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Obesity and climate change: co-crises with common solutions

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Abstract

The global obesity crisis involves an unprecedented and rapid change to the human phenotype. Conferring vast levels of avoidable morbidity and mortality at enormous cost, it has proved refractory to previous policy-led action. This article reviews recent developments in our understanding of obesity and its links to the climate co-crisis, aiming to inform evidence-based, societal-level actions to address both. Recent therapeutic developments now offer transformative interventions for millions of people living with obesity. However, treating all affected adults and children with major bariatric surgery or lifelong anti-obesity medication is unsustainable given the risks and costs. The obesity crisis has been driven primarily by the transformation of our food environment toward diets dominated by ultra-processed foods (UPFs) that exert multiple addictive and obesogenic mechanisms. Emerging evidence shows that not all UPFs have the same impact: processed meat and low-fiber, energy-dense UPFs are linked with poorer outcomes compared with less energy-dense, high-fiber, plant-rich UPFs, indicating that more nuanced classifications would be helpful. This food system also contributes significantly to climate change and other environmental harms, primarily through ruminant meat consumption. Both climate change and obesity are driven by unsustainable, but profitable, consumption. Solutions exist but have not been adequately implemented owing to a lack of political will. They require food system reforms that replace energy-dense UPFs with unprocessed foods and reduce animal-sourced foods. Accumulating evidence supports prioritizing actions to remove market distortions via increasing cost transparency, taxing unhealthy foods (redirecting the proceeds to public health), combating marketing, effective food labeling, facilitating healthy food choices, promoting healthy living environments, and public and professional education. New economic models, market demand shifts, and technological innovation should

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all be harnessed to overcome economic and political barriers, and food system reform should be integral to future actions to achieve the Sustainable Development Goals. This transformation to improve both human and planetary health will require interdisciplinary scientific advocacy and coalition-building across society. During the COVID-19 pandemic, societies recognized how rapid, concerted, science-led action can effectively address a global threat; a similar societal shift is required to motivate the political action needed to address the obesity crisis.

KEYWORDS

anti-obesity agents, bariatric surgery, climate change, food system, obesity, ultra-processed foods, environment

Key points

- Half the global population is projected to be living with excess weight and/or obesity within 10 years, placing an unsustainable burden on healthcare systems.
- The food environments driving obesity via increased consumption of energy-dense and ultra-processed foods (UPFs) are also driving climate change.
- Although bariatric surgery and incretinomimetic drugs offer important new therapeutic options, they cannot substitute for societal-level, systems-wide reform of obesogenic ecosystems.
- Reforms necessary to tackle the obesity and climate co-crises include the following: cost transparency to address market distortions, taxes on energy-dense UPFs, facilitation of healthy food choices (including subsidies to producers and consumers), food labeling, living environments that enable healthy diets and activity, and education of the public and professionals.
- Transitioning to non-obesogenic and sustainable food systems that are healthy for the planet would likely be very economically advantageous to societies.

Introduction

Over 2.6 billion people—38% of the world's population—are now living with excess weight and/or obesity. This fraction is projected to reach 50% by 2035 based on current rates of change (1). The global increase in obesity since the 1980s has been the most rapid and dramatic change in the human phenotype throughout our entire evolution.

At the simplest biological level, obesity is the accumulation of excess adipose tissue due to a prolonged surplus of energy intake over that expended. When the extent of adiposity overwhelms the capacity to buffer the energy excess, obesity becomes a complex multifactorial noncommunicable disease (NCD) and a "gateway" condition for many conditions that collectively induce the majority of the global disease burden (2–4). Obesity was first recognized as a disease by the World Health Organization in 1948. While some anthropologists contend that increased body weight is an evolutionary adaptation to changing lifestyle (5), many national and international organizations have reaffirmed its classification as a disease, and a recent international commission defined clinical obesity as a chronic, systemic disease state directly caused by excess adiposity (6). Excess weight, conventionally defined as a body mass index (BMI) >25 kg/m^2, is estimated to cause almost 500,000 deaths/year in the United States alone (7) and at least 5 million adult deaths/year globally (8, 9). It is now recognized that BMI is an imprecise measure of adiposity, affected by ethnic variations in muscle mass, and that it does not estimate visceral obesity—a major determinant of obesity-associated health outcomes. BMI is now recommended only for use as a screening tool or for epidemiology; excess adiposity should be confirmed by at least one anthropometric measure, such as waist circumference, waist-to-hip ratio, or waist-to-height ratio (6).

The global obesity epidemic is now increasing in children (1, 10) with serious lifelong consequences (11) that can be passed on epigenetically (12). Excess weight and obesity confer enormous direct and indirect economic costs, estimated at 2.19% of gross domestic product (GDP) globally in 2019 and rising (13).

While reduced energy expenditure through sedentary lifestyle patterns and automation may be a potential contributor, it is not the main driver of the obesity pandemic (14–17). Similarly, the rise in obesity does not appear to be due to increased energy intake *per se*, as evidence suggests that Americans have not been consuming more calories since 2000, especially relative to their increased body size (18). The most compelling evidence indicates that the obesity epidemic is being driven by changes in our food environment. Owing to modern food processing, our diet is increasingly diverging from that consumed during our evolution. Specifically, there has been an increase in consumption of energy-dense "Western"-style diets that are characterized by being high in refined grains, red and processed meats, confectionery, ultra-processed foods (UPFs), and sugar-sweetened beverages (SSBs). These dietary changes have been

accompanied by a reduction in home-prepared, minimally processed foods. According to a recent meta-analysis, UPFs represent up to 80% of daily energy intake in the United States and Canada (19), and their increased consumption has been reported across the world (20, 21).

In low- and middle-income countries (LMICs), the rise in obesity has occurred despite the continued prevalence of malnutrition, with a resulting growth in particular conditions termed the double burden of malnutrition (DBM) and the triple burden of malnutrition (TBM). DBM refers to the coexistence of undernutrition along with overweight or obesity within an individual (22), while TBM refers to the coexistence of undernutrition along with overweight or obesity and also micronutrient deficiency or anemia within an individual (23). These conditions particularly cluster in richer households in poorer LMICs and in poorer households in richer LMICs (24) and have been exacerbated by the rapid expansion of UPFs in the global food system, resulting in the displacement of traditional healthy diets with foods of poor nutritional value (25). Over 70% of countries, mainly LMICs such as Indonesia and Guatemala, currently experience DBM (26). While progress has been made in reducing malnutrition-related disability and mortality, these gains have been more than offset by increasing rates of obesity (27).

The trends in both malnutrition and obesity are largely due to the rapid transition of dietary habits towards energy-dense UPFs (26). In developing countries, consumption of UPFs is first adopted in richer households but soon spreads to poorer households in the same pattern as the spread of obesity (28). Coexisting malnutrition with obesity is associated with even greater risk of multiple NCDs, particularly for mothers (29), and young children can suffer stunted growth and poor cognition and educational performance (30). Such exposures during fetal and neonatal development and throughout childhood have potential lifelong consequences for the risk of obesity and other NCDs. This was originally proposed by David Barker in 1995 (31) and is now well-established (32–34).

There have been many prominent policy proposals to combat obesity in recent years (35–39). However, actions have generally been slow and inadequate, such that no nation has reversed or even halted the upward obesity trajectory. This is in stark contrast to the global COVID-19 pandemic, which caused considerable mortality and disruption worldwide but demonstrated how populations can, in general, accept dramatic upheavals to their way of life, at least for temporary periods. The COVID-19 pandemic underscored the negative impact of obesity on health outcomes, as it is a risk factor for severe COVID-19, hospitalization, and death (40). It also illustrated how rapid, concerted, science-led action can effectively address and mitigate a global public health threat. While COVID-19 presented an immediate survival threat for which societies accepted radical policies, this has not been the case for obesity, as the threat has evolved slowly over decades and has been relatively unacknowledged and/or a low priority for national health and economic strategies, despite the clear consequences it has on health and the economy. The sluggish response may also be due to social prejudices holding that obesity is self-inflicted (41). In contrast to COVID-19, obesity will require much more sustained systemic changes.

Over the same period, there has been global acceptance that climatic changes resulting from human activities are driving extreme weather events, causing considerable damage and suffering across the planet (42). Global heating now kills one person every minute around the world, accounting for around 546,000 deaths per year over the period 2012–2021, which is up 63% from the 1990s (43). Scientists warn that there is a high risk of a climate catastrophe that will threaten the health and survival of human civilizations within decades (44–46). The obesity and climate crises both relate to energy balance and, at least in part, to problems of over-consumption of food and goods from which powerful commercial entities profit—resulting in strong resistance to their mitigation from vested interests. They both represent systems problems arising from common problems in the natural and food environment that are deeply social and cultural. Addressing both crises will require political courage and urgent action at multiple levels of society, and both require all sectors to act globally.

There are two key options available to address obesity. The first option is pharmacological or surgical intervention. Until recently, doctors could only advise patients to lose weight via diet and lifestyle interventions, with limited effectiveness. The recent development of effective weight-loss medications, together with bariatric surgery for more severe cases, provides transformative treatment options for people affected by obesity. The application of glucagon-like peptide-1 receptor agonists (GLP-1RAs) for treating obesity was named *Science* magazine's breakthrough of the year in 2023 (47). However, there are deep concerns regarding the global scalability, affordability, acceptability, and long-term safety of applying medication or surgery to large populations, particularly from childhood, especially in light of the potential need for life-long medication. There is also a danger that, with effective treatments being available, policymakers will avoid addressing the food environment changes driving the obesity crisis. This is analogous to COVID-19 policymaking in some countries, where reliance was placed on rapid vaccine development rather than effective public health measures.

The second option is a food system transition toward healthier, less-processed, whole food diets to reduce the obesogenic drive, and toward more plant-based foods that would also address the multiple environmental harms from current food systems, including climate change. National dietary guidelines are becoming increasingly plant-based over time, with recent revisions to Canadian (48) German (49), Spanish (50), and Danish (51) guidelines all recommending reduced or no intake of animal-sourced products associated with high greenhouse gas (GHG) emissions. However, often there are important disconnects between national dietary guidelines and relevant government policies and subsidies (52). A food system transformation that is healthy for people and the planet would necessitate a paradigm shift in the food environment driven by appropriate policy approaches.

The growing public acceptance of the climate crisis is resulting in a societal shift in attitude and behaviors, with some people around the world shifting to more sustainable lifestyles (53), including food choices (54), consistent with a food system transformation that would help tackle obesity. Economies are also shifting, with increased investments in cleaner technologies transforming major industries such as

automobile manufacturing and energy production. This presents a critical moment to harness these societal transitions and enable sustainable living to protect the environment and avoid climate catastrophe while reducing obesity and its co-morbidities. If the global momentum for more sustainable living could be channeled towards shifting consumer demand to foods that are both non-obesogenic and that can be produced without environmental harm, similar investments could be applied to the necessary transformation of our food systems (55). It is important that food consumption is framed within a global environmental paradigm, as is already the case for fuel consumption, recycling, reusing, and upcycling.

There is also mounting recognition that preventing a climate catastrophe and protecting the environment will be less harmful and much cheaper than trying to adapt to the consequences (56). Likewise, preventing obesity by changing our food environment offers similar economic and well-being benefits over pharmacological or surgical interventions. This would avoid a future where people are condemned to surgery or lifelong medication in order to stay healthy in an environmentally unsustainable, obesogenic world. In the words attributed to Desmond Tutu, *"There comes a point where we need to stop just pulling people out of the river. We need to go upstream and find out why they're falling in."*

Here, we review the recent developments in our understanding of obesity and its treatment. Given the very broad scope of this article, we have not engaged in a formal systematic review but provide a narrative literature review. We also consider what can be learned from the co-crisis of climate change. We discuss the need for integrated multisector obesity prevention strategies that promote both a healthy lifestyle and a healthy planet. A transformative social movement and fundamental changes to our food systems will be required, combined with a realignment of education and healthcare to address these major societal challenges. This will require a variety of soft and hard policy measures and their evaluation and monitoring to ensure effective implementation.

Epidemiology: current and projected scale of the obesity pandemic

The World Health Organization (WHO) describes the global obesity epidemic as one of today's most blatantly visible—yet most neglected—public health problems (57). A clear-sighted appreciation of the current and rising scale and impact of the crisis is vital to inform action.

Obesity prevalence is rising dramatically

In 2020, 2.6 billion people aged over 5 years—roughly 38% of the world's population—were living with excess weight or obesity (1). Obesity alone accounted for 988 million people, or 14% of the population (1). Adult obesity (individuals aged ≥20 years) was found in 18% of women and 14% of men; in children (5–19 years), the rates were 10% in boys and 8% in girls. Obesity rates continue to rise globally: in 147 out of 200 countries, the lifetime risk of having a high BMI (>25kg/m^2) is now more than 50%, and in 62 countries, it exceeds 80%. The global lifetime risk of class II obesity (a BMI >35kg/m^2: the common threshold for clinical intervention) is more than 10% (58). In the United States, 80% of adults in some states are already overweight or obese. If current trends continue, projections indicate that, across the United States, one in three adolescents and two in three adults will be living with obesity by 2050 (59). There are wide geographical differences in the proportion of men and women with obesity, ranging from as low as 4% and 8%, respectively, in the South-East Asian region to as high as 32% and 37%, respectively, for the Americas (North, Central, and South America) (1) (Figure 1).

Obesity prevalence has nearly tripled over the past 50 years. While prevalence is highest in high-income countries, a large share of the increase (around 55%) has occurred in rural areas in LMICs across South-East Asia, Latin America, Central Asia, and North Africa (26). Significantly closing the gap in prevalence between urban and less-well-resourced rural areas creates "the ticking time bomb of obesity" (26). Projections suggest that by 2030, 50% of adults will be living with high BMI and 17% of men and 22% of women will be living with obesity (58) and by 2035 over 4 billion people worldwide will be living with excess weight or obesity—53% more than in 2020 (1) (Figure 1). The global obesity rate is expected to rise from 14% to 24% over this period. While a gradual rise in prevalence is forecasted for all age groups, the upward trajectory is expected to be greatest in LMICs. In some Pacific Island countries (Tonga, Samoa, Federated States of Micronesia, and Kiribati), more than two-thirds of the adult population are projected to be living with obesity by 2035.

The greatest increases are predicted in children and adolescents. Between 1975 and 2016, the prevalence of obesity increased from 0.7% to 5.6% in girls and from 0.9% to 7.8% in boys (60). This year, 2025, marks a turning point for children and adolescents (aged 5–19 years) when, for the first time, the global prevalence of obesity is now greater than that of underweight individuals (9.4% versus 9.2%) (61). Between 2020 and 2035, obesity prevalence is projected to rise from 10% to 20% in boys and from 8% to 18% in girls (1). The highest predicted annual increases are for India, Bangladesh, Myanmar, and Tanzania at 9.1%, 8.6%, 8.4%, and 8.4% per year, respectively (1). Obesity-related diseases are also being diagnosed at younger ages. Obesity in childhood is particularly damaging and can result in impaired mobility, poorer school performance, early onset puberty, stunting, skeletal anomalies, sleep apnea, stigma-induced anxiety, and mood disorders. Obesity in childhood tracks into adulthood (11) and has the potential to impact quality of life, future economic potential, and adult healthcare costs.

Obesity increases mortality and NCD rates

Obesity is a key risk factor for many of the major NCDs. Improvements in public health over recent decades have reduced the burden of disease due to communicable, maternal, and neonatal diseases, but, simultaneously, there has also been a considerable rise in the global burden due to NCDs, particularly obesity, diabetes, cardiovascular diseases, and cancer (62).

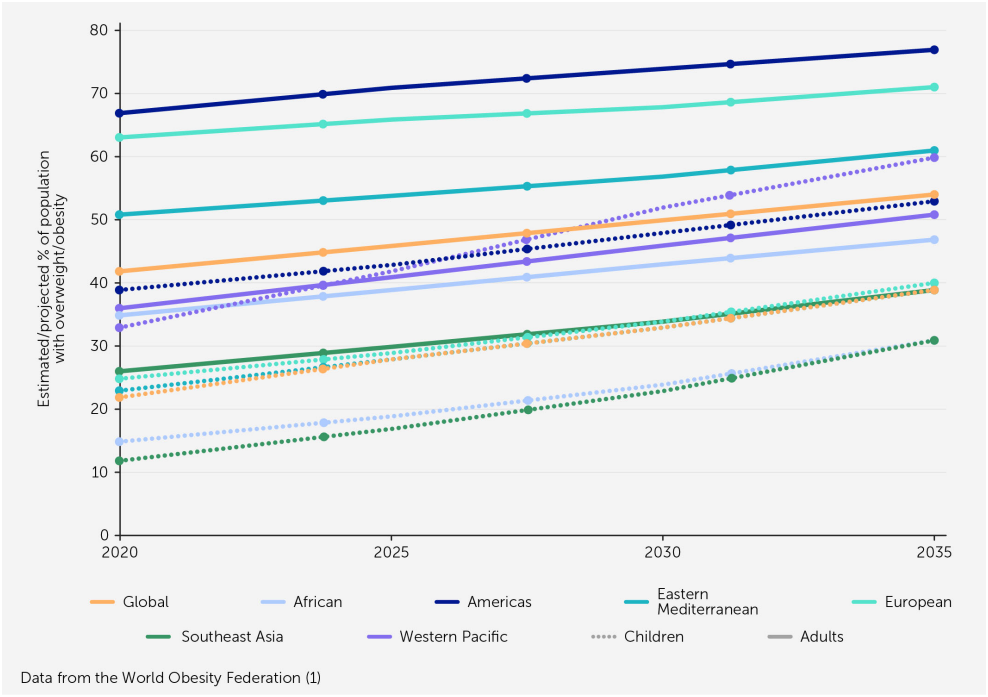


FIGURE 1
Current and projected rates of overweight and obesity prevalence in adults and children globally and by World Health Organization region. Data from the World Obesity Federation (1).

These NCDs have been termed a syndemic as they frequently overlap and co-exist within populations, share common mechanisms, and are driven by shared social, environmental, and economic factors (63). From a public health perspective, viewing these co-existing conditions as a syndemic may help convince policymakers that systemic actions involving bundles of policies in diverse but interlinked portfolios (including agriculture, industry, transport, economics, education, and healthcare) are required to tackle them (64).

