



OPEN ACCESS

EDITED BY

Mateus Vidigal de Castro,
University of São Paulo, Brazil

REVIEWED BY

Yu Jung Choi,
Korea University, Republic of Korea
Xin Gao,
Peking University, China

*CORRESPONDENCE

Hangjie Zhang
✉ hjzhang@cdc.zj.cn
Xiaofei Fu
✉ cfk@jxcdc.org.cn
Tianfeng He
✉ hetfribcdc@163.com

†These authors have contributed equally to this work

RECEIVED 22 October 2025

REVISED 22 December 2025

ACCEPTED 29 December 2025

PUBLISHED 16 January 2026

CITATION

Yu Z, Liu X, Fu J, Yang X, Liu Y, Chu Y, Jin J, Xu Z, Cao Y, Pan J, Liu S, Fu X, He T and Zhang H (2026) Influenza vaccine effectiveness among adults aged ≥ 60 years in northeastern Zhejiang Province, China, 2021–2024.
Front. Public Health 13:1730158.
doi: 10.3389/fpubh.2025.1730158

COPYRIGHT

© 2026 Yu, Liu, Fu, Yang, Liu, Chu, Jin, Xu, Cao, Pan, Liu, Fu, He and Zhang. This is an open-access article distributed under the terms of the [Creative Commons Attribution License \(CC BY\)](https://creativecommons.org/licenses/by/4.0/). 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.

Influenza vaccine effectiveness among adults aged ≥ 60 years in northeastern Zhejiang Province, China, 2021–2024

Zhao Yu^{1†}, Xinyu Liu^{2†}, Jiayun Fu^{3†}, Xiaokun Yang^{4†}, Yang Liu⁵, Yanru Chu⁶, Jialie Jin¹, Zenghao Xu¹, Yanli Cao¹, Jinren Pan¹, Shelan Liu¹, Xiaofei Fu^{5*}, Tianfeng He^{6*} and Hangjie Zhang^{1*}

¹Department of Prevention and Control of Infectious Disease, Zhejiang Provincial Center for Disease Control and Prevention, Hangzhou, Zhejiang, China, ²School of Public Health, Hangzhou Medical College, Hangzhou, Zhejiang, China, ³Department of Public Health, Central Hospital of Huashui Town, Jinhua City, Zhejiang, China, ⁴Division of Infectious Disease, Key Laboratory of Surveillance and Early-Warning on Infectious Disease, Chinese Center for Disease Control and Prevention, Beijing, China, ⁵Department of Infectious Diseases, Jiaying Center for Disease Control and Prevention, Jiaying, Zhejiang, China, ⁶Department of Infectious Diseases, Ningbo Center for Disease Control and Prevention, Ningbo, Zhejiang, China

Background: Influenza poses a particularly severe threat to older adults, yet vaccination coverage among this vulnerable population remains suboptimal in China. To address this public health challenge, Zhejiang Province initiated a free influenza vaccination program for older residents starting in 2020. This study evaluated the effectiveness of influenza vaccination in reducing outpatient visits among adults aged ≥ 60 years during three consecutive influenza seasons (2021–2024).

Methods: We employed a test-negative design (TND) among adults aged ≥ 60 years presenting with influenza-like illness (ILI) at sentinel surveillance hospitals in two cities in Zhejiang Province from October 2021 to April 2024. Standardized questionnaires were administered to collect demographic and clinical data. Respiratory specimens were tested for influenza virus types and subtypes using RT-PCR. Multivariable logistic regression models were employed to assess factors associated with vaccination status and influenza virus detection, with subsequent estimation of influenza vaccine effectiveness (VE).

Results: A total of 3,796 ILI cases were enrolled, with 644 testing positive for influenza, yielding a positivity rate of 16.97%. The results of multivariable logistic regression analysis showed that age, whether vaccinated in the current year, and whether vaccinated in the previous year were the influencing factors for influenza-positive ILI cases ($p < 0.05$). The influenza vaccination coverage in the current season was 33.14%. The overall VE was 47.21% (95% CI: 35.38 to 56.88%). Subtype-specific VE was 55.81% (95% CI: 34.83 to 70.03%) for H1N1, 40.72% (95% CI: 23.30 to 54.18%) for H3N2, and 55.16% (95% CI: 21.77 to 74.30%) for B/Victoria. Age-stratified VE analysis showed effectiveness of 70.34% (95% CI: 41.47 to 84.98%) among those aged 60–69 years, 49.48% (95% CI: 34.41 to 61.09%) in the 70–79 age group, and 38.34% (95% CI: 10.35 to 57.60%) among individuals aged 80 years and older.

Conclusion: Influenza vaccination provides moderate protection for adults aged ≥ 60 years, with effectiveness varying by subtype, age, and season, particularly limited in the older population aged ≥ 80 years.

KEYWORDS

older adults, influenza vaccine, test-negative design, vaccination, vaccine effectiveness

1 Introduction

Influenza is an acute respiratory infection caused by influenza viruses, capable of causing annual epidemics and remains a persistent public health challenge (1). Characterized by high mutability and rapid transmission, influenza viruses pose elevated risks of severe illness and complications among immunocompromised populations, particularly the older adults.

China's Technical Guidelines for Influenza Vaccination (2023–2024) recommend prioritizing vaccination for high-risk populations (e.g., individuals with chronic diseases or aged ≥ 60 years) (2). However, as influenza vaccines are not included in China's national immunization program and require self-payment, coverage rates have historically been low. An earlier study reported that only 3.8% of adults ≥ 60 years received influenza vaccination, far below the threshold needed for herd immunity (3). In contrast, many developed nations (e.g., Sweden, the UK) have implemented free vaccination policies for high-risk groups or entire populations to improve coverage (4). In China, such policies are currently limited to pilot programs in economically advanced regions like Beijing (5) and Shenzhen (6).

