rates lower than those reported in developed countries (10). Moreover, women with lower socioeconomic status exhibited even lower screening participation. Women aged 20 and above in urban areas had a screening rate of 24.6%, compared to just 15.0% in rural regions (11). The substantial gap between current screening rates and national targets highlights the urgent need to strengthen rural women's willingness to participate in BCS and to improve their overall health outcomes in China. Primary care physicians, as primary providers of breast cancer screening services (BCSs), play a critical role in improving screening rates. Research suggests that the level of knowledge, attitudes, and encouragement provided by primary care physicians are significant factors in women's willingness to undergo BCS (12, 13). Additionally, primary care physicians' recommendations and knowledge also significantly influence rural women's understanding and willingness to participate in screening programs (14, 15). These studies suggest that exploring primary care physicians' involvement could be a potential approach to enhancing BCS rates. Previous studies aimed at increasing BCS rates have mainly focused on individuals receiving these services. Most research has examined women's intentions to participate in BCS (16, 17). Existing studies have explored primary care physicians' willingness to participate in colorectal, breast, and cervical cancer screening and have identified factors such as knowledge, attitudes, and time constraints as key determinants of provider participation (18, 19). However, few investigations have specifically examined the intentions of primary care providers in rural China to offer breast cancer screening for women. Therefore, this study will apply the theory of planned behavior (TPB) to examine the predictors of primary care physicians' intentions to provide BCSs for rural women. This focus on providers offers a novel perspective on strategies to enhance screening rates.

TPB, introduced by Ajzen in 1985, is a widely applied social cognitive theory (68). It provides a robust model for predicting and understanding individual behavior across various fields (20, 21). TPB has proven particularly effective in studying healthcare professionals' behaviors. It has been validated as a useful framework for examining factors that influence physicians' referral practices and healthcare workers' job-seeking decisions (22, 23). The theory of planned behavior (TPB) has been widely applied to examine individuals' breast cancer screening behaviors (24, 25). Building upon this theoretical foundation, the present study employs the TPB framework to investigate the determinants of primary care physicians' intentions to provide BCSs. The objective of this study is to investigate the determinants of primary care physicians' intention to offer BCSs and to propose corresponding policy recommendations to strengthen their participation.

Research model and hypothesis development

The current study established a research model (Figure 1) of primary care physicians' provision of BCS for rural women in China, based on the TPB. TPB is extensively used in predicting and explaining an individual's behavior under specific conditions. It has demonstrated its effectiveness in anticipating the intentions of various healthcare professionals, including clinicians (26), pharmacists (27), and nurses (28), to provide medical services. In addition, prior meta-analyses and empirical research have indicated that the TPB demonstrates stronger explanatory capacity and clearer conceptual distinctions than alternative psychological models, including the health belief model (HBM) and the theory of reasoned action (TRA) (29, 30). According to TPB, an individual's intention is determined by three key factors: attitude toward the behavior (A), subjective norms (SN), and perceived behavioral control (PBC) (31, 32). Moreover, SN can affect attitude and PBC, thus indirectly affecting individual's intentions (see Figure 2).

Attitude refers to an individual's stable assessment and stance regarding a particular behavior. It can be influenced by strength and belief (b) as well as evaluation (e). It can be quantified by their multiplication, expressed by the equation: $AB \propto \sum b_i e_i$ (where i represents the measurement project) (31, 32). Similarly, SN refer to the belief that people will approve of and support a particular behavior, which can be determined by normative beliefs (n) and motivation to comply (m). The equation is as follows: $SN \propto \sum n_i m_i$. Moreover, PBC refers to the extent to which one assesses the difficulty of conducting a specific behavior, which is determined by two distinct factors: control beliefs (c) and perceived power (p). The corresponding equation is: $PBC \propto \sum c_i p_i$.

In this study, attitude refers to primary care physician' evaluation of providing BCSs. According to the TPB, A is an important factor that influences an individual' s intentions and subsequent behavior. Physicians' intention to provide BCSs is likely to increase if they perceive it as fulfilling personal values, achieving a sense of

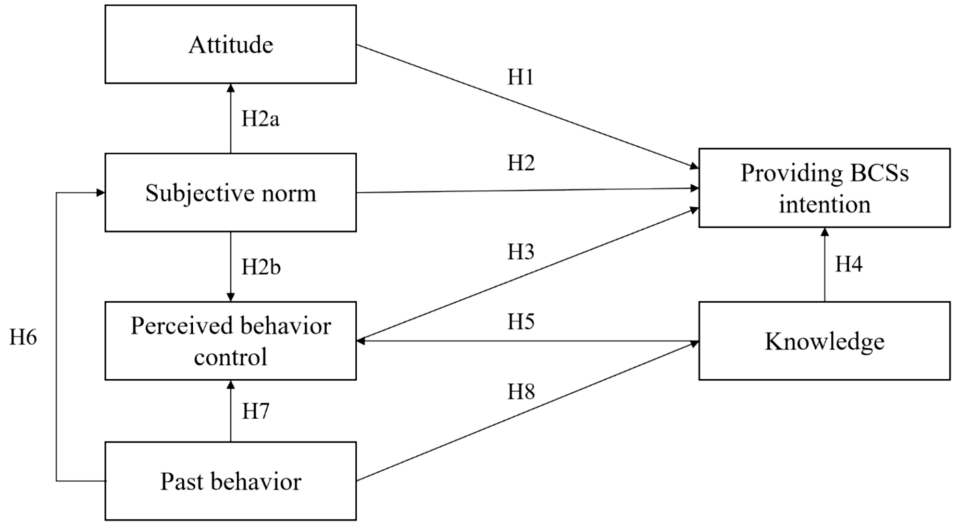


FIGURE 1
The research model of primary care physicians' providing BCSs intention.

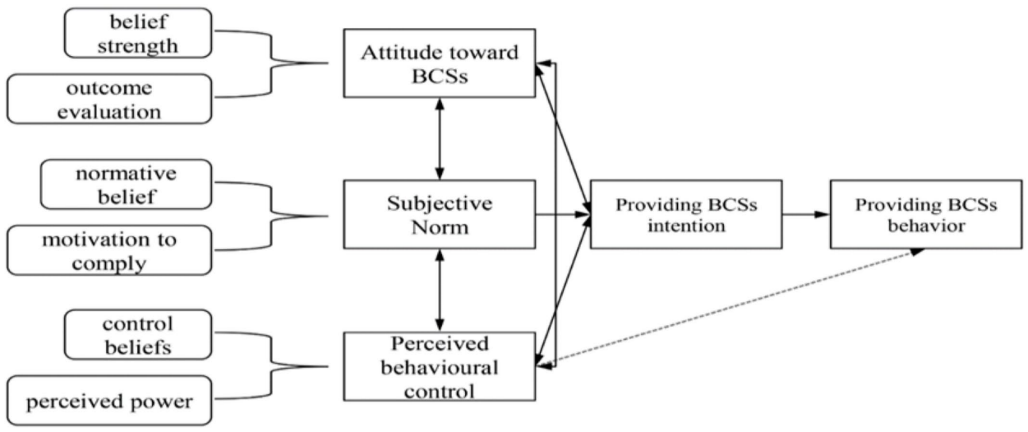


FIGURE 2
A structural model of the theory of planned behavior.

accomplishment, or recognizing the critical importance of BCS. For instance, Allenbaugh et al. (33) indicated positive attitudes among nurses and residents toward their interactions can significantly enhance the quality of care. Based on this, we propose the following hypothesis:

> Hypothesis 1: Attitude is positively correlated with primary physicians' intention to provide BCSs.

SN refer to the perceived expectations and support of relevant social referents, including colleagues, supervisors, and patients, concerning primary care physicians' engagement in BCS. Previous study has revealed that SN can directly influence physicians' intentions to provide BCSs (22, 34). Meanwhile, it can also influence their intentions indirectly by affecting their attitudes and PBC (35, 36). For instance, encouragement and support from hospital leaders, nurses, and colleagues may positively influence physicians' attitudes toward BCS, alleviate perceived challenges in providing BCSs, and further enhance their motivation. Therefore, we propose the following hypotheses:

> Hypothesis 2: SN influences primary physicians' intention positively and directly.
>
> Hypothesis 2a: The more SN primary physicians perceive, the more positive their attitude becomes.
>
> Hypothesis 2b: SN significantly affects the PBC of primary physicians during their attempt to provide BCSs.

In this study, PBC refers to primary care physicians' perceptions of how easy or difficult it is to provide BCSs, including factors such as the availability of equipment and their own level of technical proficiency. Generally, physicians with greater access to resources and better training tend to feel more confident, enhancing their PBC. According to the TPB, PBC is significantly related to an

individual's intention. Previous research has also shown that PBC effectively predicts physicians' intentions to provide medical services (34, 37). Consequently, we propose the following hypothesis:

> Hypothesis 3: PBC positively and directly influences primary care physicians' intention to provide BCSs.

The predictive utility of the TPB has been shown to improve when additional variables are integrated into the model (38, 39). Additionally, past behavior (PB) and knowledge have been incorporated into the TPB model in health-related studies, supporting their inclusion as variables to enhance the predictive power of TPB (40–42). Among primary care physicians, knowledge of BCS may indirectly influence their behavioral intentions through PBC and attitude. Greater knowledge enhances awareness of the benefits of screening, fostering a more positive attitude toward its provision. Moreover, prior experience with screening helps physicians build procedural familiarity, improving their perceived competence and reducing the perceived difficulty of the task. Such experience may also increase understanding among significant others, thereby enhancing the social support physicians receive when delivering screening services. Consequently, we propose the following hypotheses:

> Hypothesis 4: Knowledge of BCS directly and positively influences primary care physicians' attitudes toward BCSs.
>
> Hypothesis 5: Knowledge of BCS directly and positively influences primary care physicians' PBC regarding providing BCSs.
>
> Hypothesis 6: Primary care physicians' PB in providing BCSs influences their SN.
>
> Hypothesis 7: Primary care physicians' PB in providing BCSs influences their PBC.
>
> Hypothesis 8: Primary care physicians' PB in providing BCSs influences their knowledge of BCSs.

Materials and methods

Participants and data collection

This cross-sectional study was conducted from March 30 to June 1, 2020. A multi-stage stratified cluster sampling method was used to select participants. In the first stage, Jiangsu Province was chosen as the primary sampling unit. Six prefecture-level cities—Lianyungang, Yancheng, Yangzhou, Nanjing, Changzhou, and Wuxi—were selected based on geographic location, socioeconomic status, and distribution of healthcare resources. In the second stage, two rural townships were selected from each city using probability proportional to size (PPS) sampling, resulting in a total of 12 townships. All maternal and child health institutions, community health service centers, health stations, township hospitals, and village clinics within these townships were included as survey sites. In the third stage, primary care physicians at these sites were recruited as study participants. Inclusion criteria required participants to be licensed healthcare professionals with prior experience in providing breast cancer screening (BCS). Exclusion criteria applied to physicians who were ill or otherwise unable to respond. Participants were first recruited through local primary health care centers. Those who consented to take part completed the study in meeting rooms at the respective centers. The research team consisted of trained graduate students. Before the formal experiment, trained investigators distributed paper questionnaires to all participants and explained the study objectives. Upon completing the questionnaire, each participant received a small gift valued at approximately 20 RMB. The required minimum sample size was estimated using Raosoft,[1] assuming a 95% confidence level, a 5% margin of error, and a 50% response distribution, resulting in a recommended sample size of 384.

Questionnaire

The development of the questionnaire for this study followed a systematic process to ensure accuracy and validity. Based on our hypothesized model, we referred to existing literature (24, 30), utilized multiple tools to enhance the study, and refined our questionnaire. To ensure accurate representation of theoretical constructs (A, SN, PBC, PB, knowledge and intention) in the instrument, a pilot study was conducted by a panel comprising two experienced quantitative researchers and thirty primary care physicians. The panel reviewed the draft questionnaire and provided feedback to enhance its validity. Based on their suggestions, we revised the wording and phrasing of several items to improve clarity and comprehensibility. The finalized questionnaire comprises two sections:

(1) Demographic and sociological characteristics, including gender, monthly income, and educational background; (2) Intention to provide BCSs, assessed through six subscales. Contained five subscales: attitude toward BCSs, SN, PBC, behavioral intention to provide BCSs, PB and knowledge level of BCSs. The questionnaire was constructed as follows:

Attitude subscale

This subscale consisted of behavioral intention (3 items) and related outcome evaluations (3 items). These items measured three key aspects: Primary care providers' perceived value of the screening work, satisfaction with performing screening tasks, and sense of accomplishment derived from engaging in screening activities. Respondents rated each item on a five-point Likert scale, where higher scores indicated a more positive attitude toward BCSs.

Subjective norm subscale

SN was calculated by multiplying the measures of normative beliefs (3 items) and motivation to comply (3 items). Respondents rated the perceived level of support from supervisors, colleagues, and visiting women using a five-point rating scale. Higher scores were strongly correlated with a higher SN.

Perceived behavioral control subscale

PBC refers to the perception of hindering or facilitating factors and reflects the personal resources enabling primary care physicians to engage in BCSs. The scale assessed elements such as the effectiveness of hospital equipment, workload, salary, and professional skills. Respondents rated PBC on a five-point Likert scale, where higher

1 http://www.raosoft.com/samplesize.html

scores indicated greater PBC among primary care physicians in performing BCSs.

Behavioral intention subscale

Behavioral intention (BI) toward BCSs was measured by three items: "I plan to provide BCSs for rural women" "I am willing to provide BCSs for rural women" and "I try to provide BCSs for rural women." The response scale ranged from 1 (strongly disagree) to 5 (strongly agree), with higher scores indicating a stronger intention among physicians to participate in BCSs programs.

Knowledge subscale

The BCS Knowledge Index was developed to assess primary care physicians' understanding of BCS. The knowledge scale assessed participants' understanding of breast cancer and breast cancer screening, including the correct technique for breast self-examination, the appropriate sequence of palpation, and the identification of population groups requiring histopathological examination, among other related topics. It comprised six items, each scored 1 for a correct response and 0 for an incorrect one. The total score, obtained by summing the item scores, ranged from 0 to 6, with higher scores reflecting greater knowledge of BCS among primary care physicians.

Past behavior subscale

Four items were used to measure primary care physicians' past engagement in BCSs. These items evaluated their experience with conducting clinical examinations, performing mammography and ultrasonography, and providing preventive education to rural women. The response scale ranged from 1 (strongly disagree) to 5 (strongly agree), with higher scores reflecting more extensive experience in providing BCSs for rural women.

Data and statistical analysis

The database was created using EpiData version 3.1. Initially, all data were analyzed using descriptive statistics and exploratory factor analysis in SPSS version 23.0 (IBM Corp., Armonk, NY, USA). The model was constructed using exploratory factor analysis, and correlations between variables were assessed through the Kaiser–Meyer–Olkin (KMO) test and Bartlett's spherical test. Confirmatory factor analysis (CFA) was subsequently performed using structural equation modeling (SEM) to assess the model's reliability and stability. Finally, Amos version 23.0 (IBM SPSS Amos, Armonk, NY, USA) was used to fit the hypothetical research model and analyze relationships between variables through the maximum likelihood estimation (MLE) method, with statistical significance set at $p < 0.05$.

Ethics approval

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Sir Run Run Hospital, Nanjing Medical University (Protocol code: 2019-SR-017; approved on August 19, 2019). Informed consent details were provided on the first page of the questionnaire. Participants completed the questionnaire after giving informed consent. All responses were collected anonymously.

Results

Sample characteristics

A total of 1,205 questionnaires were distributed, and 1,101 valid responses were collected, resulting in a valid response rate of 91.37%. Questionnaires with extreme data were excluded. According to the recommendation by Bagozzi and Yi (43), the sample size meets the requirements for subsequent structural equation modeling analysis. The sample composition is shown in Table 1. The majority of respondents were female (90.7%), whereas only 9.3% were men. Most primary healthcare providers reported relatively low-income levels, with only 12.4% earning more than 8,000 RMB per month. In terms of educational attainment, the majority (62.5%) held a bachelor's degree. A substantial proportion (79.8%) were employed at community health service centers or township health centers.

Descriptive analysis

The results of the descriptive analysis were presented in Table 2. Primary care physicians in this study demonstrated a generally favorable attitude toward providing BCSs to rural women, the average mean score of variable attitude was 18.79 ± 4.53 (range: 5–25). However, participants reported limited support from colleagues, patients, and leaders during their daily practice of BCSs (mean = 17.00, SD = 3.94, score ranging from 5 to 25). Moreover, their PBC over engaging in BCSs was relatively low (mean = 11.18, SD = 3.76, score

TABLE 1 Demographics and relevant characteristics of participants.

Demographic variables	Frequency (N)	Percentage (%)
Gender		
Male	102	9.3
Female	999	90.7
Monthly income (RMB)		
≤3,000	112	10.2
3,000—5,000	373	33.9
5,000—8,000	479	43.5
≥8,000	137	12.4
Level of education		
Master and doctor	27	2.5
Bachelor	688	62.5
Associate degree	297	27
Others	89	8.1
Type of hospital		
Township health center	431	39.1
Village clinic	76	6.9
Rural community health center	448	40.7
Rural maternal and child health center	91	8.3
Other	55	5

10.3389/fpubh.2025.1674081

TABLE 2 The result of descriptive statistics.

Variable	Mean ± SD	Range
Attitude	18.79 ± 4.53	5–25
Subjective norm	17.00 ± 3.94	5–25
Perceived behavioral control	11.18 ± 3.76	5–25
Intention	4.07 ± 0.63	1–5
Knowledge of BCSs	3.93 ± 1.28	0–6
Past behavior	12.43 ± 3.70	4–20

ranging from 5 to 25). Despite these challenges, the study revealed that primary care physicians exhibited a relatively high intention to provide BCSs for rural women (mean = 4.07, SD = 0.63, score ranging from 1 to 5) and demonstrated a good knowledge level of BCSs, with a mean score of 3.93 ± 1.28 (range: 0–6). However, their experience in providing BCSs for rural women was relatively limited, with a mean score of 12.43 ± 3.70 (range: 4–20).

Instrument reliability and validity

SPSS 23.0 was employed to perform exploratory factor analysis on the collected data to verify the validity and reliability of the questionnaire. We conducted both exploratory factor analysis (EFA) and confirmatory factor analysis (CFA). The sample was randomly divided into two groups, and half of the original data (N = 550) was used to perform the EFA. Factor analysis was first conducted. The Kaiser-Meyer-Olkin (KMO) value was 0.848 > 0.5, the approximate chi-square value of Bartlett's test of sphericity was 4438.024, and the significance probability was less than 0.001. These results indicate that the data were highly suitable for factor analysis (44). Principal component analysis was applied to extract common factors, and the maximum variance orthogonal rotation method was employed for data analysis. Four common factors with characteristic root exceeding 1 were extracted, with a cumulative contribution rate of 77%. The factor loadings of individual items ranged from 0.752 to 0.867. Cronbach's alpha coefficients for all four dimensions were above 0.8, indicating high internal reliability.

Confirmatory factor analysis (CFA) was conducted on the remaining half of the data (n = 551) using AMOS 23.0 to assess structural, convergent, and discriminant validity. The maximum likelihood method was applied to assess the model fit. The results indicated that the χ^2/df ratio was 2.211 (<5), RMSEA (root mean square error of approximation) was 0.047 (<0.050), and SRMR (standardized root mean square residual) was 0.034 (<0.08). Additionally, CFI (comparative fit index), TLI (Tucker-Lewis index), and NFI (normed fit index) values all exceeded 0.90, demonstrating strong structural validity and a satisfactory model fit (45). As shown in Table 3, the standardized path coefficients for the four latent variables were all above 0.5. The average variance extracted (AVE) for each latent variable exceeded 0.5 (46), and the combined reliability surpassed 0.7 (47), indicating that the convergent validity is acceptable. Discriminant validity was assessed using the Fornell-Larcker criterion (46, 48). As shown in Table 4, Attitude, SN, PBC, and BI were significantly correlated (p < 0.001), yet the correlations between constructs were all lower than the square root of their respective AVEs, indicating adequate discriminant validity. This finding indicates that the variables were closely interrelated yet distinct from one another. Therefore, the scale demonstrated satisfactory discriminant validity (49).

TABLE 3 Convergent validity test (n = 550).