Despite improvements in their treatment, the global burden due to this syndemic is projected to continue to increase due to population growth and aging (65). The food environment plays a central role in driving this syndemic (66), and obesity can be viewed as a gateway condition for many of the other NCDs (2–4). In 2019, more than 5 million deaths globally were attributed to obesity-related ill-health, with more than half occurring amongst persons aged under 70 years (13). A high BMI is among the top three causes of death in all geopolitical regions except Sub-Saharan Africa (26). The Organisation for Economic Co-operation and Development (OECD) estimates that excess weight and obesity reduce life expectancy in member countries by an average of 2.7 years (67).

Obesity drives cardiovascular risk factors, including dyslipidemia, type 2 diabetes (T2D), hypertension, and sleep disorders, and the development of cardiovascular disease independently of other cardiovascular risk factors (68). One in five adults with obesity also has T2D, with the risk increasing with higher BMI (69). Obesity has also been linked with numerous common cancers, including breast, colorectal, esophageal, kidney, gallbladder, uterine, pancreatic, and liver cancer (70–72). Excess BMI leads to a 17% increased risk of cancer-specific mortality (70) and is the third-highest risk factor for cancer after smoking and alcohol use (9).

The effect of obesity in driving cancer incidence among children and young adults is of particular concern. A recent analysis of a population-based cancer registry in China, covering around 12–14 million individuals from 2007–2021, found that almost half of incident cancers were obesity related. Obesity-related cancers increased in incidence by 3.6%/year overall, but the rate of increase was highest in younger generations, e.g., 15.28% in those aged 25–29 years versus 1.55% in those aged 60–64 years. The alarming rise documented in the obesity-related cancer incidence rate ratio in successive generations since the 1980s points to an emerging major public health concern (73).

Obesity also increases the risk of osteoarthritis, non-alcoholic fatty liver disease, cirrhosis, gall bladder disease, gout, some pulmonary diseases, and autoimmune diseases (e.g., type 1 diabetes).

Economic impact of obesity

Obesity also presents a huge economic burden. In 2020, the economic costs of obesity ranged from 1.2% of GDP in the African region to 3.2% in the Americas (13). Indirect costs arising from premature mortality and lost productivity accounted for more than two-thirds of this cost, with the remainder being direct medical costs. The OECD estimated that obesity effectively reduces the workforce by 54 million persons/year across 52 countries (67).

Given current trends, the global economic costs of obesity (including healthcare and economic productivity) are projected to rise from just below US$2 trillion in 2020 to over US$3 trillion by 2030, over US$4 trillion by 2035, and to US$18 trillion by 2060—reaching 3.29% of total GDP (1, 13).

Obesity pathogenesis and drivers

The lack of progress on addressing obesity may be partly due to the common misconception that it results simply from an energy imbalance caused by increased consumption of energy-dense foods accompanied by reduced energy expenditure associated with sedentary lifestyles. This has perpetuated the belief that the solution is for individuals to eat less and exercise more, which stigmatizes individuals who cannot sustain such habits. In reality, the evidence suggests that much more complicated mechanisms are at play.

Obesity develops due to complex interactions between multiple factors. These include genetic predisposition, environmental exposures (primarily nutrition), epigenetics and developmental programming, and endocrine, metabolic, immune, microbiome, social/cultural, political, economic, and psychological/behavioral factors. The causes of the global obesity epidemic are not fully clear, but its rapid onset and worldwide spread across many cultures and all age groups exclude many factors, such as changes in genetic predisposition.

Obesity models

There are several theories for the obesity epidemic, including the energy storage model (74), the developmental origins of obesity model (75), the energy balance model (76), and the carbohydrate-insulin model (77). The latter two paradigms can be simplistically summarized as "push" and "pull" models, respectively. The push model postulates that obesity is driven by increased consumption of readily available, inexpensive, energy-dense foods. In contrast, the pull model postulates that consumption of food with a high glycemic load stimulates insulin, which alters fuel partitioning, inhibiting mitochondrial respiration and fatty acid utilization (78, 79) and promoting fat deposition into adipose tissue, stimulating hunger and further consumption. These different models have generated considerable academic debate, especially regarding whether all calories have the same metabolic or adipogenic potential and the circular question of whether people develop obesity due to excessive caloric intake or whether their obesity drives excessive caloric intake. Excessive caloric intake resulting in severe, early-onset obesity can be driven by mutations in appetite regulation genes, including melanocorticopin 4 receptor, leptin, and the leptin receptor; however, such cases are relatively uncommon, and the greatest proportion of obesity is likely driven by shifts in the modern food environment affecting individuals according to their genetic predisposition. Despite these debates, the models have significant overlap, and it is possible that both the push and pull models are correct and operate to varying extents in different contexts and/or in different individuals (80). There is, however, common agreement that (i) the epidemic is caused essentially by a change in the food environment, (ii) obesity is an endocrine disorder, and (iii) it is not a personal health issue but a public health crisis.

Energy intake and activity

The obesity epidemic has been most evident in the United States, where the obesity prevalence has tripled since 1980 (81). Yet, this does not appear to be due to increased energy intake: evidence from self-reported recall data and food availability estimates indicates that consumption and availability of dietary energy increased rapidly until around 2000 and subsequently declined by a small but significant amount (18). Theories blaming obesity on macronutrients have been proposed, initially implicating fats and then sugars (82). However, this is also not consistent with evidence suggestive of slight dietary improvements in the United States since around 2000 (83–86). Similarly, although energy expenditure appears to have decreased early in the epidemic, evidence from the United States and Europe suggests that, since 1990, exercise reductions associated with occupation, travel, and being within the home have been offset by an increase in leisure-time exercise (14, 16, 17). More energy is expended to move as individuals become larger; therefore, reduced physical activity does not necessarily equate to reduced absolute energy expenditure. Longitudinal data also suggest that increased adiposity predicts less physical activity but reduced physical activity does not predict increased adiposity (15).

Higher rates of cardiovascular disease and obesity have been associated with the global increase in urbanization, with the fraction of the global population living in urban settings having risen from 36.6% in 1970 to 44.8% in 1994, and being projected to reach 61.1% by 2025 (87, 88). The lower prevalence of obesity in rural areas was proposed to be due to food consumption being restricted by lower incomes (89) and because energy expenditure was higher due to agricultural work and domestic activities such as water and firewood collection (90). However, this does not now apply to all regions: in middle-income countries, agriculture is increasingly mechanized, cars are used for transport, and homes are supplied with water and domestic fuels (91). In addition, the theory that increased urbanization has driven obesity is also not supported by more recent data, as the majority of the global increase in obesity has been in rural areas: 55% of the global increase in mean BMI from 1985 to 2017 occurred in rural areas, and, for some LMICs, rural areas accounted for 80% of the rise (92).

Reduced physical activity does not appear to play a major role in driving the obesity epidemic, which appears to be primarily due to the amount and quality of food intake (93). However, a sedentary lifestyle is a risk factor for weight gain. It is also clear that physical activity has many benefits for cardiometabolic health independent of BMI changes (94). Reducing weight by combining physical activity with diet induces additional improvements in metabolic health, as compared with a similar loss of weight by diet alone (95). As such, a more nuanced analysis of energy balance with greater appreciation of energy partitioning and diet quality is required.

Ultra-processed foods: the key driver of obesity?

As a response to food security concerns in the mid-20th century, investments in the "Green Revolution" drove a dramatic increase in crop yields, with much of the increased grain then used to feed cows, pigs, and chickens, which, together with the use of antibiotics, enabled the industrialization of livestock production. Contemporaneously, Western lifestyles moved away from home-prepared meals made with minimally processed whole foods to ready-to-eat meals, snacks, and convenience foods (96–98). Consumer demand for ready-to-eat foods drove a change in food production that enabled the growth of large national and international food conglomerates, which, in response to demand and to enhance profits, led to the development of UPFs (99). The rise of UPF consumption is now broadly seen as the key factor driving the obesity epidemic (Figure 2).

What are UPFs?

While food processing, such as cooking, fermenting, pickling, curing, and smoking, has been essential throughout history, UPFs are industrially produced, containing ingredients that would not be found in most normal homes. Today, the classification of food as UPFs is based on the NOVA system, which classifies foods into four broad groups: unprocessed or minimally processed foods, processed culinary ingredients, processed foods, and UPFs. In NOVA, UPFs are conceptually defined as formulations of food substances and additives containing little if any whole food, designed to replace the other NOVA food groups and their culinary preparation while maximizing industry profits. Operationally, they are defined as formulations containing one or more markers of food ultra-processing, either sensory-related classes of food additives or food substances of no culinary use (97, 99). Reservations have been raised that classifying foods based on processing is too broad, lacks clarity over the specific food components of concern, and is not consistent with nutritional recommendations, which are generally based on specifying nutrients and food groups (100). In many high-income countries, UPFs are already dominant in the food system and contribute considerably to daily nutrient and energy intake, whereby restricting or removing UPFs requires replacement with appropriate unprocessed or minimally processed foods such that nutrient deficiencies do not occur. Further, the health effects are not the same across UPF subgroups. In a European study, high consumption of animal-based UPFs and SSBs increased risks of cardiometabolic disease and cancer multimorbidity, while breads, cereals, and plant-based UPFs did not (101). Similarly, in an analysis of three large prospective cohorts in the United States, SSBs and processed meats largely explained the overall UPF association with cardiovascular disease outcomes, and for stroke, when SSBs and processed meats were excluded, the association with UPF became inverse (102). Another prospective study in the United States found an association between UPF consumption and mortality, but ultra-processed vegetables and legumes were associated with a reduced risk of mortality (103). However, this apparent heterogeneity of health effects across UPF subgroups is contentious and may reflect biases and flawed comparisons with "the rest of the diet" rather than with non-ultra-processed counterparts (104). However, despite possible limitations of the NOVA system, nearly all of the evidence from hundreds of studies linking food processing levels with obesity risk has been obtained using this system (105).

The industrialization of food production involves the deconstruction of whole foods, obtained cheaply due to the farming revolution, into their component parts. These are then subjected to mechanical, thermal, fermentative, enzymatic, and decontamination treatments. Finally, they are reformulated to add "value" and enhance profitability. This may involve modification, fortification with vitamins and minerals, enhancement of taste with artificial flavorings and sweeteners, enhancement of appearance with artificial colorants, foaming or anti-foaming agents, clarifying agents, and bleaching agents, enhancement of texture and "palatability" with more artificial additives (such as acidity regulators, emulsifiers, gelling agents, glazing agents, and thickeners), and, finally, enhancement of shelf life with artificial stabilizers, antioxidants, and preservatives (106, 107).

UPF consumption: implications for diet quality and obesity

As a result of these changes in farming and lifestyle, together with aggressive marketing, UPF sales have grown rapidly across all countries (20, 21). UPFs now form a major part—in some countries, the main part—of Western diets. The proportion of the diet comprised of UPFs is directly correlated with national wealth (28). An Australian study indicated that 56% of grocery energy was from UPFs, and these were cheaper and purchased by lower lower socioeconomic status groups (108). In the United States and Canada, around half of daily energy intake is now obtained primarily from cookies, pastries and sweet bread, packaged bread, fast foods, SSBs, and processed sweets (19). According to a recent meta-analysis, UPFs comprise almost 80% of all calories consumed in these two countries, and their consumption was inversely related to the intake of unprocessed foods (19). This is evidence that UPFs have displaced whole foods and formed the main part of Western diets. A higher UPF intake is associated with lower intake of fruits, vegetables, legumes, and seafood. Consequently, increased amounts of refined grains, starchy vegetables, and chemical additives and reduced amounts of non-starchy vegetables and whole grains, fibers, probiotics, prebiotics, flavonoids, and phytonutrients are now consumed.

Accumulating evidence indicates that the consumption of a UPF-dominant diet is detrimental to health. Meta-analyses, systematic and umbrella reviews, including many cohort studies across the globe covering millions of individuals, showed that high UPF diets increased the risk of all-cause mortality and were associated with 32 specific adverse health outcomes (109–113). According to prespecified evidence classification criteria, convincing evidence (Class 1) supported direct associations with cardiovascular disease, common mental health disorders, overweight and obesity, and T2D (110). A recent systematic review found 104 prospective observational studies assessing the

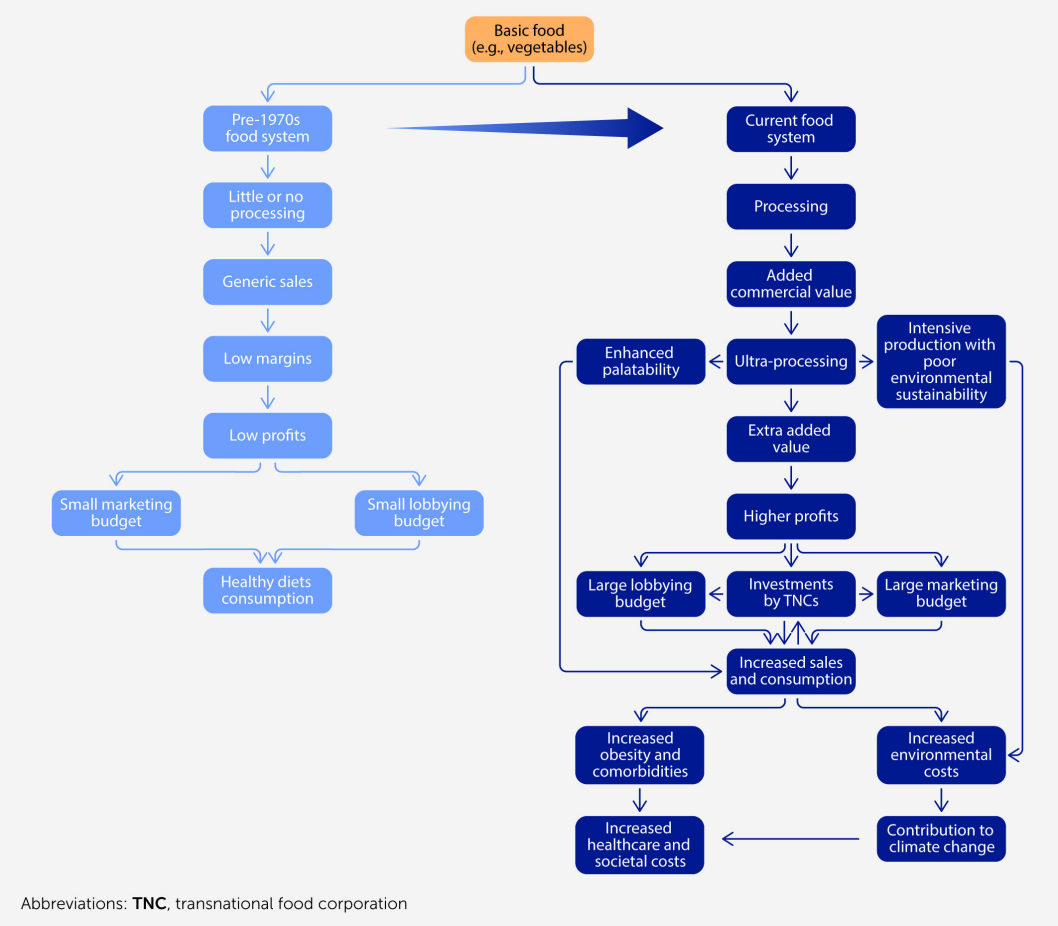


FIGURE 2
Food system transition driving ultra-processed food (UPF) consumption—the key driver of obesity.

effects of UPFs in the diet on chronic disease risk, of which 92 found that greater consumption of UPFs increased the risk of one or more chronic diseases, with 78 of these reporting significant linear trends (28). In meta-analyses of outcomes, which were included in at least four of the studies, significant associations were found with 12 outcomes, including excess weight or obesity, abdominal obesity, and T2D (28). A study assessing the contribution of dietary UPFs to premature deaths across eight countries with very different levels of consumption estimated that in Colombia, UPFs account for just 4% of all-cause premature mortality, whereas in the United States and the United Kingdom, the estimate was 14% (112).

In contrast to changes in energy intake or energy expenditure, the increase in UPF consumption has paralleled the rise in obesity in adults (114–116) and children (117). UPF consumption predicted increased general and abdominal obesity in all prospective epidemiological studies systematically reviewed (118). A systematic review of observational studies found a dose-response relationship, with every 10% increase in daily UPF consumption being associated with a 6% increase in obesity (119). A prospective cohort study across nine European countries found, after multivariate adjustment, that every additional standard deviation of UPF consumption was associated with a weight gain of 0.12 kg [95% confidence interval (CI): 0.09–0.15] over 5 years (120). In the United Kingdom, a longitudinal study of over 9,000 children followed from age 7 to 24 years found accelerated BMI growth in those in the highest quintile for UPF consumption, with similar increases for other adiposity measures (121). A study of children and adolescents in 185 countries found that SSB intake increased globally by an average of 23% between 1990 and 2018 and paralleled the increase in prevalence of obesity in these populations (122). Evidence indicates that UPFs and SSBs account for at least a third of total energy intake for adolescents in Argentina, Belgium, Chile, and Mexico and at least half in Australia, Canada, the United States, and the United Kingdom (61). Consumption of UPFs in early childhood may have lasting effects as taste preferences are set early childhood, and early exposure may determine lifelong preferences for sweet, salty, and artificially flavored foods (123).

The most convincing evidence for a role in obesity comes from Latin America, where UPF classification has been widely accepted and the transition to UPF-dominated diets has been rapid and was strongly correlated to equally rapid increases in national obesity prevalence (124). In 2013, the cross-national annual retail sales per capita of UPFs, after controlling for confounders (national income, urbanization, and deregulation), correlated strongly with the

national prevalence of obesity across 14 nations, and for 12 of these Latin American countries, the temporal changes from 2000 to 2009 in annual retail sales per capita of UPFs correlated strongly with the change in national mean BMI (125).