Since 2020, Zhejiang Province has progressively expanded free vaccination eligibility: initially covering adults ≥ 70 years with local household registration under government livelihood projects, then extending to ≥ 65 years (2021), and finally to ≥ 60 years (2024) (7). This policy initiative has been associated with a substantial increase in vaccination coverage at the local level. For example, in Ningbo city, vaccination coverage among older adults increased from 1.14% in the 2017–2018 season to 33.41% in 2022–2023, with coverage specifically reaching 50.03% among the target population aged ≥ 70 years (8). A district-level analysis in Yinzhou further documented a 29.1% absolute increase in vaccination rates following policy implementation (9).

While previous studies have estimated influenza vaccine effectiveness (VE) among older adults in Zhejiang Province, most were limited to single seasons or individual cities. Multi-season, subtype-stratified, and age-stratified VE data under the free vaccination policy remain scarce. To address this evidence gap, this study aims to estimate the protective effectiveness of influenza vaccination against outpatient influenza infections among individuals aged ≥ 60 years over three consecutive influenza seasons (2021–2024), utilizing surveillance data from sentinel hospitals in Ningbo and Jiaying cities of Zhejiang Province. The findings are expected to provide evidence-based insights for optimizing influenza vaccination strategies for the aging population in China.

2 Methods

2.1 Study population

This study employed a test-negative design (TND), a widely used observational study design for evaluating influenza VE. Influenza-like illness (ILI) patients aged 60 and above who were eligible for the local free influenza vaccination policy and were treated in the influenza surveillance sentinel hospitals in Jiaying and Ningbo, Zhejiang Province from October 2021 to April 2024 were selected. ILI refers to patients with an acute onset (duration of illness ≤ 7 days), a maximum body temperature of ≥ 37.5 °C, and accompanied by either cough or sore throat. Cases were excluded if they met any of the following conditions: (a) Contraindications to influenza vaccination; (b) Residency in nursing homes or living outside the surveillance area; (c) 7 days between symptom onset and medical visit, or prior use of antiviral medications; (d) inability to communicate effectively with the patient or guardian; (e) Declined to participate or unable to provide informed consent.

2.2 Data collection

At the time of patient enrollment, uniformly trained medical staff administered an electronic questionnaire for ILI immediately following specimen collection and prior to any diagnostic testing. The questionnaire collected demographic data, vaccination history, clinical symptoms, specimen details, and laboratory results.

The questionnaire was developed by the research team in collaboration with influenza vaccine experts and the Zhejiang Provincial Center for Disease Control and Prevention (CDC). To ensure validity, a pilot test was conducted with 10 older adults (not included in the final analysis). All data were anonymized, and written/verbal informed consent was obtained prior to participation.

Vaccination records for the study period were primarily retrieved from the Zhejiang Provincial Immunization Registry, a mandatory reporting system that captures influenza vaccinations administered at all accredited healthcare facilities across the province. This registry uses unique citizen identification numbers to ensure accurate individual-level linkage, providing a reliable and nearly complete source of vaccination data. Study participants were classified as vaccinated if the registry indicated receipt of a seasonal influenza vaccine at least 14 days prior to their ILI symptom onset. For the primary analysis, “vaccinated” status was assigned solely based on receipt of the current season's vaccine.

2.3 Laboratory confirmation

Pharyngeal swab specimens were collected from participants and tested for influenza virus nucleic acids using real-time reverse transcription polymerase chain reaction (RT-PCR). First nucleic acids were tested for influenza viruses A (A) and B (B); A-positive specimens

Abbreviations: ILI, Influenza-like Illness; TND, Test-negative Design; VE, Vaccine Effectiveness; RT-PCR, Reverse Transcription Polymerase Chain Reaction; CDC, Center for Disease Control and Prevention; aOR, Adjusted Odds Ratio; CI, Confidence Interval; IQR, Interquartile Range.

then went on to be tested for A (H1N1) and A (H3N2), and B-positive specimens were tested for the B/Victoria lineage and the B/Yamagata lineage, and the cases that were positive for influenza viruses were formed into a case group, and those that were negative for influenza viruses were formed into a control group. Throughout the study period, the trivalent influenza vaccine administered in Zhejiang Province followed WHO recommendations for the Northern Hemisphere. National surveillance indicated that influenza B/Victoria predominated in 2021–2022, A/H3N2 and A/H1N1 co-circulated in 2022–2023, and A/H3N2 was the dominant subtype in 2023–2024 (10, 11).

2.4 Statistical analysis

Variable selection for the multivariable logistic regression model was based on biological plausibility, prior knowledge, and associations ($p < 0.10$) observed in bivariate analyses. A TND was employed to estimate influenza VE by comparing influenza positivity rates between vaccinated and unvaccinated individuals. Categorical variables were analyzed using chi-square tests. Logistic regression models were used to identify factors associated with both vaccination status and influenza positivity. Adjusted odds ratio (aOR) with 95% confidence intervals (CI) were calculated after controlling for potential confounders in the final model, which included sex, age group, underlying medical conditions, influenza season, and vaccination status in the previous season. Model fit was assessed using the Hosmer-Lemeshow goodness-of-fit test, which indicated adequate fit ($p > 0.05$). Multicollinearity was evaluated using variance inflation factors (all < 2.0). VE was calculated as $100\% \times (1 - \text{aOR})$, with $p < 0.05$ indicating a statistically significant difference.