Variables			Factor loading	CR	AVE
Attitude	←	A1	0.901	0.892	0.735
	←	A2	0.933		
	←	A3	0.724		
SN	←	SN1	0.761	0.884	0.656
	←	SN2	0.896		
	←	SN3	0.848		
PBC	←	PBC1	0.848	0.852	0.596
	←	PBC2	0.587		
	←	PBC3	0.909		
	←	PBC4	0.784		
BI	←	BI1	0.774	0.824	0.664
	←	BI2	0.800		
	←	BI3	0.911		

A, attitude; SN, subjective norm; PBC, perceived behavior control; BI, behavior intention; CR, combined reliability; AVE average variance extracted.

TABLE 4 Discriminant validity test (n = 551).

Variable	Attitude	SN	PBC	BI
Attitude	**0.857**			
SN	0.591***	**0.810**		
PBC	0.284***	0.375***	**0.772**	
BI	0.494***	0.546***	0.348***	**0.815**

SN, subjective norm; PBC, perceived behavioral control; BI, behavior intention; Diagonals (in bold) represent the square root of the AVE. ***, p< 0.001.

TABLE 5 Results of structural equation modeling analysis (n = 1,101).

χ^2/df	CFI	TLI	NFI	RMSEA	SRMR
2.618	0.969	0.964	0.950	0.038	0.0411

χ^2/df, relative chi-square and degrees of freedom; GFI, goodness of fit index; TLI, Tucker-Lewis index; NFI, normative fit index; RMSEA, root mean square error of approximation; SRMR, standardized root mean square residual.

Test of structural equation model

In this study, the extended structural equation model included knowledge and PB as additional predictors of primary care physicians' breast cancer screening behavior. Model fit and path analyses were performed using AMOS software. As shown in Table 5, the goodness-of-fit indices indicated that the model achieved a satisfactory fit. The standardized path coefficients between latent variables are presented in Figure 3, while the hypothesis testing results are summarized in Table 6, the relationships among the variables in the structural equation model are all statistically significant (p < 0.001). Thus, all ten

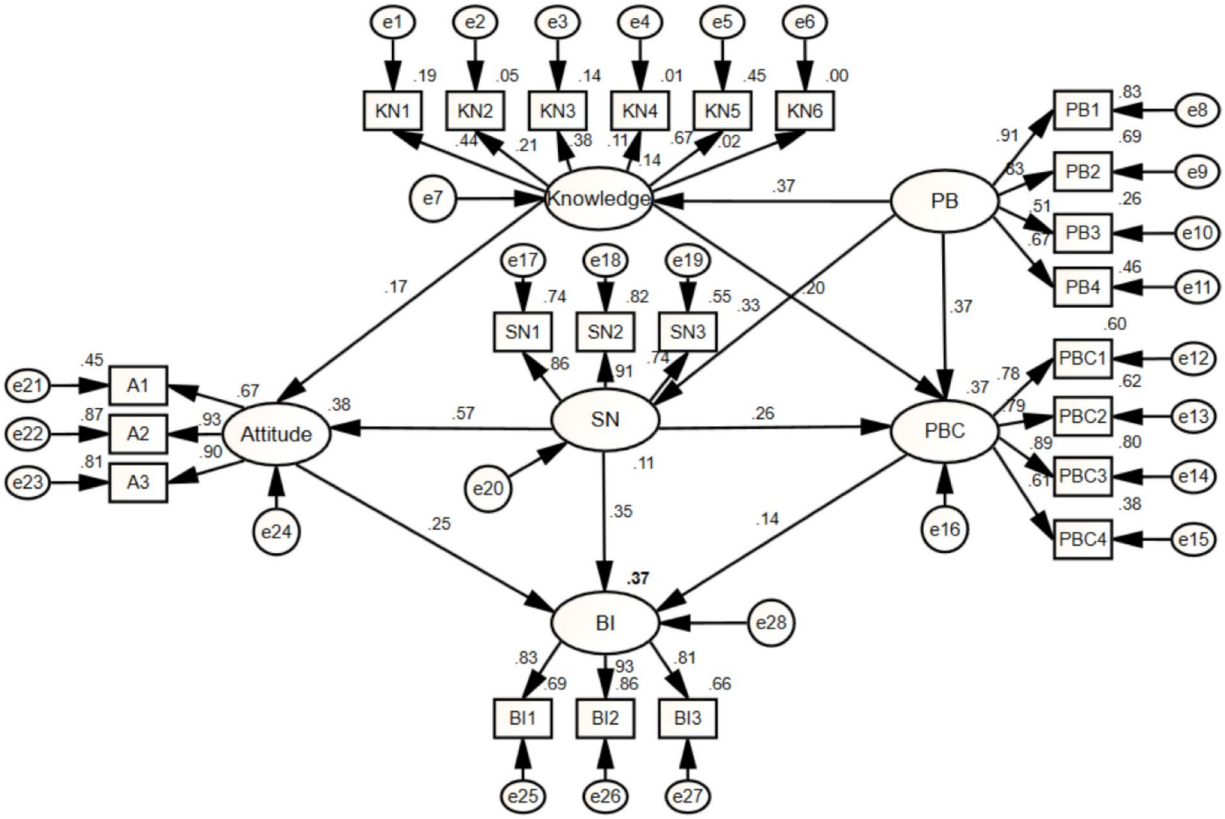


FIGURE 3
The results of SEM analysis. BI, behavior intention; SN, subjective norm; PBC, perceived behavior control; PB, past behavior.

hypotheses were supported, indicating that the relationships among the variables were statistically validated. As indicated by the results, attitudes towards BCS ($\beta = 0.251$, $p < 0.001$) and PBC ($\beta = 0.140$, $p < 0.001$) were significantly associated with primary physicians' intention to provide BCSs. SN were strongly associated with attitudes among primary care physicians ($\beta = 0.573$, $p < 0.001$) and moderately associated with PBC ($\beta = 0.258$, $p < 0.001$) and BI ($\beta = 0.352$, $p < 0.001$). Additionally, knowledge about BCS significantly influenced PBC ($\beta = 0.204$, $p < 0.001$) and attitudes ($\beta = 0.168$, $p < 0.001$) among primary care physicians. However, past screening behavior had moderate effects on SN ($\beta = 0.326$, $p < 0.001$) and PBC ($\beta = 0.370$, $p < 0.001$) and knowledge ($\beta = 0.368$, $p < 0.001$).

Discussion

This study examined the multifaceted predictors of primary care physicians' intention of providing BCSs to rural women. To our knowledge, this is the first study to examine physicians' BCS behaviors using the TPB as a conceptual framework. Notably, 90.7% of participants were female, a pattern that aligns with the gender composition of rural primary healthcare personnel in China and the breast cancer screening context (50). In general, the results showed that primary care physicians held high intentions to provide BCSs. The findings of the present study align closely with those of a previous investigation conducted in Tianjin, China, which reported that approximately two-thirds of physicians were willing to engage in cancer screening (18). The high intention demonstrated by primary care physicians in this study may be attributed to a national BCS program launched in 2009 to provide screening services for women (51). This program highlights the importance of promoting BCS and reflects the government's commitment to its widespread implementation. Such emphasis may increase primary care physicians' willingness to provide screening services. The expanded TPB model accounted for 37% of the variance in consumption intentions, aligning with results reported in previous studies (52, 53). In accordance with the hypotheses based on the TPB, the results of the path analysis test ascertained that primary care physicians' attitude, SN, PBC, PB and knowledge level can all directly or indirectly affect their intention to perform the BCSs. These findings confirm suggestions that the TPB is a suitable theoretical basis for understanding physicians' intentions and behaviors (54–56).

In this study, attitude was found to have a positive impact on the BI of primary care physicians, this finding indicates that physicians' awareness of the significance of BCS, combined with a sense of fulfillment and professional value derived from delivering such services, is positively associated with their intention to engage in this behavior. This conclusion aligns with research by Heena et al. (12) and Malve et al. (57). In this study, primary care physicians demonstrated positive attitudes toward BCS, suggesting broad acceptance of screening services within China's primary care system. Additionally, we found that screening-related knowledge indirectly influenced physicians' intention to offer services through its impact on attitudes, this indicates that improving knowledge may help providers better

TABLE 6 Results of structural equation modeling analysis.

The hypothesis (H)		S.E.	C.R.	Estimate	P	Supported
H1:	BI ← attitude	0.031	0.004	0.251	***	Yes
H2:	BI←SN	0.053	0.006	0.352	***	Yes
H2a:	Attitude ← SN	0.704	0.038	0.573	***	Yes
H2b:	PBC ← SN	0.258	0.031	0.258	***	Yes
H3:	BI←PBC	0.021	0.005	0.140	***	Yes
H4:	Attitude ← knowledge	6.197	1.379	0.168	***	Yes
H5:	PBC ← knowledge	6.148	1.322	0.204	***	Yes
H6:	SN ← PB	1.233	0.125	0.326	***	Yes
H7:	PBC ← PB	1.399	0.138	0.370	***	Yes
H8:	Knowledge ← PB	0.046	0.007	0.368	***	Yes

BI, behavior intention; SN, subjective norm; PBC, perceived behavior control; PB, past behavior.

understand the importance of BCS, thereby fostering stronger support for its implementation. A previous study indicates that in resource-limited settings, physicians' knowledge of tele-surgery is significantly associated with their attitudes toward its use (58). Furthermore, our findings suggest that external support—from colleagues or supervisors—can enhance service willingness by shaping more favorable attitudes, this may be because support from significant others helps create a more favorable work environment, thereby enhancing primary care providers' perceived value of participating in screening programs. For physicians with negative attitudes, developing deeply tailored messages to address their specific concerns can effectively help reshape their perspectives (38). For example, emphasizing that BCS is a priority in national health initiatives, highlighting the significant demand for these services among women, and underscoring the scarcity of providers can all serve to counteract negative attitudes and foster a more positive attitude.

In this study, SN has the most significant impact on the intention of primary physicians to provide BCSs. This suggests that physicians who receive support from their supervisors, colleagues, and patients are more likely to have a stronger intention to perform screening activities. Moreover, SN indirectly influenced BI through attitudes and PBC. These findings were consistent with previous studies, a study examining BI among family medicine residents identified SN as the strongest predictor of intention ($\beta = 0.56$, $p < 0.001$) (59). Another study demonstrated that conformity to colleagues' practices or expectations significantly predicted healthcare providers' intentions to perform vaginal examinations for female patients (60). Among all variable, SN2 (support from visiting women) had the highest factor loading (0.906), indicating that support from patients is the most influential factor in motivating primary care physicians, this finding underscores the importance of enhancing rural women's recognition of primary care physicians as a method to strengthen physicians' intentions to provide BCSs. In Chinese cultural contexts, rural women often hold more conservative attitudes toward their bodies and are therefore more likely to experience embarrassment or feelings of shame when undergoing physical examinations by others (25, 53). Discrete choice experiment result has also indicated that women prefer screening services provided by primary healthcare workers with a more positive attitude (61). Therefore, fostering a positive doctor-patient relationship and enhancing rural women's support for BCS conducted by primary healthcare providers may be an important way to strengthen these providers' willingness to offer such services. A potentially feasible strategy is to disseminate accurate information about BCS to rural women, ensuring they have a comprehensive understanding of the basic procedures and what to expect during the screening process. This knowledge can help alleviate fear stemming from uncertainty. Moreover, hospitals should create a supportive environment, enhance the communication skills of primary healthcare providers, and build a trustworthy image of BCSs providers. Rural women who receive high-quality BCSs are more likely to support BCSs providers, thereby encouraging primary care physicians to provide these services with stronger intention and greater quality. Such reciprocal dynamics can create a virtuous cycle: support and encouragement from rural women increase primary care physicians' SN and strengthen their intention to provide BCSs. In turn, these physicians are more capable of providing high-quality BCSs, further reinforcing rural women's trust and support.

According to the TPB, PBC is a key predictor of an individual's intention to perform a given behavior (31). In this study, participants reported the lowest scores on the PBC dimension, suggesting that primary care physicians in rural areas face considerable challenges in providing BCSs. These challenges include heavy workloads, insufficient equipment, and limited technical skills. Such practical barriers significantly undermine physicians' intention to engage in BCSs. The significant disparities in financial resources and healthcare infrastructure between urban and rural regions in China have created persistent challenges for rural primary care facilities. Experienced and skilled physicians often prefer working in urban areas with better infrastructure and resources. In contrast, rural primary care facilities, which typically lack adequate support and opportunities, struggle to retain such professionals (62). Meanwhile, studies have indicated that rural primary healthcare institutions in China are often understaffed and lack essential screening equipment such as ultrasound and mammography devices. Only a small proportion are equipped to perform ultrasound imaging, mammography, HPV testing, and liquid-based cytology (63, 64). These findings underscore the pressing need to address systemic issues limiting access to adequate equipment, resources, and skill training in rural areas. The health authority equipping primary care physicians with the skills and resources on BCSs would provide a pathway to improve their

BCSs delivery behaviors. The central government should play a key role in balancing healthcare supply and demand by promoting more equitable allocation of medical resources across regions. To reduce barriers faced by primary care providers in delivering BCSs, rural health institutions should focus on both talent recruitment and professional development. On one hand, regular training programs should be provided to primary care physicians involved in screening to strengthen their knowledge and technical capacity (65). On the other hand, policies aimed at attracting and retaining skilled medical professionals in rural areas are essential (66). These include creating clear career advancement pathways, supporting continuing education, increasing investment in screening equipment, and improving government coordination and institutional support for screening programs at all levels of the rural healthcare system.

Our study also revealed that PB, as an external variable, indirectly influenced primary care physicians' intentions to provide BCSs through its effects on knowledge, SN, and PBC, this finding aligns with some previous studies. Shi et al. incorporated past related health behaviors into the TPB model and found that elementary school students' past oral health behaviors were associated with their intention to improve oral health behaviors (67). The overall level of PB reported in our sample was relatively low, suggesting that such screening is not yet routine among primary care providers, particularly in rural areas. These results emphasize the need to strengthen physicians' screening experience and incorporate habit-forming strategies into policy interventions. Institutions may leverage this insight by creating opportunities for physicians with screening experience to share their knowledge and serve as role models. Therefore, institutions can take advantage of this finding. For instance, primary physicians who have been participating in screening services may set up a special team to regularly publicize their experience. At the same time, more obstetrics and gynecology specialists and general practitioners may be involved in BCS, so as to build a professional team.

Strength and limitations

One major strength of this study is its relatively large sample size (n = 1,101), which enhances the robustness of the findings. Another strength of this study lies in the adoption of a well-established social psychological framework—the TPB. Moreover, the inclusion of knowledge and PB as additional variables further enriched and refined the research model. Finally, unlike earlier research that focused primarily on the demand side, this study adopts a supply-side perspective by examining the factors influencing primary care physicians' intention to provide BCSs.

Our study has limitations. Firstly, this is a cross-sectional study. As a result, the causal relationship between variables needs to be further verified. Secondly, this research only investigated factors of BI of primary medical staff instead of investigating the specific screening behavior. Although there is a strong correlation between intention and behavior, there remains a need to investigate actual screening service conducted by primary physicians. Moreover, only primary care physicians were studied in this research, many other allied health care professionals can impact screening behaviors. While this ensures a cohort with similar characteristics and measurable this is useful to prove efficacy it would be valuable to further study a more diverse cohort, the samples may be expanded in future studies. Finally, this study included only primary care physicians from Jiangsu Province, which may limit the generalizability of the findings. Future research should recruit physicians from additional provinces to enhance external validity.

Conclusion

Our study extended the TPB model by incorporating knowledge and PB to predict primary care physicians' intention to provide BCSs for rural women in China. The study found that attitude, SN, PBC, knowledge and PB significantly influenced physicians' intentions. These factors should be given greater attention in efforts to improve health outcomes among rural women. Furthermore, targeted interventions that enhance physicians' knowledge and skills related to BCS, including regular training programs, professional competitions, educational lectures, and other structured activities, may effectively promote physicians' engagement in BCS initiatives.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Author contributions

YZ: Software, Visualization, Writing – original draft, Formal analysis, Resources, Data curation, Funding acquisition, Project administration, Supervision, Conceptualization, Writing – review & editing, Investigation, Methodology, Validation. ZZ: Writing – original draft. YubH: Investigation, Data curation, Software, Writing – original draft, Methodology. ZG: Methodology, Investigation, Writing – review & editing, Data curation, Software. FY: Conceptualization, Project administration, Supervision, Funding acquisition, Resources, Software, Writing – original draft. ZH: Project administration, Supervision, Conceptualization, Methodology, Writing – review & editing, Investigation, Software, Data curation, Visualization, Resources, Funding acquisition. YuaH: Conceptualization, Methodology, Software, Resources, Supervision, Project administration, Writing – original draft.

Funding

The author(s) declare that financial support was received for the research and/or publication of this article. The author gratefully acknowledge the financial support provided by the Ministry of education of Humanities and Social Science project of China (22YJC820051), and the support provided by the Talent Startup Fund

of Nanjing University of Information Science & Technology (2024r115).

Acknowledgments

The authors would like to express their appreciation for all the research assistants in data collection—special thanks to the reviewers and the editors for their useful comments.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The authors declare that Gen AI was used in the creation of this manuscript. The author affirms full responsibility for the content of this manuscript. Generative artificial intelligence (AI) tools were used solely to assist in language translation during the manuscript preparation process. All intellectual content, including study design, data analysis, interpretation, and conclusions, was entirely developed by the authors. The final manuscript was thoroughly reviewed and revised by the authors to ensure accuracy, clarity, and compliance with ethical standards.

Any alternative text (alt text) provided alongside figures in this article has been generated by Frontiers with the support of artificial intelligence and reasonable efforts have been made to ensure accuracy, including review by the authors wherever possible. If you identify any issues, please contact us.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

References

1. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. (2024) 74:229–63. doi: 10.3322/caac.21834

2. Wilkinson L, Gathani T. Understanding breast cancer as a global health concern. *Br J Radiol*. (2022) 95:20211033. doi: 10.1259/bjr.20211033

3. Fan L, Zheng Y, Yu KD, Liu GY, Wu J, Lu JS, et al. Breast cancer in a transitional society over 18 years: trends and present status in Shanghai, China. *Breast Cancer Res Treat*. (2009) 117:409–16. doi: 10.1007/s10549-008-0303-z

4. Zheng R, Zhang S, Zeng H, Wang S, Sun K, Chen R, et al. Cancer incidence and mortality in China, 2016. *J Natl Cancer Cent*. (2022) 2:1–9. doi: 10.1016/j.jncc.2022.02.002

5. Cao W, Chen HD, Yu YW, Li N, Chen WQ. Changing profiles of cancer burden worldwide and in China: a secondary analysis of the global cancer statistics 2020. *Chin Med J*. (2021) 134:783–91. doi: 10.1097/CM9.0000000000001474

6. Moss SM, Wale C, Smith R, Evans A, Cuckle H, Duffy SW. Effect of mammographic screening from age 40 years on breast cancer mortality in the UK age trial at 17 years' follow-up: a randomised controlled trial. *Lancet Oncol*. (2015) 16:1123–32. doi: 10.1016/S1470-2045(15)00128-X

7. Massat NJ, Dibden A, Parmar D, Cuzick J, Sasieni PD, Duffy SW. Impact of screening on breast cancer mortality: the UK program 20 years on. *Cancer Epidemiol Biomarkers Prev*. (2016) 25:455–62. doi: 10.1158/1055-9965.EPI-15-0803

8. Plevritis SK, Munoz D, Kurian AW, Stout NK, Alagoz O, Near AM, et al. Association of screening and treatment with breast cancer mortality by molecular subtype in US women, 2000-2012. *JAMA*. (2018) 319:154–64. doi: 10.1001/jama.2017.19130

9. Bleyer A, Welch HG. Effect of three decades of screening mammography on breast-cancer incidence. *N Engl J Med*. (2012) 367:1998–2005. doi: 10.1056/NEJMoa1206809

10. Zhang M, Bao H, Zhang X, Huang Z, Zhao Z, Li C, et al. Breast cancer screening coverage—China, 2018–2019. *China CDC Wkly*. (2023) 5:321–6. doi: 10.46234/ccdcw2023.062

11. Zhang M, Zhong Y, Bao H, Zhao Z, Huang Z, Zhang X, et al. Breast cancer screening rates among women aged 20 years and above—China, 2015. *China CDC Wkly*. (2021) 3:267–73. doi: 10.46234/ccdcw2021.078

12. Heena H, Durrani S, Riaz M, AlFayyad I, Tabasim R, Parvez G, et al. Knowledge, attitudes, and practices related to breast cancer screening among female health care professionals: a cross sectional study. *BMC Womens Health*. (2019) 19:122. doi: 10.1186/s12905-019-0819-x