How UPFs drive obesity

The relationship between food and obesity is complex. Obesity is not determined by energy intake alone. Rather, different foods can promote obesity by inducing a variety of metabolic changes (Figure 3). In recent decades, the food industry has invested heavily in developing convenient, highly palatable foods using chemicals whose health effects are poorly understood. More than 10,000 chemical additives are estimated to be present in foods in the United States (126). Of 766 introduced there since 2000, only 10 were formally approved by the Food and Drug Administration; the other 756 were self-approved by industrial companies (127). This has become a very active field of research, but only after the realization that a metabolic health crisis had been created. Many unknowns remain regarding the long-term health effects of the numerous stabilizers, emulsifiers, preservatives, colorants, and other chemicals now present in food and the concomitant reductions in fiber, probiotics, flavonoids, and phytonutrients. It is increasingly clear that there are also many complex interactions between all of these agents and factors; more research is required to clarify their effects, particularly potential epigenetic effects on appetite, satiety, and metabolic pathways. With so many chemicals now present in foods that have numerous potential interactions, the traditional strategies for testing and regulation that examine one chemical at a time are impractical and prohibitively expensive. This has led to suggestions for a new approach to determine toxic chemical exposures utilizing many recently developed technologies. There are now several initiatives such as the "Human Exposome Project," analogous to the "Human Genome Project," which incorporates the Implementation Moonshot Project for Alternative Chemical Testing (IMPACT), which aims to revolutionize traditional toxicology (128, 129), using multiomics technologies, biomonitoring, big data analytics, microphysiological systems, and artificial intelligence to identify chemical exposures within the complex environment that impact human health.

Energy density and palatability

The highly palatable nature of many UPFs, along with their low cost and convenience, alters the way and the amount we eat. Accumulating evidence indicates that energy-dense UPFs promote adiposity by altering energy partitioning within the body. The food industry has engineered the precise formulations of fats, carbohydrates, sugars, and salt to maximize palatability such that neuroendocrine signaling to reward centers is reinforced (130, 131). Indeed, neurological signals induced by highly palatable UPFs are very similar to those activated by addictive substances (132). Furthermore, these potentiated reward signals may be perturbed in people with obesity, such that they do not perceive the food addiction (133).

UPFs tend to have lower nutrient density, higher energy density, and lower cost compared with unprocessed foods (134). In contrast, healthier foods are generally more expensive (135). This aligns with the recognized associations between lower socioeconomic status, overt poverty, lower education, and obesity prevalence (136). Another factor may be eating rate: faster eating is associated with higher total energy intake (137). As UPFs are generally softer and more energy dense than conventional foods, they promote rapid energy consumption, further compounding total energy consumption (138). In a recent randomized clinical trial, a time-restricted eating regimen was as effective as calorie restriction at reducing energy intake and inducing weight loss (139, 140). The most compelling evidence of the obesogenic effect of UPFs comes from randomized crossover trials. A month-long, inpatient, randomized, crossover feeding trial assessed *ad libitum* energy intake of adults presented with a diet of UPFs compared with an unprocessed diet matched for palatability, calories, sugars, carbohydrates, fats, sodium, and fiber (141). On the UPF diet, participants consumed around 500 kCal/day more and gained more weight than when on the unprocessed diet. On further analyses, eating rate was associated with energy intake for both diets, but the additional energy intake on the UPF diet was related to energy density and palatability (142). A similar, 1-week, randomized, crossover feeding trial in Japan tested UPF and non-UPF diets matched for total energy, macronutrient levels, and energy density (143). On the UPF diet, participants consumed more daily calories and gained more weight; further, the eating rate was faster with lower chewing frequency and a significantly lower number of chews per calorie consumed, indicating mechanisms for the increased caloric intake observed. Outside such controlled environments, an 8-week randomized crossover trial in free-living participants compared a UPF-diet with a diet composed of minimally processed foods (MPF); both diets followed national healthy dietary guidelines (144). Whilst both diets caused weight loss, the degree of weight, BMI, and fat mass loss on the MPF diet was greater than that on the UPF diet, together with significantly lower energy intake. Favorable improvements in craving control and hedonic appetite were observed on the MPF diet despite greater weight loss and lower flavor and taste ratings. In the prespecified sensitivity analysis, the results were consistent.

Modern food processing has resulted in an increasing divergence between what we now consume and what we have traditionally eaten. One emerging strand of research is the discordant activation of central neuronal pathways affecting reward, satiety, and appetite that do not match the nutritional content of the UPFs being consumed. It is relatively rare for natural, unprocessed foods to be rich in both fats and carbohydrates, whereas many UPFs are deliberately high in both to enhance palatability. High dietary intake of simple carbohydrates (sugars) alters the gut microbiome, which, in turn, alters the gut immune system, resulting in greater lipid absorption and systemic inflammation (145). The gut-brain neuronal signaling differs when consuming fats (146) or carbohydrates (147). Consuming foods rich in both may reinforce reward center activation (131). The promotion of hedonic eating, eating when not hungry, and overriding homeostatic food intake controls has been designed by food producers.

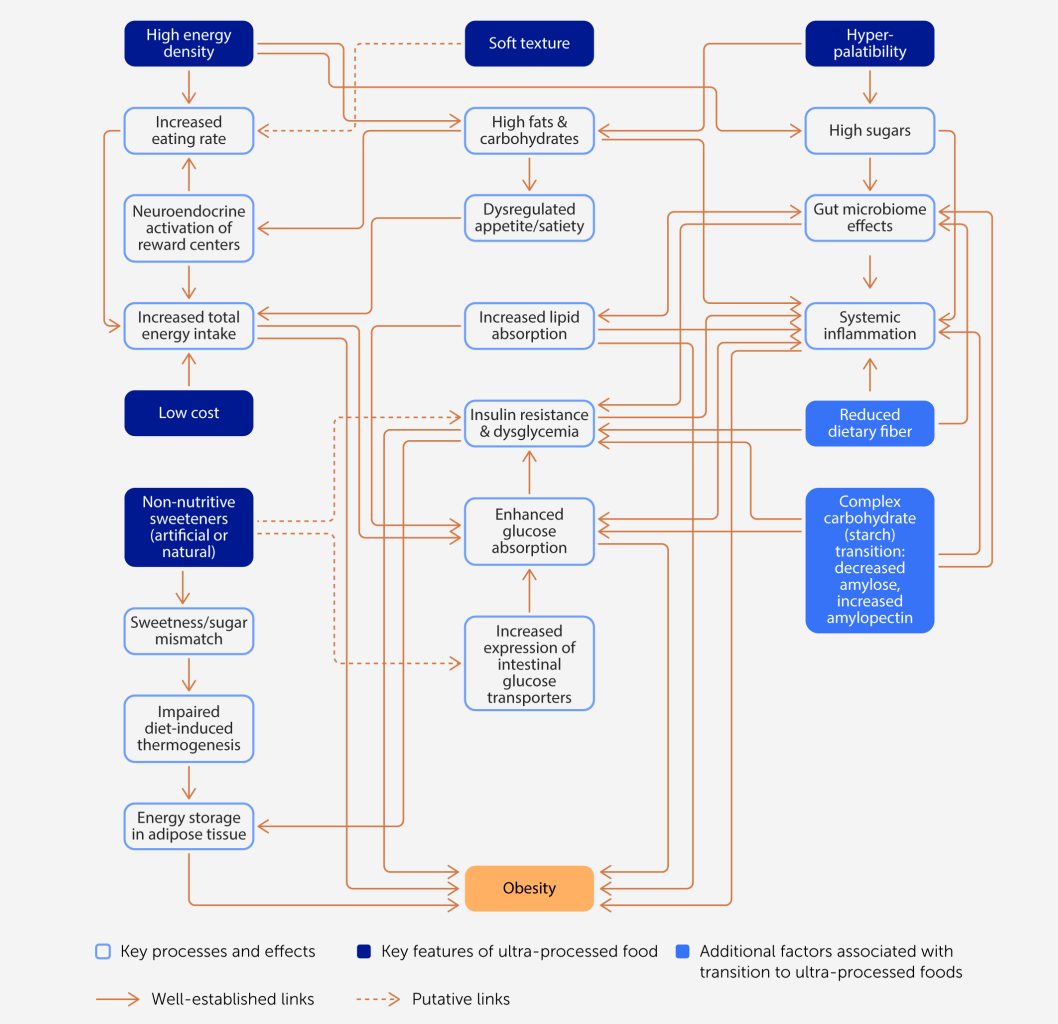


FIGURE 3
Ultra-processed foods (UPFs) may promote obesity by various mechanisms. Key characteristics of UPFs, such as high energy density, soft texture, hyper-palatability (fat, carbohydrate, and sugar ratios), non-nutritive sweeteners, and low cost in conjunction with reductions in dietary fiber and changes in complex carbohydrate intake, can interact in complex ways with multiple interconnected physiological systems and processes to drive obesity. The figure illustrates the relationships between the key mechanisms outlined in the text but is not intended to be exhaustive.

The multiple ingredients of UPFs are generally either industrially synthesized or purified from raw foods, resulting in an acellular composition lacking the structural matrix of normal raw foods. Independent of the food nutrient composition, this lack of matrix has many effects on human health similar to a lack of fiber, including the extent of chewing required (thereby impacting momentum of and volume of consumption), satiety control, digestive tract transit speed, gastrointestinal hormonal secretions, nutrient bioaccessibility/bioavailability, microbiota diversity, and metabolic utilization (148, 149). The dominance of UPFs in the diet is associated with a reduction of diversity in the diet and an altered pattern of nutrient intake with higher consumption of free sugars, sodium, and total-, saturated- and trans-fats and lower consumption of many micronutrients, including vitamins A, E, C, B9, B12, zinc, calcium, iron, magnesium, potassium, and phosphorus (150, 151). The full effects of these changes in diet diversity and the mix of macro- and micronutrients on weight gain are far from fully understood (152).

Sweetness

Generally, the sweetness of natural foods is directly linked to their sugar content. In contrast, many UPFs contain artificial (e.g., saccharin, sucralose, or aspartame) or natural non-nutritive sweeteners (e.g., steviol glycosides, monk fruit, or xylitol). These sweeteners cause a mismatch between the sweetness and the sugar consumed. Although these additives do not contain calories, they can impact metabolic responses. For example, a sweetness/sugar consumption mismatch impairs diet-induced thermogenesis, which normally reduces energy partitioning, to promote storage in adipose tissue (153). Some non-nutritive sweeteners enhance glucose absorption by increasing intestinal mucosa expression of sodium glucose cotransporter-1 and glucose transporter 2 (154). The use of non-nutritive sweeteners does not necessarily reduce the intake of sugars since activation of neural reward centers requires glucose utilization rather than sweet taste (155). In addition, sucralose consumption along with sucrose blunts the brain response to

sucrose, reducing insulin sensitivity and impairing glucose tolerance (156). Non-nutritive sweeteners also impact glucose tolerance by adversely altering the intestinal microbiome (157).

One of the most important sweeteners is high-fructose corn syrup (HFCS), introduced in the 1960s due to its low cost (in part due to subsidy structures) and plentiful supply. The sudden large increase in dietary fructose stimulated considerable interest in its potential role in the obesity epidemic. Despite the concern, the pattern of HFCS consumption has not been compatible with the global increase in obesity, either temporally or geographically (158). Although HFCS is not implicated in the global obesity epidemic, there is compelling evidence that high consumption adversely affects metabolic health (159, 160). For instance, the incidence of T2D is 20% higher in countries with high HFCS consumption compared with those with low consumption (158).

Altered complex carbohydrates

The nature of complex carbohydrates (starches) in our diet has also changed, in parallel with the increase in UPFs, with shifts in consumption of the main starches, amylose, and amylopectin. Amylose, the main starch in legumes such as beans, lentils, and chickpeas, consists of simple glucose chains that are only digested from their ends. This results in slower processing in the upper intestine and allows more amylose to pass into the large intestine, where much of it is utilized by the microbiome via bacterial fermentation, limiting the absorption of glucose into the host. In contrast, amylopectin, the main starch in wheat, rice, pasta, and potatoes, has a complex, highly branched structure, allowing it to be digested by several enzymes and more rapidly absorbed in the upper intestine, presenting the liver and pancreas with a greater glucose load and hence a greater insulin response. Amylose consumption has decreased in the transition to UPFs, whereas the consumption of amylopectin has increased. Cereal crops in which the starch branching enzymes are inhibited to increase amylose content are currently being engineered (161).

Reduced fiber

The reduction in dietary fiber due to the removal of plant structures from UPFs also impacts how the gut processes food and partitions consumed energy. Dietary fibers form a gel on the lining of the duodenum, reducing nutrient absorption by up to 25–30%, lowering the glucose load, and increasing the flux of nutrients to the microbiome in the large intestine (162). This also affects the response of gastrointestinal hormones to food entering the gut, with reduced glucose-dependent insulinotropic polypeptide (GIP) and ghrelin and increased cholecystokinin (CCK) and peptide YY (PYY) impacting insulin secretion and central regulation of satiety and appetite (163). This gel lining the duodenum is lacking with low fiber consumption, facilitating greater small intestine absorption and reducing nutrient supply to the large intestine. This then enhances insulin secretion and lipid deposition but also starves the gut microbiome of nutrients, switching it to digesting the colonic mucus barrier, resulting in "leaky gut," inflammation, and insulin resistance (164).

Microbiome and obesity

Changes in the gut microbiome are another potential driver of the obesity pandemic, receiving significant attention recently. The gut microbiome comprises roughly the same number of cells as there are human cells in the whole body, but due to bacterial diversity, its total genome is estimated to have 150-fold more genes than the human genome—and these are capable of producing considerably more enzymes for digesting our food (165). The gut microbiome consists of 95% anaerobic bacteria that can consume between 7 and 22% of ingested energy via fermentation (166, 167).

Individuals vary considerably in their metabolic response to the ingestion of identical meals, with variants in the human genome contributing little to these differences (168). In contrast, our microbiome strongly determines our metabolic response to food, and microbiome composition is highly associated with the quality of dietary intake, with microbiome diversity increased by healthy plant-based foods (169). Microbiota composition also mediates the effect of some ingested nutrients on visceral fat mass, a major risk factor for cardiometabolic disease (170). In addition, a healthy microbiome facilitates the formation of secondary bile acids, which have important metabolic actions (171). Microbiome bacterial diversity is reduced in individuals with obesity, although whether this dysbiosis contributes to, or results from, obesity remains unclear. Nevertheless, dysbiosis can have many effects on the host metabolism (166, 167).

A further related concern comes from the prophylactic use of low-dose antibiotics in agriculture, not just to prevent infections but historically as growth promoters. In 2015, it was estimated that approximately 80% of antibiotics sold in the United States were used in livestock agriculture (172). In some parts of the world, antibiotics have been added to food or water for livestock for over 70 years, with residual antibiotics being present in the food chain. This led to the hypothesis that ingestion of antibiotic-contaminated foods could cause gut microbiome dysbiosis, thereby contributing to obesity (173). Antibiotic use may cause livestock microbiome dysbiosis; possible zoonotic transfer of consequent gut microbes to humans could also contribute to obesity (174). However, the use of antibiotics in livestock is not uniform and has varied considerably between countries and over time (175), and patterns of use do not seem to relate to the global rise in human obesity. There is, however, some evidence that antibiotic use in human infants younger than 6 months, or exposure to more than three courses of antibiotics in childhood, and the use of broad-spectrum antibiotics may increase the risk of subsequent obesity (176).

Evidence from mouse models linking the microbiome causatively to obesity engendered interest in microbiota transfer as a potential treatment. However, studies in humans have failed to replicate the effects seen in mice (177).

Genetic variants and obesity

The recent rise in obesity levels across most societies cannot be attributed to changes in the human genetic code. Genetic differences between individuals (and ethnic groups) may favor weight gain and poorer outcomes in terms of metabolic disease (e.g., cardiovascular disease and T2D). The idea that famines throughout evolution favored genetic variants promoting adiposity, a "thrifty genotype" (178), has been challenged by an alternative view that, once we no longer needed to escape predators or forage for food, there was no evolutionary pressure for variants favoring leanness, a "drifty genotype" (179). Studies of families and twins indicate that heritability explains 40–70% of the individual variation in BMI (180) as well as more precise measures of adiposity, including abdominal fat (181).

There are rare, highly penetrant genetic variants associated with excessive weight gain that control feeding circuits. Initially implicated genes were identified from "genetic experiments": the variants are usually recessive in humans, and their effects are therefore the result of consanguineous marriage. For example, mutations in genes encoding for the satiety hormone leptin and its receptor result in dramatic obesity associated with impaired satiety and feeding behaviors (182). Leptin interacts with satiety circuits in feeding centers in the ventromedial and lateral hypothalamus (183), whose importance is demonstrated by the severely obese phenotypes of human subjects when target genes are disrupted (184). These findings point strongly to feeding behavior—specifically, constant craving for food—as the driver for weight gain, rather than any shift towards enhanced deposition of fat or a "slowing" of metabolism.

Subsequently, genome-wide BMI association studies over the past 16 years have described more than 1,100 common variants associated with obesity, which together account for only around 6% of BMI variation (183, 185–188). For the vast majority of these variants, it is not known which loci may have a causal effect on BMI or what mechanism may have been involved. The fat mass and obesity-associated (*FTO*) gene was identified in the first of these screens (185), but later studies showed its effect was more likely caused by the neighboring iroquois homeobox 3 (*IRX3*) gene (189, 190). Other implicated loci also encode genes controlling circuits involved in feeding and satiety (191–193).

Population and twin studies have indicated the presence of gene–environment interactions, and epigenetic studies are now helping to clarify the mechanisms involved. A study of 1,850 twins aged 4 years found that BMI heritability was 86% for those living in lower socioeconomic environments but only 39% for those in higher socioeconomic environments (194). The heritability of adiposity is markedly attenuated by a healthy diet (195–197) or by increased physical activity (198–200). Studies also demonstrate that excess energy exposure *in utero* and infancy can lead to early weight gain and obesity via epigenetic alterations to gene expression (201–203). These findings indicate that genetic variance and epigenetic mechanisms can affect the susceptibility of an individual to gain weight in response to an unhealthy environment or lifestyle.

The role of epigenetics in obesity is one of the most rapidly emerging research fields with many studies of DNA modifications (mainly methylation thus far), histone modifications, non-coding RNAs, and, more recently, chromatin structure, as described in many recent reviews (204–208). As it is now clear that many epigenetic marks are modifiable, there is much hope that such studies will eventually yield epigenetic markers of exposures, such as foods and the microbiome, and methylation risk scores that will predict an individual's risk of developing obesity. They may even give insights into intergenerational epigenetic inheritance of obesity. The impact of early-life exposures on subsequent risk of obesity and other NCDs, as posited in the Developmental Origins of Health and Disease (DOHaD) model, is now recognized to mainly operate via epigenetics (207–209).

As many genetic variants each account for a very small amount of susceptibility to gain weight, we are a long way from being able to apply these for any individualized, precision medicine approaches to predicting risk or prognosis.