2.5 Ethics statement

This study was approved by the Ethics Review Committee of the Zhejiang CDC and was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants prior to their inclusion in the study.

3 Result

3.1 Participants characteristics

During the study period, a total of 5,225 questionnaires were distributed to eligible ILI patients. After applying the inclusion and exclusion criteria, 3,796 valid questionnaires were included in the final analysis, yielding an effective response rate of 72.7%. The primary reasons for exclusion were not meeting the ILI case definition (e.g., duration of illness > 7 days), residing outside the surveillance area, or declining to participate.

These 3,796 enrolled patients had a nearly equal sex distribution, including 1894 male cases (49.89%) and 1902 female cases (50.11%). The median age was 76 years (IQR: 72–82 years), distributed across age groups as follows: 405 (10.7%) aged 60–69 years, 2093 (55.1%) aged 70–79 years, and 1,298 (34.2%) aged ≥ 80 years. Underlying medical conditions were present in 2568 patients (67.7%).

3.2 Influenza vaccination

Among 3,796 ILI cases, 1,258 (33.14%) received influenza vaccination during the current season (Table 1). Vaccination rates for the 2021–2022, 2022–2023, and 2023–2024 seasons were 32.10, 31.27, and 34.87%, respectively. Males had a significantly higher vaccination rate (34.88%) than females (31.40%; $p = 0.023$). Age-specific vaccination coverage was 25.43% (103/405) in the 60–69 age group, 35.36% (740/2093) in the 70–79 group, and 31.97% (415/1298) in the ≥ 80 group. Regarding vaccination history, 20.60% (782/3796) were vaccinated in both the current and previous seasons, 12.54% (476/3796) only in the current season, 9.72% (369/3796) only in the previous season, and 57.09% (2,167/3796) were unvaccinated in both seasons.

3.3 Influenza positivity

Among 3,796 ILI cases, 644 tested positive for influenza, with a positivity rate of 16.97%. Of these, 552 were influenza A infections, predominantly H3N2 (355 cases, 55.12% of positives), followed by H1N1 (188 cases, 29.19%). Influenza B was detected in 90 cases, mostly of the B/Victoria lineage (81 cases, 12.28%); the remaining positive cases were not subtyped. No significant difference in influenza positivity rates by sex was observed: 17.00% in males (322/1894) and 16.93% in females (322/1902) ($p = 0.959$). However, significant differences were observed across age groups. The positivity rate was highest among those aged 60–69 years (24.69%, 200/405), followed by 70–79 years (17.77%, 372/2093), and lowest in those aged ≥ 80 years (13.25%, 172/1298) ($p < 0.001$). The positivity rate was 17.21% among individuals with underlying diseases and 16.45% among those without, a difference that was not statistically significant ($p = 0.558$), as shown in Table 1.

3.4 Multivariate analysis

After adjustment for potential confounders, the analysis indicated that gender and age were significantly associated with influenza vaccination rates ($p < 0.05$). Specifically, women were significantly more likely to be vaccinated than men (aOR = 1.18, 95% CI: 1.03–1.35). Compared with adults aged 60–69, those in the 70–79 and ≥ 80 age groups had 1.62 (95% CI: 1.28–2.07) and 1.40 (95% CI: 1.09–1.80) times higher odds of being vaccinated, respectively (Table 2).

Using influenza virus positivity as the dependent variable, and age group, presence of underlying diseases, current-season vaccination status, and previous-season vaccination status as independent variables, a multivariable logistic regression analysis was performed. The results indicated that age, current-season vaccination, and previous-season vaccination were significantly associated with influenza positivity among ILI cases ($p < 0.001$). Age ≥ 70 years was identified as a protective factor. Compared with the 60–69 age group, the odds of influenza positivity were 0.70 times (95% CI: 0.54–0.90) in the 70–79 age group and 0.48 times (95% CI: 0.36–0.63) in the ≥ 80 age group. Compared to unvaccinated individuals, getting vaccinated against seasonal influenza can effectively reduce the risk of infection (OR = 0.63, 95% CI: 0.50–0.78). Similarly, previous-season vaccination also showed a protective effect (OR = 0.76, 95% CI: 0.61–0.96; $p = 0.019$), as shown in Table 3.

TABLE 1 ILI case vaccination characteristics and infection characteristics.