13. Grady KE, Lemkau JP, McVay JM, Reisine ST. The importance of physician encouragement in breast cancer screening of older women. *Prev Med*. (1992) 21:766–80. doi: 10.1016/0091-7435(92)90083-t

14. Gu C, Chan CW, Twinn S, Choi KC. The influence of knowledge and perception of the risk of cervical cancer on screening behavior in mainland Chinese women. *Psychooncology*. (2012) 21:1299–308. doi: 10.1002/pon.2037

15. Kwok C, White K, Roydhouse JK. Chinese–Australian women's knowledge, facilitators and barriers related to cervical cancer screening: a qualitative study. *J Immigr Minor Health*. (2011) 13:1076–83. doi: 10.1007/s10903-011-9491-4

16. Zhang M, Wei W, Li Q, Chen X, Zhang M, Zuo D, et al. Determinants of intention to participate in breast cancer screening among urban Chinese women: an application of the protection motivation theory. *Int J Environ Res Public Health*. (2021) 18:11093. doi: 10.3390/ijerph182111093

17. Nazari M, Ghazaani FM, Kaveh MH, Karimi M, Ghahremani L. Investigating the predictors of breast cancer screening behaviors (breast self-examination, clinical examination or examination by physician/midwife and mammography) based on protection motivation theory (PMT) in women. *J Prev Med Hyg*. (2021) 62:E736–41. doi: 10.15167/2421-4248/jpmh2021.62.3.1857

18. Zheng S, Zhang X, Greuter MJW, de Bock GH, Lu W. Willingness of healthcare providers to perform population-based cancer screening: a cross-sectional study in primary healthcare institutions in Tianjin, China. *BMJ Open*. (2024) 14:e075604. doi: 10.1136/bmjopen-2023-075604

19. Ramos M, Esteva M, Almeda J, Cabeza E, Puente D, Saladich R, et al. Knowledge and attitudes of primary health care physicians and nurses with regard to population screening for colorectal cancer in Balearic Islands and Barcelona. *BMC Cancer*. (2010) 10:500. doi: 10.1186/1471-2407-10-500

20. Haubenstricker JE, Lee JW, Segovia-Siapco G, Medina E. The theory of planned behavior and dietary behaviors in competitive women bodybuilders. *BMC Public Health*. (2023) 23:1716. doi: 10.1186/s12889-023-16568-w

21. Pelling EL, White KM. The theory of planned behavior applied to young people's use of social networking web sites. *Cyberpsychol Behavior*. (2009) 12:755–9. doi: 10.1089/cpb.2009.0109

22. Zhao D, Chen S, Jin S, Chen L, Zheng C, Wang X, et al. Predictors of referral behaviour and intention amongst physicians in a medical consortium based on the theory of planned behaviour: a cross-sectional study in China. *Front Public Health*. (2023) 11:1159207. doi: 10.3389/fpubh.2023.1159207

23. Jia H, Yu J, Feng T, Ning L, Cao P, Shang P, et al. Factors influencing medical personnel to work in primary health care institutions: an extended theory of planned behavior. *Int J Environ Res Public Health*. (2022) 19:2785. doi: 10.3390/ijerph19052785

24. Wang X, Chen D, Xie T, Zhang W. Predicting women's intentions to screen for breast cancer based on the health belief model and the theory of planned behavior. *J Obstet Gynaecol Res*. (2019) 45:2440–51. doi: 10.1111/jog.14109

25. Sun Y, Yuan J, Liu W, Qin B, Hu Z, Li J, et al. Predicting rural women's breast Cancer screening intention in China: a PLS-SEM approach based on the theory of planned behavior. *Front Public Health*. (2022) 10:858788. doi: 10.3389/fpubh.2022.858788

26. Galaviz K, Jauregui-Ulloa E, Fabrigar L, Latimer-Cheung A, Lopez y Taylor J, Lévesque LJ. Physical activity prescription among Mexican physicians: a structural

equation analysis of the theory of planned behaviour. *Int J Clin Pract*. (2015) 69:375–83. doi: 10.1111/ijcp.12546

27. Herbert KE, Urmie JM, Newland BA, Farris KB. Prediction of pharmacist intention to provide Medicare medication therapy management services using the theory of planned behavior. *Res Social Adm Pharm*. (2006) 2:299–314. doi: 10.1016/j.sapharm.2006.02.008

28. Via-Clavero G, Guàrdia-Olmos J, Gallart-Vivé E, Arias-Rivera S, Castanera-Duro A, Delgado-Hito P. Development and initial validation of a theory of planned behaviour questionnaire to assess critical care nurses' intention to use physical restraints. *J Adv Nurs*. (2019) 75:2036–49. doi: 10.1111/jan.14046

29. Alhamad H, Donyai P. The validity of the theory of planned behaviour for understanding people's beliefs and intentions toward reusing medicines. *Pharmacy (Basel)*. (2021) 9:58. doi: 10.3390/pharmacy9010058

30. Gerend MA, Shepherd JE. Predicting human papillomavirus vaccine uptake in young adult women: comparing the health belief model and theory of planned behavior. *Ann Behav Med*. (2012) 44:171–80. doi: 10.1007/s12160-012-9366-5

31. Ajzen I. The theory of planned behavior. *Organ Behav Hum Decis Process*. (1991) 50:179–211. doi: 10.1016/0749-5978(91)90020-T

32. Ajzen I. Constructing a theory of planned behavior questionnaire: Conceptual and methodological considerations. University of Massachusetts, Amherst. (2002) Available online at: https://people.umass.edu/aizen/pdf/tpb.measurement.pdf

33. Allenbaugh J, Corbelli J, Rack L, Rubio D, Spagnoletti C. A brief communication curriculum improves resident and nurse communication skills and patient satisfaction. *J Gen Intern Med*. (2019) 34:1167–73. doi: 10.1007/s11606-019-04951-6

34. Kiyang LN, Labrecque M, Doualla-Bell F, Turcotte S, Farley C, Cionti Bas M, et al. Family physicians' intention to support women in making informed decisions about breast cancer screening with mammography: a cross-sectional survey. *BMC Res Notes*. (2015) 8:663. doi: 10.1186/s13104-015-1608-8

35. Deng Q, Zeng Z, Zheng Y, Lu J, Liu W. Predictors of physicians' intentions to use clinical practice guidelines on antimicrobial in tertiary general hospitals of China: a structural equation modeling approach. *Antimicrob Resist Infect Control*. (2021) 10:97. doi: 10.1186/s13756-021-00966-z

36. Deng Q, Liu W. The effect of social norms on physicians' intentions to use liver Cancer screening: a cross-sectional study using extended theory of planned behavior. *Risk Manag Healthc Policy*. (2022) 15:179–91. doi: 10.2147/RMHP.S349387

37. Liu C, Liu C, Wang D, Deng Z, Tang Y, Zhang X. Determinants of antibiotic prescribing behaviors of primary care physicians in Hubei of China: a structural equation model based on the theory of planned behavior. *Antimicrob Resist Infect Control*. (2019) 8:23. doi: 10.1186/s13756-019-0478-6

38. Tama RAZ, Ying L, Yu M, Hoque MM, Adnan KM, Sarker SAJ. Assessing farmers' intention towards conservation agriculture by using the extended theory of planned behavior. *J Environ Manag*. (2021) 280:111654. doi: 10.1016/j.jenvman.2020.111654

39. Tengku Ismail TA, Wan Muda WA, Bakar MI. The extended theory of planned behavior in explaining exclusive breastfeeding intention and behavior among women in Kelantan, Malaysia. *Nutr Res Pract*. (2016) 10:49–55. doi: 10.4162/nrp.2016.10.1.49

40. Hu Z, Sun Y, Ma Y, Chen K, Lv L, Wang L, et al.Examining primary care physicians' intention to perform cervical cancer screening services using a theory of planned behavior: A structural equation modeling approach. (2022) 10:893673.

41. Dumitrescu AL, Wagle M, Dogaru BC, Manolescu B. Modeling the theory of planned behavior for intention to improve oral health behaviors: the impact of attitudes, knowledge, and current behavior. *J Oral Sci*. (2011) 53:369–77. doi: 10.2334/josnusd.53.369

42. Bruno F, Abondio P, Laganà V, Colao R, Curcio SM, Frangipane F, et al. Using the theory of planned behavior and past behavior to explain the intention to receive a seasonal influenza vaccine among family caregivers of people with dementia. *Int J Transl Med*. (2023) 3:246–54. doi: 10.3390/ijtm3020017

43. Bagozzi RP, Yi Y. Specification, evaluation, and interpretation of structural equation models. *J Acad Mark Sci*. (2012) 40:1. doi: 10.1007/s11747-011-0278-x

44. Kaiser HF. Little jiffy, mark IV. *Educ Psychol Meas*, (1974). 34:111–7. doi: 10.1177/001316447403400115

45. Hu L, Bentler PMJSEM. Cutoff criteria for fit indexes in covariance structure analysis: conventional criteria versus new alternatives. *Struct Equ Modeling*. (1999) 6:1–55. doi: 10.1080/10705519909540118

46. Fornell C, Larcker DF. Evaluating structural equation models with unobservable variables and measurement error. *J Mark Res*. (1981) 18:39–50.

47. Hair JF, Black WC, Babin BJ, Anderson RE. Multivariate data analysis: a global perspective. Upper Saddle River, NJ: Pearson, (2010).

48. Hair JF, Hult GTM, Ringle CM, Sarstedt M. A primer on partial least squares structural equation modeling (PLS-SEM). Thousand Oaks, CA: Sage Publications (2019).

49. Gefen D, Straub D, Boudreau MC. Structural equation modeling and regression: guidelines for research practice. *Commun Assoc Inf Syst*. (2000) 4:7. doi: 10.17705/1CAIS.00407

50. Liu B, Xue Q, Li X, Sun J, Rao Z, Zou G, et al. Improving primary healthcare quality in China through training needs analysis. *Sci Rep*. (2024) 14:30146. doi: 10.1038/s41598-024-81619-0

51. Sudharsanan N, Ali MK, McConnell M. Hypertension knowledge and treatment initiation, adherence, and discontinuation among adults in Chennai, India: a cross-sectional study. *BMJ Open*. (2021) 11:e040252. doi: 10.1136/bmjopen-2020-040252

52. Kortteisto T, Kaila M, Komulainen J, Mäntyranta T, Rissanen P. Healthcare professionals' intentions to use clinical guidelines: a survey using the theory of planned behaviour. *Implement Sci*. (2010) 5:51. doi: 10.1186/1748-5908-5-51

53. Schliemann D, Hoe WMK, Mohan D, Allotey P, Reidpath DD, Tan MM, et al. Challenges and opportunities for breast cancer early detection among rural dwelling women in Segamat District, Malaysia: a qualitative study. *PLoS One*. (2022) 17:e0267308. doi: 10.1371/journal.pone.0267308

54. Samuels EA, Dwyer K, Mello MJ, Baird J, Kellogg AR, Bernstein E. Emergency department-based opioid harm reduction: moving physicians from willing to doing. *Acad Emerg Med Off J Soc Acad Emerg Med*. (2016) 23:455–65. doi: 10.1111/acem.12910

55. Alradini F, Bepari A, AlNasser BH, AlGheshem EF, AlGhamdi WK. Perceptions of primary health care physicians about the prescription of antibiotics in Saudi Arabia: based on the model of theory of planned behaviour. *Saudi Pharm J*. (2021) 29:1416–25. doi: 10.1016/j.jsps.2021.10.011

56. Wang D, Zhang X, Chen H, Liu C. Applying theory of planned behavior to understand physicians' shared decision-making with patients with acute respiratory infections in primary care: a cross-sectional study. *Front Pharmacol*. (2021) 12:785419. doi: 10.3389/fphar.2021.785419

57. Malve H, Sathe P, Chakravarty P, Thakor P, Tesado C. Knowledge, attitudes, and practices regarding Oral fluid, electrolyte, and energy Management in Acute Nondiarrheal Illnesses among physicians in India. *J Assoc Physicians India*. (2023) 71:11–2. doi: 10.5005/japi-11001-0249

58. Reda MM, Gashu KD, Beshir MA, Butta FW. Physicians' knowledge and attitudes towards telesurgery and its associated factors in a resource-limited setting, Northwest Ethiopia, 2022: a cross-sectional study design. *BMJ Open*. (2024) 14:e079046. doi: 10.1136/bmjopen-2023-079046

59. Grierson LE, Fowler N, Kwan MY. Family medicine residents' practice intentions: theory of planned behaviour evaluation. *Can Fam Physician*. (2015) 61:e524–31.

60. Mwaliko E, Van Hal G, Bastiaens H, Van Dongen S, Gichangi P, Otsyula B, et al. Early detection of cervical cancer in western Kenya: determinants of healthcare providers performing a gynaecological examination for abnormal vaginal discharge or bleeding. *BMC Fam Pract*. (2021) 22:52. doi: 10.1186/s12875-021-01395-y

61. Sun Y, Wang Y, Zhang H, Hu Z, Ma Y, He Y. What breast cancer screening program do rural women prefer? A discrete choice experiment in Jiangsu, China. *Patient*. (2024) 17:363–78. doi: 10.1007/s40271-024-00684-9

62. Di J, Rutherford S, Chu C. Review of the cervical cancer burden and population-based cervical cancer screening in China. *Asian Pac J Cancer Prev*. (2015) 16:7401–7. doi: 10.7314/apjcp.2015.16.17.7401

63. Zheng S, Zhang X, Greuter MJW, de Bock GH, Lu W. Determinants of population-based Cancer screening performance at primary healthcare institutions in China. *Int J Environ Res Public Health*. (2021) 18:3312. doi: 10.3390/ijerph18063312

64. Xia C, Basu P, Kramer BS, Li H, Qu C, Yu XQ, et al. Cancer screening in China: a steep road from evidence to implementation. *Lancet Public Health*. (2023) 8:e996–e1005. doi: 10.1016/S2468-2667(23)00186-X

65. Sangwan RK, Huda RK, Panigrahi A, Toteja GS, Sharma AK, Thakor M, et al. Strengthening breast cancer screening program through health education of women and capacity building of primary healthcare providers. *Front Public Health*. (2023) 11:1276853. doi: 10.3389/fpubh.2023.1276853

66. Noya F, Freeman K, Carr S, Thompson S, Clifford R, Playford D. Approaches to facilitate improved recruitment, development, and retention of the rural and remote medical workforce: a scoping review protocol. *Int J Health Policy Manag*. (2021) 10:22–8. doi: 10.34172/ijhpm.2020.27

67. Shi H, Wang J, Huang R, Zhao J, Zhang Y, Jiang N, et al. Application of the extended theory of planned behavior to understand Chinese students' intention to improve their oral health behaviors: a cross-sectional study. *BMC Public Health*. (2021) 21:2303. doi: 10.1186/s12889-021-12329-9

68. Ajzen I. From intentions to actions: A theory of planned behavior. In Action-Control: From Cognition to Behavior, eds. Kuhl *J, and Beckmann J. Berlin: Springer*. (1985), 11–39. doi: 10.1007/978-3-642-69746-3_2

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 14 November 2025
DOI 10.3389/fpubh.2025.1683074

Check for updates

OPEN ACCESS

EDITED BY
Xin Long Xu,
Hunan Normal University, China

REVIEWED BY
Ebenezer Kwabena Tetteh,
University of Ghana, Ghana
Rubén Avilés-Reyes,
Universidad Autónoma de Baja California, Mexico

*CORRESPONDENCE
Wu Lei
✉ wulei@hrbeu.edu.cn

RECEIVED 11 August 2025
ACCEPTED 20 October 2025
PUBLISHED 14 November 2025

CITATION
Guanyi Y, Lei W, Heng C and Zhengliang D (2025) Study on the relationship between buyer market power, spatial spillover effect, and profit in China's pharmaceutical industry. *Front. Public Health* 13:1683074. doi: 10.3389/fpubh.2025.1683074

COPYRIGHT
© 2025 Guanyi, Lei, Heng and Zhengliang. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

Study on the relationship between buyer market power, spatial spillover effect, and profit in China's pharmaceutical industry

Yu Guanyi[1], Wu Lei[1]*, Chen Heng[1] and Ding Zhengliang[2]

[1]School of Economics and Management, Harbin Engineering University, Harbin, China, [2]Decision-Making Consultation Department, Party School of Heilongjiang Provincial Committee of Communist Party of China (Heilongjiang Academy of Governance), Harbin, China

Previous studies have extensively explored industrial innovation, but the impact of downstream buyer market power on upstream industries remains underexamined. Using a spatial Durbin model (SDM) and data from China's medical and pharmaceutical sectors (2001–2021), we analyze how buyer market power affects pharmaceutical industry profitability. Key findings include: (1) local buyer market power reduces local pharmaceutical profitability and may also negatively affect other regions through spatial spillover, though this spillover effect is weak. (2) Stronger regional economic ties amplify the impact of local medical industry power on pharmaceutical profitability. (3) Supplier countervailing power can mitigate the negative effects of buyer power on pharmaceutical profits. (4) Buyer market power significantly harms pharmaceutical profitability in western China and low capital-intensity sectors, but not in eastern or central regions and high capital-intensity sectors. (5) Asset specificity intensifies the negative impact of buyer power, while larger firm size helps reduce it. (6) Buyers can lower pharmaceutical profitability by reducing R&D investment. This study contributes to industrial organization theory by revealing how downstream buyer power affects upstream profitability. It expands empirical methods by incorporating spatial econometrics and offers policy suggestions for improving pharmaceutical industry performance from a vertical chain perspective.

KEYWORDS

buyer market power, seller countervailing power, profit, spatial Durbin model, spatial spillover effect

1 Introduction

Buyer power refers to the market power possessed by the buyer in a market transaction. Galbraith (1) expressed the buyer power for the first time as the market power owned by the buyer, being able to countervail with the manufacturer. He believed that when the seller occupies a dominant position in the industrial chain, the buyer can rely on the counterbalance power to pass on the cost savings to consumers, finally reducing the product price and improving consumer welfare. Galbraith (1) affirmed the emergence and effect of buyer counterbalance power.

In the previous studies on the buyer counterbalance power the implied background of the industrial chain is that the buyer power is relatively small and the seller power is

dominant, thus it is called "buyer counterbalance power." As the market power from of downstream customers increased gradually, the position of buyers and sellers in market transactions shifted. In this situation, countervailing power of buyers to only necessary to counter dominant supplier market power, but previous studies do not consider what the impact on social welfare (however defined) will be if buyer market power becomes dominant. Theoretically, in the case of the industrial chain dominated by downstream buyer, the effect of the buyer power may be the same as the effect of counterbalance power. However, it may not be the same, because the balance of the power between buyers and sellers shifted, and buyer power has become a new kind of power.

Relying on the realistic background of the Chinese market, we choose the pharmaceutical industry to carry out the research, a typical industry with prominent buyer power. By virtue of professional diagnosis, treatment knowledge and services, doctors extend their market power in the diagnosis and treatment market to the drug sales market. In this way, hospitals turned into very powerful negotiating buyers, they tend to possess a strong and indisputable bargaining power when facing pharmaceutical companies. Compared with other industries, the pharmaceutical industry is a typical industry where buyer power is prominent. Therefore, it can be used as the appropriate research object of buyer power effect.

The purpose of this paper is to empirically explore the influence of buyer power on the supplier's profit in the case of the new buyer-led vertical relationship when the position of the buyer and the seller changes. This paper adds to or expands on existing literature on buyer countervailing or counterbalance power in pharmaceutical markets. This study confirms that the buyer power faced by pharmaceutical enterprises (the large buyer counterbalance power developing to a certain stage) does exist and is universal. When the position of the buyer and the seller changes, in the case of the new buyer-led vertical relationship, the distortion of the vertical relationship caused by the buyer power will have a negative impact on the upstream industry. This effect is in contrast to the beneficial effect of buyer counterbalance power (1).

Based on the spatial econometric model, this paper innovates the research method of vertical relationship, which provides evidence of the interaction between upstream and downstream industries. Specifically, from the perspective of spatial spillover effect, this paper empirically studies the inter-industry influence mechanism, which explores the effect of excessive downstream power on upstream industry. We have proved the theoretical inference of the negative influence of buyer power on suppliers' profits and provided evidence and theoretical enlightenment in this regard, which is the unique theoretical significance of this paper and its contribution to the research field of vertical relationship.