Psychological and behavioral drivers

It is vital to understand the processes of hunger, wanting, craving, satiation, and post-meal satiety, which stimulate or inhibit eating behavior. People living with obesity, particularly those who binge eat or have a higher BMI status, exhibit weakened within-meal satiation (210). Rather than the rate of food intake naturally decelerating during a meal, as ingestion generates inhibitory signals, eating continues at the same pace. Similarly, post-meal satiety is weaker and hunger rebounds sooner after consumption. These differences, which reflect the underlying biology of obesity, make it far harder for people with obesity to limit their food intake. With uncontrolled hunger and disinhibition of eating behavior, reward-driven eating dominates, placing greater demands on the cognitive and behavioral resources of those with obesity (211). Indeed, the inability to control their hunger is the key barrier to weight loss for adolescents living with obesity (212).

Weight loss through dieting results in persistent changes in the hormones regulating appetite and aggravates underlying hunger (213). Consequently, people living with obesity face a double challenge. Consistent food restriction or dieting increases hunger and food cue responsiveness, undermining inhibitory control and other executive functions. This, in turn, undermines the ability to cope and maintain dietary preferences, particularly in an environment with constant exposure to food cues through pervasive food advertising. This, in turn, negatively affects mood, reinforcing food-related coping strategies. Weakened appetite control is further undermined by physiological and neurochemical responses to reductions in body mass—the so-called "adipostat" (214).

Compounding these neurohumoral responses driving food ingestion are psychological factors that impact mental health and secondarily drive food intake. Whether in clinical samples (e.g., patients waiting to undergo bariatric surgery) or in population studies, obesity is associated with levels of psychological disorders

that exceed population norms, including depression, anxiety, substance abuse, and eating disorders. Meta-analyses indicate that greater consumption of UPFs is associated with depression both cross-sectionally and prospectively (215). The relationship between obesity and depression appears bidirectional, with depression increasing the likelihood of developing obesity and vice versa (216). This relationship is apparent even in children as young as 7 years (217). A high proportion of adolescents living with obesity report poor mental health and low self-esteem (212) Struggling with weight at an earlier age is not only associated with higher adult weight and poorer weight management outcomes but also with increased feelings of helplessness (218).

Personal circumstances and life events have well-established impacts on both mental health and weight gain. Adverse life events or past trauma are associated with obesity (219). Stress is associated with visceral obesity (220) and mood impairment, undermining dietary restraint and thus leading to increased vulnerability to temptations (the urge to break the diet) and lapses (when the diet is broken). In turn, these reinforce feelings of failure and guilt, undermining general self-esteem and the success of weight management (221).

Social ecosystems and living environments

The built environment shapes the living space individuals must negotiate, their food access, and their liberty to be physically mobile. Environments affect the prevalence of obesity by influencing both energy intake, via access to healthy foods (222, 223), and energy expenditure, via access to an environment conducive to physical activity (224–227). Specifically, sociodemographic risk factors for obesity include safety, food security, food access, access to safe public transportation, car commute times, and safe walking pathways (228–230). The past century has witnessed significant shifts in the built environment through rapid urbanization, mass transport, increased mechanization, and labor-saving technologies, which have affected all domains of life (231). Coupled with the growth of service industries, these factors have profoundly changed the food environment and reduced physical activity (26).

Food environment: a key driver of obesity prevalence

Studies of dietary habits of communities stratified by socioeconomic status have shown that poorer neighborhoods have greater access to corner and convenience stores (232) and fast-food restaurants, with residents consuming more fried foods, oil, and less-healthy snacks, and not meeting recommended daily intakes of fruit and vegetables (233). Such areas with high density of fast-food and "junk food" relative to healthy food access are often called "food swamps" (234). Food swamps strongly relate to high obesity prevalence (234) and obesity co-morbidities (235). For example, among 3038 United States counties, those with the highest food swamp scores had a 77% (95% CI: 1.43–2.19) increased age-adjusted odds of high obesity-related cancer mortality versus areas with low scores (235). Even after adjusting for age, race, and poverty rates, counties with a high food swamp score had almost 30% increased odds of high obesity-related cancer mortality (1.29; 95% CI: 1.03–1.63). "Food deserts," where residents have limited access to nutritious foods, also exist within cities, rural areas, and remote areas (222) and are related to increased risk of obesity (234) and associated health outcomes (235).

The existence of food swamps and deserts could also be considered as a commercial strategy whereby certain lower socioeconomic status areas are profiled and provisioned with low-quality, energy-dense and nutrition-poor foods (with high rates of UPFs) for consumers with lower food literacy and little choice (236, 237).

Physical activity

There is a strong association between neighborhood characteristics and obesity. For example, a recent systematic review showed that green space, parks, and recreation facilities are beneficial for children's weight (238). The availability of schools, parks, and playgrounds plays a key role in promoting physical activity in rural communities in the United States (239). Likewise, studies of adults in Spain and throughout Latin America found that higher exposure to green space was associated with reduced rates of obesity (240–242).

A review of 13 studies concluded that walkability generally promoted more active lifestyles, although not all of the studies supported this conclusion (243). However, changes in the built environment have reduced the walkability of neighborhoods: for example, settings may not be considered safe or may lack footpaths or amenities within walking distance. An analysis of data from 93,280 individuals with obesity from 10 countries found that higher intersection density was associated with higher levels of BMI and obesity, although, unlike other studies, it did not establish a link between urban sprawl and higher BMI or obesity (242).

Education

There are complex, often bidirectional and culturally determined relationships between education and obesity. In high-income countries, there is a strong link between childhood obesity and a lower level of maternal education (244). However, in China and other LMICs, the opposite is apparent, with childhood obesity relating to a higher level of maternal education (245). This may be confounded by other cultural factors, such as excess weight being regarded as a sign of financial success.

Children with obesity show different educational outcomes compared to their peers, indicating early divergence in trajectories. Prospective Swedish data show that childhood obesity predicts fewer years of education achieved by early adulthood (246). This may be explained by lower parental education influencing expectations and trajectories but also by the known discrimination against children who live with obesity. For example, teacher-dependent weight bias is associated with the award of lower academic marks in children who have obesity, particularly girls (247, 248). There is further evidence of subjective downgrading of assessments of children who have obesity, regardless of their objective performance (249). The stigma of obesity plus lower

educational achievement imposes a double disadvantage on girls. Employment discrimination, a key determinant of financial success, is evident against adult women living with obesity (250). Income gradients are also evident in women who live with excess weight or obesity and are, in turn, linked to less frequent access to health screening and interventions (251).

The importance of education is discussed later with respect to its foundational importance to the success of public health measures to improve diet and lifestyle.

Obesity management: options and limits

Appropriate management of excess weight and obesity is patient-centered, such that the clinician considers the patient's needs and wishes (252–254). A recent series of Cochrane Collaboration systematic reviews of interventions for childhood obesity concluded that dietary interventions alone result in little to no difference. For children aged 5–11 years, school-based physical activity interventions, alone or combined with dietary interventions, may show modest beneficial effects over the short and medium term but not at long-term follow-up. In adolescents aged 12–18 years, there was low certainty in evidence that physical activity interventions may have a small beneficial effect in the medium and long term (255–257). Recent medical and surgical interventions have transformed weight loss for adults, and there are no relevant and contemporary Cochrane reviews for adult obesity.

Dietary management

Key to obesity management is a comprehensive behavioral program that includes both diet and physical activity that helps the patient either lose or maintain a healthy weight (see Presentation 1: Supplementary Table 1). Dietary modifications are estimated to account for 80% of weight loss following behavioral programs and physical activity for the remaining 20% (258).

There is strong evidence for many different types of diets that vary in micronutrient content, nutrient or energy density, or other weight loss strategies (e.g., meal timing, intermittent fasting, or use of meal replacements) (see Presentation 1: Supplementary Table 2). Although many of these diets were introduced more than 10 years ago, they remain valid and in agreement with the current treatment paradigm. There has been much recent emphasis on dietary patterns, defined as quantities, proportions, varieties, or the combination of foods, drinks, or dietary nutrients and frequent habitual consumption of these foodstuffs (see Presentation 1: Supplementary Table 3 for examples) (259). Attention has also been given to meal patterns, relating to when individuals eat rather than what they eat, for example, intermittent fasting, time-restricted eating, or other forms of timing or regularity of eating plans. There have been some indications that intermittent fasting can result in cardiovascular benefits (including blood pressure and improved dyslipidemia) and weight loss (260). A comprehensive review found improved overall health outcomes for intermittent fasting (261). A review of intermittent fasting concluded that it may be helpful for the treatment of obesity, producing weight losses of 0.8–13.0% (262). Benefits of other types of fasting regimens have also been reported (263). However, studies so far have been small and short term. Whether intermittent fasting can be sustained in the long term given an individual's work life, family life, and level of motivation is an open question.

Long-term adherence to a diet is key for success and can be enhanced if the hunger that accompanies weight loss is controlled, the diet is individualized, and food intake is self-monitored (264). Weight loss is accompanied by adaptations in the gut, including altered release of appetite-regulating hormones such as ghrelin, CCK, and PYY, resulting in an increased drive to eat that may offset the loss of weight. The induction of ketosis appears to blunt these changes (265, 266). This has increased interest in very low-energy diets (VLEDs), of the order of 800 calories daily, to promote rapid weight loss with the benefit of ketosis (267). Clinical trials have indicated that VLEDs can enable sustainable weight reduction with greater adherence than gradual weight loss (267, 268). Many patients find that faster weight loss enhances motivation and improves compliance. Weight reductions of 10–15% and remission from T2D have been reported for VLEDs, offering an intervention with a response intermediate between the more extreme intervention of bariatric surgery and conventional diets (269). Although the changes in gastrointestinal hormones following a VLED are not as great as those induced by bariatric surgery, the changes in ratings of postprandial hunger and fullness were comparable (270). A potential problem is that VLEDs do not provide sufficient nutrients and nutrient supplements are required. Ketones appear on day 3 and can suppress hunger better than most medications. Hunger hormone levels change very soon after weight loss starts (271), and ketones blunt some of these changes (272, 273). In addition, ketones enter the same pathway that glucose uses to suppress hunger. As patients approach their target weight, or earlier in patients who cannot avoid carbohydrates, hunger-suppressing medications may become necessary over the long term because the hormone changes leading to increased hunger remain. Hunger can be managed by a range of medications, individualized for the patient, including semaglutide, tirzepatide, bupropion/naltrexone, and phentermine. As multiple hormones suppress hunger after a meal, it may be necessary to use low doses of multiple medicines.

Medical mitigation

Given the difficulties in achieving and maintaining weight loss via diet and physical activity, the global rise in obesity incidence, and the overwhelming medication market potential, the search for effective and safe medical interventions has exploded. Owing to past failures of evidence-based medical treatments, an enormous industry selling alternative weight-loss products—worth US$33 billion/year in the United States alone—has grown, even though such products generally result in only a 3% loss in weight (274). However, there have been significant recent breakthroughs in

medical treatments. Here we outline these and their implications, though potential future agents fall outside the scope of this review.

Effectiveness and safety of incretinomimetics

Currently, incretinomimetics appear to be the most efficacious anti-obesity agents: these include the GLP-1RA agonists, semaglutide and liraglutide, and the combined GLP-1RA and GIP agonist, tirzepatide. A multitude of other agents are in development for T2D, including the GLP-1/GIP/glucagon ("triple-G") agonist retatrutide, and non-incretinomimetic agents. Recent results indicate a 24% loss of weight after 48 weeks of treatment with retatrutide (275). It has also recently been suggested that GLP-1RAs may provide a novel means of directing other drugs (e.g., glutamate receptor agonists) to relevant neurons involved in satiety, achieving even greater effects on body weights than the incretin itself (276).

These medications have a multitude of effects that manifest as altered eating and drinking behaviors that reduce energy intake, improve satiety with earlier cessation of food intake during a meal, and reduce food cravings (277, 278). Efficacy in weight loss and weight loss durability (while on trial) have been demonstrated in large, randomized clinical trials (summarized in Presentation 1: Supplementary Table 4).

However, there are important safety and side effect considerations. Indeed, 25 anti-obesity medications have been withdrawn since 1975 (279). Safety remains a fundamental concern, both short and long term, since obesity will not be "cured" by a 3-month or 3-year treatment period. The incretinomimetic clinical trials for obesity have been relatively short-term (Presentation 1: Supplementary Table 4). Currently, medication-specific adverse effects from incretinomimetics are predominantly gastroenterological and often dose-related, particularly in the initial dose-escalation phase, including nausea, vomiting, diarrhea, and constipation. Gastro-esophageal reflux disease (GERD) symptoms can worsen. Reports of pancreatitis indicate cautious use of these agents in susceptible patients, including those with underlying pancreatic disease or excess ethanol consumption and possibly prior colonic or neuroendocrine malignancies. The rapid weight loss that can occur during therapy requires ongoing clinical management, including careful dosage adjustment for existing medications and, in the elderly, a concurrent exercise program to avoid the risk of sarcopenia (280). Given the relative novelty of GLP-1RAs, medium-term evidence on safety in people with normoglycemic obesity is only just being reported. For example, the incidence of death from cardiovascular causes, non-fatal myocardial infarction, or stroke was reduced by 20% at a mean of almost 40 months of follow-up with semaglutide (47, 281).

With the current agents, once stopped, the weight lost is regained within a year, implying a requirement for lifelong intervention. The real-world long-term tolerability of current agents is low: only 27% of patients remained on the prescribed drug after 1 year in one large study (282). As obesity increasingly affects younger people, and hence pharmacotherapy is extended to adolescents and potentially children, incretinomimetics and other effective agents require long-term safety surveillance, including their effects during growth and pubertal development, before and after pregnancy, and on cardiovascular, gastroenterological, mental, and cognitive health. A final concern is the impact of the "medicalization" of such a large proportion of the world's population on the constrained resources of health systems.

Effective pharmacotherapy may undermine the importance of ongoing lifestyle change, with attendant health impacts. Alternatively, it may create space for lifestyle change for people who have not been able to make sustained lifestyle and food behavioral changes in a hostile food environment.

Costs and access parity

The need for continued treatment, poor tolerability, and high cost indicate that these newer medications are currently not cost-effective, especially when compared to bariatric surgery (283, 284). At a population level, 93 million American adults currently meet the criteria for prescription of GLP-1RA: at current prices, the annual cost would amount to $US600 billion, which is equivalent to all other prescription drugs combined (285). The population-level costs of these interventions are set to balloon with obesity projected to affect more than 50% of many populations (1, 286) and the age of onset decreasing into early childhood.

The United States Congressional Budget Office estimates that authorizing the use of anti-obesity medications to all Medicare beneficiaries with obesity, and some classified as overweight, would increase *net* federal spending by about US$35 billion between 2026 and 2034. It projects that total direct federal costs of covering these agents would increase from US$1.6 billion in 2026 to US$7.1 billion in 2034, far exceeding total savings from beneficiaries' improved health (287).

In Denmark, reimbursement of proprietary semaglutide alone for the 900,000 citizens with BMI ≥30 would reportedly cost the state the equivalent of US$3.5–4 billion/year based on 2023 prices (288).

The idea that wider use and competition will reduce costs is not encouraging, given trends for prices for other medications such as insulin. Initial indications suggest that pharmaceutical companies have already planned strategies for price protection with some GLP-1RAs and their delivery systems covered by 20 patents each, extending protection to 2040 or beyond (289).

Examination of a US database revealed that only 2.4% of people with obesity in 2010–2019 accessed pharmacotherapy (290). Obvious factors may include socio-demographics; however, this was prior to the reporting of the efficacy of newer GLP-1RAs. Frameworks for the fair allocation of such drugs that are limited in supply are currently being debated (291). Evidence on variations in access to these therapies within and between nations is needed, particularly in nations where socio-demographic factors affect healthcare access. Medical treatments could be made more widely available and affordable by using GLP-1RAs for initial weight loss and then switching to older, less effective drugs and/or lifestyle modifications for maintenance (261 Such options need to be evaluated.

Re-engineering the human body: bariatric surgery

Despite recent advances in pharmacotherapy, surgery remains the most effective treatment for morbid obesity, given the strength of evidence for durability in long-term weight loss and resolution of the consequent disease sequelae. Surgical techniques have evolved for over six decades following the observation that patients undergoing subtotal gastrectomy for cancer subsequently experienced sustained weight loss (292). The original aims of bariatric surgery were to reduce gastric capacity or to create a diversion bypassing sections of the gastric tract, thereby restricting food intake and/or absorption. However, the actual mechanisms of weight loss are more complex and may also involve changes in neural signals affecting central appetite control, the release of gut hormones, changes in gut microbiota, and bile acids (293).

Bariatric surgery has become more prevalent with increasing obesity rates and is now almost a routine surgical procedure in many countries. In 2018, around 400,000 patients worldwide underwent bariatric surgery (294), with an estimated 250,000 procedures in the United States alone (295). Recent guidelines for bariatric surgery are for individuals with a BMI ≥35 kg/m^2 and those with a BMI of 30.0–34.9 kg/m^2 when obesity-related comorbidities are present (296). The lower limit was recommended for patients with T2D for whom adequate glycemic control could not be achieved by lifestyle or optimal medications (297, 298).

The quality of surgical expertise and post-operative care has improved following the implementation of standardized protocols, with the incidence of complications and mortality reduced to 1.4% and 0.04%, respectively, for minimally invasive procedures in the United States (299, 300). However, bariatric surgery remains underutilized relative to need, with around 0.5% of patients who meet the indications undergoing surgery in the United States (299). This is despite the improvements in safety and despite surgery remaining the most cost-effective intervention over time—its initial high cost being far outweighed by the accrued long-term savings in health costs due to greater weight loss and T2D remission (301–304). The recent development of effective incretinomimetics and other drugs for obesity may reduce requests for and uptake of bariatric surgery in the future.

Procedures and effectiveness

Around 98% of bariatric surgical procedures are now laparoscopic, with many undertaken as day cases (299, 305). Various procedures have evolved, differing in their complexity, particularly in the number of new intestinal connections, or anastomoses, required (Figure 4). The most straightforward is vertical sleeve gastrectomy (VSG), which involves no anastomosis but just a vertical dissection to drastically reduce the size of the stomach. VSG has become the most popular bariatric procedure in the last 10 years owing to its excellent efficacy and safety profile (306, 307). In contrast, Roux-en-Y gastric bypass (RYGB) involves the creation of a small gastric pouch and two anastomoses so that ingested food bypasses most of the stomach and the first portion of the digestive tract. Simpler procedures have gained popularity, including the "mini-gastric bypass" or one-anastomosis gastric bypass (OAGB) (308) and the single anastomosis duodeno-ileal bypass (SADI-S). These achieve results comparable to or better than RYGB but with shorter operating times and lower complication rates (309, 310). Robotic bariatric surgery has recently become popular with results comparable to laparoscopic surgery despite longer operative time and higher costs (311, 312).