Characteristic	Total	Vaccination status		Statistics		Influenza detection		Statistics	
		Vaccinated	Unvaccinated	χ^2	p	Influenza negative	Influenza positive	χ^2	p
No. (%)	3,796 (100)	1,258 (33.14)	2,538 (66.86)			3,152 (83.03)	644 (16.97)		
Season				$\chi^2 = 4.67$	0.097			$\chi^2 = 159.70$	< 0.001
2021–2022	835 (21.99)	268 (32.10)	567 (67.90)			809 (96.89)	26 (3.11)		
2022–2023	1,180 (31.09)	369 (31.27)	811 (68.73)			971 (82.29)	209 (17.71)		
2023–2024	1,781 (46.92)	621 (34.87)	1,160 (65.13)			1,372 (77.04)	409 (22.96)		
Sex				$\chi^2 = 5.18$	0.023			$\chi^2 = 0.00$	0.959
Male	1894 (49.89)	661 (34.88)	1,234 (65.12)			1,572 (83.00)	322 (17.00)		
Female	1902 (50.11)	597 (31.40)	1,304 (68.60)			1,580 (83.07)	322 (16.93)		
Age group				$\chi^2 = 16.30$	< 0.001			$\chi^2 = 30.84$	< 0.001
60–69 y	405 (10.67)	103 (25.43)	302 (74.57)			305 (75.31)	100 (24.69)		
70–79 y	2093 (55.14)	740 (35.36)	1,353 (64.64)			1721 (82.23)	372 (17.88)		
≥ 80 y	1,298 (34.19)	415 (31.97)	883 (68.03)			1,126 (86.75)	172 (13.25)		
Underlying diseases ^a				$\chi^2 = 0.66$	0.416			$\chi^2 = 0.34$	0.558
Yes	2,568 (67.65)	840 (32.71)	1,728 (67.29)			2,126 (82.79)	442 (17.21)		
No	1,228 (32.35)	418 (34.04)	810 (65.96)			1,026 (83.55)	202 (16.45)		
Vaccinated in the previous season				$\chi^2 = 903.21$	< 0.001			$\chi^2 = 24.85$	< 0.001
Yes	1,151 (30.32)	782 (67.94)	369 (32.06)			1,009 (87.62)	142 (12.38)		
No	2,645 (69.68)	475 (17.98)	2,167 (82.02)			2,142 (81.00)	503 (19.00)		
Vaccinated in the current season								$\chi^2 = 36.12$	< 0.001
Yes	1,258 (33.14)	-	-			1,110 (88.24)	148 (11.76)		
No	2,538 (66.86)	-	-			2042 (80.46)	496 (19.54)		

^aUnderlying diseases included a range of chronic conditions as reported by patients or recorded in medical charts, including but not limited to: asthma, chronic obstructive pulmonary disease, hypertension, coronary heart disease, diabetes, chronic kidney disease, cerebrovascular disease, and malignancy.

3.5 Vaccine effectiveness

After adjusting for confounding factors such as gender, age group, underlying diseases, and flu season, the overall VE was 47.21% (95% CI: 35.38–56.88%). Subtype-specific VE was 55.81% (95% CI: 34.83–70.03%) against A/H1N1, 40.72% (95% CI: 23.30–54.18%) against A/H3N2, and 55.16% (95% CI: 21.77–74.30%) against B/Victoria. VE varied by age group: 70.35% (95% CI: 41.47–84.98%) in the 60–69 age group, 49.48% (95% CI: 34.41–61.09%) in the 70–79 group, and 38.34% (95% CI: 10.35–57.60%) among those aged 80 years or older. Across influenza seasons, VE was 70.78% (95% CI: 11.83–90.32%) in 2021–2022, 56.00% (95% CI: 36.00–69.74%) in 2022–2023, and 43.58% (95% CI: 27.61–56.03%) in 2023–2024, as shown in Figure 1.

Further stratification by influenza subtype revealed additional heterogeneity. In the 2021–2022 season, all influenza cases were due to B/Victoria, with a VE of 58.56% (95% CI: –10.82– 88.04%). In 2022–2023, when both influenza A subtypes co-circulated, VE against A/H1N1 was 50.21% (95% CI: 27.07–66.82%) and against A/H3N2 was 52.94% (95% CI: –15.23–84.29%). In 2023–2024, VE was highest against A/H1N1 at 83.15% (95% CI: 13.1–99.08%), followed by B/Victoria at 51.18% (95% CI: 9.99–75.49%), and was lowest against the predominant A/H3N2 at 35.19% (95% CI: 15.74–50.52%), as shown in Figure 2. It should be noted that some estimates, particularly those for subtypes with a small number of positive cases (e.g., A/H1N1 in

2023–2024, $n = 12$), are associated with wide confidence intervals and should be interpreted with caution.

4 Discussion

This study assessed influenza VE in adults ≥60 years in Zhejiang over three seasons (2021–2024). The overall VE was 47.21%, with substantial variation by season (70.78, 56.00, 43.58%), subtype (higher for A/H1N1 and B/Victoria than A/H3N2), and age (declining from 70.35% in 60–69 years to 38.34% in ≥80 years). These findings demonstrate that while influenza vaccination provided moderate overall protection in this older population, its effectiveness was influenced by season, viral subtype, and markedly by age.

These findings hold particular significance given China’s rapidly aging population. By the end of 2023, individuals aged 60 and above accounted for 21.1% of the total population (12). Older adults face elevated risks of infection and severe outcomes from influenza. Vaccination remains a cornerstone of preventive strategy for this growing demographic, underscoring the need to understand its real-world effectiveness.

In China, influenza vaccination is included in the non-immunization program, and coverage remains low among older adults nationwide. During the 2021–2022 and 2022–2023 influenza seasons, the estimated influenza vaccination rates

TABLE 2 Multivariate logistic regression analysis of influenza vaccination status.

Characteristic	OR	95% CI	<i>p</i>
Sex (Reference: Male)			
Female	1.18	1.03–1.35	0.020
Age group (Reference: 60–69 y)			
70–79 y	1.62	1.28–2.07	< 0.001
≥ 80 y	1.40	1.09–1.80	
Underlying disease (Reference: No)			
Yes	0.93	0.80–1.07	0.313

TABLE 3 Multivariate logistic regression analysis of influenza-positive ILI cases.