This paper can enrich the theory of industrial organization and verify the effects and mechanisms of counterbalance power. The significance of this paper is that it not only enriches the theory of industrial organization and verifies the effects and mechanisms of countervailing power. In terms of practical significance, when facing the social problems of "high drug prices and expensive medical treatment," it can also provide references for the anti-monopoly authorities to impose price cuts on drugs in the industrial chain, limit the price regulation and reduce the drug expenses for residences.

2 Conceptual framework

2.1 Buyer market power and pharmaceutical industry's profits

Under the context of vertical relationships in the industry chain, the role of customers has become increasingly prominent in the suppliers' decision-making process and future development prospects with the deepening division of labor and cooperation between upstream and downstream industries (2, 3). Downstream customers act as a link between suppliers' products and consumers. They transmit valuable feedback to manufacturers regarding consumer preferences, and further convey essential information related to product distribution. Moreover, they also provide sales platforms for marketing suppliers' products. Customers, as direct downstream participants with a direct interest in suppliers, are the source of suppliers' profits and the basis of their survival, as well as the most important stakeholders of the suppliers, other than the investors. The buyer market power formed by the bargaining power of downstream customers is related to the suppliers' bargaining position in market transactions, and their operations and roles in price negotiations, which further affects the suppliers' business performance (4, 5).

First, the competitive advantage perspective. Buyers in dominant negotiating positions in market transactions often seek to maximize their own profits by means such as replacing trading partners or taking products off the shelves (6–8). Decreasing the suppliers' operating efficiency and profitability could be achieved by diverse tools, such as extracting rent from suppliers, deferring payments to suppliers despite having sufficient funds, capturing the downstream market and thus firmly control sales channels, obtaining better trading conditions than competitors, appropriating suppliers' working capital through commercial credit financing, prolonging suppliers' business cycles, etc. (9, 10).

Second, the resource-dependence perspective. When the market concentration of downstream customers is high or when their purchases account for a relatively large proportion of the suppliers' sales, the suppliers are heavily dependent on downstream customers and the buyers have strong market power this moment (11–13). Relying on strong bargaining power, in addition to forcing the suppliers to make greater concessions on their profits through strategic behavior, buyers also puts the suppliers at risk of terminating the relationships at any time and replacing the counterparties (14, 15). Due to the practical need to prevent the loss of customer resources and the breakdown of cooperative relationships, suppliers must actively maintain close contractual relationships with downstream customers so as to ensure the stability of their market share (16, 17). Thus, suppliers need to pay a high cost to maintain these contractual relationships, while reducing their own profitability (18, 19).

Third, the perspective of relationship-specific investments and transaction costs. When there is a particular relationship-specific investment between a supplier and a buyer, the supplier' operational flexibility and the right of independent decision-making is also reduced by the increased switching cost (20–22). In case a downstream customer is facing a financial crisis or is on the verge of bankruptcy, given the stable sales channels, relatively fixed trading rules, and mutually agreed trading

mechanisms established between the supplier and the downstream customer over a long period of time, the supplier is likely to face the risk of sales disruption due to the termination of the trading relationship if it is difficult to find another alternative buyer within a short period of time (23, 24). In this case, the relationship-specific assets between the supplier and the downstream customer will lose a lot of or even their entire original value (25–27), thereby pushing up the supplier's transaction costs, resulting in lower market performance.

Fourth, the perspective of operational and financial risks. When the market power of the downstream buyers is strong, it means that there is higher market concentration of the downstream customers and more frequent trading relationship between the suppliers and the downstream customers (28–30). This over-dependence on close trading relationships tends to increase the potential risks for suppliers (31–33). On the one hand, it is highly likely that downstream customers will achieve a backward integration strategy by virtue of their competitive advantage and break their partnership with the suppliers, the suppliers then face difficulty in bringing products to market, and their business risks rise (34–36). On the other hand, in case a downstream customer is facing a financial crisis or is on the verge of bankruptcy, it will largely transfer its own financial risk to its trading partners, resulting in a significant reduction in suppliers' profitability (37–39).

Hypothesis H_1a: buyer power of local medical institutions can diminish the profits of the local pharmaceutical industry via various means of vertical control.

Hypothesis H_1b: local medical institutions, following the same mechanism in market transactions, can also transmit the market power to pharmaceutical industries in other regions and depress their profits.

Hypothesis H_1c: buyer power of local medical institutions reduces pharmaceutical industry profits in all provinces.

2.2 Buyer market power, corporate size, and profit

Large-scale enterprises are more effective innovators and have a bigger impact on the market (40). Their competitive edge comes from a variety of business models and the advantages of economies of scale, which allow them to cut costs, more effectively use resources for R&D, and spread risk. These benefits improve the external environment for innovation within these businesses, fostering their passion for creative endeavors and giving them more chances to succeed in innovation (41–43). This relieves the pricing pressure and the risk of innovative rents being extracted imposed by powerful downstream consumers to some extent, which ultimately increases their overall profitability (44–47). Based on this, we propose the following hypothesis.

H_2: The pharmaceutical industry is more likely to offset the negative impact of the buyer market power on profits as companies grow in size.

2.3 Buyer market power, asset specificity, and profit

Due to its higher level of asset specialization, the pharmaceutical sector differs from the whole industry in a number of distinctive ways. Specific assets are characterized by difficult conversion toward alternative uses, low liquidity, and high conversion costs. As a result, attempts to rearrange these specific assets have a major negative impact on their value (48, 49). Suppliers are vulnerable to post-negotiation risks related to the specific asset investment when they are faced by powerful downstream purchasers. These risks include the possibility for exploitation, entrapment, and unfavorable posture (50, 51). As a result, suppliers' revenues are reduced since they must comply with the stringent requirements put out by buyers (52). Thus, we propose the following hypothesis:

H_3: The pharmaceutical industry experiences reduced profitability when there is a higher degree of asset specificity, as greater buyer market power exerts a negative influence.

3 Methodology

3.1 Establishment of vertical relationship

Sales revenue is the main source of profit for industrial businesses, the claims presented in this research are well-supported by the substantial correlation between profit and sales revenue, which is measured at 0.9843 by using the Stata14.0 program. It is crucial to understand that the pharmaceutical industry in each particular location depends on sales revenue from 30 other buyer markets in addition to the local buyer market when taking that sector into account. A complex dynamic is introduced by the vertical connection between the 31 pharmaceutical corporations acting as sellers and the 31 medical enterprises acting as buyers.

In others terms, hospitals in any region have an impact on the sales income (and subsequently the profit) of both local pharmaceutical industry and pharmaceutical industries in nearby regions. Figure 1 shows a vertical spatial relationship between the independent and dependent variables, as opposed to the more obvious 1×1 relationship depicted in Figure 2. In essence, the independent variable has spatial and geographic implications on the dependent variable.

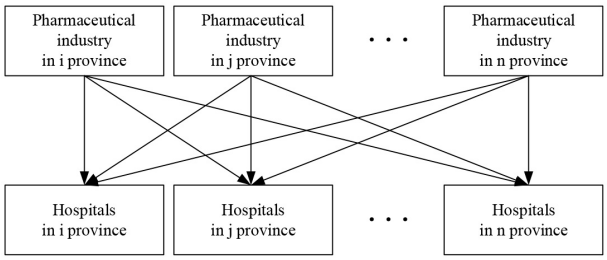


FIGURE 1
Interaction diagram of regional vertical relationship.

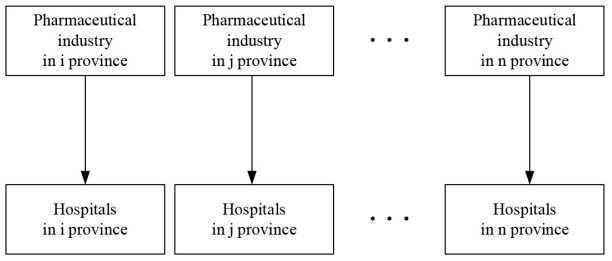


FIGURE 2
Vertical 1×1 relationship diagram.

3.2 Establishment and test of spatial Durbin model (SDM)

By taking into account the spatial linkages between all of the sections, the spatial panel analysis differs from the traditional panel technique. As geographic information is added based on the differentiated individual variables, it improves the accuracy of estimation results and captures the influence of local independent variables on local and regional dependent variables by including spatial data with individual variables. Its usefulness is increased as a result.

Spatial panel models include spatial autoregressive model (SAR), spatial error model (SEM), and spatial Durbin model (SDM). The general form of the spatial panel models is as follows:

$$y_{i,t} = \rho \sum_{j=1}^{N} W_{i,j} y_{j,t} + \beta x_{i,t} + \delta \sum_{j=1}^{N} W_{i,j} x_{j,t} + u_i + \eta_t + \varepsilon_{i,t} \quad (1)$$

For the SDM model, its estimation procedure is as follows. Firstly, Wald or LR statistics are used to test the two assumptions: ①H_0^1:$\delta = 0$, ②H_0^2:$\delta + \rho\beta = 0$. The two sets of hypothesis conditions are employed to determine whether it is possible to simplify the SDM into SAR or SEM. If both sets of hypotheses are disproven, the choice is in favor of the SDM. Secondly, The Hausman test is applied to determine the appropriate model specification between fixed-effect and random-effect. Thirdly, if the fixed-effect model is chosen as the appropriate specification, we need to choose among the optimal estimation model among no fixed effect, spatial fixed effect, temporal fixed effect, and spatial-temporal bidirectional fixed effect.

Compared to ordinary least squares (OLS), SDM allows decomposition of variable effects (especially the impact of market power of local medical institutions, as large buyers, on industry profits) into direct, indirect and total effects. Direct effect, indirect effect, and total effect of SDM are presented in the Appendix.

3.3 Sources of data, explanations of variables, and descriptive statistics

We used panel data samples from all 31 Chinese provinces, autonomous regions, and centrally managed municipalities, covering the years 2001 to 2021. The information was extracted from a number of government sources, including the China Statistics Yearbook on High Technology Industry, China Health and Family Planning Yearbook, China Industry Economy Statistical Yearbook, China Urban Life and Price Yearbook, and China Statistical Yearbook. Extreme values for all continuous variables were submitted to a Winsorization technique at the 1% level in order to reduce the influence of outliers. Stata 14.0, ArcGIS 10.2, and Matlab (56) were used for the empirical analysis and measurement. Attached Table 1 provides comprehensive information on variable units, symbols, and definitions whereas Attached Table 2 provides descriptive statistics for all variables.

3.3.1 Dependent and independent variables

(1) Dependent variable: it represents the yearly net earnings of the regional pharmaceutical industry, adjusted by the GDP deflator to eliminate the influence of inflation.

(2) Independent variable: the buyer market power is the main independent variable being considered. In a novel vertical relationship where the buyer retains dominance, the goal of this study is to empirically investigate how the buyer market power affects the profitability of suppliers. Buyer market power is evaluated by counting all the hospitals in a particular area. However, enterprise size may have an impact on the indication of the seller countervailing power, measured by the total number of pharmaceutical companies in a province. Given the accessibility of data, it is possible to improve the model by including such metrics, the total assets of pharmaceutical industry in a province and the total industrial output value of the pharmaceutical industry in a province, adjusted for inflation, to assure the stability of the predictions.

In the study of the vertical relationship of industrial organization, the market power of buyers and sellers is interdependent, as the buyer market power gradually increases, the seller power plays a countering function. This is known as the interaction term of the buyer power and the seller countervailing power. As a result, the seller power functions as a countervailing power in the interaction term and acts as a moderating factor to influence the relationship between the buyer market power and the profitability of the pharmaceutical industry.

3.3.2 Moderating variables and mediating variables

Enterprise size and asset specificity, two moderating factors that can be evaluated separately, are both included in this study. Asset specificity can be assessed by calculating the ratio of fixed asset investment in the pharmaceutical industry relative to the total asset investment at the end of the year, while corporate size can be calculated by dividing the total industrial output value of the pharmaceutical sector by the number of pharmaceutical companies. Additionally, we included mediating variables to investigate how the buyer market power affects supplier's profit. The pharmaceutical industry's R&D investment is a proxy for these mediating factors, and it is quantified as the ratio of internal R&D spending to sales revenue.

3.3.3 Control variables

We also chose to evaluate a number of significant aspects in light of the results of the available research results. The barrier to entry is one of them, and its impact is determined by the amount of fixed asset investment. Additionally, it takes into account government price regulation, which is established by ex-factory price index of pharmaceutical industry divided by ex-factory price index of the general industrial products in a province. The difference between the current sales revenue and the previous sales revenue divided by the current sales revenue is used to compute the market demand growth rate. Per capita GDP; Return on assets (calculated as net profits divided by total assets); Capital density (determined by dividing fixed asset investments by the number of employees); the density of R&D personnel (determined by the ratio of R&D personnel to all employees), and the quantity of new product development projects are additional factors considered. The profitability of the pharmaceutical sector is significantly influenced by these control variables.

3.4 Estimation strategy

3.4.1 Estimation method

Through this research, we tried to handle the complex longitudinal many-to-many interaction by using the SDM approach in cases when there is a paucity of granular data. Using the ordinary least squares (OLS) method could result in biased estimation findings due to the endogeneity problem, which is caused by the dependent variable being encapsulated within the independent variable. We propose using the Maximum Likelihood Estimation (MLE) method to estimate the model parameters in accordance with earlier works, including Elhorst (53) and Lee and Yu (54).

3.4.2 The setting of benchmark model

The following spatial measurement model is constructed in accordance with the chosen dependent variables, independent variables, and control variables, as well as the goals of this research:

$$Profit_{i,t} = \rho \sum_{j=1}^{N} W_{i,j} Profit_{j,t} + +\beta_1 Bmp_{j,t} + \beta_2 Smp_{i,t} + \beta_3 Bmp_{i,t} \cdot Smp_{i,t} + \delta \sum_{j=1}^{N} W_{i,j} Bmp_{j,t} + \alpha X'_{i,t} + u_i + \eta_t + \varepsilon_{i,t} \quad (2)$$

In the model, $Profit_{i,t}$ stands for the profit, $Bmp_{i,t}$ for the buyer power, $Smp_{i,t}$ for the seller power, $X'_{i,t}$ for the matrix composed of control variables, α for the coefficient vector corresponding to the control variable matrix, $\beta_1 \sim \beta_3$ for the coefficient of the corresponding independent variable, and $W_{i,j}Bmp_{j,t}$ for the spatial spillover effect of the buyer power.

3.4.3 Construction of inverse distance space weight matrix (*W*1) and economic distance spatial weight matrix (*W*2)

$W1$ is constructed based on the linear Euclidean distance between the two capital cities. When the buyer power in regions i and j is equal, the influence on area k diminishes as the distance between the two regions rises. This is the economic implication of the inverse distance spatial weight matrix $W1$. This idea is consistent with Tobel's first law of geography, according to which everything is connected to everything else, although connections between distant objects are weaker than connections between objects that are near to one another.

$W1 = \begin{cases} 0 & (i=j) \\ 1/d_{ij} & (i \neq j) \end{cases}$, d is the linear Euclidean distance between the two capital cities.

When establishing the spatial weight matrix, it is essential to consider two key factors: geographical distance and economic distance. The buyer market power, serving as the central variable, plays a pivotal role in the spatial spillover effect. To put it differently, when regions i and j have the same geographical distance as region k, the level of impact is positively associated with the buyer power in regions i and j. In typical circumstances, when the buyer power in region i surpasses that in region j but is farther away from the seller, determining the extent of impact on region k becomes challenging. In accordance with previous research by Li et al. (55), an economic distance spatial weight matrix $W2$ is established, incorporating both the buyer power and geographical distance factors, as illustrated below:

$$W2 = W1 \cdot U = W1 \cdot \mathrm{diag}\left(\frac{\bar{E}_1}{\bar{E}}, \frac{\bar{E}_2}{\bar{E}}, \cdots, \frac{\bar{E}_n}{\bar{E}}\right)$$

$$U = \mathrm{diag}\left(\frac{\bar{E}_1}{\bar{E}}, \frac{\bar{E}_2}{\bar{E}}, \cdots, \frac{\bar{E}_n}{\bar{E}}\right)$$

$$\bar{E}_i = \frac{1}{t_1 - t_0 + 1} \sum_{t=t_0}^{t_1} E_{i,t}$$

$$\bar{E} = \frac{1}{N(t_1 - t_0 + 1)} \sum_{i=1}^{N} \sum_{i=t_0}^{t_1} E_{i,t}$$

In the equation, U stands for the diagonal matrix, which is used to measure the relative size of the buyer power in different regions; $\bar{E}_i$ stands for the average of the total number of hospitals in i region, $\bar{E}$ is the average of the total number of hospitals in all provinces, autonomous regions, and municipalities directly under the central government, and t for different periods, $t \in [2001, 2021]$, $t_0 = 2001$, $t_l = 2021$. $W2$ stands for the influencing mechanism of the buyer under the joint action of market power and spatial location on the profit of pharmaceutical industry in different regions.

3.5 Robustness test

3.5.1 Cluster standard error regressions for the OLS

In the further test, the basic econometric specification is also added to this paper, we use cluster standard error regressions for the OLS as one of the robustness of the estimates, the regression results are shown in Attached Table 3.

3.5.2 Measurement of the seller power according to the total assets of the regional pharmaceutical industry and total industrial output value of the regional pharmaceutical industry

It becomes vital to carry out a robustness test when comparing the seller countervailing power in region i relative to region j by taking the number of pharmaceutical businesses into consideration. This criteria is crucial to removing the influence of the scale of enterprises from the calculation of relative power. To be clear, even if both locations have an equal number of pharmaceutical businesses, their relative market power may vary if the pharmaceutical industry in one is more developed and includes larger organizations. Therefore, it is essential to use measurement indicators from diverse viewpoints. Examining the total assets of the regional pharmaceutical industry and the total industrial output value of the regional pharmaceutical industry is one way to address this problem. We use Figure 3 to assess the sensitivity of results to different measurement and spatial weight matrices, it is presented as follows.

4 Results

4.1 Spatial weights matrices results

4.1.1 Regression analysis for inverse distance space weight matrix ($W1$)

After testing, with respect to inverse distance space weight matrix $W1$, all of the Wald statistics reject the null hypothesis of $\delta = 0$ and $\delta + \rho\beta = 0$ at the significance level of 0.01, indicating that the spatial Durbin model is the best choice. Hausman test determines that the spatial-temporal bidirectional fixed effect is the optimal estimation model, and the regression results are shown in Table 1.

From Table 1, it can be known that:

(1) The coefficient δ of spatial spillover effect of the core variable, buyer market power, exhibits a negative direction, and it does not demonstrate statistical significance, indicating that the spatial spillover effect of buyer market power is not significant.

(2) The buyer market power has a noteworthy negative direct effect with a significance level of 0.01. This suggests that the buyer market power of local medical institutions can substantially diminish the local pharmaceutical industry's profits, confirming Hypothesis H_1a. Furthermore, the adverse indirect effect implies that local medical institutions, while decreasing the local pharmaceutical industry's profitability through diverse vertical strategic actions, can also employ this same mechanism to transfer their market power to pharmaceutical industries in other regions, thereby reducing their profits as well. Therefore, Hypothesis H_1b is verified. Nonetheless, the insignificance of the coefficient suggests that within the context of spatial spillover effects in the transmission mechanism, the local buyer market power does not have a significant impact on reducing pharmaceutical industry's profits in other regions. This aligns with the observed direction and significance level of $W1_{ij} \cdot Bmp_{jt}$. The overall effect is negative, indicating that it reduces the profit of the pharmaceutical industry in all regions. Therefore, Hypothesis H_1c is verified.

(3) The absolute value of the coefficient of indirect effect is significantly lower than the absolute value of the coefficient of direct effect. This suggests that market players within the same region have closer economic ties and market transaction relationships. In this situation, the pharmaceutical industry, acting as the supplier, is subject to a stronger vertical constraint from the medical industry, acting as the buyer. Additionally, rather than extending to other regions, the main sales channel

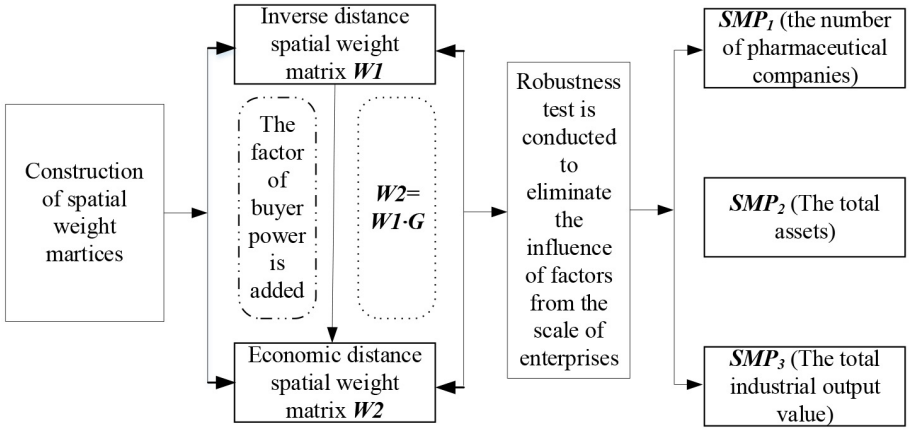


FIGURE 3
Robustness test of the sensitivity of results.