Compared with optimal medical therapy plus lifestyle management, bariatric surgery resulted in almost double the weight loss after 12 years, and a significantly higher T2D remission rate, according to combined data from four randomized trials (298). Remission from T2D progressively declined following surgery from 51% at 1 year to 13% at 12 years; this might be explained by progressive lapses in adherence to post-operative lifestyle regimens or to continued β-cell functional decline despite the sustained weight loss (313). Given the slow development of T2D with progressive β-cell failure, earlier surgical intervention may achieve better long-term remission. Trials comparing outcomes following bariatric surgery versus the new GLP-1RAs are currently underway (314).

Bariatric surgery also results in sustained improvements in most adverse sequelae associated with morbid obesity and extends life expectancy (315, 316). Cardiovascular health is significantly improved along with long-term improvements in nonalcoholic steatohepatitis (NASH) and liver disease (317–320). The risks of several obesity-related cancers are also significantly reduced (321–323). Bariatric surgery can help patients meet BMI eligibility criteria for access to renal and heart transplantation (324, 325) or even obviate the need for heart transplantation (326, 327). Bariatric surgery also results in improvements in osteoarthritis, reducing the need for pain management and orthopedic surgery (328, 329). Bariatric surgery can reduce depressive symptoms, improve memory, attention, and executive function, and induce long-term changes in brain structure (330–332). Nevertheless, 52.5% of adolescents in one study still showed mild cognitive impairment 10 years after bariatric surgery (333). Longitudinal studies will be required to establish whether cognitive deficits are more immutable when obesity occurs at an early age.

Risks and limits of surgery

Bariatric surgery remains a major re-engineering of the human body, and there are potential adverse events. After 12 years, patients who underwent surgery had higher rates of anemia and fractures (possibly due to greater weight loss or potential nutritional deficiencies), and more adverse gastrointestinal events, than those treated with medical plus lifestyle management (298). The most common procedure, VSG, is associated with a high rate of GERD (334), and, most concerning, 8% of patients develop the premalignant condition Barrett's esophagus (335). The profound weight loss and anatomical changes also have significant effects on the uptake and pharmacokinetics of orally administered drugs (336, 337). This necessitates careful consideration of alternatives or adjustment of dosages to ensure efficacy and avoid toxicities.

Bariatric surgery has long-term consequences and requires life-long multidisciplinary follow-up, monitoring, and aftercare to

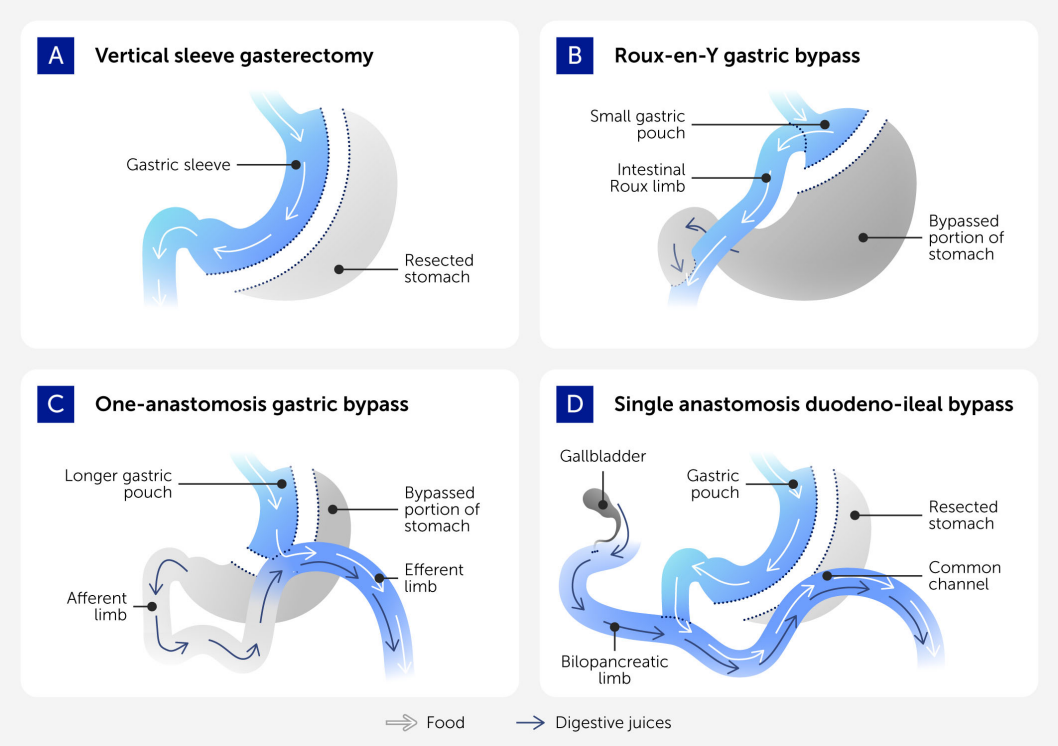


FIGURE 4
Bariatric surgery procedures include **(A)** vertical sleeve gastrectomy, which involves no anastomosis but just a vertical dissection to reduce the size of the stomach, **(B)** Roux-en-Y gastric bypass (RYGB), which involves the creation of a small gastric pouch and two anastomoses so that ingested food bypasses most of the stomach and the first portion of the digestive tract, **(C)** "mini-gastric bypass" or one-anastomosis gastric bypass (OAGB), and **(D)** single anastomosis duodeno-ileal bypass (SADI-S).

achieve optimal outcomes and minimize the risk of complications. Even more essential is careful patient selection, preoperative evaluation, and preoperative work-up (338). This should include education and counseling to manage expectations and ensure adherence to strict postoperative nutrition and eating behaviors. Weight loss prior to surgery may reduce the risk of surgical complications (338, 339), and initial findings suggest that GLP-1RAs may be appropriate (340).

The challenge of weight loss maintenance

Many weight loss strategies do not appear to have long-term durability (or "fail") due to a number of adaptive responses that have evolved over millennia to defend the body's energy stores. These include a rise in the level of ghrelin (341) and a fall in the many hormones that suppress hunger, including leptin, CCK, GLP-1, amylin, and pancreatic polypeptide, promoting food seeking and hunger. These hormonal changes are upregulated with even minor weight loss (even as little as 5 kg) (272) and persist long term (342) in the context of reduced energy expenditure (343). The resilience and effectiveness of these adaptive responses to weight reduction require additional interventions to prevent weight regain and remain a strong argument for the primacy of the prevention of obesity.

The challenge of holistic care in medical mitigation

Well-developed strategies for the management of other chronic diseases should be adopted for people with obesity. For example, there is much to learn from care models for ischemic heart disease, T2D, and even cancer risk reduction in highly susceptible groups. Since there are many similar comorbidities and complications of obesity, prevention and treatment strategies applied in each of these conditions could be replicated for the care of people living with obesity. These approaches include optimizing blood pressure, lipid, and glucose levels and supportive management of sleep apnea or hypoventilation syndrome and GERD. Specific physical regimens are recommended for people impaired by degenerative joint disease.

Cancer risk mitigation is a specific health need for people living with obesity, and yet this group experiences barriers to screening for bowel, breast, and cervical cancer (344). Women with obesity less frequently pursue breast and cervical cancer screening (345) and have larger breast cancers when detected by screening (346). Women with oligoamenorrhea require interventions that reduce endometrial cancer risk.

In conclusion, medical mitigation of obesity and its consequences requires intense lifestyle support, pharmacotherapy, and consideration of bariatric procedures. The co-morbidities of

obesity require medical intervention, perhaps for life. This paradigm has an immense impact on personal and national health resources, particularly in resource-poor settings. Given the potential long-term consequences, the inflated costs of interventions (347), and limitations on medical resources, the future must be in obesity prevention (348).

The obesity and climate co-crises

Rapid global economic growth throughout the 20th century is at risk of being undone in the 21st century due to human-induced climate change, environmental damage, and biodiversity loss (349). Similarly, the dramatic global health gains seen in the second half of the 20th century are at risk of reversing due to the syndemic of obesity, undernutrition, and climate change (36). The obesity and climate crises are inter-linked: climate change aggravates obesity, and obesity aggravates factors contributing to climate change—with both crises resulting from forms of overconsumption of food and goods (Figure 5). In this section, we review these inter-relationships as a basis for reflection on future action to tackle both crises.

Climate change aggravates obesity risks

Increasing temperature may make a very small contribution to obesity through reduced adaptive thermogenesis. Adaptive thermogenesis is a core function to maintain body temperature and can amount to up to 10% of total energy expenditure; as environmental temperatures rise, less energy is expended in adaptive thermogenesis, and more consumed calories are partitioned to adipose storage (350, 351). Individuals living with obesity are less able to tolerate increased temperatures owing to a diminished ability to dissipate heat (352), resulting in a greater risk of heatstroke and heat-related poor health (353). In the 2003 heatwave in Europe, obesity doubled the risk of death in the elderly (352). The recent Lancet Countdown on Health and Climate estimated that, on average globally, the number of heatwave days that people over the age of 65 years were exposed to in 2024 had increased by 304% compared to the average exposure over the period 1986–2005 (43).

Obesity accelerates climate change via food systems

Obesity prevalence rates in different world regions correlate with GHG emissions (36). Obesity contributes to increased GHG emissions from transport systems (through the movement of increased weight) and, most importantly, via food systems (354). Maintaining obesity requires sustained energy over-consumption, which increases energy demands and hence the associated emissions. Compared with a normal BMI, the over-consumption required to sustain obesity generates 20% higher GHG emissions, mainly from the additional food production (354). An analysis of the effects of changes in the weight of individuals between 1975 and 2014 on food requirements across 186 countries estimated that increased weight (adjusted for changes in age distribution) added a further 13% to the food energy requirements over this period, equivalent to the needs of 286 million adults (355).

At the global level, the increased consumption of UPFs that underlie the obesity crisis, the processed meats in those UPFs, and the large-scale monoculture of crops required for producing UPFs accelerate the contribution of food production to climate change and environmental damage, including via land clearance, degradation, and biodiversity loss. While the emphasis has been on transforming energy systems to phase out the burning of fossil fuels, the evidence clearly shows that our current food systems are also a major contributor to climate change. Food production accounts for 25–33% of global GHG emissions, depending on how widely you draw the system boundary, for example, whether decomposition emissions and what forms of land use change are included (356, 357). It has been estimated that current food systems will add nearly 1°C to global warming by the end of this century (358). Even if all fossil fuel emissions were halted immediately, the current food system on its own could be enough to breach 1.5°C and potentially 2°C climate targets (359).

Agriculture occupies around 40% of ice-free land across the planet, 70–80% of which is used for animal protein production (360, 361), and is responsible for 70% of freshwater use (362). Food production is the largest cause of land clearance and hence loss of ecosystems and biodiversity (363). Clearance of forests, savannas, and grasslands and draining of wetlands releases carbon dioxide (CO_2) and also removes important sites of carbon sequestration. This has created a vicious cycle with changes in land use and climate change then threatening mass species extinctions and the collapse of the natural world; over 30 years, the global population of flying insects has decreased by 70%, and over 15 years, farmland bird populations have reduced by 30% (364). This compromises food production, as flying insects are responsible for the fertilization of many crops.

Climate change affects food systems in various other ways. Increasing atmospheric CO_2 reduces the yield and nutrient content of most crops, such as maize, rice, and soy, although wheat yields increase (365, 366). However, estimations of the impact of climate change must also account for the effects of increases in extreme weather events and losses to pests. The chance of multi-breadbasket failures due to extreme weather events increases rapidly at 1.5 and 2°C (367). Global crop losses to insect pests due to climate change increase by 10–25% per degree of warming (368). Likely, the impacts of climate change on food systems have been systemically underestimated, similar to the impacts on sea level rise, ice-sheet loss, and other large-scale transitions (369).

The food systems contributing to obesity also have local socioeconomic impacts. The activities of transnational food corporations (TNCs) in poorer nations result in loss of intergenerational subsistence farms, often subsumed into mega-plantations utilizing cheap local labor—exacerbating local poverty and land degradation, particularly where governments do not have robust controls or monitoring (370, 371).

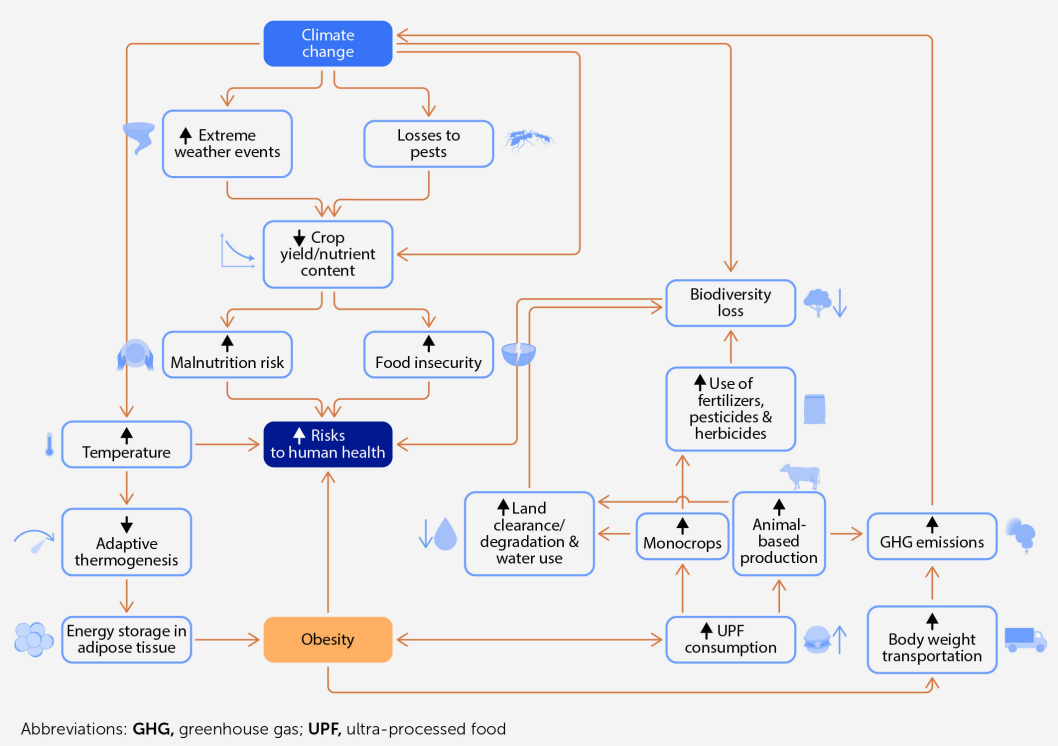


FIGURE 5
Inter-relationships between the obesity and climate co-crises.

Animal-based foods confer the most environmental impact

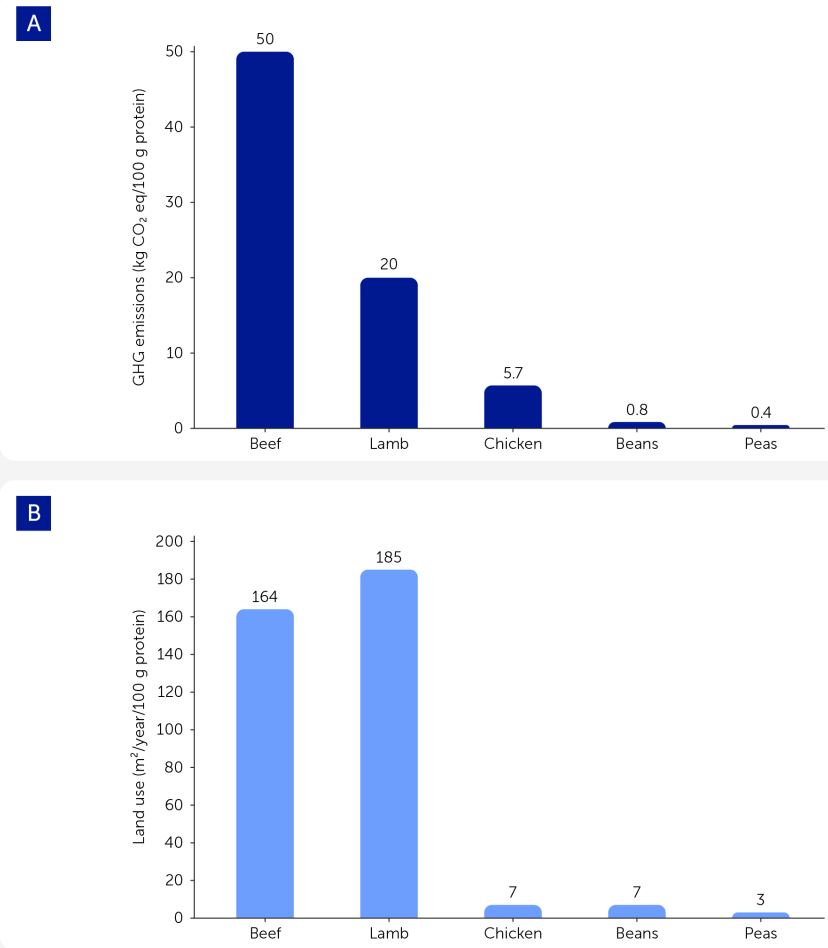
Our foods and their production methods vary considerably in terms of their impact both on our health and on the climate. The increasing global consumption of UPFs that adversely affect human health has also accelerated the environmental damage attributed to food production. UPFs are generally manufactured using ingredients extracted from a small number of high-yield mono-crops, such as soy, maize, wheat, and oil-seed crops, and—more importantly—animal-based ingredients that are obtained from animals fed on the same crops, all of which use large amounts of land, water, fertilizers, and herbicides and accelerate climate change (372–374).