Characteristic	OR	95% CI	<i>p</i>
Sex (Reference: Male)			
Female	1.03	0.86–1.22	0.771
Age group (Reference: 60–69 y)			
70–79 y	0.70	0.54–0.90	< 0.001
≥ 80 y	0.48	0.36–0.63	
Underlying disease (Reference: No)			
Yes	1.11	0.92–1.33	0.284
Vaccinated in the current season (Reference: No)			
Yes	0.63	0.50–0.78	< 0.001
Vaccinated in the previous season (Reference: No)			
Yes	0.76	0.61–0.96	0.019

among adults aged ≥ 60 years were only 3.75 and 4.16%, respectively (13). Certain regions report even lower rates; for example, the highest annual vaccination rate in Henan Province between 2020 and 2022 was merely 3.15% (14), and in Anhui Province from 2021 to 2023, it was only 1.84% (15). In contrast, the present study found that the influenza vaccination rates among ILI patients aged ≥ 60 years were 32.10, 31.27, and 34.87% during the 2021–2022, 2022–2023, and 2023–2024 influenza seasons, respectively. These findings are consistent with a previous report showing an influenza vaccination rate of 36.95% among residents aged ≥ 50 years in Zhejiang Province in 2022 (16).

A study involving older adults aged 60 and above in Ningbo, Zhejiang Province from 2018–2019 to 2021–2022 found that the overall VE of influenza vaccines was 63.5% (95% CI: 56.3–69.5%) (17). A study conducted during the 2019–2020 influenza season showed that the VE of influenza vaccines among older adults aged 60 and above was 37.04% (95% CI: 9.43–56.23%) (18), and the VE found in our study was slightly higher. In this study, the overall VE of influenza vaccines in the three influenza seasons from 2021 to 2024 was 47.21%, and the VEs in the three seasons were 70.78, 56.00, and 43.58%, respectively. The notably high pooled VE in the 2021–2022 season (70.78%) coincided with a season of very low influenza activity, resulting in only 26 positive cases, all of which were influenza B/Victoria. Consequently, this estimate is highly unstable, as reflected by its wide confidence interval. In the 2022–2023 season, with increased activity yielding 209

positive cases. However, subtype-specific estimates for A/H1N1 ($n = 176$) and A/H3N2 ($n = 28$) in this season remain based on limited numbers and should be interpreted with caution. The 2023–2024 season provided the largest sample (409 positive cases) and the most stable estimates. The overall VE was 43.58%, with the lowest point estimate observed against the predominant A/H3N2 subtype (35.19%). In contrast, the VE against A/H1N1 was 83.15%, but this is based on only 12 positive cases and has an extremely wide confidence interval, precluding any reliable conclusion about high effectiveness against this subtype. These findings, particularly the moderate overall protection and lower effectiveness against A/H3N2, are consistent with a recent large-scale, population-based TND study conducted in Southern China during the same season (19). That study, which included over 200,000 participants, reported an overall VE of 49.4% (95% CI: 47.8–50.9%) against laboratory-confirmed influenza. It also found lower VE against influenza A (41.9%) compared to influenza B (59.9%), aligning with our observation of lower effectiveness against the predominant A/H3N2 subtype.

Our pooled VE against influenza A (H1N1: 55.81%; H3N2: 40.72%) is broadly comparable to the VE of 51% against any influenza A reported in Italian older adults (≥ 65 years) during the 2023–2024 season (20). However, our estimates are substantially higher than those reported from other settings. For the 2022–2023 season, our adjusted overall VE was 56.00%, with subtype-specific estimates of 50.21% against A/H1N1 and 52.94% against A/H3N2. These figures are substantially higher than the VE of 29% (95% CI: 12–42%) against any influenza A reported in a European multi-country study among individuals aged ≥ 65 years during the same season (21). Similarly, a US study focusing on influenza-associated hospitalization in 2022–2023 reported a VE of 28% in adults aged ≥ 65 years (22). For the 2023–2024 season, our overall VE was 43.58%, with the lowest point estimate observed against the predominant A/H3N2 subtype (35.19%). However, early estimates from South Korea for 2023–2024 indicated a non-significant VE of 13.5% (95% CI: –17.9 to 36.6%) in adults aged ≥ 65 years (23).

The relatively higher VE observed in our study may have been influenced by a better antigenic match between the vaccine strains and the locally circulating influenza viruses during the study period. Although detailed local genetic characterization data are limited, national surveillance reports suggested a generally good match for the predominant lineages in these seasons. A meta-analysis showed that the VE in the case of matching between the prevalent strain and the vaccine strain (44.38, 95% CI: 22.63–60.01%) was higher than that in the case of mismatch (20.00, 95% CI: 3.46–33.68%) (24). Additionally, the distinct history of prior influenza exposures and vaccinations in our population could have shaped a different baseline immunity, potentially modulating the response to the current season's vaccine (25).

We observed a marked decline in VE with increasing age. The VE of the 60–69 age group was 70.35%, that of the 70–79 age group was 49.48%, and that of the ≥ 80 age was 38.34%, showing a trend that the protective effect of the vaccine decreases with age. This pattern may be attributed to immunosenescence; namely, the age-related deterioration of immune function commonly observed in older populations (26).