TABLE 1 The regression results for inverse distance spatial weight matrix.

Explanatory variable	Profit			
	Direct effect	Indirect effect	Total effect	Pool regression
Buyer Power	−0.028*** (−4.545)	−0.010 (−1.3054)	−0.038*** (−4.791)	−0.022*** (−4.042)
Seller power1	0.094*** (3.663)	0.582*** (3.925)	0.676*** (4.441)	0.084*** (3.354)
Buyer Power·Seller power1	1.850*** (9.591)	6.835*** (3.682)	8.685*** (4.717)	1.725*** (8.907)
Enterprise size	6.866*** (3.384)	7.298** (2.094)	14.164** (2.155)	6.173*** (2.987)
Asset specificity	−142.368* (−1.774)	−199.833** (−2.148)	−342.201** (−2.145)	−137.992*** (−3.627)
Barriers to entry	0.162*** (11.816)	−0.365*** (−3.310)	−0.204* (−1.887)	0.169*** (11.812)
Government price regulation	−20.921 (−1.542)	−1.361 (−0.022)	−22.282 (−0.378)	−21.228 (−1.566)
Market demand	3.930 (1.065)	16.014 (0.552)	19.944 (0.716)	3.581 (0.914)
Per capita GDP	2.410** (2.448)	−4.664 (−1.072)	−2.254 (−0.526)	2.459** (2.540)
Return on assets	248.756*** (3.696)	52.968 (0.175)	301.724 (0.973)	250.217*** (3.612)
Capital density	7,462.076*** (3.120)	53,054.168*** (5.669)	60,516.244*** (6.694)	7,504.870*** (3.165)
Density of R&D personnel	71.506*** (3.227)	577.733** (2.548)	649.239*** (2.924)	61.523*** (2.696)
New products	0.006** (2.235)	0.054** (2.661)	0.060*** (3.003)	0.005* (1.766)
W_1·Bmp	−0.714 (−0.954)			
R^2	0.920			
Maximum likelihood	−1,813.259			

***Means that it is significant at the 0.01 level.
**Means that it is significant at the 0.05 level.
*Means that it is significant at the 0.1 level.
The z value of the regression coefficient is in parentheses; The same as below. Due to the limitation of the software program on the exact number of decimal places, Bmp·Smp in the data matrix is recorded in tens of thousands. The figures in brackets are standard errors, the same treatment has been applied to Tables 2–6 and the Appendix.

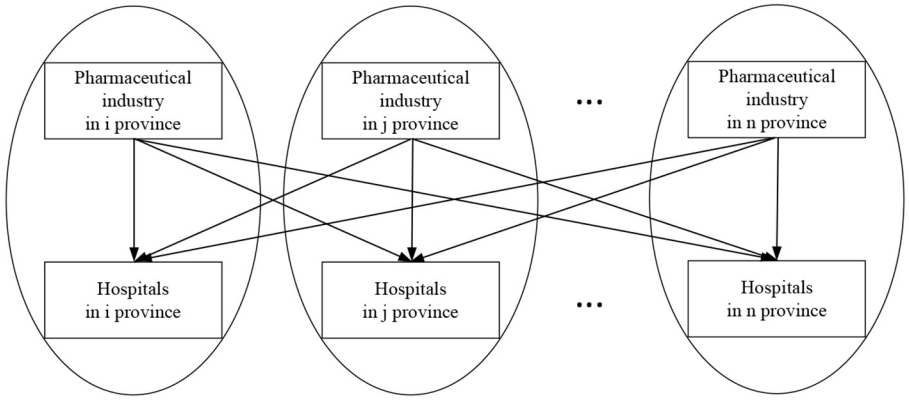


FIGURE 4
Economic implications for vertical markets.

for medications primarily operates inside the local area. This circumstance creates what can be called an "economic circle." Figure 4 provides a visual representation of this idea, showing how the downstream hospitals in region i and the upstream pharmaceutical sector are essentially encircled in this economic circle.

(4) The coefficient of direct effect of $Bmp_{it} \cdot Smp_{1it}$ showing the interaction of the vertical market power is positive and significant at the level of 0.010. According to Equation 2, the partial derivation of the dependent variable of profit to the independent variable of the buyer power can lead to the expression: $\partial Profit_{it}/\partial Bmp_{it} = \beta_1 + \beta_3 Smp_{it}$. In which, Q25(Smp) = 384, median(Smp) = 607, mean(Smp) = 684.5685, Q75 (Smp) = 926.5. In this way, the effect of profit as a function of Bmp depends on the value of Smp is well reflected, which avoids the effect of Bmp would be the effect of this variable when Smp = 0. If the seller countervailing power is taken into account as a moderating element, it can

help balance the negative impacts of the buyer power on the seller's profitability, thus lessening the negative effects of the buyer power. In essence, pharmaceutical companies have some market power, namely, if they have a countervailing power, they may be able to increase their own profits. The significance of coefficient suggests that both buyers and sellers in the same region exist as market trading entities with closer economic relationships, and the downstream industry has a larger vertical influence over suppliers. This is consistent with the fact that the absolute value of buyer power has a much higher direct effect than it does an indirect one.

(5) As to control variables, barrier to entry reduce industry competition, as a result, incumbent businesses can profit for a longer period of time from being the first to enter the market. Pharmaceutical companies may be forced to abandon R&D initiatives with uncertain or low-profit prospects due to government-mandated price reductions and maximum price regulations for particular medications. Expected returns in the pharmaceutical industry are consequently drastically reduced. Strong market demand produces a steady and regular cash flow, which boosts the profits made by the pharmaceutical industry. Profitability in the pharmaceutical industry is positively correlated with the degree of economic development in a certain area. Investments in innovation are supported by revenue from business growth and profitability, which also improves business performance. Employee training and advanced knowledge are linked to a company's capacity for research and development, which considerably boosts earnings. The pharmaceutical industry has a high concentration of R&D workers, which is indicative of the industry's overall R&D capacity and long-term growth potential, which benefits performance. Market demand is determined by a drug's efficacy, with specialized pharmaceuticals with intricate production methods and high levels of science and technology displaying promising market potential and sizable earnings in comparison to conventional drugs. National patent protection technology also enables brand-name medicine producers to continue profiting from their patents for an extended length of time.

4.1.2 Regression analysis for economic distance spatial weight matrix ($W2$)

After testing, the Wald statistics of $W2$ reject the null hypothesis of $\delta = 0$ and $\delta + \rho\beta = 0$ at the significance level of 0.01 both, which means that the SDM is the best choice. The Hausman test indicates that the spatial fixed effect is the optimal estimation model, and the regression results are shown in Table 2.

$W2$ further contends that buyer power has a negative impact on local and other regional earnings of pharmaceutical industry. However, there are no noticeable knock-on effects in other places as a result of this impact. Our hypotheses H1a, H1b, and H1c are therefore supported. There are closer trading relationships and economic connections between the vertical industry chain market entities in the same region. When pharmaceutical industry has a countervailing power, they may be able to increase their own profits. In terms of direction and significance level, the coefficients of the control variables closely match the results shown in Table 1.

4.2 Robustness test results

4.2.1 Regression analysis for OLS

As can be seen in attached Table 3, according to the coefficient symbol and significance level of core variables $Bmp_{i,t}$, $Smp_{i,t}$, $Bmp_{it} \cdot Smp_{2it}$ and control variables, the robustness of the regression results can also be proved When the total number of regional hospitals is used to measure the buyer power, and the number of pharmaceutical enterprises is used to measure the seller power under the setting of the inverse distance spatial weight matrix and the economic distance spatial weight matrix.

4.2.2 Regression analysis for measurement of the seller power according to the total assets of the regional pharmaceutical industry and total industrial output value of the regional pharmaceutical industry

When buyer power is gauged by assessing the combined count of regional hospitals, while the total assets of the regional pharmaceutical industry are used to measure the seller countervailing power. According to the Hausman test, the results of the robustness test $W1$ using time fixed effects are shown in Panel A of attached Table 4, whereas the results of the robustness test $W2$ using both space and time bidirectional fixed effects are shown in Panel B of attached Table 4. It also proves the robustness of the regression results under the setting of $W1$ and $W2$.

The buyer power is gauged by assessing the combined count of regional hospitals, while seller countervailing power is evaluated by considering pharmaceutical industry's total industrial output. In accordance with the Hausman test, the outcomes of the robustness tests, labeled as $W1$ and conducted with space and time bidirectional fixed effects, are displayed in Panel A of attached Table 5. Additionally, Panel B of attached Table 5 presents the findings of the $W2$ robustness test, which employs a time fixed effect. The robustness of the regression findings are further demonstrated.

4.3 Further analysis of heterogeneous competitive environments

From the perspective of vertical relationships in the industrial chain, the supplier's competitive position and relative advantage inside the vertical market are significantly shaped by the heterogeneous external competitive environment. As a result, this further affects the supplier's negotiating position when dealing with buyers, which ultimately affects their innovation performances. In this study we further groups the pharmaceutical industry according to different categories, and analyzed heterogeneity in terms of geographic location and capital intensity. Table 3 presents the results of our regression analysis.

10.3389/fpubh.2025.1683074

TABLE 2 The regression results for economic distance spatial weight matrix.

Explanatory variable	Profit			
	Direct effect	Indirect effect	Total effect	Pool regression
Buyer power	−0.026*** (−3.360)	−0.006 (−0.176)	−0.031* (−1.042)	−0.026*** (−3.490)
Seller power1	0.067** (2.642)	0.035 (0.514)	0.102 (1.607)	0.068*** (2.730)
Buyer Power·Seller power1	1.664*** (8.578)	−0.271 (−0.386)	1.393* (1.958)	1.665*** (8.800)
Enterprise size	4.141** (2.157)	15.742*** (3.009)	19.883*** (2.911)	3.569** (2.319)
Asset specificity	−178.337** (−2.114)	−238.217* (−1.8.8)	−416.554** (−2.278)	−183.224* (−1.859)
Barriers to entry	0.163*** (11.834)	−0.005 (−0.127)	0.159*** (4.002)	0.164*** (11.734)
Government price regulation	−16.423 (−1.341)	13.223 (0.694)	−3.200 (−0.417)	−16.640 (−1.338)
Market demand	5.250 (1.396)	−9.556 (−0.925)	−4.306 (−0.417)	5.170 (1.374)
Per capita GDP	4.293*** (4.689)	6.407* (1.978)	10.700*** (3.496)	4.279*** (4.876)
Return on assets	152.162** (2.245)	734.298 (1.048)	886.460 (1.235)	155.536** (2.217)
Capital density	4,098.043* (1.786)	91,800.137*** (3.526)	95,898.179*** (3.666)	4,329.165* (1.927)
Density of R&D personnel	63.552*** (2.908)	109.807 (1.221)	173.359 (0.510)	63.860*** (2.959)
New products	0.004 (1.546)	−0.024*** (−2.922)	−0.020*** (−2.343)	0.004 (1.469)
*W*2·Bmp	−0.166 (−0.183)			
R^2	0.975			
Maximum likelihood	−1,838.134			

***Means that it is significant at the 0.01 level. **Means that it is significant at the 0.05 level. *Means that it is significant at the 0.1 level.

TABLE 3 Regression results for heterogeneous competitive environment.

Panel A classification by geographical region						
	Eastern regions		Central regions		Western regions	
Buyer power	*W*1	*W*2	*W*1	*W*2	*W*1	*W*2
Direct effect	−0.266* (−1.834)	−0.397* (−1.827)	−0.186* (−1.797)	−0.448* (−1.801)	−0.586*** (−3.004)	−0.608*** (−4.742)
Indirect effect	−0.098 (−1.297)	−0.063 (−1.278)	−0.042 (−0.897)	−0.112 (−1.416)	−0.188 (−1.137)	−0.315 (−1.304)
Total effect	−0.364* (−1.776)	−0.460* (−1.815)	−0.231* (−1.860)	−0.560* (−1.791)	−0.773*** (−3.118)	−0.924*** (−3.303)
Pool regression	−0.220* (−1.858)	−0.325* (−1.879)	−0.191* (−1.850)	−0.404* (−1.862)	−0.524*** (−3.920)	−0.584*** (−3.178)
Control Variables	Control	Control	Control	Control	Control	Control
Panel B classification by capital intensity						
	High capital intensity		Low capital intensity			
Buyer power	*W*1	*W*2	*W*1	*W*2		
Direct effect	−0.125* (−1.826)	−0.255* (−1.822)	−0.375*** (−5.008)	−0.662*** (−3.381)		
Indirect effect	−0.044 (−0.917)	−0.090 (1.070)	−0.092 (−1.271)	−0.129 (−1.267)		
Total effect	−0.169* (−1.832)	−0.345* (−1.903)	−0.466*** (−2.992)	−0.791*** (−4.098)		
Pool regression	−0.113* (−1.777)	−0.244* (−1.791)	−0.399*** (−4.579)	−0.689*** (−3.639)		
Control variables	Control	Control	Control	Control		

***Means that it is significant at the 0.01 level. **Means that it is significant at the 0.05 level. *Means that it is significant at the 0.1 level.

In the situation where data is unavailable, this paper can only obtain data on the number of new products developed. We use the mean value of capital intensity of the pharmaceutical industry as categorical variables, the pharmaceutical industry is divided into different categories of high capital density and low capital density. By analyzing the correlation between capital intensity in the pharmaceutical industry and the number of new products developed using Stata 14.0 program, it can be concluded that the correlation coefficient between the two variables is 0.9194. The result indicates that capital intensity has a significant positive correlation with the number of new products developed.

In the further analysis combined with Table 3 above, with respect to inverse distance space weight matrix *W*1, the coefficients of indirect effect do not pass the significance test, in accordance

TABLE 4 Regression results of corporate size as a moderating variable.

Explanatory variable	Profit			
	Direct effect	Indirect effect	Total effect	Pool regression
Panel A $W1$				
Buyer power	−0.369** (−2.157)	−0.109 (−0.917)	−0.478** (−2.453)	−0.341** (−2.216)
Enterprise size	5.597*** (4.679)	10.121* (1.886)	15.718* (1.816)	5.179*** (3.619)
Buyer power·Enterprise size	3.641*** (2.774)	9.168** (2.126)	12.809** (2.371)	3.215*** (3.091)
Control variables	Control	Control	Control	Control
Panel B $W2$				
Buyer power	−0.706** (−2.422)	−0.243 (−0.752)	−0.949** (−2.355)	−0.749** (−2.356)
Enterprise size	3.546* (1.860)	22.175 (1.507)	25.721** (2.337)	3.383** (2.158)
Buyer power·Enterprise size	4.091*** (3.561)	5.658 (1.121)	9.750** (2.189)	4.233*** (3.237)
Control variables	Control	Control	Control	Control

***Means that it is significant at the 0.01 level. **Means that it is significant at the 0.05 level. *Means that it is significant at the 0.1 level.

TABLE 5 Regression results of asset specificity as a moderating variable.

Explanatory variable	Profit			
	Direct effect	Indirect effect	Total effect	Pool regression
Panel A $W1$				
Buyer power	−0.247** (−2.171)	−0.057 (−1.326)	−0.303* (−1.856)	−0.212** (−2.324)
Asset specificity	−165.058* (−1.871)	−217.116** (−2.306)	−382.174** (−2.164)	−170.153* (−1.796)
Buyer power·Asset specificity	−0.241*** (−3.030)	−0.512** (−2.116)	−0.753** (−2.216)	−0.272*** (−3.647)
Control variables	Control	Control	Control	Control
Panel B $W2$				
Buyer power	−0.425*** (−2.997)	−0.116 (−1.171)	−0.541** (−2.143)	−0.463*** (−3.371)
Asset specificity	−189.784* (−1.907)	−252.656** (−2.613)	−442.441* (−1.863)	−195.271** (−2.124)
Buyer power·Asset specificity	−0.512* (−1.872)	−0.687 (−0.912)	−1.199** (−2.448)	−0.501** (−2.034)
Control Variables	Control	Control	Control	Control

***Means that it is significant at the 0.01 level. **Means that it is significant at the 0.05 level. *Means that it is significant at the 0.1 level.

with the regression results in Panels A and B of Table 3, which are consistent with the influence and transmission mechanism of local buyer market power on pharmaceutical industry's profit in other regions as shown in Tables 1, 2. The coefficient of Bmp_{it} of pharmaceutical industry located in western region (defined by low capital intensity) shows extremely significant coefficients of direct and total effect at the 0.01 level. The pharmaceutical industry located in the eastern and central regions (characterized by high capital intensity) are weakly significant. The finding is evidence buyer power is not of great concern for, at least, value-adding innovations of new products developed, or even potential patented value-adding innovations. Additionally, the absolute values of the coefficients of Bmp_{it} for the direct effect, indirect effect, and total effect for the pharmaceutical industry in the western region (defined by low capital intensity) are noticeably higher than those for the pharmaceutical industry in the eastern and central regions (characterized by high capital intensity). This pattern is valid under the $W2$ conditions. An increased reliance on sellers in market transactions has resulted from the growth of pharmaceutical technology in the eastern and central regions as well as pharmaceutical businesses' ability in research and development to produce new pharmaceuticals. As a result, this has limited the outside options that downstream customers have, increasing the supplier's bargaining power. High capital intensity businesses are more likely to seek innovation, and their capacity to create innovative products strengthens their clout in vertical transactions. In consequence, this reduces the downstream customers' market power while increasing the suppliers' countervailing power.

4.4 The test of moderating effect

In order to test Hypothesis 2 and Hypothesis 3, we established Model (3):

$$\begin{aligned} Profit_{i,t} = {} & \rho \sum_{j=1}^{N} W_{i,j} Ip_{j,t} + \beta_1 Bmp_{i,t} + \beta_2 K_{i,t} + \beta_3 Bmp_{i,t} \cdot K_{i,t} \\ & + \delta \sum_{j=1}^{N} W_{i,j} Bmp_{j,t} + \alpha_1 Govr_{i,t} + \alpha_2 Demand_{i,t} \\ & + \alpha_3 Reg_{i,t} + \alpha_4 Sprofit_{i,t} + \alpha_5 Roa_{i,t} + \alpha_6 Capital_{i,t} \\ & + u_i + \eta_t + \varepsilon_{i,t} \end{aligned} \tag{3}$$

In the model, the moderating variable $K_{i,t}$ includes the two variables of corporate size (Size) and asset specificity (Asset). The regression results are shown in Tables 4, 5.

Through the partial derivation of the dependent variable innovation performance to Bmp_{it} in Equation 3, the following equation can be obtained: $\partial Profit_{it}/\partial Bmp_{it} = \beta_1 + \beta_3 Size_{it}$; combined with the coefficient signs and significance levels of Bmp_{it}, $Size_{it}$, $Bmp_{it} \cdot Size_{it}$ as shown in Table 4, the following conclusion can be reached: when corporate size is used as a moderating element, it can improve the vertical squeeze of downstream customer market power on the profits of the pharmaceutical industry, and weaken the negative effect of buyer power. In other words, the scale of the enterprise can play a positive regulatory role, to a certain extent, alleviate the adverse effects of buyer power. As a result, Hypothesis H_2 is confirmed.

Through the partial derivation of the dependent variable innovation performance to Bmp_{it} in Equation 3, the following equation can be obtained: $\partial Profit_{it}/\partial Bmp_{it} = \beta_1 + \beta_3 Asset_{it}$. Combined with the coefficient signs and significance levels of Bmp_{it}, $Asset_{it}$, $Bmp_{it} \cdot Asset_{it}$ in Table 5, the following conclusion can be reached: when asset specificity is used as a moderating factor, it has the ability to intensify the damaging impact of downstream customers' market dominance on pharmaceutical industry's earnings, and enhance the negative effects of the buyer market power. To put it another way, asset specificity can work as a negative moderating element within the pharmaceutical industry, further aggravating the unfavorable influence of the buyer market power. Consequently, this validates the validity of Hypothesis H_3.