Animal-based foods account for a large proportion of the environmental impact of food production (364). Grazing livestock alone contributes 9.3% of total global GHG emissions (375). If current dietary trends continue, GHG emissions from food production would increase by 80% by 2050 (376). In particular, the production of ruminant meat, primarily beef and dairy, has increased dramatically. This has a particularly high environmental impact, primarily due to the greater use of land, freshwater, and fertilizers in beef production: beef requires 28-fold more land and 11-fold more freshwater than poultry production (377). On average, the production of 100 g of protein from beef generates 50 kg CO_2, compared with 20 kg from lamb, 5.7 kg from chicken, 0.84 kg from beans, and 0.44 kg from peas (361) (Figure 6). Moreover, livestock production is responsible for 37% of anthropogenic emissions of methane (52, 364), which has an 85-fold greater warming potential than CO_2 over a 20-year timeframe. Methane has particular environmental significance as it is oxidized in the troposphere and cleared from the atmosphere within 12 years (378). Therefore, although reducing CO_2 emissions is essential to prevent further global warming, decreasing the huge number of ruminants could reduce near-term temperatures, as the methane that they produce would rapidly disappear. Hence, reducing meat consumption is a critical practical measure to rapidly reduce global warming. For the livestock sector to comply with Paris Agreement 1.5°C climate targets, climate experts estimated that a 61% reduction in global emissions due to livestock would be needed by 2036 (379).

As with fossil fuel emissions, the contributions of food production to climate change differ greatly between world regions. According to estimates, if everyone in the world adopted the lifestyle and diet of the average middle-class American, then the planet could only support a quarter of its current population (354).

Reforming obesogenic ecosystems

Following current trends, more than 50% of all humans will be living with excess weight or obesity by 2035, costing the global economy around US$4 trillion/year and conferring a potentially unsustainable burden on health systems. It is a societal crisis that requires societal solutions. There is a growing consensus that the primary driver has been a dramatic change in the food environment (36). The food environment is determined by individual factors,



Data from (361). All data are means.
Abbreviations: **CO_2,** carbon dioxide; **GHG,** greenhouse gas

FIGURE 6
Environmental costs of different foods. Figure shows **(A)** greenhouse gas emissions and **(B)** land use to produce 100g of protein. Data from (361).

such as living conditions, socioeconomic status, food literacy, and personal preferences, but also by societal/environmental factors, such as food security and the availability and affordability of healthy food choices. United Nations (UN) agencies highlight that current global food systems are failing to provide affordable and healthy foods, while simultaneously driving substantial harm to the environment (380). In short, current food systems are failing to eradicate malnutrition and contribute to the global pandemic of obesity, cardiometabolic diseases, and cancer. Concurrently, the food system has been a major contributor to climate change, causing widespread environmental, land, and soil degradation, loss of biodiversity and ecosystems, considerable GHG emissions, and workforce exploitation (380). Both food and environmental impacts threaten our healthcare systems (36).

Changes to the food system required to help achieve the targets necessary to prevent climate catastrophes could also address the nutritional requirements to mitigate the obesity pandemic and many other chronic diseases. However, there are strong political and market incentives to avoid or delay systems change. This leads to a "papering over the cracks" of the problem, for example, the use of medical or surgical interventions to treat obesity or strategies such as geoengineering for climate change, both of which can have long-term consequences that are not easily reversed (381). Indeed, the GLP-1RAs have considerably improved the treatment options for the millions currently living with obesity, and their effectiveness should help sway the argument from obesity being due to a failure of willpower to it being recognized as a disease associated with a hormonal imbalance. However, a downside could be that politicians may argue that effective treatments remove the need for societal, policy-level action (sometimes characterized as "nanny-state" interventions): such arguments should be negated by the economic and health benefits of prevention. This is similar to the concerns that CO_2 removal strategies to combat climate change may make policymakers and the public imagine that there is no need to reduce the burning of fossil fuels because the emissions can be offset, which has been termed the "moral hazard" (382).

Our current food environment is characterized by the ready availability of cheap and unhealthy foods that are addictive. There is overwhelming evidence that a diet dominated by energy-dense UPFs is detrimental to human health and a critical factor in the obesity pandemic. Some have argued that, as the precise mechanism linking UPF consumption to obesity has not been verified, it is too soon to recommend changes (383). However, there are many potential mechanisms, and likely many of these are working simultaneously. There is also no evidence suggesting it would be safe or healthy for humans to rapidly switch to consuming the complex, artificial mixtures and formulations typical in UPFs. With such strong evidence of harm, gold-standard evidence from long-term, randomized clinical trials is unlikely to be obtained and would probably be unethical owing to the anticipation of adverse outcomes.

There are major, complex environmental factors contributing to the challenge of food selection, including food access, food insecurity, and food literacy, particularly for people residing in lower socioeconomic status areas. To change this ecosystem, healthy food options need to be made more available and more affordable and unhealthy foods made less attractive by ensuring that their harms to health and the environment are accurately reflected in their costs. The Food Insecurity in people living with Obesity Initiative (FIO) articulates a multipronged approach to tackling this issue in the United Kingdom (384). Different strategies and approaches will likely be necessary in nations with other approaches to public health, where responsibility for health is devolved to the individual regardless of their health literacy or access to resources.

In this section, we review recent evidence that i) supports a transition to food systems that are both healthier and more environmentally sustainable, ii) explains why previous obesity strategies and policies have failed, and iii) indicates which options are key to reforming obesogenic ecosystems (Figure 7).

Transitioning to a healthy and sustainable food system

The transformation of agriculture was largely successful in enabling the production of sufficient food for expanding populations at an affordable cost. The drive for large-scale farms with a monoculture of crops and industrialization of animal farming and food production enhanced profits but caused environmental damage, contributed to climate change, and has chronic adverse effects on human health (385). It is now recognized that a new transition is required to develop sustainable food systems.

A healthy and sustainable food system that also counters the obesity epidemic will need a gradual shift away from the high proportion of energy-dense, low-fiber UPFs in diets. A recent systematic review concluded that for this to be accomplished, policies are needed to address the UPF products themselves, but also food supply chains, food environments, UPF corporations, and fast-food and supermarket corporations (386). In 2019, the EAT-Lancet Commission on healthy diets from sustainable food systems (364) used the planetary boundaries framework (387) to develop safe operating boundaries for the global food system. It concluded that a transition to a healthy and sustainable food system will require a >50% reduction in the consumption of unhealthy foods, particularly red meat, UPFs, and sugars, replaced by a >100% increase in the consumption of healthy foods, such as fruits, vegetables, nuts, and legumes (364). However, even a small increase in consumption of red meat or dairy foods would make it difficult or impossible to maintain the planet in a safe operating space. The Commission estimated that the adoption of a largely plant-based diet by 2050 could reduce food-related GHG emissions by 80%, that more efficient food production could reduce emissions a further 10%, and halving food waste could reduce another 5%.

The Commission recommended diets aimed at improving both human and planetary health. These include a range of food groups but with between zero to moderate animal product intake at a much lower level than in high-income countries today (364). The Commission used a Mediterranean diet as an example of a healthy, sustainable diet that traditionally was largely plant-based and low in red meat but high in legumes and fat, predominantly olive oil. The energy-reduced Mediterranean diet can mitigate the potential negative effects of age-dependent changes in body composition with a reduction in total and visceral fat and a maintenance of lean body mass (388).

The Commission has recently published an update in which they emphasize that the evidence has become even more compelling for an urgent need for a radical transformation of global food systems to ensure the health of humans and to ensure that the planet remains within safe boundaries for sustaining life (389). They report that food systems are the largest single cause of the transgression of five of the six planetary boundaries that have already been breached, these being biodiversity, freshwater flows, biogeochemical flows (nitrogen and phosphorus cycles), and novel entities (pesticides and antimicrobial use) (389). Food systems have also had a notable impact on the climate and ocean acidification boundaries, with agricultural and food systems contributing 30% of total global GHG emissions. That diets proposed by the Lancet Commission as sustainable for a healthy planet can also reduce the risk of obesity was confirmed by a recent umbrella review of food groups associated with excess weight and obesity (390). The risk of being overweight or obese was lowest in those with a high intake of whole grains, legumes, nuts, and fruits and highest in those with a high intake of red meat and SSBs (390).

Recent studies have analyzed the environmental impacts of different diets and attempted to define an ideal diet that, in contrast to diets previously designed solely for weight loss, would be healthy for both humans and the planet. An analysis of dietary data from a large United Kingdom population estimated that the GHG emissions associated with a vegan diet were 74.9% lower than for high meat diets, and the environmental impacts of high meat consumption were at least 30% higher compared to those whose diet included low levels of meat (391). Similarly, a comparison of the environmental impacts of a Mediterranean diet with the current Spanish diet and a cafeteria-style American diet, using food balance sheets from the UN Food and Agriculture Organization (FAO), indicated that meat product consumption was the main contributor

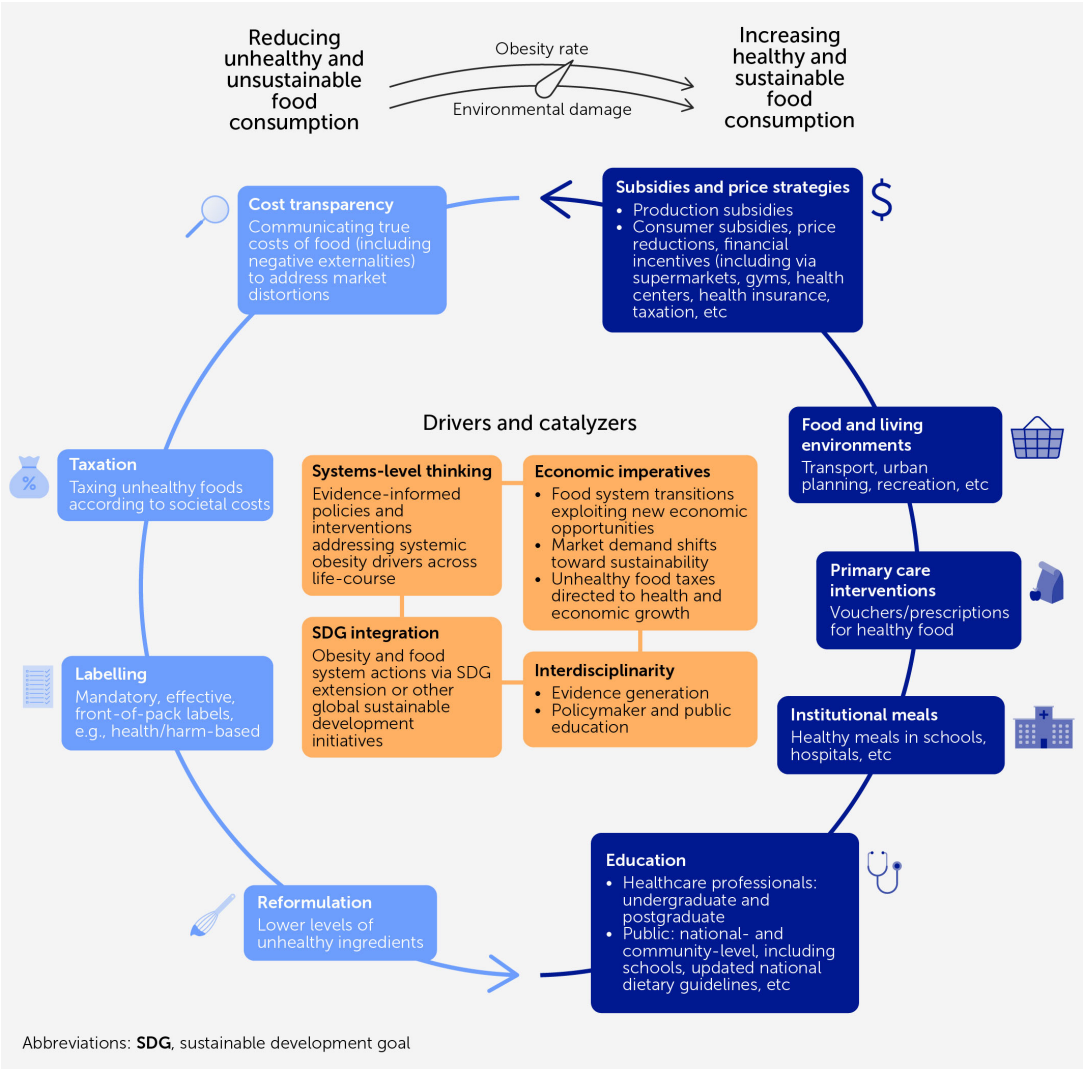


FIGURE 7
Reforming food systems and environments to address obesity and climate co-crises. Multicomponent interventions are needed to "move the dial" on obesity rates via actions to reduce unhealthy, unsustainable food consumption and increase healthy, sustainable food consumption. Multisectoral engagement spans health, agriculture, transport, planning, recreation and parks, industry, education, and the media. The figure illustrates the key interventions and drivers or "catalyzing" factors.

to large differences in GHG emissions. Emissions could be 72% lower if the Spanish population adopted a Mediterranean diet (392). Recent comparisons of common American diets also showed ruminant meat consumption to be the main factor driving environmental impact (393, 394).

Recent large prospective cohort studies have quantified the human and planetary co-benefits of sustainable diets. For example, in Europe, it was estimated that up to 10–39% of incident cancers and 19–63% of deaths could be prevented over 20 years by different levels of adherence to the EAT-Lancet diet. Higher adherence could potentially reduce food-associated GHG emissions and land use by up to 50% and 62%, respectively, compared with lower adherence (395). In the United States, adherence to this diet was associated with lower risk of total mortality, and mortality due to cardiovascular disease, cancer, and other NCDs, together with lower environmental impacts (396).

A recent meta-analysis concluded that an ideal, sustainable diet should be very similar to the diet that our ancestors evolved to consume and should be based on whole foods, specifically a high-fiber, largely plant-based diet consisting mainly of whole grains, legumes, tubers, roots, bulbs, nuts, seeds, vegetables, and fruits, with reduced quantities of meat and dairy (52).

There are further climate and health benefits from dietary change, given the large-scale land use of animal agriculture. Dietary shifts offer the option of returning large areas of land to nature, resulting in carbon sequestration, biodiversity protection, recreational areas, better floodwater retention, and more. If people in high-income nations were to adopt an EAT-Lancet Commission diet, then dietary GHG emissions could be reduced by around 60% (364, 397). This potential could double if the land currently occupied by animal agriculture were returned to nature, drawing down carbon into the land (397, 398). This so-called "double

dividend" would also result in additional nature areas closer to urban centers that could help address access to nature, along with mental and physical challenges. It may also result in increased resilience to climate change (e.g., via better floodwater retention versus pasture) and to shocks to the food supply (by releasing land that can be used as a buffer against interruptions) (399). A recent modeling study indicated that a transition to the EAT-Lancet diet would make the pathway to the climate target of 1.5°C much more feasible due to the reduction of GHG emissions, especially methane from ruminants, requiring less CO_2 removal and reducing pressure on GHG prices, energy prices, and food expenditures (400).

Despite a wealth of data, there is a lack of wider appreciation of the problems with the current food system and the changes and targets necessary to achieve a sustainable food system that would ensure both human and planetary health. Achieving the required changes will be complex owing to the need for alignment between many stakeholders, including medical and public health professionals, nutritionists, dietitians, educators, policymakers, agriculture, retailers, food industries, and the general public. For example, the recent Danish Plant-Based Action Plan covers a suite of measures along the supply chain to encourage increased intake of plant-based foods (401).

The required transformation of our food system presents particular challenges for LMICs, where food insecurity, malnutrition, and poor diets are common. The rapid rise in UPF consumption in LMICs adds to these existing challenges (20). In LMICs, any food transformation needs to also address sanitation, adequate clean water, and, where appropriate, fortification and micronutrient supplement strategies. Food already represents a much greater proportion of income in such countries, and affordability is critical (402). With economic improvements resulting in higher incomes, food can become more affordable, but this may not translate into healthier diets as it is generally accompanied by rapid expansion in the availability of UPFs and SSBs and increased exposure to advertising of unhealthy foods (20, 403, 404). Many LMICs currently import a substantial portion of their vegetables, fruits, nuts, and legumes, making them especially vulnerable to international price variations (389). Targeted policy interventions may be required in such countries to build infrastructure, such as storage and transport, and to ensure the affordability of a healthy diet. Furthermore, a large proportion of the population may be employed in the agriculture sector in many LMICs, which can also constitute up to 40% of national GDP, in contrast to less than 5% for high-income countries (405). These factors present additional challenges for transforming food systems within LMICs.

Why have previous obesity strategies and policies failed?

Many national and international institutions have produced reports and recommendations to address the obesity pandemic. In response, many governments and international bodies have endorsed or enacted policies in attempts to reduce obesity rates, but until recently, none have had any meaningful effect. At the highest international level, for example, the WHO agreed a Global Action Plan for the Prevention and Control of Non-Communicable Diseases 2013–2020, with a target to prevent any further increase in the rates of obesity by 2025 (406). Yet, the World Obesity Federation (WOF) concluded that not one country was on target to meet this goal, and most countries had a ≤5% chance of doing so (407). WHO has subsequently updated its objective with the Global Noncommunicable Diseases Compact 2020–2030 and, in 2022, published the Acceleration Plan to Stop Obesity (408).

Evaluating obesity strategies to date

The failure to reduce obesity rates indicates that most national public health policies have been largely ineffective. A review of regulatory approaches to control the obesity pandemic adopted across the United States and European Union (EU) between 2004 and 2013 concluded that these had been limited in reach and scope with no widespread consistent policies adopted (409). Policies were frequently restricted to subpopulations, such as schools, rather than the general population, and governments generally preferred providing consumer information over direct taxes or market restrictions. The policies that have been adopted were generally too brief for effects on obesity or health to become apparent (409).

A more global review of policies concluded that governments have generally lacked sufficient commitment to take effective action; this was at least partly due to insufficient influence from consumers and civil society coupled with the food industry's ability to moderate policies to protect commercial interests (410). In the United Kingdom, analysis of 14 strategies and 689 specific policies between 1992 and 2020 identified a number of issues (411). Only one strategy was based on an independent evaluation of previous government strategies, and only 24% of the proposed policies included any details for monitoring or evaluation. Only 19% cited any evidence to support the policy, and only 9% included any costings or allocated budget. Many of the proposed policies were similar or identical to ones previously proposed, while several were proposed multiple times but with no reference to their prior proposal and failure to be implemented. The majority of policies were not set out in a manner that would lead to implementation, and they relied heavily on behavioral changes by individuals rather than changes to the food environment (411). A major contributor to such ineffective policies in countries such as the United Kingdom and United States has been conflicts of interest (412, 413). To counter such issues, countries such as Brazil and Mexico have adopted evidence-based policy recommendations developed by experts without commercial conflicts of interest (387, 414).