The impact of repeated influenza vaccination on VE remains a subject of ongoing debate. This study found no significant difference in protection between those vaccinated only in the current season and those vaccinated repeatedly. However, compared with individuals unvaccinated in both seasons, both

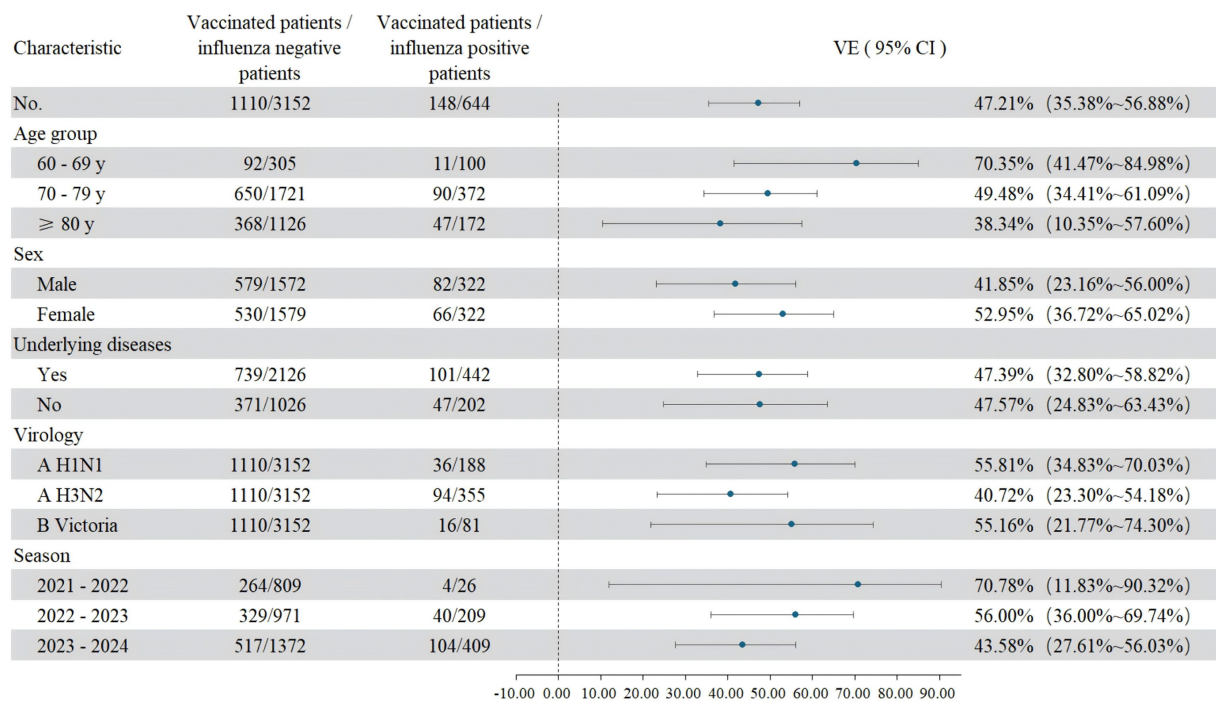


FIGURE 1 Influenza vaccine effectiveness (VE) in adults ≥60 years by demographic and clinical characteristics, Zhejiang Province, China, 2021–2024.

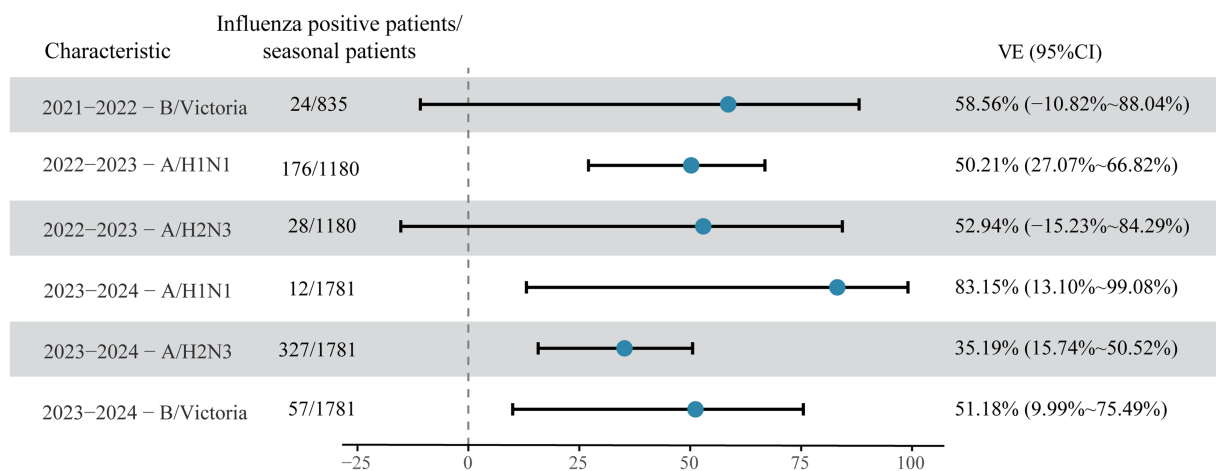


FIGURE 2 Stratified influenza vaccine effectiveness (VE) by season and predominant subtype among adults aged ≥60 years in Zhejiang Province, China, 2021–2024.

single-season and repeated vaccination provided measurable protection to older adults, which is consistent with previous meta-analyses (27).

4.1 Limitations

The findings of this study are primarily derived from data collected from influenza sentinel hospitals in Ningbo and Jiaying cities of Zhejiang Province. Therefore, the research results have certain limitations when applied to different regions and

populations across the province and even the country. Furthermore, as the data were obtained from sentinel surveillance systems, selection bias may exist due to the underrepresentation of individuals with mild or asymptomatic infections who did not seek medical care. Notably, some season-subtype strata contained very few positive cases. VE estimates derived from such small samples are inherently unstable and have wide confidence intervals, which may lead to overestimation or imprecise representation of the true protective effect. Additionally, a precise assessment of the antigenic match between the vaccine strains and the locally circulating influenza viruses for each season could

not be conducted due to the unavailability of detailed local viral genetic characterization data.