4.5 Test of action mechanism

The pharmaceutical industry's cutting-edge technological features attract R&D spending, which is essential for boosting product competitiveness, growing market presence, and attaining steady growth. Downstream buyers using their market power to limit suppliers' R&D spending will inevitably lead to insufficient innovation spending, which will stifle performance in this area. In this study, we aim to strengthen the logical framework by studying the impact mechanism utilizing mediating variables given that the inverse association between a buyer's influence and innovation performance in the pharmaceutical industry has already been verified. Model (4) is introduced in this study to examine if buyer market power affects the pharmaceutical industry's R&D investment.

$$Rnd_{i,t} = \rho \sum_{j=1}^{N} W_{i,j} Rnd_{j,t} + \beta_1 \text{ Bmp }_{i,t} + \beta_2 Smp_{i,t} + \beta_3 Bmp_{i,t} .Smp_{i,t} + \delta \sum_{j=1}^{N} W_{i,j} Bmp_{j,t} + \alpha X_{i,t} + u_i + \eta_t + \varepsilon_{i,t} \quad (4)$$

In the model, $Rnd_{i,t}$ stands for R&D investment and the remaining variables have the same meanings as those in Equation 2. It is worth mentioning that in the pharmaceutical industry within any given region, when R&D investment is measured as the ratio of internal R&D spending to sales revenue, considering that the R&D spending is conducted across the entire country and the sales revenue comes from both local and other regional buyer markets, there exists a complex interaction in the vertical relationship. This interaction remains to be addressed through a spatial measurement model. The specific regression results are presented in Table 6.

Table 6 shows that the coefficient of Bmp_{it} demonstrates substantial negative values at varied levels in the regression findings for $W1$ and $W2$. This suggests that the influence of buyer power causes upstream suppliers in the industry chain to reduce their R&D investments, which has a negative impact on earnings owing to innovation limits. This thereby validates the method by which buyer power affects the earnings of the pharmaceutical industry.

In further research, this paper explores the subdivision of R&D spending into product R&D spending and process R&D spending in depth, so as to observe the impact of buyer power on the two forms of R&D spending respectively. $Rnd_{i,t}$ is divided into $Product\ Rnd_{i,t}$ and $ProcessRnd_{i,t}$, the remaining variables have the same meanings as those in Equation 2. The specific regression results are presented in Tables 7, 8 respectively.

According to Tables 7, 8, the coefficient of Bmp_{it} demonstrates substantial negative values at varied levels in the regression findings for $W1$ and $W2$. This suggests that the influence of buyer power causes upstream suppliers in the industry chain to reduce their product R&D investment and Process R&D Investment both, the negative effect on earnings still holds when different forms of innovative activities are constrained.

5 Conclusions and policy recommendations

5.1 Conclusions

Using the data of China's pharmaceutical industry and medical industry from 2001 to 2021, this paper selects the pharmaceutical industry, a typical industry with prominent buyer power, for research based on the realistic background of China's market. This paper studied the upstream and downstream rivalries in the pharmaceutical industry in the provinces of China. From the perspective of spatial spillover effect, we construct a vertical relationship between pharmaceutical industries in the 31 provinces of the seller and medical industries in the 31 provinces of the buyer, and empirically studies the influence mechanism between industries, which explores the influence of market power from downstream customers on the profits of pharmaceutical industry in industrial organizations, as well as the effect on upstream industries when the downstream power is too powerful. We found the following conclusions.

(1) The buyer power faced by pharmaceutical industry (the large buyer counterbalance power developing to a certain stage) does exist and it is universal. When the position of the buyer and the seller changes, in the case of the new buyer-led vertical relationship, the distortion of the vertical relationship caused by buyer power will have a negative impact on the upstream industry. This effect is in contrast to the beneficial effect of buyer counterbalance power (1).

(2) Factors that affect the decision-making of enterprises include not only the structural characteristics of the industry

10.3389/fpubh.2025.1683074

TABLE 6 Buyer power and R&D investment in the pharmaceutical industry.

Independent variable	Rnd			
	Direct effect	Indirect effect	Total effect	Pool regression
Panel A $W1$				
Buyer power	−0.132** (−2.056)	−0.031 (−1.124)	−0.163 (−1.350)	−0.131* (−1.957)
Control variables	Control	Control	Control	Control
Panel B $W2$				
Buyer power	−0.422*** (−2.952)	−0.031 (−0.821)	−0.453*** (−3.194)	−0.408** (−2.338)
Control variables	Control	Control	Control	Control

Due to the limitation of the software program on the exact number of decimal places, Bmp, Smp, and Bmp·Smp in the data matrix are all recorded in tens of thousands. ***Means that it is significant at the 0.01 level. **Means that it is significant at the 0.05 level. *Means that it is significant at the 0.1 level.

TABLE 7 Buyer power and product R&D investment in the pharmaceutical industry.

Independent variable	Product Rnd			
	Direct effect	Indirect effect	Total effect	Pool regression
Panel A $W1$				
Buyer power	−0.078** (−2.371)	−0.019 (−1.116)	−0.094 (−1.437)	−0.066** (−2.099)
Control variables	Control	Control	Control	Control
Panel B $W2$				
Buyer power	−0.257*** (−3.855)	−0.017 (−0.659)	−0.267*** (−4.337)	−0.209** (−2.616)
Control variables	Control	Control	Control	Control

Due to the limitation of the software program on the exact number of decimal places, Bmp, Smp, and Bmp·Smp in the data matrix are all recorded in tens of thousands. ***Means that it is significant at the 0.01 level. **Means that it is significant at the 0.05 level. *Means that it is significant at the 0.1 level.

TABLE 8 Buyer power and process R&D investment in the pharmaceutical industry.

Independent variable	Process Rnd			
	Direct effect	Indirect effect	Total effect	Pool regression
Panel A $W1$				
Buyer power	−0.054** (−2.368)	−0.014 (−1.385)	−0.079 (−1.447)	−0.049* (−1.896)
Control Variables	Control	Control	Control	Control
Panel B $W2$				
Buyer power	−0.165*** (−3.649)	−0.014 (−0.968)	−0.179*** (−3.822)	−0.178** (−2.035)
Control variables	Control	Control	Control	Control

Due to the limitation of the software program on the exact number of decimal places, Bmp, Smp, and Bmp·Smp in the data matrix are all recorded in tens of thousands. ***Means that it is significant at the 0.01 level. **Means that it is significant at the 0.05 level. *Means that it is significant at the 0.1 level.

in the horizontal market, but also the vertical power characteristics in the industrial organization. Downstream industry characteristics also play a role in the decision-making of upstream industries, in which market power is the typical representative. This paper extends the industrial chain hierarchy, the market power from downstream customers in the industrial organization is included in the analysis of the impact on the profits of upstream industry. The results show that the local buyer power reduces the profit of the pharmaceutical industry in the local and other provinces at the same time, but the spatial spillover effect is not significant.

(3) The absolute value of the coefficient of direct effect is significantly greater than that of the indirect effect. The pharmaceutical industry and medical institutions within the same region have closer market transaction relationship and economic connection. In this situation, the pharmaceutical industry, acting as the supplier, is subject to a stronger vertical constraint from the medical industry, acting as the buyer.

(4) The interaction term of market power indicates that when the seller counterbalance power is taken as the moderating variable, the counterbalance power of the supplier can improve the negative influence of the buyer power on its own profit and weaken the negative effect of buyer power. In other words, the pharmaceutical industry also has market power, when it has a counterbalance power, its own profits would increase.

(5) When we take the number of regional hospitals as the buyer power, the total assets and the total industrial output value of the pharmaceutical industry as the measure of

the seller power, the conclusions above are also proved to be robust.

(6) This article explores the differentiation of countervailing power among different categories of pharmaceutical industries in a heterogeneous competitive environment, and confirms that the pharmaceutical industry in the eastern and central regions, as well as the high capital density (western regions, low capital density), have stronger (weaker) countervailing power compared to buyers.

(7) This article confirms that enterprise size can alleviate the adverse impact of buyer market power on the profits of the pharmaceutical industry, while asset specificity can exacerbate this adverse impact. Furthermore, this study explores its mechanism of action and confirms that the underlying mechanism behind the negative impact of buyer market power on the profits of the pharmaceutical industry is to reduce the R&D investment level of the latter.

5.2 Policy recommendations

The pharmaceutical industry chain consists of the Active Pharmaceutical Ingredient suppliers (API suppliers), the pharmaceutical industry, and the medical industry (mainly hospitals as the distribution terminal). The profit shares of each stakeholder in the vertical market come from patients as a specific consumer group. This study empirically concludes that the market power of medical institutions drives the profits of the pharmaceutical industry to flow to medical institutions and reduces the performance of the pharmaceutical industry. The immediate policies are as follows: (1) Regulatory bodies should cater for heterogenous preferences of customers to encourage the development of private hospitals, those who prefer (lower-priced) public hospitals will use them and those who prefer (higher priced) private facilities get what they want, thus reducing society's reliance on public hospitals. Increasing the number and geographical distribution of community pharmacies in an equitable fashion so as to increase market demand facing manufacturers and extend patients' choices of medicines, in order to increase access to care (demand) for patients. In addition to overseeing the wholesale price of medicines, regulators should also focus on supervising the price of medicines sold at medical terminals. (2) Regulatory bodies should strictly regulate and control the transaction behavior of downstream customers, especially the medical industry, and crack down on all kinds of unfair competition imposed on pharmaceutical companies by the medical industry drawing on their dominant market position and abusing their market power. (3) Pharmaceutical companies in weaker market positions or complex competitive environments need to continue harmonious relationships with customers while also holding high cash reserves to guard against unfavorably effect on short-term production and operations brought by cash-flow risks and adverse external shocks.

The pharmaceutical industry in China faces powerful downstream buyers, and under the context that "hospitals" and "drugs" are difficult to be separated in the short run, the inhibitory effects of buyer power on the economic effect and behavioral decisions of pharmaceutical companies will remain in place for a longer period. The influence of horizontal market factors on pharmaceutical companies changes with the external environment. In the face of strong buyers, pharmaceutical companies could boost their counterbalance power through a variety of channels. The short-run policies are as follows: (1) With respect to supply chain management, pharmaceutical companies should optimize their relationships with downstream customers in the industrial chain, both to preserve the stability of partners and to expand the range of external options for downstream customers to develop a diversified relationship network of suppliers-customers. (2) The pharmaceutical enterprises not only need to rely on continuous investment in research and development to maintain its technological advantage but also must adopt effective market strategies and product innovations to maintain its market shares. At the same time, while pursuing short-term returns, pharmaceutical enterprises should place greater emphasis on the sustainability of future profit growth and their long-term production and management capacity, in order to cope with fierce horizontal market competition as well as vertical market competition from downstream customers. (3) With respect to vertical cooperation, pharmaceutical companies should establish new information shared mechanisms of teamwork, risk-sharing, and mutually-supported with large customers, extend and strengthen the industry chain, enhance the level of trust between both parties, so as to mitigate the negative effects of buyers on suppliers' profits. (4) With respect to negotiation skills and public relations, pharmaceutical companies should establish professional negotiation teams and devise differentiated negotiation strategies for different downstream customers, so as to strategically cushion the adverse effects of their inherent weaknesses relative to the healthcare industry in market transactions, with a view to securing more benefits in market transactions.

The long-run policies are as follows: (1) With respect to corporate management, pharmaceutical companies should strengthen the development of their independent innovation capabilities and gain competitive advantages through product and technological innovation in a fiercely competitive market environment, with the aim of enhancing their performance. Pharmaceutical companies should improve their governance structure, optimize resource allocation, and implement diverse strategies for innovation investment, in order to enhance their competitive advantages in the market. (2) With respect to product production, pharmaceutical companies should actively adjust their development strategies to adapt to changes in market demand, focus on a specific area of better medicine production (safer, more health benefits, more cost-effective with lower manufacturing costs), and enhance their bargaining power in market transactions through value-adding products and services. (3) With respect to market support and regulation, the government should build a comprehensive innovation system, such as by increasing innovation investment in basic research of pharmaceutical companies and assisting pharmaceutical companies in their innovative R&D. The government should formulate targeted and differentiated subsidy policies based on the R&D situations of different types of pharmaceutical companies and their market

positions in the industrial chain, with the aim of guiding companies to optimize the efficiency of their R&D investment.

6 Discussion

The findings of this study not only provide theoretical foundations and practical approaches for regulating large buyer groups (cartels) in vertical market transactions, but also assist regulatory authorities in identifying and preventing potential market risks, thereby safeguarding fairness and efficiency in market competition. At the same time, the results help promote more balanced interactions among upstream and downstream enterprises in the pharmaceutical industry chain, and enhance the overall stability and resilience of the industry chain. Against the backdrop of multiple uncertainties facing the global pharmaceutical supply chain, this research offers important insights for policymakers and business leaders to optimize governance mechanisms and strengthen risk resistance capabilities.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

YG: Validation, Data curation, Conceptualization, Project administration, Supervision, Writing – review & editing, Methodology, Investigation, Writing – original draft, Resources, Visualization, Formal analysis, Software, Funding acquisition. WL: Writing – review & editing, Data curation, Methodology, Supervision, Conceptualization. CH: Conceptualization, Methodology, Supervision, Writing – review & editing. DZ: Supervision, Data curation, Writing – original draft, Investigation, Software, Conceptualization, Methodology, Resources, Funding acquisition, Visualization, Project administration, Formal analysis, Validation.

Funding

The author(s) declare that financial support was received for the research and/or publication of this article. This research was supported by Heilongjiang Postdoctoral Funding LBH-Z22014; National Social Science Fund: 23BGL076.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The author(s) declare that no Gen AI was used in the creation of this manuscript.

Any alternative text (alt text) provided alongside figures in this article has been generated by Frontiers with the support of artificial intelligence and reasonable efforts have been made to ensure accuracy, including review by the authors wherever possible. If you identify any issues, please contact us.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2025.1683074/full#supplementary-material

References

1. Galbraith JK. *American Capitalism: The Concept of Countervailing Power*. New York, NY: Houghton Mifflin (1952).

2. Beckert W. An empirical analysis of countervailing power in business-to-business bargaining. *Rev Ind Organ.* (2018) 52:369–402. doi: 10.1007/s11151-017-9607-7

3. Gu T, Sanders NR, Venkateswaran A. CEO incentives and customer-supplier relations. *Produ Operat Manag.* (2017) 26:1705–27. doi: 10.1111/poms.12715

4. Chen ZQ. Supplier innovation in the presence of buyer power. *Int Econ Rev.* (2019) 60:329–53. doi: 10.1111/iere.12355

5. :Krolikowski M, Yuan XJ. *Friend or foe: customer-supplier relationships and innovation. J Bus Res.* (2017) 78:53–68. doi: 10.1016/j.jbusres.2017.04.023

6. Inderst R, Valletti TM. Market analysis in the presence if indirect constraints and captive sales. *J Compet Law Econ.* (2007) 3:203–31. doi: 10.1093/joclec/nhl025

7. Inderst R, Shaffer G. Retail mergers, buyer power and product variety. *Econ J.* (2007) 117:45–67. doi: 10.1111/j.1468-0297.2007.02001.x

8. Dobson PW, Inderst R. *The Waterbed Effect: Where buying and selling power come together*. Wisconsin Law Review. Madison, WI: University of Wisconsin Law School (2008). p. 331–57.

9. Weiss CR, Wittkopp A. Retail concentration and product Innovation in food manufacturing. *Eur Rev Agric Econ.* (2005) 32:219–44. doi: 10.1093/eurrag/jbi022

10. Fumagalli C, Motta M. Buyers' miscoordination, entry and downstream competition. *Econ J.* (2008) 118:1196–222. doi: 10.1111/j.1468-0297.2008.02166.x

11. Pan X, Zang SW, Hu YY, Liu JY. Identifying the positive sides of power use between (in)congruence in distributive fairness perception and supplier-buyer relationship quality. *Ind Mark Manag.* (2020) 91:362–72. doi: 10.1016/j.indmarman.2020.09.013

12. Dhaliwal D, Michas PN, Naiker V, Sharma D. Greater reliance on major customers and auditor going concern opinions. *Contemp Account Res.* (2020) 37:160–88. doi: 10.1111/1911-3846.12551

13. Ellison SF, Snyder CM. Countervailing power in wholesale pharmaceuticals. *J Ind Econ*. (2010) 58:32–53. doi: 10.1111/j.1467-6451.2010.00408.x

14. Hada M, De Bruyn A, Lilien GL. Horizontal referrals in B2B markets. *J Market Res*. (2024) 61:143–64. doi: 10.1177/00222437231175415

15. Geiger I, Naacke D. "What's it really worth?" A meta-analysis of customer-perceived relationship value in B2B markets. *J Bus Ind Market*. (2023) 38:751–73. doi: 10.1108/JBIM-09-2021-0438

16. Geiger I, Salmen A, Zerres A. Is the buyer really king? A meta-analysis of the buyer advantage in sales negotiation. *Ind Mark Manag*. (2024) 123:372–85. doi: 10.1016/j.indmarman.2024.11.004

17. Mirzabeiki V, He Q, Sarpong D. Sustainability-driven co-opetition in supply chains as strategic capabilities:drivers, facilitators, and barriers. *Int J Produ Res*. (2023) 61:4826–52. doi: 10.1080/00207543.2021.1988749

18. Dhaliwal D, Judd JS, Serfling M, Shaikh S. Customer concentration risk and the cost of equity capital. *J Account Econ*. (2016) 61:23–48. doi: 10.1016/j.jacceco.2015.03.005

19. Giannetti M, Burkart M, Ellingsen T. What you sell is what you lend? Explaining trade credit contracts. *Rev Financ Stud*. (2011) 24:1261–98. doi: 10.1093/rfs/hhn096

20. Huo B, Guo M, Tian M. The impact of supply chain specific investments on firms' market performance:the mediating role of innovation. *J Bus Ind Mark*. (2023) 38:208–22. doi: 10.1108/JBIM-03-2021-0162

21. Jia N. Competition, governance, and relationship-specific investments:theory and implications for strategy. *Strateg Manag J*. (2013) 34:1551–67. doi: 10.1002/smj.2077

22. Chen PY, Chen KY, Wu LY. The impact of trust and commitment on value creation in asymmetry buyer-seller relationships:the mediation effects of specific assets investments. *J Bus Ind Market*. (2017) 32:457–71. doi: 10.1108/JBIM-09-2014-0171

23. Saghiri SS, Mirzabeiki V. *Buyer-led environmental supplier development: can suppliers really help it? Int J Prod Econ*. (2021) 233:107969. doi: 10.1016/j.ijpe.2020.107969

24. De Stefano MC, Montes-Sancho MJ. Supply chain environmental R&D cooperation and product performance: exploring the network dynamics of positional embeddedness. *J Purch Supply Manag*. (2018) 24:288–303. doi: 10.1016/j.pursup.2018.10.003

25. Williamson OE. *Markets and Hierarchies: Analysis and Antitrust Implications*. New York, NY: The Free Press (1975).

26. Willamson OE. *The Economic Institute of Capitalism. New York, NY: Free Press* (1985). p. 528–30.

27. Hertzel MG, Li Z, Officer M, Rodgers K.Inter-firm linkages and the wealth effects of financial distress along the supply chain. *J Finan Econ*. (2008) 87:374–87. doi: 10.1016/j.jfineco.2007.01.005

28. Hou WJ, Li SC, Zhang XY, Wu HF. When buyer transparency really stimulates supplier innovation: a motivation-opportunity–ability perspective. *J Innov Knowl*. (2025) 10:1–15. doi: 10.1016/j.jik.2025.100805

29. Sadeghi J, K, R, Azadegan A, Ojha D, Ogden J, et al. Benefiting from supplier business continuity: the role of supplier monitoring and buyer power. *Ind Market Manag*. (2022) 106:432–43. doi: 10.1016/j.indmarman.2022.09.009

30. Fabbri D, Menichini AMC. Trade credit, collateral liquidation, and borrowing constraints. *J Finan Econo*. (2010) 96:413–32. doi: 10.1016/j.jfineco.2010.02.010

31. Siemieniako D, Makkonen H, Kwiatek P, Karjaluot H. Empowering value co-creation: product and technology development in power asymmetric buyer-supplier relationships from the perspective of a weaker supplier. (2025) 124:128–49. doi: 10.1016/j.indmarman.2024.11.008