Commercial obstacles to obesity strategies and polices

A recent analysis of 1,500 climate change policies implemented in 41 countries between 1998 and 2022 found that only 63 were successful (415). A common feature between climate and obesity policy is that, in both cases, powerful commercial entities invest large amounts in lobbying policymakers who are persuaded to choose policies that have no effect and often focus on individual

actions rather than those that are more likely to work at a systemic level but at the expense of the dominant commercial actors (416). This is despite the accumulation of evidence indicating that obesity is due to system-level factors and not due to individual fallibility, including strong evidence that people who migrate, over time, adopt the obesity characteristics of their new location (417, 418).

Obesity-reduction strategies relying on industry self-regulation and public-private engagement have proved ineffective, owing to conflicts of interest (419–421). The UPF, SSB, and fast-food companies, and animal agriculture industries, hold disproportionate influence over food environments, particularly for children, and leverage vast financial resources and immense political influences to resist policies aimed at creating healthier and more equitable food environments (61). Indeed, a fundamental transformation of the food environment will involve changes resisted by these very powerful food and agricultural sectors. These sectors together account for some of the largest employers globally: in the United States, one in 10 jobs is in the food production sector (422). Economies of scale have enabled TNCs to generate huge profits by selling processed foods at low prices. Over the period 2009 to 2023, the global sales of UPFs grew from US$1.5 trillion to US$1.9 trillion, with eight TNCs dominating the market and accounting for 42% of the sector's total assets in 2021 (423). These eight TNCs all have headquarters based in North America and Western Europe, with nearly half located near the decision-making centers of Washington, DC and Brussels (423). The over-consumption of food driving obesity was estimated in 2015 to be worth US$60 billion per year to the food industry in the United States alone, equivalent to around US$80 billion today (424). Between 1962 and 2021, more than half of the shareholder payouts in the food sector were distributed just by the TNCs manufacturing UPFs (425). These profits have attracted investors such that the TNCs are now themselves dominated by a small number of hedge-fund managers and private equity firms who generally oppose public health proposals from other shareholders in favor of maximizing financial returns (425–427). The success of TNCs or managed funds in creating wealth attracts support from governments wanting to promote national economic growth.

A recent international synthesis of the evidence for global action on UPFs concluded that the main obstacle to effective policies was the internationally coordinated political activities of the TNCs that included direct lobbying, infiltrating government agencies, and legal actions to restrict regulation, promote TNC-friendly governance, and manufacture scientific doubt (423). Corporate financial influence has had a negative effect on the adoption of WHO-recommended policies to restrict the consumption of unhealthy foods across the globe (428). Similar to climate controls, the ability of national governments to legislate to control their obesity epidemics can be limited by "free trade" deals that empower TNCs, who have used World Trade Organization (WTO) mechanisms to restrain the ability of governments to regulate their own food systems (429–431). The TNCs have also employed intensive lobbying of UN and WTO bodies to oppose food regulation policies (432). Similar to the strategies employed by the tobacco industry, these powerful bodies have also skewed the scientific debate by sponsoring research, scientific conferences, and organizations to counter the impact of evidence that implicates their food products in driving obesity, and the strategies suggested to restrict these (433–436). With sales of UPFs and ultra-processed beverages becoming saturated in high-income countries, the TNCs have focused on the potential of middle-income countries, where the sales of UPFs are projected to match those of high-income countries this year and those of ultra-processed beverages are already greater (434). The success of the food industry strategies can be seen in China, where the industry-funded International Life Sciences Institute is embedded within the Chinese Centre for Disease Control and Prevention and successfully reframed Chinese obesity policy to emphasize interventions based on physical activity rather than diet, which is at odds with the consensus scientific evidence (437).

In contrast to national-level policies, commercial pressures have been less effective at curtailing municipal authorities. The Milan Urban Food Policy Pact was launched in 2014 with recommendations for food policies, including 620 specific actions covering governance, food production, supply, distribution and waste, social and economic equity, and sustainable diets and nutrition. With 55% of the global population now living in urban centers, projected to rise to 68% by 2050 (438), and with 290 cities (with a combined population of 490 million people) already signed up to the Pact, this has the potential to significantly transform food systems (439).

In 2019, the Lancet Commission on "The Global Syndemic of Obesity, Undernutrition, and Climate Change" called for governance levers to be strengthened at local, national, and international levels; for more policy actions from governments; to reduce commercial entity influence and lobbying on such policies or to make them more transparent; to strengthen accountability for policy actions; and for the creation of sustainable and health-promoting business models that prioritize societal and environmental benefits and not just profits (36).

Removing market distortions: cost transparency

As described, large TNCs have been successful in marketing UPFs, making them ubiquitous in the food environment and generating huge profits (440). The mass production of UPFs adds considerable profit for the food industry and provides cheap food for consumers. Generally, food producers add more salt, low-quality fats, and sugars to UPFs to make them highly palatable and then heavily promote them to increase sales and profits despite their known adverse effects on health (441). Unhealthy diets are much cheaper than healthy diets, and this price differential most impacts lower socioeconomic groups (442, 443). However, the low price of processed foods does not reflect their true cost to society and our environment, often termed negative externalities (380).

These distortions need to be addressed systemically and across the policymaking domain in order for people to make informed, healthy choices while living sustainably. A common libertarian refrain claims that a "nanny state" would intrude into private

lives and restrict individual choice (444, 445). However, the current system already makes explicit and implicit decisions on the food choices available to people. Incentives that actively "tilt" the playing field to incentivize further externalization of costs are common. For example, an estimated 82% of EU agricultural subsidies are embedded in animal products that are responsible for 84% of the GHG emissions from EU food production but only supply 35% of the calories (446).

The first step in enabling free transparent choices and making food systems sustainable is to inform consumers of the true costs of food (447) (Figure 8). For example, Americans spend a total of US $1.1 trillion a year on food, yet when the impacts of the food system on rising healthcare costs, climate change, and biodiversity loss were factored in, costs were three-fold higher—at least US$3.2 trillion a year (448).

Taxing unhealthy foods to redress their true societal cost

Internalizing all negative externalities into the cost of food would likely make many foods unaffordable in most countries. However, an understanding of all of the true costs would enable policymakers to use levers for reducing external costs while informing citizens of the real cost of their choices. Many nations have introduced taxes on unhealthy foods, the most common being taxes on SSBs adopted to varying degrees by 103 countries covering 51% of the global population (449). Meta-analysis of 62 studies indicated that such taxes resulted in average reductions of 15% in sales and 18% in intake of SSBs (450).

Latin American nations (451, 452) and Pacific islands (453) have consistently been at the forefront in applying policies to control obesity. This is likely a result of their recent rapid trends in obesity prevalence that are more clearly linked to food system changes. The influence of the food industry to impede political actions in these nations may also be less entrenched than elsewhere, as TNCs are generally not based in these countries. For example, in 2014, Mexico imposed a tax of 1 peso/L on SSBs, representing a small 5.3% increase in the purchase price, and an 8% *ad valorem* tax on non-essential energy-dense foods. After 3 years, SSB purchases decreased by 7.6% and taxed foods by 6%, with larger reductions in lower socioeconomic status groups (454, 455). Within 2 years, there was a 1.3% decrease in the prevalence of excess weight and obesity in adolescent girls (456). Modeling studies have indicated that if Mexico increased these taxes then obesity rates could be reduced with huge savings for the national economy (457), with a 30% tax projected to reduce obesity by 9.1% after 10 years, which translates to 3.8 million fewer cases, with a saving of US$17.9 billion in costs to the economy (458). In the United States, California saw reductions in the rates of excess weight and obesity of 5.5% in children aged 2–5 years and 4.2% in those aged 6–11 years within 4–6 years after city-level SSB taxes were implemented (459). In 2016, the Indian state of Kerala levied an indirect tax of 14.5% on fast foods sold at branded restaurants (rather than targeting specific nutrients), with the revenue generated directed to public health initiatives. The tax only remained for 11 months before being dropped when a new federal tax system was implemented. However, it proved effective with reductions in fast food purchases of 3.9–5.6% over the duration of the tax and in the following period (460).

Combating marketing and implementing effective food labeling

The high profits made from UPFs enable considerable advertising budgets, price promotions, and other marketing techniques that drive further demand. In 2024, just three of the TNCs manufacturing UPFs spent a combined US$13.2 billion on marketing, which was nearly four times that of WHO's total operating budget (423). Advertisements for UPFs are ubiquitous in many societies, with particularly high exposure among lower socioeconomic status groups (461). Children are most vulnerable as they are highly impressionable, motivated by immediate gratification, and have underdeveloped nutritional knowledge. Marketing for adolescents is also of particular concern since food choices made at this critical stage of development set the foundation for a healthy life (123, 462). This problem has been intensified by digital marketing, which has enabled children and adolescents to be targeted with precision with personalized UPF advertisements and gaming platforms that blur the boundaries between entertainment and advertisement (463). The WHO has recently strengthened its guidelines for mandatory policies to protect children from marketing for unhealthy foods, although some consider that the recommendations should go further (464). Evidence indicates causality between food marketing and childhood obesity (465), while a systematic review of policies to restrict marketing to children concluded that these can be effective (466).

Nutritional- or harm-based labels on food products, like those on cigarettes, have also been proven to work and have been adopted in over 20 countries. Graphic labels depicting health effects have the most impact on consumer choice; lists of nutrient contents have the least impact (467, 468). A systematic review of the effect of front-of-pack nutrition labeling on food industry practices found that labels with numerical information had no impact, but labels with intuitive information led to product reformulation, generally reducing sodium, sugar, or calorie content (469). More consistent effects on product reformulation were observed if the food labeling was mandatory compared with voluntary policies that have been found to have little impact (470). The effects of labels specifically warning that foods are UPFs are not yet known and online experiments have yielded differing results: a study of 600 adults in the United States indicated that it would discourage them from purchasing such products (471) whereas a similar online study of 1004 adults in Brazil found that such labeling would not affect purchasing intentions (472).

In the United States, analyses of purchasing datasets from some states show that listing calories on menus in restaurants and

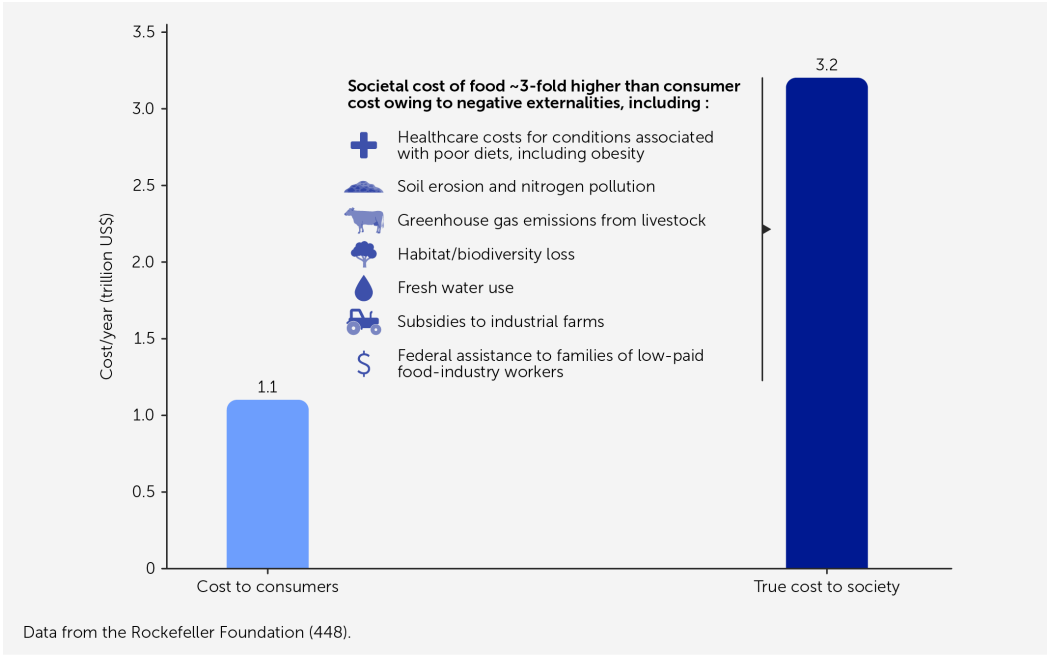


FIGURE 8
Comparing consumer and true costs of foods, taking into account negative externalities. Estimated annual costs in the United States. Data from the Rockefeller Foundation (448).

supermarket prepared foods can result in a 5% reduction in calories per purchase (473, 474). WHO recommends that for a healthy diet, less than 30% of total energy intake should be from fat, with saturated fat under 10% of total energy, and free sugars under 10% of total energy. For salt, the recommendation is less than 5 grams per day. Various countries have introduced labeling of foods to help people adhere to these guidelines by flagging foods that are high in fats, sugars, and salt (HFSS). In 2016, Chile was the first nation to introduce mandatory, national front-of-pack warning labels on unhealthy foods and beverages, restrictions on marketing such products to children, and a ban on their sales in schools. Unhealthy foods had to have a distinctive black octagon on the front of the pack displaying the words "high in" sugar, sodium, saturated fat, and/or calories. In addition, harmful nutrients are treated as added ingredients rather than intrinsic components of foods, and their content is regulated (475). After Phase 1, there were decreases in household purchases of total calories (4%), sugars (10%), saturated fat (4%), and warning-labeled foods (24%) (476). Even larger changes are expected after Phase 2 and Phase 3. In Phase 3, the thresholds for HFSS were lowered to 10 g sugar, 4 g saturated fat, 400 mg sodium, and 275 kcal energy per 100 g for solids or per 100ml for liquids. This was accompanied by a complete ban on television advertisements of warning-labeled foods between 6 am and 10 pm and a ban on the sale, promotion, or marketing of such foods within schools. An initial analysis indicated that this resulted in improved diets with increased intake of healthy nutrients in children within schools (477). Warning labels on foods can also have indirect effects by creating incentives for food manufacturers and retailers to reformulate their products (478). Recent evidence indicates that this has been the case after full implementation of Phase 3 in Chile, with many producers reformulating packaged foods with reduced contents of fats, sugars, and salt (479). Similar warning labels have now been adopted across much of Latin America (Figure 9). Such policies are more effective when they are coordinated with other mutually reinforcing policies, such as those in Chile (475) and in Colombia, where food labeling is reinforced with taxes on UPFs and SSBs (480).

With the rapid growth of obesity in children, the extension of warning labels to UPFs and HFSS foods that are targeted at infants and young children and stricter regulation of their marketing are particularly needed (466, 481–483).

Facilitating healthy food choices

Strategies to make healthy foods more affordable and readily available include subsidies, either at the level of producer or consumer, particularly for fruit and vegetables; primary care-based nutritional interventions, such as vouchers or prescriptions for healthy meals; and provision of healthy meals in schools, hospitals, and other institutions. Strategies for improving the availability of healthy foods should increase the availability and affordability of unprocessed or minimally processed foods, including ready-to-consume and ready-to-heat minimally processed foods (386). There have been insufficient studies of the impact of pricing strategies such as price reductions, subsidies, or financial incentives for healthy food, and these have mainly been of short duration. However, they generally indicate that availability, purchases, and consumption of fruit and vegetables can be increased with potential health benefits (484–486). A recent meta-analysis of 14 studies indicated that a 20%

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FIGURE 9
World Health Organization Region of the Americas (AMRO) countries that had adopted a front-of-pack nutrition labeling (FORNL) system as of August 2022. ©Elsevier, 2023. Re-printed with permission from (468).

price reduction could increase fruit and vegetable purchases by 16.6% (486). Subsidies for healthy foods can be funded by levying taxes on unhealthy foods such as UPFs (487, 488).

Financial incentives can be established through links between supermarkets, gymnasiums, health centers, and health insurance or taxation schemes, depending on the national context. Targeted food subsidies can have indirect effects on the food environment. For example, in the United States, subsidies introduced in the Special Supplemental Nutrition Program for Women, Infants, and Children resulted in increased availability and variety of healthy foods, especially in low-income neighborhoods, as grocery stores responded to demand (489). Subsidies targeting families with young children can also help to develop a healthy preference learning environment at home. The United States "Food is Medicine Movement" aims to overcome the interlinked issues of lack of available, affordable healthy food, and the growing healthcare costs. This involves people with obesity and cardiometabolic diseases being treated with medically tailored meals, prescription programs, and subsidies for healthy foods such as fruit and vegetables (490, 491). The Food is Medicine Movement has also created community teaching kitchens to provide education on healthy dietary behaviors to communities and especially undergraduate students in medicine, nursing, nutrition, and dietetics, as well as doctors and other healthcare professionals (492). These can be established by healthcare professionals in collaboration with schools, universities, and medical colleges, together with local agriculture, including farms, community gardens, and urban agriculture groups. They can be delivered by various combinations of dietitians, physicians, other healthcare workers, and chefs in different formats, including virtual (videos or podcasts) or in-person classes in community facilities, schools, colleges, and businesses. A similar program of community-based teaching kitchens developed by a celebrity chef, Jamie Oliver, has been implemented in the United Kingdom and Australia (493). These can build cross-disciplinary communities, increasing awareness and engagement with the critical role of nutrition and the food system in maintaining healthy lifestyles and a healthy planet (492). These initiatives have often been transient; long-term funding and structures need to be established for them to have greater impact.

In addition to improving the availability of healthy foods, there have been a few studies of behavioral interventions aimed at promoting more environmentally sustainable diets. A systematic review indicated that the use of multicomponent interventions through education, persuasion, and environmental restructuring was most effective, but that more high-quality studies were needed (494).

Living environments enabling healthy diets and activity

Given that living environments help shape health both via dietary patterns and physical activity levels, a systems approach is needed. This requires the engagement of all sectors of society and government—including transport, planning, recreation and parks, industry, education, and the media—rather than health alone.

Changes in the built environment that would enhance physical activity could also reduce climate impacts. The WHO Global Action Plan on Physical Activity 2018–2030 recommends a multifaceted approach combining both upstream policy actions that support the integration of physical activity into multiple settings with downstream, individually focused approaches that empower people to become active (495). A survey of physical activity surveillance, policy, and research in 164 countries found large disparities between countries with only modest progress between 2015 and 2020 (496). Urban and transport planning need to be strengthened and closely integrated to develop compact, highly connected neighborhoods with access to safe and expedient public transport options, thereby reducing car dependency (495). Commitment to a more holistic approach to urban planning is essential (497).