5 Conclusion

Influenza vaccination provides a moderate overall protective effect against influenza infection in adults aged 60 years and above. Both age and vaccination status were identified as significant factors influencing influenza infection. VE varied across influenza subtypes, age groups, and epidemic seasons, and showed a declining trend with increasing age, particularly among individuals aged 80 years or older, where protection was more limited. To further optimize immunization strategies for older adults, future large-scale, multi-center, and long-term real-world studies are recommended to develop more targeted and differentiated vaccination policies.

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.

Ethics statement

Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

ZY: Investigation, Methodology, Writing – original draft. XL: Data curation, Writing – original draft. JF: Data curation, Writing – original draft. XY: Formal analysis, Methodology, Writing – original draft. YL: Data curation, Investigation, Writing – review & editing. YCh: Data curation, Investigation, Writing – review & editing. JJ: Formal analysis, Investigation, Writing – review & editing. ZX: Formal analysis, Investigation, Writing – review & editing. YCa: Data curation, Investigation, Writing – review & editing. JP: Formal analysis, Investigation, Writing – review & editing. SL: Formal analysis, Investigation, Writing – review & editing. XF: Conceptualization, Resources, Writing – review & editing. TH: Conceptualization, Resources, Writing – review & editing. HZ: Conceptualization, Funding acquisition, Writing – review & editing.

References

1. Tenforde, MW, Kondor, RJG, Chung, JR, Zimmerman, RK, Nowalk, MP, Jackson, ML, et al. Effect of antigenic drift on influenza vaccine effectiveness in the United States—2019–2020. *Clin Infect Dis.* (2020) 73:e4244–50. doi: 10.1093/cid/ciaa1884
2. Feng, LZ, Peng, ZB, Wang, DY, Yang, P, Yang, J, Zhang, YY, et al. Technical guidelines for seasonal influenza vaccination in China (2018–2019). *Zhonghua Yu Fang Yi Xue Za Zhi.* (2018) 52:1101–14. doi: 10.3760/cma.j.issn.0253-9624.2018.11.003
3. Fan, J, Cong, S, Wang, N, Bao, H, Wang, B, Feng, Y, et al. Influenza vaccination rate and its association with chronic diseases in China: results of a National Cross-Sectional Study. *Vaccine.* (2020) 38:2503–11. doi: 10.1016/j.vaccine.2020.01.093
4. Achterbergh, RCA, McGovern, I, and Haag, M. Co-Administration of Influenza and Covid-19 vaccines: policy review and vaccination coverage trends in the European Union, UK, US, and Canada between 2019 and 2023. *Vaccine.* (2024) 12:216. doi: 10.3390/vaccines12020216

Funding

The author(s) declared that financial support was received for this work and/or its publication. This work was supported by the National Natural Science Foundation of China (82302519); the key grants of Department of Science and Technology of Zhejiang Province (2024C03216, 2025C02186); the Key Program of Health Commission of Zhejiang Province/Science Foundation of National Health Commission (WKJ-ZJ-2523); the National Key Research and Development Project by the Ministry of Science and the Technology of China (2023YFC2308705); the Zhejiang Provincial Medical and Health Science and Technology Plan (2023RC143); the Zhejiang Provincial Disease Prevention and Control Science and Technology Plan (2025JK014).

Acknowledgments

We acknowledge the physicians and staff of the sentinel hospitals and reference laboratories for their excellent work on specimen collection, epidemiology surveys, and laboratory testing. We are also grateful to all patients of this study.

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.