32. Montes-Sancho M, J, Tachizawa EM, Blome C. Financial and market impacts of buyer-supplier sustainability asymmetries: empirical evidence from sensitive industries. *J Clean Produ*. (2022) 370:133256. doi: 10.1016/j.jclepro.2022.133256

33. Fabbri D, Klapper LF. Bargaining power and trade credit. *J Corp Finan*. (2016) 41:66–80. doi: 10.1016/j.jcorpfin.2016.07.001

34. Minerbo C, Samartini AL, Brito LAL. Sharing the benefits: how different dimensions contribute to value creation and capture. *Ind Market Manag*. (2023) 108:251–62. doi: 10.1016/j.indmarman.2022.11.015

35. Cool K, Henderson J. Power and firm profitability in supply chains: French Manufacturing Industry in 1993. *Strat Manag J*. (1998) 19:909–26. doi: 10.1002/(SICI)1097-0266(199810)19:10<909::AID-SMJ991>3.0.CO;2-K

36. Kelly T, Gosman ML. Increased buyer concentration and its effects on profitability in the manufacturing sector. *Rev Ind Organ*. (2000) 17:41–59. doi: 10.1023/A:1007870816171

37. Makkonen H, Siemieniako D, Mitrega M. Structural and behavioral power dynamics in buyer-supplier relationships: a perceptions-based framework and a research agenda. *Tech Anal Strat Manag*. (2023) 35:1099–113. doi: 10.1080/09537325.2021.1991574

38. Köhler C, Rammer C. *Buyer Power and Suppliers' Incentives to Innovate*. Zew Discussion papers (2012). p. 1–25. doi: 10.2139/ssrn.2141963

39. Köhler C. *Bargaining in Vertical Relationships and Suppliers' R&D Profitability*. Zew Discussion Papers (2014). p. 1–30. doi: 10.2139/ssrn.2523374

40. Toraubally WA. Comparative advantage with many goods: new treatment and results. *Eur J Operat Res*. (2023) 311:1188–1201. doi: 10.1016/j.ejor.2023.05.027

41. Jung SH, Kouvelis P. On co-opetitive supply partnerships with end-product rivals:information asymmetry, dual sourcing and supply market efficiency. *Manuf Serv Oper Manag*. (2022) 24:1040–55. doi: 10.1287/msom.2021.0982

42. Shriver SK, Bollinger B. Demand expansion and cannibalization effects from retail store entry: a structural analysis of multichannel demand. *Manag Sci*. (2022) 68:8829–56. doi: 10.1287/mnsc.2022.4308

43. Moon SK, Phillips GM. Outsourcing through purchase contracts and firm capital structure. *Manag Sci*. (2020) 67:363–87. doi: 10.1287/mnsc.2019.3443

44. Gu W, Liu YJ, Song YN, Shang J, Cheng JCE. The impact of retailer regret in two-stage supply chains: various structures and buyer power. *Eur J Operate Res*. (2024) 319:587–99. doi: 10.1016/j.ejor.2024.07.005

45. Revilla A, Fernandez Z. Environmental dynamism, firm size and the economic productivity of R&D. *Ind Innov*. (2013) 20:503–52. doi: 10.1080/13662716.2013.833374

46. Czarnitzki D, Toole AA. The R&D investment-uncertainty relationship: do strategic rivalry and firm size matter? *Manag Decis Econ*. (2013) 34:15–28. doi: 10.1002/mde.2570

47. Foellmi R, Zweimuller J. Is inequality harmful for innovation and growth? Price versus market size effects. *J Evol Econ*. (2017) 27:359–78. doi: 10.1007/s00191-016-0451-y

48. Coase RH. The nature of the firm. *Economica*. (1937) 4:86–405. doi: 10.1111/j.1468-0335.1937.tb00002.x

49. Luo A, Kumar V. Recovering hidden buyer-seller relationship states to measure the return on marketing investment in business-to-business markets. *J Market Res*. (2013) 50:143–60. doi: 10.1509/jmr.11.0295

50. Ovchinnikov A, Pun H, Raz G. The impact of inventory risk on market prices under competition. *Decis Sci*. (2023) 54:29–42. doi: 10.1111/deci.12520

51. Perera HN, Fahimnia B, Tokar T. Inventory and ordering decisions:a systematic review on research driven through behavioral experiments. *Int J Operat Produ Manag*. (2020) 40:997–1039. doi: 10.1108/IJOPM-05-2019-0339

52. Niu BZ, Lai CW, Zheng ZB, Zeng FZ, Dai ZP. Will supplier's quality improvement discourage competing buyers' joint procurement? Impact of product differentiation and manufacturing cooperation. *Int J Prod Econ*. (2025) 286:109666. doi: 10.1016/j.ijpe.2025.109666

53. Elhorst JP. *Spatial Panel Data Models//Handbook of Applied Spatial Analysis Software Tools, Methods and Applications*. Berlin, Heidelberg, Germany: Springer Press (2010). p. 377–407. doi: 10.1007/978-3-642-03647-7_19

54. Lee L, Yu J. Estimation of spatial autoregressive panel data models with fixed effects. *J Econom*. (2010) 154:165–85. doi: 10.1016/j.jeconom.2009.08.001

55. Li J, Tan QM, Bai JH. Spatial econometric analysis on region innovation production in China. *Manag World*. (2010) 7:43–55. doi: 10.19744/j.cnki.11-1235/f.2010.07.006

56. MathWorks. *MATLAB R2018b (Version 9.7) [Computer software]*. Natick, MA: The MathWorks Inc (2018).

frontiers | Frontiers in Public Health

TYPE Original Research
PUBLISHED 11 December 2025
DOI 10.3389/fpubh.2025.1655280

Check for updates

OPEN ACCESS

EDITED BY
Kevin Lu,
University of South Carolina, United States

REVIEWED BY
Muhammad Fawad Rasool,
Bahauddin Zakariya University, Pakistan
Ricardo De Moraes E. Soares,
Naval School, Portugal

*CORRESPONDENCE
Shiya Zuo
452351069@qq.com
Ling Lin
linl@hku-szh.org

RECEIVED 27 June 2025
REVISED 22 November 2025
ACCEPTED 26 November 2025
PUBLISHED 11 December 2025

CITATION
Zuo S and Lin L (2025) Characteristics of hospitalization patterns and expenditures in cross-border medical tourism: a knee replacement surgery cohort study. *Front. Public Health* 13:1655280. doi: 10.3389/fpubh.2025.1655280

COPYRIGHT
© 2025 Zuo and Lin. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

Characteristics of hospitalization patterns and expenditures in cross-border medical tourism: a knee replacement surgery cohort study

Shiya Zuo[1]* and Ling Lin[2]*

[1]Department of Pediatric Dentistry, School and Hospital of Stomatology, Guangdong Engineering Research Center of Oral Restoration and Reconstruction & Guangzhou Key Laboratory of Basic and Applied Research of Oral Regenerative Medicine, Guangzhou Medical University, Guangzhou, Guangdong, China, [2]The University of Hong Kong-Shenzhen Hospital, Shenzhen, China

Objective: Using knee arthroplasty as a case study, this research explores the characteristics of length of stay (LOS) and hospitalization costs for Hong Kong residents receiving medical treatment in mainland China.
Methods: Utilizing front-page medical record data of patients who underwent knee arthroplasty at Hospital H, descriptive statistics, univariate analysis, and mediation effect tests were conducted to analyze the impact of being a Hong Kong patient on LOS and hospitalization costs.
Results: The study included 356 patients, predominantly older adults over 65 years old (77.25%), with a similar gender distribution. Hong Kong patients had shorter LOS, shorter postoperative LOS, and lower hospitalization costs, laboratory and examination costs, and medication costs. LOS fully mediated the effect of being a Hong Kong patient on hospitalization costs.
Conclusion: Hong Kong residents seeking medical care in mainland China are driven by factors distinct from those of non-local patients within mainland China, with medical quality, efficiency, and cost being significant drivers of cross-border healthcare seeking. It is essential to strengthen cross-border medical collaboration between Shenzhen and Hong Kong, and the Greater Bay Area as a whole, through institutional mechanisms, welfare benefits, long-term follow-up, and health monitoring to ensure tangible medical benefits for Hong Kong patients.

KEYWORDS

seeking medical care in mainland China, cross-border medical cooperation, knee arthroplasty, length of stay, hospitalization costs

1 Introduction

The construction of healthcare integration in the Guangdong-Hong Kong-Macao Greater Bay Area has provided institutional breakthroughs for innovations in cross-border medical services. Since the *Outline Development Plan for the Guangdong-Hong Kong-Macao Greater Bay Area* proposed the "Healthy Bay Area" strategy, policymakers have gradually established a multidimensional framework for Shenzhen-Hong Kong medical collaboration. This framework includes opening cross-border practice qualifications for Hong Kong doctors, optimizing access mechanisms for pharmaceuticals and medical

devices from Hong Kong and Macao, and promoting mutual recognition of hospital accreditation standards between the two regions (1, 2). These measures systematically address institutional barriers to cross-border healthcare resource flows. This policy system not only facilitates northbound healthcare-seeking for Hong Kong residents but also reshapes the spatial distribution of medical resource allocation within the Greater Bay Area through deep integration of healthcare service supply (1).

Under the impact of special public health events, the healthcare system in Hong Kong has faced practical pressures such as a backlog of elective surgeries and extended service delivery cycles, which further intensified the "demand spillover" effect of cross-border medical care (3). During this period, medical institutions in mainland China, leveraging their efficient service response capabilities, became a significant supplementary force in alleviating the healthcare difficulties faced by Hong Kong residents. Existing research on cross-border medical behaviors has primarily focused on medical tourism, border medical care, and healthcare demands arising from cross-border work. The driving forces behind patient mobility include shorter distances, higher-quality medical services, or lower medical costs, exemplified by individuals traveling to Hungary for dental and orthopedic treatments or UK-supported NHS patients seeking care in Brussels and France in the early 2000s. Notably, previous studies have generally identified a "dual-high" phenomenon—longer length of stay (LOS) and higher medical costs—among non-local patient groups compared to local patients at the destination (4, 5). The reasons for this involve both objective differences in patient case complexity and the relative highlighting effect, under payment policy reforms, of better cost control for local patients compared to non-local patients (4).

When Hong Kong residents seek medical treatment in mainland China, do their characteristics of length of stay and costs still align with the patterns observed in non-local medical care models? On the one hand, compared to domestic non-local medical care within China, which often occurs within the same social system, medical seeking from Hong Kong to the mainland involves crossing different social systems. Does this confer new characteristics in terms of hospitalization costs and LOS? On the other hand, compared to existing international cross-border medical care, which often occurs across nations but within similar social systems, this scenario is distinct. Therefore, this study focuses on analyzing the characteristics of LOS and hospitalization costs for voluntary cross-border medical care within a single country but across different social systems.

This study focuses on knee arthroplasty procedures performed in the orthopedic department of Hospital H, a preferred institution for Hong Kong patients. As a demonstrative platform for Shenzhen-Hong Kong medical cooperation, Hospital H recorded 3,676 inpatient discharges and 128,500 outpatient and emergency visits for Hong Kong patients in 2023. The orthopedic department had the highest number of inpatient discharges among Hong Kong patients, with knee arthroplasty (including bicompartmental and total knee arthroplasty) being the most common procedure. Hospital H has established a significant brand aggregation effect in the field of joint arthroplasty. Its patient volume and procedural standardization level provide an ideal observation window for studying cross-border medical care. Furthermore, hospital H operates under a fixed annual salary system modeled after Hong Kong's public hospital compensation structure. This system eliminates any financial incentive for physicians to treat local and cross-border patients differently. Building upon the homogeneous clinical pathway for knee arthroplasty, this unique salary model at Hospital H, and the concentrated flow of cross-border patients, this study aims to descriptively analyze the differences in length of stay, costs, and related patterns between Hong Kong medical tourists and local mainland patients undergoing elective arthroplasty at a specific center in mainland China. It further seeks to explore the underlying reasons and policy implications.

2 Materials and methods

2.1 Sample and data sources

Case data for this study were extracted from the front pages of medical records of patients who underwent knee arthroplasty at Hospital H between July 2023 and June 2024, totaling 363 cases. To ensure data validity and analytical accuracy, data cleaning was performed to verify consistency between ICD-9-CM3 procedure codes and Chinese surgical names, with the primary procedures identified as bicompartmental knee arthroplasty or total knee arthroplasty. Patients with missing addresses, bilateral knee arthroplasty, hospitalization costs exceeding three times the mean were excluded. The final study cohort comprised 356 patients (see Supplementary Figure 1). Their demographic characteristics showed no statistically significant differences from the original sample upon statistical analysis and comparison, as detailed in Supplementary Table 1.

2.2 Variable definitions

The independent variable in this study was "whether the patient is a resident of Hong Kong" (identified based on permanent residence being Hong Kong). The dependent variables were "length of hospital stay" and "hospitalization costs," with "length of hospital stay" also serving as the mediating variable. Existing research suggests that hospitalization costs and length of stay for knee arthroplasty are primarily influenced by disease-related factors such as comorbidities, cost of medical consumables, history of prior knee arthroplasty, and anesthesia method, as well as demographic factors like gender and age. Socioeconomic factors, including family support and personal financial conditions, also play a role (6–8). Considering data availability, this study ultimately incorporated the following measurement indicators: age and gender for demographic information, marital status for family support, comorbidity status (Carlson Comorbidity Index, CCI score) for comorbidities, and anesthesia method (spinal anesthesia/general anesthesia) and history of prior knee arthroplasty for disease and treatment characteristics. The CCI score was calculated by extracting ICD-10 codes from other diagnoses listed on the front page of medical records and computing a total score based on the CCI index calculation table. Total hospitalization costs include only the expenses

TABLE 1 Demographic and clinical characteristics of the sample.

Variables	Category	Mainland patients 143 (40.17%)	Hong Kong patients 213 (59.83%)	Total 356 (100%)	$t/^2$	*P*
Age	y≤65	31 (21.68%)	50 (23.47%)	81 (22.75%)	0.396	0.82
	65<y≤75	90 (62.94%)	127 (59.62%)	217 (60.96%)		
	y>75	22 (15.38%)	36 (16.90%)	58 (16.29%)		
Sex	Male	42 (29.37%)	108 (50.70%)	150 (42.13%)	15.971	<0.001***
	Female	101 (70.63%)	105 (49.30%)	206 (57.87%)		
Marital status	Currently single	23 (16.08%)	55 (25.82%)	78 (21.91%)	4.742	0.029*
	Married with partner	120 (83.92%)	158 (74.18%)	278 (78.09%)		
CCI score	0	80 (55.94%)	125 (58.69%)	205 (57.58%)	0.556	0.754
	1	47 (32.87%)	69 (32.39%)	116 (32.58%)		
	≥2	16 (11.19%)	19 (8.92%)	35 (9.83%)		
Anesthesia type	Spinal anesthesia	84 (58.74%)	137 (64.32%)	221 (62.08%)	1.131	0.288
	General anesthesia	59 (41.26%)	76 (35.68%)	135 (37.92%)		
Prior knee arthroplasty	No	117 (81.82%)	171 (80.28%)	288 (80.90%)	0.131	0.718
	Yes	26 (18.18%)	42 (19.72%)	68 (19.10%)		
Hospital stay duration		9.87 ± 4.07	8.93 ± 3.02	9.31 ± 3.50	6.156	0.014*
Preoperative days		3.19 ± 1.95	3.04 ± 1.75	3.10 ± 1.83	0.546	0.460
Postoperative days		6.68 ± 3.40	5.89 ± 2.55	6.21 ± 2.94	6.193	0.013*
Medical service fees		10,728.91 ± 2,333.31	10,282.07 ± 1,783.42	10,461.56 ± 2,031.07	4.178	0.042*
Examination/laboratory fees		2,655.57 ± 804.84	2,459.11 ± 811.84	2,538.03 ± 813.63	5.045	0.025*
Material costs		12,799.82 ± 1,235.31	12,856.64 ± 1,095.11	12,833.82 ± 1,152.11	0.208	0.649
Medication costs		803.99 ± 547.15	670.36 ± 296.16	724.04 ± 420.04	8.852	0.003**
Hospital-acquired infections		0	0	0	–	–
Total costs		26,988.29 ± 3,285.29	26,268.18 ± 2,737.06	26,557.44 ± 2,985.97	5.033	0.025*

*$P < 0.05$; **$P < 0.01$; ***$P < 0.001$.
Age and CCI index were adjusted using the Bonferroni correction.

incurred during the hospital stay and do not cover post-discharge care costs.

2.3 Research hypotheses

H1: Hong Kong patients have a longer length of hospital stay compared to mainland patients.

H2: Hong Kong patients incur higher hospitalization costs compared to mainland patients.

2.4 Statistical analysis methods

Data organization and analysis were performed using SPSS 25.0 statistical software. Mediation effect testing was conducted using the Process v2.13 plugin. Statistical analysis methods included descriptive statistics, univariate analysis, and mediation effect testing (Bootstrap method).

3 Results

3.1 Demographic and clinical characteristics

As shown in Table 1, the study included 356 patients undergoing unilateral knee arthroplasty, with 213 (59.83%) being Hong Kong residents. The majority (217, 60.96%) were aged 65–75 years, with a higher proportion of females (206, 57.87%) than males. Most patients (278, 78.09%) were married and not divorced. Clinically, most patients (205, 57.58%) had a CCI score of 0, 221 (62.08%) underwent spinal anesthesia, and 68 (19.10%) had a prior history of knee arthroplasty.

3.2 Univariate analysis

As presented in Table 1, compared to non-Hong Kong patients, Hong Kong patients showed a higher proportion of females,

TABLE 2 Results of multivariable linear regression analysis and mediation effect test for hospital stay duration and hospitalization costs in patients undergoing knee arthroplasty.

Variable	Mediator: hospital stay duration				Dependent variable: hospitalization costs			
	Coeff	*Boot Mean*	*LLCI*	*ULCI*	*Coeff*	*Boot Mean*	*LLCI*	*ULCI*
constant	8.92	8.95	6.87	11.00	19,323.05	19,323.97	18,182.00	20,416.07
HK patient	−0.93	−0.94	−1.70	−0.21	16.30	12.32	−363.80	399.79
Married with partner	−1.24	−1.24	−2.38	−0.18	−174.52	−179.67	−611.62	250.51
General anesthesia	0.50	0.49	−0.25	1.26	685.84	689.75	264.61	1,111.37
Prior knee arthroplasty	−0.48	−0.49	−1.35	0.41	−731.57	−729.09	−1,214.74	−280.27
Female	0.36	0.36	−0.34	1.04	61.05	60.85	−296.22	428.29
Age (ref: ≤65 years)								
65<y≤75	0.35	0.35	−0.45	1.13	101.03	102.69	−345.41	533.69
y>75	1.72	1.71	0.51	2.91	437.12	433.95	−216.07	1,062.50
CCI score (ref: 0)								
1	0.53	0.53	−0.26	1.36	674.34	668.50	264.40	1,079.89
≥2	0.72	0.70	−0.51	2.00	1,105.19	1,095.93	446.24	1,821.56
Hospital stay duration	641.68	641.81	578.45	707.30				
$R^2 = 0.822$, $P < 0.001$					$R^2 = 0.397$, $P < 0.001$			
	Effect	*BootSE*	*BootLLCI*	*BootULCI*				
X→ Y	16.30	196.19	−369.59	402.19				
X→ M→ Y	−599.23	243.77	−1,097.71	−133.79				

The analysis excluded variables with VIF >2 to mitigate multicollinearity.
Bootstrap samples = 5,000, Confidence level for confidence intervals = 95%.

a lower proportion of married individuals, shorter hospital stay durations, and lower hospitalization costs. No significant differences were observed in prior knee arthroplasty history, anesthesia type, or comorbidity status. The shorter hospital stay duration was attributed to reduced postoperative hospitalization time, with no significant difference in preoperative stay. Regarding costs, Hong Kong patients incurred lower medical service fees, examination/laboratory fees, and medication costs, except for material costs. Regarding medical quality, none of the knee arthroplasty patients experienced complications or hospital-acquired infections during their hospitalization.

3.3 Mediation effect test of length of hospital stay

A mediation effect test was conducted with hospitalization costs as the dependent variable, length of hospital stay as the mediating variable, whether the patient was from Hong Kong as the independent variable, and age, gender, marital status, comorbidities, anesthesia method, and history of prior knee arthroplasty as control variables. The results are presented in Table 2. After controlling for other factors, Hong Kong patients undergoing knee arthroplasty had an average hospital stay 0.93 days shorter than non-Hong Kong patients. Compared to the group aged 65 and below, the average length of stay increased by 0.35 days and 1.72 days for the groups aged 65–75 and over 75, respectively. Patients who were married with a living spouse or not divorced had an average hospital stay 1.23 days shorter than those who were unmarried, divorced, or widowed. In contrast, gender, comorbidities, and history of prior knee arthroplasty had no significant impact on the length of stay.