Education: public and professional

Public health strategies may provide education to improve diets and lifestyles, but individuals' access is fundamentally dependent on their basic education level, language, and literacy. Many consumers do not possess sufficient knowledge to assess nutrient content from food labels (498). More nutrition education is needed to help consumers make healthier choices and to increase awareness of the role that nutrition plays in preventing chronic diseases. Education needs to be implemented throughout schools and colleges in a culturally appropriate manner (499). National food guidelines need to be updated to not just consider individual nutrients but also view food systems and environments holistically in order to address the interplay between all components and characteristics of food. This should include formulation and processing, with recommendations to favor unprocessed natural whole foods and avoid UPFs—as have been adopted to varying degrees in Brazil, Canada, Ecuador, Denmark, Germany, Peru, and Uruguay (20).

Better education regarding nutrition and obesity is also particularly important for healthcare professionals. Health professionals need to be trained and equipped in the prevention, management, and treatment of obesity and in addressing weight bias, which remains a systemic barrier to access and effective implementation of care. Obesity bias is widespread among healthcare professionals and is associated with poor patient outcomes (500, 501). Many medical students start with unconscious obesity bias (502, 503). Moreover, evidence indicates that physicians are not adequately prepared educationally to tackle the obesity crisis. A systematic review concluded that there is a paucity of education on obesity in medical schools worldwide (504). For example, a survey of United States medical schools found an average of 10 hours of obesity education, and fewer than 40% indicated that their medical program covered any obesity-related topic well; only 10% were confident that their students were "very prepared" to manage patients with obesity (505). A United Kingdom-based survey revealed that 70% of medical students could only recall 2 hours devoted to nutrition throughout their 7 years of training; only 26% of doctors were confident in their nutrition knowledge, and 74% gave nutritional advice less than once a month in their clinical practice (506, 507). A similar Canadian survey found that over 87% of medical students thought more time should have been dedicated to nutrition education (508). A survey of United States medical interns found that only 29% considered that they had sufficient education in nutrition (509), and although 94% of internal medicine residents agreed that nutritional counselling was essential, only 14% suggested that they were adequately trained to deliver this (510). In 2022, the United States House of Representatives passed a resolution calling on medical schools to ensure more meaningful nutrition education in their medical curricula, but changes still need to be implemented (511).

A new way forward: catalyzing policy action to tackle obesity

For more than a decade, WHO and repeated Lancet features and Commissions on obesity have called for a switch in emphasis from individual responsibility and the view that the solution was for people to "eat less and move more" to acknowledgement that personal choices for diet and physical activity are greatly constrained by our obesogenic environments and these can only be addressed by more governmental action (36, 440, 512). This was recently reiterated by the WOF (513). To overcome the global lack of progress on policies attempting to limit the obesity pandemic, the WOF and other obesity organizations have developed a framework with five objectives based around the acronym "ROOTS": Recognition of obesity; Obesity monitoring; Obesity prevention; Treatments of obesity; and a Systems-based approach (407). This ROOTS approach is proposed to be applied to the management of obesity and to the environmental, social, and commercial roots of obesity.

In this final section, we outline approaches to catalyze actions on these fronts and to overcome key barriers to change.

Promoting system-level thinking

The challenge is to shift the focus of policymakers from the misconception that obesity can be addressed by nudges to correct the "failures" of individuals to government actions that enable societal or environmental interventions that directly address the systemic drivers of obesity. Governments should recognize that obesity is a disease and invest in its prevention, management, and treatment. Such recognition could reduce the potential harm of weight stigma, which has deleterious effects contributing to additional weight gain (514). Governments must introduce

policies that are informed by evidence and address the primary drivers of obesity from a societal perspective. With obesity onset increasingly occurring in childhood, with serious long-term consequences through to adulthood, interventions must address the entire life-course. For these actions to be effective, they need to include a clear plan for implementation, clear targets and timeframes, accepting appropriate time-lags between changes in dietary behavior and obesity prevalence, and an established process for ongoing independent monitoring and evaluation.

Experiences in Latin America and the Pacific Islands are beginning to demonstrate effective multipronged approaches with the potential to transform our food system. These include taxes, tariffs, subsidies, warning labels on unhealthy foods, education, and making healthy foods affordable and available through primary care-based nutritional interventions, vouchers or prescriptions for healthy meals, provision of healthy meals in schools, hospitals, and other institutions, and via community measures such as the facilitation of local markets, local whole food production, and communal kitchens. Such measures may be particularly valuable in LMICs where financial resources are limited and where provisions such as school meal coverage are currently very low and would cost a significant proportion of GDP (515). An example is the National School Feeding Program that has been adopted in Brazil and currently feeds over 40 million children: this requires that food procured for schools to be at least 90% unprocessed or minimally processed with a maximum of 10% processed or UPF and 30% to be obtained from local family farmers (516, 517). The use of local family farms increased the proportion of fruit, vegetables, and legumes in school meals (518), generated local employment, and stimulated national GDP (519). Another innovative approach has been taken in Vietnam with their Home-Grown School Feeding Program, which promotes the use of school gardens to produce fresh foods for the children (520).

Overcoming commercial pressures opposing change

As described, for consumers, the attractions of UPFs have been their affordability, convenience, and palatability, but the main drivers of UPF proliferation have been commercial. Removing the current distortions and constraints and enabling genuine informed choices will require multi-faceted, interdisciplinary solutions involving policymakers, industrial leaders, institutions, educators, and the public coming together in collaborative policy shifts to change behaviors and transform our food system. Increasing transparency and awareness of the true costs of food is key to helping transform food systems without compromising wealth creation. It should not be a choice, or a contest, between healthy profits or healthy people. As with the transition to green energy, rather than being framed as a threat to economic growth, the emphasis should be on new opportunities. A transition of the food system could provide many opportunities for new developments and employment for the food industry, provided appropriate investment is made available. Schemes such as the Just Energy Partition Partnerships initiated at the 26th Conference of the Parties to the UN Framework Convention on Climate Change (COP26), involving a consortium of countries supporting fair and inclusive economic development (521), could be adopted not just for energy but also for food production. For example, sugar consumption is a major contributor to human obesity, but its production is important for the economies of several countries. A reduction in human consumption could, however, provide several opportunities, such as switching land to grow other food crops or rewilding for environmental gains. In addition, sugar crops could be retained but the sugar utilized for other purposes, such as the production of microbial protein, biofuels, and bioplastics that could mitigate the economic consequences (522). It has been estimated that switching sugar from direct human consumption to microbial protein production could meet the protein needs of 521 million adults with considerable environmental gains (522). Indeed, microbial protein production is just one of many opportunities for developing alternative foods with a much lower environmental footprint, such as synthetic meats, algae, insect-derived proteins, hybrid foods combining any of the previous with plant-based materials, genetically modified crops, and 3D-printed foods (523–526). One recent example is rice-based meat developed by combining technologies involving hybrid rice grains, nanocoating, and animal cell culture (527). Most of these new experimental foods are being developed in response to environmental and sustainability concerns; however, there is no evidence, as yet, that they would impact human obesity. Their impact on obesity should be a major consideration in their development and evaluated before widespread adoption. The challenge for science and the food industry is to provide innovative technologies to enable a further transition of the food industry that is both economically sound and, most importantly, benefits both human and planetary health. These new developments will also challenge the bluntness of the NOVA classification of UPFs, as most of the experimental foods would currently be classified as UPF, and this may require a new nomenclature for advanced processed foods that are healthy for both the environment and humans.

The most important barriers to change are the power imbalances between the TNCs and the health sector, conflicts of interest, and industry interference (528, 529). Governments have a responsibility to promote both the health and wealth of their populations, and when corporations profit from products, such as tobacco and foods that harm health, this creates conflicts. Governments could assert sovereignty over their food systems and the rights of their citizens to healthy and challenge foreign investments by TNCs in foods that are detrimental to health, national economies, and sustainable development (423). A bold move in this direction has been made in Mexico with their new General Law on Adequate and Sustainable Nutrition (530). The challenge is to convince communities and governments to confront powerful TNCs in such ways with policies that transform the food environment to promote better health and less environmental harm, but without compromising economic development. This calls for an innovative economic system that

promotes not just financial success but also human, social, and land health (531). This will clearly require engagement with debates and policy arenas with other sectors and disciplines beyond health and science. For instance, if superannuation policyholders were engaged, they could demand that funds be invested only in ethical industries. TNCs have long recognized this: for example, when taxes on SSBs were imposed in some markets, TNCs invested in new markets, lobbying policymakers, and promoting the role of physical activity in combating obesity rather than regulating foods and beverages (437).

Changes in market demand considerations could also help drive change. While food producers and retailers may be reluctant to forego the enormous profit from foodstuffs driving obesity, they would respond to demand and economic pressures in the same manner as industries are responding to societal shifts caused by climate breakdown. Global economies rely on competition, and if the market demands healthier foods and eschews UPFs, food producers would be financially imprudent to continue to pursue current trends despite declining sales. Surveys of young adults show increased interest in sustainable methods of food production and healthy eating practices (532, 533), although the targeted marketing of unhealthy foods to adolescents requires action since food choices made at this critical stage of development are recognized to set the foundation for a healthy life (462).

Central to overcoming commercial obstacles to food system transformation will be the emphasis on the economic imperatives: that actions will be less damaging to wealth creation than inaction and taxes and tariffs can provide resources for the required investments and services (13). In 2001, Thailand established the Thai Health Promotion Foundation to promote public health using resources financed by an additional 2% tax levy on alcohol and tobacco products (534). Such a system could be extended to use taxes and tariffs on unhealthy foods, UPFs, and SSBs to promote healthy local whole foods and the development of healthcare infrastructure. In turn, a healthier population reduces healthcare costs, is more productive, and pays more taxes. However, the classification process of UPFs will be important to avoid discriminating against plant-based products that would have both health and environmental benefits. WHO has a number of guidelines in development scheduled for 2027: a guideline for the optimal intake of animal-sourced foods, which will incorporate considerations of food processing and sustainability, an operational definition of UPFs to support national policy making, and a guideline on the consumption of UPFs (535). A more nuanced definition of UPFs is needed to distinguish unhealthy UPFs from those that are made with less-processed ingredients, such as whole grains, fruits, vegetables, and legumes, or which generally have neutral or positive health associations (536).

Globally, it has been estimated that reducing projected excess weight and obesity by 5% annually from current trends or keeping it at 2019 levels will translate into average global annual reductions of US$429 billion or US$2.2 trillion in costs, respectively, between 2020 and 2060 (13). According to the Food System Economics Commission, *"The economic value of the human suffering and planetary harm … [resulting from food systems] … is well above US$10 trillion/year, more than food systems contribute to global GDP. In short, our food systems are destroying more value than they create"* (55).

Obesity and the Sustainable Development Goals

A recent analysis of the relationships between global obesity and human development concluded that the increasing prevalence of obesity was linked to economic development, with a shift from agrarian to more industrialized societies, with a concomitant shift to more convenience and processed foods (537). In 2015, the UN General Assembly approved Sustainable Development Goals (SDGs) to address the health and development challenges faced by humanity, to be achieved by 2030 (538). These SDGs were widely endorsed by governments around the world. Despite obesity being a major global health issue with many interrelationships to the SDGs, and which clearly poses challenges to human development, it was surprisingly omitted from the original SDGs, and sustainable agriculture was only included as part of the goal to end hunger (407). With the realization that the SDGs cannot be met by 2030, there have been recent proposals to allow more time and extend the goals to 2050 and include the incorporation of an objective to achieve food systems that are aligned with the climate goals and have net-zero emissions (539). This acknowledges that targets to lessen the harms of climate change cannot be met without reforming current food systems but still omits any mention of obesity despite it compromising human health and development. In 2021, the UN held its first Food System Summit from which a collaboration emerged, the Food System Countdown to 2030 Initiative (FSCI), to provide a framework for the development of new food systems when the current SDGs expire (540). The FSCI framework objective is that a new food system transition should ensure that "all people have access to healthy diets, produced in sustainable, resilient ways that restore nature and deliver just and equitable livelihoods" (540). The FSCI proposes that a sustainable new food system should consider human diets, nutrition and health, the environment, natural resources, livelihoods, poverty, equity, governance, and resilience (541).

Role of interdisciplinary advocacy

The medical and public health communities need to provide evidence both for the drivers of, and solutions to, the obesity crisis, to educate the public and, most importantly, to engage and educate policymakers. The drivers of political action are complex and require the engagement of multiple actors that can muster public opinion and ultimately political will to enact change (528). Trust in nutrition science among the public and policymakers needs to be improved (542). Co-framing the parallel and overlapping threats and common solutions involved in reducing obesity, improving health, reforming unsustainable food systems, protecting the environment, and avoiding climate breakdown should help to build the networks and coalitions across society required to

overcome the complexities and barriers to convince governments to make radical changes (538). Examples of effective coalitions driving political change are the Chilean Labelling and Marketing Law, which was established after the Ministry of Health worked with experts and advocacy groups to sustain political momentum (452), and the Ghanian Government, which assembled a similar health coalition to deliver coordinated policies for front-of-pack labeling, marketing restrictions, food taxes, and public food procurement (543). Health professionals and policy advocates need to build networks and alliances to present a united approach to policymakers and frame proposed policies so that they align with the ideology and objectives of their politicians and provide them with clear evidence, particularly for the cost-effectiveness of proposals. A set of mutually reinforcing policies is required. The recent Lancet EAT commission concluded that evidence indicated individual policies and interventions were insufficient to bring about the changes needed to the food system and that bundles of multiple coherent interventions needed to be implemented simultaneously (389). Economically, prevention should be the prime objective with linked policies introduced to address all components of the obesogenic environment in a coordinated manner, as initiated in Chile (544). People living with obesity should be involved throughout—in policy setting, service design, guidelines, and professional training.

Conclusion

Obesity is a complex disease—a societal problem requiring societal solutions. Recent developments in treatment have provided important new options for the millions currently living with obesity to reduce morbidity and mortality. However, the availability of effective surgical and medical treatments could be used to justify circumventing strategies for prevention. This would perpetuate the cycle where market forces ensure considerable profits from both producing unhealthy foods that promote obesity and then producing drugs to alleviate the consequent harm.

There is now good evidence for effective prevention strategies by improving the food system, such as taxes, front-of-pack warning labels on unhealthy foods, and increased availability of healthy foods. In addition to the health benefits, these measures can provide economic benefits that can then be used to subsidize the provision of healthy foods (13). The stigma surrounding obesity has been a major obstacle and has been exploited by stakeholders who have framed obesity as a lifestyle issue and a matter of personal responsibility, to which strategies should be addressed. This has contributed to national strategies with emphasis on personal responsibility and the reliance on small single policies that have been insufficient in terms of having an impact on population weight. The recent international consensus recognition that obesity is a disease shifts the responsibility to that of society and policymakers. Reframing obesity as a disease should also help to reduce the influence of commercial entities and critically enhance the involvement of people living with obesity in the policy-making process.

At the societal level, ecosystem changes are paramount to address the global challenge of obesity in a sustainable manner. Although many factors have been postulated to contribute to the global obesity epidemic, it is widely agreed that the primary driver has been the transformation of our food environment and, in particular, the adoption of UPF-dominated diets. Specific policies that explicitly target UPFs are needed to counter their impact on obesity and other NCDs (386). These will be assisted by the new UPFs guidelines in development by WHO (535), particularly a new operational definition of UPFs. In countries where UPFs are already dominant, policies to reduce UPF consumption will be needed, but in many LMICs, UPF prevention strategies will be required, and these will need to be integrated with policies addressing undernutrition and the multiple nutritional challenges facing their populations (545).

The transformed food system has also been a major contributor to climate change, which, like obesity, is driven by unsustainable, but profitable, consumption. Both climate and obesity issues require a change to the entire food environment, which will have to overcome strong political and market obstacles empowered by the commercial success of TNCs. At some stage, the costs incurred by wildfires, floods, droughts, crop failures, and other consequences of climate change will be so great that policymakers will be compelled to take more effective actions. The challenge for climate scientists is to convince policymakers to act before too many of the planet's safe operating boundaries have been crossed.

Similarly, the costs of the obesity pandemic will eventually be so great that the case for prevention will be compelling. And again, the challenge for the health community is how to convince policymakers to act before more harm is incurred. The economic argument is clear, the cost to transform the food system to address both co-crises is affordable. The global cost for implementing a core bundle of five interventions proven effective at combating obesity (subsidies and taxes, marketing restrictions, food labeling, school policies, and reformulations) was estimated by the UN International Children's Emergency Fund (UNICEF) to be US$24.6 billion over a 10-year period based on 2024 values, compared with the global economic burden of obesity of US$4 trillion by 2035 (61). For many high- and middle-income countries, this can largely be achieved by redirecting existing government subsidies: the public funding for agricultural subsidies for the 54 OECD countries in 2023 was US$400 billion, whereas the cost to totally transform the global food system is estimated as US$215 billion (55). This would not be feasible for many LMICs with little agricultural subsidies to reallocate but could be achieved with more equitable international funding; currently, only 4.5% (around US$12 billion) of all international development funds are targeted at agriculture, forestry, and fishing (55).

The need to transform the food system to avoid a climate catastrophe may help to drive coalitions across society to deliver momentum and foster the political will for the necessary transformations that will simultaneously tackle the obesity pandemic. For both the climate and obesity co-crises, there are considerable economic benefits in preventing and addressing the known causes rather than mitigating them. In the post-COVID-19 era, societies may be more accepting of such broad structural changes.

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fsci.2025.1613595/full#supplementary-material

PRESENTATION 1: SUPPLEMENTARY TABLE 1
Comprehensive lifestyle intervention for obesity treatment and management.

PRESENTATION 1: SUPPLEMENTARY TABLE 2
Diets found to be effective for weight loss.

PRESENTATION 1: SUPPLEMENTARY TABLE 3
Dietary patterns designated as healthy or potentially unhealthy.

PRESENTATION 1: SUPPLEMENTARY TABLE 4
Incretinomimetic trials in people with normoglycaemic obesity: the evidence base to February 2024.

Statements

Author contributions

PB: Conceptualization, Writing – original draft, Writing – review & editing.

CMC: Conceptualization, Writing – original draft, Writing – review & editing.

JCGH: Conceptualization, Writing – original draft, Writing – review & editing.

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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.

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