5. Lv, M, Fang, R, Wu, J, Pang, X, Deng, Y, Lei, T, et al. The free vaccination policy of influenza in Beijing, China: the vaccine coverage and its associated factors. *Vaccine*. (2016) 34:2135–40. doi: 10.1016/j.vaccine.2016.02.032
6. Jiang, SQ, Cai, YW, Zuo, R, Xu, L, Zheng, J, Yi, H, et al. Analysis of influenza vaccination coverage, recommendation behaviors and related factors among health care workers in Nanshan District of Shenzhen City under the free policy between 2019 and 2020. *Zhonghua Yu Fang Yi Xue Za Zhi*. (2022) 56:1565–70. doi: 10.3760/cma.j.cn112150-20211217-01164
7. Wang, X, Jiang, W, Yu, Z, Jiang, W, Zhu, X, Wang, Z, et al. Government livelihood project - free influenza vaccination for the older population in China: the example of Zhejiang Province. *Front Public Health*. (2025) 13:1499. doi: 10.3389/fpubh.2025.1571499
8. Ye, L, Chen, J, Mei, Q, Sun, Y, and Yang, T. The impact of the Covid-19 pandemic and the free vaccination policy on seasonal influenza vaccination uptake among older adults in Ningbo, eastern China. *Hum Vaccin Immunother*. (2024) 20:999. doi: 10.1080/21645515.2024.2370999
9. Liu, G, Liu, Z, Zhao, H, Sun, Y, Shen, P, Lin, H, et al. The effectiveness of influenza vaccine among elderly Chinese: a regression discontinuity design based on Yinzhou regional Health information platform. *Hum Vaccin Immunother*. (2022) 18:5751. doi: 10.1080/21645515.2022.2115751
10. Wu, H, Xue, M, Wu, C, Ding, Z, Wang, X, Fu, T, et al. Estimation of influenza incidence and analysis of epidemic characteristics from 2009 to 2022 in Zhejiang Province, China. *Front Public Health*. (2023) 11:4944. doi: 10.3389/fpubh.2023.1154944
11. Chinese Center for Disease Control and Prevention (China CDC). (2024). National sentinel surveillance of acute respiratory infectious diseases. Available at: https://www.chinacdc.cn/jksj/jksj04_14275/ (Accessed July 12, 2025).
12. Fang, J, Liu, Y, An, Y, and Zhou, K. The macroeconomic impact of demographic shifts: aging populations and their socioeconomic consequences. *Law Econ*. (2023) 2:37–43. doi: 10.56397/le.2023.11.05
13. Lixue, C, Li, L, Lei, C, Yifan, S, Zhaonan, Z, and Zhundong, Y. Vaccination coverage of three non-epi vaccines among the national population aged ≥ 60 years from 2019 to 2023. *Chin Prev Med*. (2024) 25:592–7. doi: 10.16506/j.1009-6639.2024.05.014
14. Xiaoxiao, Z, Kaichao, Y, Binghui, D, Yanfang, J, Lubin, S, Jun, L, et al. Current status of influenza vaccination among persons aged ≥ 60 years in Henan Province, 2020–2022. *Modern Dis Cont Prev*. (2024) 35:166–8+78. doi: 10.13515/j.cnki.hnjpm.1006-8414.2024.03.004
15. Leijing, M, Xianwei, L, Ling, L, Mingxue, R, Yan, D, and Binbing, W. The status of influenza vaccination among people aged 60 years and above in Anhui Province from 2021 to 2023. *J Prev Med Inform*. (2025) 41:515–20. doi: 10.19971/j.cnki.1006-4028.240457
16. Zixin, L, Shenyu, W, Xiaotong, Y, Jinhang, X, Yue, X, Sheng, W, et al. Coverage and influencing factors of influenza and pneumococcal vaccination among urban and rural residents 50 years old and over in Zhejiang Province, 2022—a cross-sectional survey. *Chin J Public Health*. (2024) 40:44–9. doi: 10.11847/zgggws1142709
17. Yang, T, Tang, L, Li, P, Li, B, Ye, L, and Zhou, J. Effectiveness of inactivated influenza vaccine against laboratory-confirmed influenza among Chinese elderly: a test-negative design. *BMC Geriatr*. (2024) 24:404. doi: 10.1186/s12877-024-05003-3
18. Xiaokun, Y. Chinese Center for Disease Control and Prevention (China CDC). Evaluation of influenza vaccine effectiveness in China (2021). doi: 10.27511/d.cnki.gzyyy.2021.000053
19. Gao, X, Sun, Y, Shen, P, Guo, J, Chen, Y, Yin, Y, et al. Population-based influenza vaccine effectiveness against laboratory-confirmed influenza infection in southern China, 2023–2024 season. *Open Forum Infect Dis*. (2024) 11:456. doi: 10.1093/ofid/ofae456
20. Domnich, A, Icardi, G, Panatto, D, Scarpaleggia, M, Trombetta, C-S, Ogliastro, M, et al. Influenza epidemiology and vaccine effectiveness during the 2023/2024 season in Italy: a test-negative case-control study. *Int J Infect Dis*. (2024) 147:107202. doi: 10.1016/j.ijid.2024.107202
21. Rose, AMC, Pozo, F, Martínez-Baz, I, Mazagatos, C, Bossuyt, N, Cauchi, JP, et al. Vaccine effectiveness against influenza hospitalisation in adults during the 2022/2023 mixed season of influenza a(H1N1)Pdm09, a(H3N2) and B circulation, Europe: Vebis sari Ve hospital network. *Influenza Other Respir Viruses*. (2024) 18:e13255. doi: 10.1111/irv.13255
22. Lewis, NM, Zhu, Y, Peltan, ID, Gaglani, M, McNeal, T, Ghamande, S, et al. Vaccine effectiveness against influenza a-associated hospitalization, organ failure, and death: United States, 2022–2023. *Clin Infect Dis*. (2024) 78:1056–64. doi: 10.1093/cid/ciad677
23. Choi, YJ, Song, JY, Wie, SH, Lee, J, Lee, JS, Jeong, HW, et al. Early and late influenza vaccine effectiveness in South Korea during the 2023–2024 season. *Vaccines*. (2025) 13:197. doi: 10.3390/vaccines13020197
24. Darvishian, M, van den Heuvel, ER, Bissielo, A, Castilla, J, Cohen, C, Englund, H, et al. Effectiveness of seasonal influenza vaccination in community-dwelling elderly people: An individual participant data Meta-analysis of test-negative design case-control studies. *Lancet Respir Med*. (2017) 5:200–11. doi: 10.1016/s2213-2600(17)30043-7
25. Kitamura, S, Matsushita, M, Komatsu, N, Yagi, Y, Takeuchi, S, and Seo, H. Impact of repeated yearly vaccination on immune responses to influenza vaccine in an elderly population. *Am J Infect Control*. (2020) 48:1422–5. doi: 10.1016/j.ajic.2020.05.011
26. Yuelong, S, and Siming, W. Research progress on factors influencing the protective effects of influenza vaccines. *J Shandong Univ*. (2021) 59:1–7. doi: 10.6040/j.issn.1671-7554.0.2021.0319
27. Belongia, EA, Skowronski, DM, McLean, HQ, Chambers, C, Sundaram, ME, and De Serres, G. Repeated annual influenza vaccination and vaccine effectiveness: review of evidence. *Expert Rev Vaccines*. (2017) 16:554. doi: 10.1080/14760584.2017.1334554