After controlling for other factors, there was no significant difference in average hospitalization costs between Hong Kong and non-Hong Kong patients undergoing knee arthroplasty. Compared to patients with a CCI score of 0, the average hospitalization costs increased by CNY 649.44 and CNY 1,082.54 for those with scores of 1 and 2 or above, respectively. Patients who received general anesthesia had an average hospitalization cost increase of CNY 731.74 compared to those who received spinal anesthesia. For each additional day of hospital stay, the average hospitalization cost increased by CNY 641.73. At this point, age, gender, marital status, and other factors had no significant impact on hospitalization costs.

The length of hospital stay fully mediated the effect of whether the patient was from Hong Kong on hospitalization costs.

3.4 Mediation effect analysis of hospitalization and cost structure

Using hospitalization costs as the dependent variable, and preoperative length of stay, postoperative length of stay, medical service fees, laboratory and examination fees, material costs, and medication costs as mediating variables, with Hong Kong

patient status as the independent variable and age, gender, marital status, comorbidities, anesthesia method, and history of prior knee arthroplasty as control variables, a mediation effect analysis was conducted. The results, as shown in Supplementary Tables 1–6, are as follows: the mediation effect of preoperative length of stay was not significant; postoperative length of stay fully mediated the effect of Hong Kong patient status on hospitalization costs; medical service fees partially mediated this effect; laboratory and examination fees fully mediated the effect; the mediation effect of material costs was not significant; and medication costs fully mediated the effect of Hong Kong patient status on hospitalization costs. This indicates that Hong Kong patients had shorter postoperative hospital stays and lower laboratory/examination and medication costs, while no significant differences were observed in preoperative length of stay or material costs compared to mainland patients.

4 Discussion and conclusion

The results of this study indicate that Hong Kong patients undergoing knee arthroplasty exhibited both lower hospitalization costs and shorter lengths of stay, contrasting with the "dual-high" phenomenon observed in domestic non-local medical care. This suggests that the drivers for Hong Kong patients seeking medical care outside their region may differ from those in other parts of the country. Mediation effect analysis revealed that the length of hospital stay fully mediated the impact of Hong Kong patient status on hospitalization costs. Structurally, Hong Kong patients had shorter postoperative hospital stays and lower laboratory/examination and medication costs. However, in terms of healthcare quality, none of the patients acquired a hospital infection during their hospitalization, indicating that the quality of care was not compromised. Nevertheless, due to the lack of long-term follow-up data, we cannot assess whether the long-term outcomes are comparable. Thus, this study demonstrates that for knee arthroplasty, Hong Kong patients seeking medical care in mainland China can achieve a balance among medical efficiency, quality, and economic benefits.

4.1 Institutional drivers for optimized hospitalization cycles among Hong Kong patients

The findings of this study are completely opposite to the initial hypotheses (H1, H2). The study originally hypothesized that Hong Kong patients would have longer hospital stays and higher costs. This assumption was potentially based on factors faced by cross-border patients, such as language and cultural barriers, unfamiliarity with the local healthcare system, and potentially more complex preoperative conditions, all of which could prolong hospitalization and increase medical expenses (9, 10). However, this hypothesis overlooked a more critical determinant: the unique healthcare-seeking motivations of the medical tourist cohort.

On one hand, the primary motivation for Hong Kong patients seeking care in mainland China is likely to circumvent the protracted waiting times in Hong Kong's public hospitals. Although the Hong Kong public healthcare system adheres to the principle of universal access (2), it faces persistent pressure from long waiting lists for elective surgeries. As of June 30, 2024, the number of patients waiting for total joint replacement in Hong Kong reached 33,951, with the median waiting time being longest in Kowloon West at 51 months and shortest in New Territories West at 7 months (3). This situation objectively creates a push factor for patients to seek care in regions with higher service efficiency. On the other hand, evidence suggests that if the waiting time for knee arthroplasty exceeds three months, it can lead to increased healthcare costs and reduced health-related quality of life (HRQoL) over the subsequent decade (11). In a different context, another study indicates that Australia's knee arthroplasty registry represents a cost-effective undertaking for the government (12).

From the patient's perspective, when considering healthcare accessibility, safety, and economic factors, the inability of the local Hong Kong system to meet timely demand makes seeking cross-border alternatives a rational choice to overcome resource constraints. It is noteworthy that although the Hong Kong SAR government has attempted to alleviate cross-border healthcare barriers through extended welfare schemes, institutional gaps in inpatient coverage remain, leaving patients highly sensitive to indirect costs. Currently, no Hong Kong government medical welfare schemes provide coverage for inpatient care; arrangements like the Elderly Health Care Voucher are only applicable to outpatient services. Consequently, these patients prioritize highly efficient and expedited services. Once clinical discharge criteria are met, they have a strong incentive to be discharged quickly and return to Hong Kong.

On the other hand, Hospital H operates under a fixed salary system, eliminating any financial incentive for physicians to prolong hospital stays or increase services for revenue generation. For self-paying Hong Kong patients, shortening the LOS directly reduces their total costs. The standardized clinical pathway management implemented at Hospital H effectively balances healthcare quality with patient preferences. By employing flexible discharge mechanisms that return postoperative decision-making power to patients, this institutional design aligns supply-side capabilities with demand-side preferences, constituting a key factor in reducing the hospitalization cycle.

Therefore, the rejection of our research hypotheses powerfully demonstrates that under specific institutional arrangements and driven by patient motivations, cross-border healthcare can manifest as a model characterized by higher efficiency and lower costs. This finding provides a fresh perspective for understanding the diverse models of cross-border medical care. Furthermore, although the mediation analysis confirmed that LOS is a key mechanism explaining the cost differences—a relatively direct causal pathway—this study lacks qualitative data (e.g., in-depth patient decision interviews, healthcare provider perspectives) to uncover the root causes behind the observed differences in LOS. Investigating these underlying reasons represents a crucial direction for future research.

4.2 Cross-border synergistic effects in cost control mechanisms

This study found that the reduction in hospitalization costs was primarily associated with decreases in laboratory/examination fees and medication costs, while no significant change was observed in material costs. This may be related to the clinical pathway for knee arthroplasty, where postoperative expenses largely consist of imaging evaluations, laboratory monitoring for conditions such as thrombosis, and daily prophylactic medications for infection and thrombosis prevention (13). The shortened hospital stay may have directly influenced the arrangement of postoperative monitoring and medication use, or partially shifted inpatient medical services to outpatient care in Hong Kong (13, 14). However, due to the lack of available data, it is not possible to further investigate whether these medical measures were implemented during subsequent follow-ups.

The differentiated performance of cross-border medical costs reveals a deeper interaction between payment systems and organizational incentives. Unlike the conventional pattern in which non-local patients in mainland China incur higher costs due to treatment complexity, the cost control observed among Hong Kong patients stems from multi-system synergies: First, the decision-making motivation for cross-border medical care has shifted from "technical attraction" to "efficiency priority," reducing the potential for cost premiums associated with critical conditions (5, 15). Second, the fixed salary system at Hospital H, modeled after Hong Kong's public sector, severs the link between physician income and medical practices, transforming clinical pathway implementation from passive compliance to active optimization (16). Third, the integration of healthcare management philosophies between Shenzhen and Hong Kong has fostered a unique cost containment mechanism—while hospitals in mainland China generally face pressure to shift costs under payment reform, Hospital H has achieved endogenous compression of hospitalization costs through institutional coupling (17, 18). This cross-border synergistic cost-control pathway suggests that the marginal benefits of payment policy adjustments may be limited and need to resonate with organizational reforms in personnel management and quality culture (19, 20).

4.3 Conclusion

This study demonstrates that the hospitalization duration and cost characteristics of Hong Kong residents seeking medical care in mainland China reflect a unique cross-border healthcare logic: the long-standing pressure from elective surgery waiting times within Hong Kong's public healthcare system, coupled with gaps in cross-border inpatient coverage, drives patients toward efficiency-oriented mainland institutions to achieve optimal outcomes in medical quality, efficiency, and cost at the individual level. By implementing standardized clinical pathways and flexible discharge mechanisms, Hospital H ensures medical quality while meeting patients' demands for autonomous decision-making during postoperative recovery, forming the core driver for optimized hospitalization cycles. At the cost control level, the institutional synergy between Shenzhen and Hong Kong is the fixed salary system eliminates financial incentives for overutilization of medical services, while efficiency-driven healthcare decisions reduce non-essential service consumption, collectively shaping a cost-containment paradigm for cross-border care. However, due to the lack of long-term follow-up data, it remains unclear whether accelerated discharge affects long-term outcomes or offsets the survival benefits gained from timely treatment. This study indicates that current Shenzhen-Hong Kong medical collaboration has evolved from mere service substitution to systemic rule restructuring, urgently requiring institutional innovations to overcome barriers to resource mobility and achieve a transition from short-term resource complementarity to long-term system integration.

4.4 Policy recommendations

First, establish a tiered cross-border healthcare security system. Priority should be given to expanding direct payment channels for inpatient costs incurred by Hong Kong residents in the mainland, and exploring the development of cross-border settlement platforms for commercial health insurance. This would gradually upgrade the current transitional "welfare portability" into institutionalized arrangements. Second, innovate cross-border tiered healthcare collaboration models. Leveraging Hong Kong's specialist expertise and the mainland's primary care network, joint efforts should be made to develop referral guidelines and teleconsultation mechanisms. This would facilitate the diversion of elective surgeries such as knee arthroplasty to the mainland, while preserving Hong Kong's core role in managing complex cases. Third, strengthen postoperative follow-up and the monitoring of patient-reported outcomes. By utilizing information technology, we can achieve remote high-quality follow-ups, health monitoring, and health education, thereby better evaluating the effectiveness of cross-border medical services.

4.5 Study limitations

(1) The most significant limitation of this study is selection bias. The Hong Kong patient cohort represents a self-selected group who may possess greater payment capacity, higher health literacy, and more urgent healthcare needs, while simultaneously facing the pressure of out-of-pocket payments. Consequently, the observed differences in length of stay and costs between them and local patients likely reflect these pre-existing characteristics rather than a pure effect of geographical origin. Therefore, the findings of this study should be interpreted as a description of a specific medical tourism model, not as conclusions from a strict comparative effectiveness analysis.

(2) The study's sample size is relatively limited, drawing data only from patients who underwent knee arthroplasty at

Hospital H within a one-year period, which may be insufficient to fully represent the overall landscape of northbound healthcare-seeking from Hong Kong. Furthermore, the study focused solely on knee arthroplasty and did not encompass other types of cross-border medical services, thus the generalizability of the conclusions requires further validation. Although multiple influencing factors were considered, other unmeasured variables might also affect length of stay and costs, potentially limiting the precision of the analytical results. Moreover, the absence of long-term follow-up data prevents any assessment of long-term efficacy benefits.

(3) The hospitalization costs in this study only reflect the direct costs incurred during the hospital stay from the healthcare provider's perspective. They do not include the additional expenses borne by Hong Kong patients and their families, such as transportation, accommodation, meals, and potential costs for accompanying persons. These costs effectively shift a portion of the economic burden from the healthcare system to patient families. Similarly, post-discharge expenses for rehabilitation, follow-up visits, or complication management were not included. Thus, our conclusion of lower costs is strictly confined to the inpatient hospitalization period.

(4) The conclusions of this study are primarily applicable to medical institutions that have implemented a fixed annual salary system. This characteristic of Hospital H makes it not broadly representative of hospitals in mainland China, and caution is warranted when extrapolating these findings to settings where fixed salaries constitute a low proportion of physician compensation. However, as China is currently promoting an increase in the proportion of fixed salaries within physician compensation from the top down, this study may hold some reference value for future healthcare scenarios.

Future research should expand sample sizes, integrate patient-reported outcomes, link outpatient and inpatient data, broaden the range of diseases studied, and comprehensively calculate the full patient disease burden. This would enable a precise assessment of the short-, medium-, and long-term impacts of changes in costs and efficiency, thereby enhancing the reliability, applicability, and practical significance of the conclusions.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

SZ: Writing – original draft. LL: Writing – review & editing.

Funding

The author(s) declare that financial support was received for the research and/or publication of this article. This study was supported by the National Health Commission of the People's Republic of China (Research on the Impact of DIP Payment Reform on the Operational Management of Public Hospitals).

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The author(s) declare that no Gen AI was used in the creation of this manuscript.

Any alternative text (alt text) provided alongside figures in this article has been generated by Frontiers with the support of artificial intelligence and reasonable efforts have been made to ensure accuracy, including review by the authors wherever possible. If you identify any issues, please contact us.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpubh.2025.1655280/full#supplementary-material

References

1. Ai X, Yao XC. Research on the portability mechanism of cross-border healthcare in the Guangdong-Hong Kong-Macao Greater Bay Area under the "Healthy Bay Area" initiative. *Chin Health Serv Manag.* (2024) 41: 11–8.

2. Zhao Z, Wang JH, He JW. The operational mechanism and implications of the Hong Kong Special Administrative Region Government's purchase of medical services in China. *Chinese Health Resour.* (2021) 24:713–8. doi: 10.13688/j.cnki.chr.2021.210218

3. Hospital Authority of Hong Kong. *Booking of total joint replacement surgery.* (2024). Available online at: https://www.ha.org.hk/visitor/ha_visitor_index.asp?Content_ID=221223&Lang=CHIB5&Dimension=100&Parent_ID=214172 (Accessed August 27, 2024).

4. Ma C, Du YR, Tang RY, Xu W, Wang TY. DIP payment reform, medical cost control, and short-term strategic responses of hospitals. *World Econ.* (2022) 45:177–200. doi: 10.19985/j.cnki.cassjwe.2022.11.009

5. Han JS, Lyu CA. Analysis of medical costs for non-local and local inpatients under DRG payment: an empirical study based on a cancer hospital. *China Health Insur.* (2023) 2023:55–8. doi: 10.19546/j.issn.1674-3830.2023.1.009

6. Bullock DP, Sporer SM, Shirreffs TG. Comparison of simultaneous bilateral with unilateral total knee arthroplasty in terms of perioperative complications. *J Bone Joint Surg Am.* (2003) 85:1981–6. doi: 10.2106/00004623-200310000-00018

7. Ethgen O, Bruyère O, Richy F, Dardennes C, Reginster JY. Health-related quality of life in total hip and total knee arthroplasty: a qualitative and systematic review of the literature. *J Bone Joint Surg Am.* (2004) 86-A:963–74. doi: 10.2106/00004623-200405000-00012

8. Insall JN, Binazzi R, Soudry M, Mestriner LA. Total knee arthroplasty. *Clin Orthop Relat Res.* (1985) 192:13. doi: 10.1097/00003086-198501000-00003

9. Jevnikar BE, Khan ST, Emara AK, Elmenawi KA, Deren M, Piuzzi NS. Robotic total hip and knee arthroplasty: economic impact and workflow efficiency. *J Robot Surg.* (2025) 19:578. doi: 10.1007/s11701-025-02698-3

10. Witthayapipopsakul W, Asavamongkolkul A, Mills A, Gurol-Urganci I, van der Meulen J. Use of total knee arthroplasty by type of public insurance scheme: a cross-sectional study based on claims data in Thailand. *BMJ Open.* (2025) 15:e093576. doi: 10.1136/bmjopen-2024-093576

11. Scott C, Yapp LZ, Makaram NS, Karayiannis PN, and Clement ND. The false economy of increased waiting times for hip and knee arthroplasty: a cost consequence analysis. *Bone Joint J.* (2025) 107-B:905–14. doi: 10.1302/0301-620X.107B9.BJJ-2024-0974.R2

12. Okafor C, Nghiem S, Holder C, Vertullo C, Byrnes J. Are joint replacement registries cost-effective? Economic evaluation of the Australian orthopaedic association national joint replacement registry. *Arch Orthop Trauma Surg.* (2025) 145:408. doi: 10.1007/s00402-025-06029-x

13. Liu HW. Enhanced recovery after surgery in older patients with total knee arthroplasty: a systematic review and meta-analysis. *J Orthop.* (2025) 68:230–7. doi: 10.1016/j.jor.2025.05.060

14. Hoskins W, Bingham R, Corfield S, Harries D, Harris IA, Vince KG. Do the revision rates of arthroplasty surgeons correlate with postoperative patient-reported outcome measure scores? A study from the Australian orthopaedic association national joint replacement registry. *Clin Orthop Relat Res.* (2024) 482:98–112. doi: 10.1097/CORR.0000000000002737

15. Yu W, Sun YL, Zheng YJ, Tang XL, Huang W, Chen Y, et al. Study on the impact of DIP payment reform on hospitalized lung cancer patients with different types of care-seeking. *Health Econ Res.* (2025) 42:75–8. doi: 10.14055/j.cnki.33-1056/f.2025.08.019

16. Fu CZ, Pang YY. From "pilot" to "model": the mechanism of cross-border medical integration at the University of Hong Kong-Shenzhen Hospital from the perspective of institutional entrepreneurship. *J Fujian Prov Comm Party Sch CPC.* (2021) 2021:104–16. doi: 10.15993/j.cnki.cn35-1198/c.2021.05.003

17. Zhang LJ, Wang KQ, Yang HY, Feng ZC, Wang CS, Song ZJ. Research on the linkage between salary and performance of doctors in domestic public hospitals. *Chinese Hosp.* (2025) 29:77–82. doi: 10.19660/j.issn.1671-0592.2025.12.18

18. Liu H, Wang QL, Yu J. Design and simulation analysis of multi-task incentive contracts for public hospital doctors from the perspective of principal-agent theory. *Chinese Hosp.* (2025) 29:12–6. doi: 10.19660/j.issn.1671-0592.2025.4.03

19. Zou K, Li HY, Zhou D, Liao ZJ. The effects of diagnosis-related groups payment on hospital healthcare in China: a systematic review. *BMC Health Serv Res.* (2020) 20:112. doi: 10.1186/s12913-020-4957-5

20. Wu XF, Zhong YJ. Cross-border medical cooperation from the perspective of strong-weak institutional interaction evolution: a case study of the University of Hong Kong-Shenzhen Hospital. *J Guangdong Inst Public Admin.* (2021) 33:32–9, 98. doi: 10.13975/j.cnki.gdxz.2021.04.004

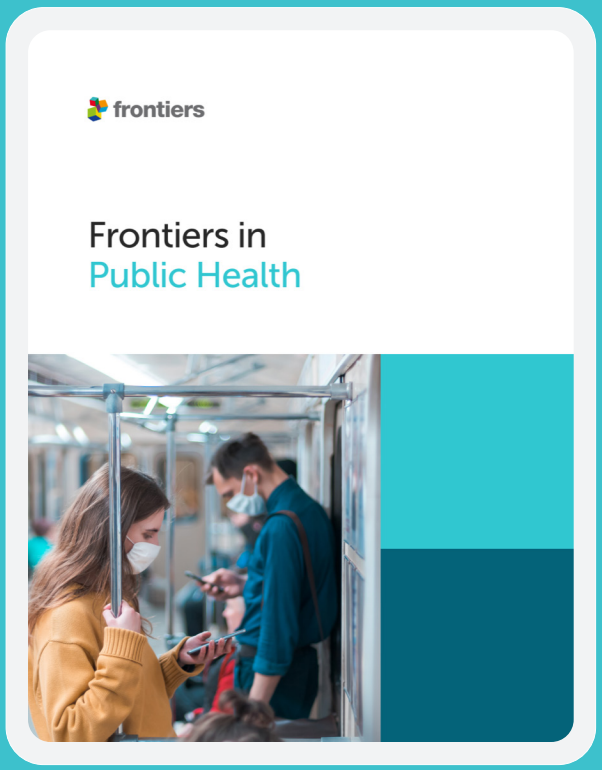
Frontiers in Public Health

Explores and addresses today's fast-moving healthcare challenges

One of the most cited journals in its field, which promotes discussion around inter-sectoral public health challenges spanning health promotion to climate change, transportation, environmental change and even species diversity.

Discover the latest Research Topics

See more →



Frontiers

Avenue du Tribunal-Fédéral 34
1005 Lausanne, Switzerland
frontiersin.org

Contact us

+41 (0)21 510 17 00
frontiersin.org/about/contact