The worldwide prevalence of overweight and obesity has nearly tripled over the past four decades, and represents one of the most serious unmet public health challenges of the 21st century. Pooled estimates from population-based studies from across the globe show that the prevalence of obesity increased between 1975 and 2016, from <1% to 6–8% among children, from 3% to >11% among men and from 6% to 15% among women. Over 2.1 billion people, or nearly 30% of the global population, have overweight or obesity, giving rise to substantial health, social and economic costs. Excess weight is the leading risk factor for type 2 diabetes mellitus (T2DM) and can also lead to a number of related chronic conditions, including coronary heart disease (CHD), stroke and many cancers. The global economic effect of obesity is estimated to be ~2 trillion US dollars, or 2.8% of global gross domestic product, which is roughly equivalent to the global economic effect of smoking or armed conflict.

Obesity is a complex condition that results from various physiological, environmental, behavioural and socio-political factors, which all contribute to a positive energy balance. Maintaining a healthy weight is in large part a function of modifiable lifestyle choices that are shaped by the broader food environment, including availability, price and marketing. Among these factors, sugar-sweetened beverages (SSBs) have emerged as an important risk factor, with a robust body of evidence linking SSBs to weight gain and risk of T2DM, cardiovascular disease (CVD) and certain cancers. Collectively, SSBs are the largest source of added sugar in the diet; a typical 12 fl oz (355 ml) serving of soda delivers 35.0–37.5 g of sugar and 140–150 calories (Box 1). Numerous health authorities have called for reductions in SSB consumption. In addition, a number of public policies have been implemented to limit SSB intake in order to improve health and curtail escalating health-care costs.

In this Review, we provide an overview of the role of SSBs in the obesity epidemic. We consider global trends in intake, alternative beverages (including artificially-sweetened beverages) and policy strategies targeting SSBs that have been implemented in different settings. Strong evidence from cohort studies on clinical outcomes and clinical trials assessing cardiometabolic risk factors supports an aetiological role of SSBs in relation to weight gain and cardiometabolic diseases. Many populations show high levels of SSB consumption and increasing consumption patterns are associated with urbanization and economic growth. As such, more intensified policy efforts are needed to reduce intake of SSBs and the global burden of obesity and chronic diseases.
Reviews

Key points

* Sugar-sweetened beverages (SSBs) are consumed on a global scale, with intake levels above the recommended daily limits for free sugar in many high-income countries and on the rise in low-income and middle-income countries.
* Prospective cohort studies of clinical outcomes and clinical trials assessing intermediate risk factors provide strong evidence for an aetiological relationship between SSBs and weight gain and the risk of related chronic diseases.
* SSBs promote weight gain through adding additional liquid calories to the diet, from hyperinsulinaemia induced by the rapid absorption of glucose, and possibly from activation of the dopaminergic reward system.
* SSBs contribute to chronic disease risk through weight gain, through development of risk factors precipitated by adverse glycaemic effects and through hepatic metabolism of excess fructose from sugars in SSBs.
* Several policy and regulatory strategies exist across different levels of governance that can be adopted concurrently to change social norms and limit intake of SSBs among individuals and populations.
* Given the consistency of the evidence across different populations and high intake levels globally, reducing intake of SSBs is one important step to improving overall diet quality and cardiometabolic health.

Sugar-sweetened beverages (SSBs). Beverages that contain added sugar, including carbonated and non-carbonated soft drinks, fruit drinks, and sports and energy drinks that are typically low in nutritional quality.

145 kcal per day from SSBs, which corresponds to 6.5% of daily calories. This intake level alone nearly meets the daily recommendation of no more than 10% of total calories coming from added sugar or free sugar (added sugars plus sugars that are naturally present in honey, syrup and fruit juices) suggested by multiple health authorities including the Dietary Guidelines for Americans and WHO. In the US population, higher intakes have been reported among youth and young adults, among non-Hispanic Black individuals and among Hispanic men and women, compared with other demographics. These intake trends track with disparities in obesity and chronic disease prevalence. Similar trends of a decline or plateauing of SSB intake have been observed in other high-income countries. By contrast, intake of SSBs is increasing in many low-income and middle-income countries (LMICs), as widespread urbanization and economic development have increased the availability of these beverages.

A survey of SSB consumption in adults in 187 countries found that intake was higher in middle-income countries compared with either high-income or low-income countries. Of the seven super-regions (groupings of world regions) evaluated, SSB consumption was highest in Latin America and the Caribbean, with a steady rise in intake from 1990 to 2015, and intake was lowest in Asia, with generally higher intakes observed among men than among women in all global regions (Fig. 1). In comparing global intakes of SSBs in individual countries in 1990 and 2015, marked increases are observed in countries in South and Central America, and parts of southern and north Africa (Fig. 2).

Intake trends among youth have generally paralleled those in adults. Survey data from adolescents in 53 LMICs showed that SSB intake was highest in Central and South America, and lowest in Southeast Asia. Of note, 54% of adolescents consumed SSBs at least once per day. Daily intake of SSBs was shown to decrease between 2002 and 2018 among adolescents in eastern Europe, with larger declines observed in more affluent groups. These downward trends are consistent with observations in western Europe, the USA and Canada.

SSBs and cardiometabolic disease

Obesity. An analysis of historical data from the USA illustrates parallel trends between the rise in consumption of added sugar (largely from SSBs) and epidemics of obesity and T2DM. Obesity prevalence has not declined despite the decline in SSB intake since the early 2000s; however, this observation does not refute the association between SSBs and weight gain. Weight change is a gradual process and major reversals in obesity prevalence would not yet be expected at the population level. Moreover, since obesity and T2DM are complex conditions, causation cannot be inferred from time-trend data alone. Rather, we consider evidence from prospective cohort studies and randomized clinical trials (RCTs), which are able to establish temporality between SSB intake and weight change, or development of obesity and related sequelae.

A number of meta-analyses have synthesized the evidence on SSBs and weight gain and obesity. The majority have shown positive associations, although a meta-analysis of studies among children found a null association. However, this meta-analysis included estimates that were adjusted for total energy intake, which attenuated the overall association. SSBs add calories to the diet and adjusting for total energy intake is equivalent to assessing SSB-induced effects on body weight that are independent of total energy intake. Our previous meta-analysis of cohort studies found that each serving per day increment in SSB consumption was associated with a weight gain of 0.12 kg (0.26 lb) in 1 year among adults and an increase in BMI of 0.05 kg/m² in 1 year among children. We included estimates that were not adjusted for total energy intake, which might explain some of the differences observed between studies. We also included studies that evaluated the change in intake...
of SSBs in relation to weight change. These studies are able to simulate quasi-experimental studies that are generalizable to a real-world setting. Although the results of our meta-analysis seem modest, weight gain is a gradual process, with an average weight gain in adults of about 0.45 kg (1 lb) per year. Therefore, limiting SSB consumption could be an effective way to prevent age-related weight gain. Limiting SSB intake among children is an important strategy for them to develop healthy weight trajectories.

Findings from cohort studies are supported by our previous analysis of gene–SSB interactions. Using data from three large cohorts, we found that people who consumed one or more SSB servings per day had a stronger genetic risk of having an elevated BMI and obesity; this risk was twice that in people who consumed less than one serving per month. This finding suggests that individuals with a genetic predisposition to obesity compared with those without might be more susceptible to adverse associations between SSB consumption and weight gain. Further support for the link between SSBs and weight gain has been provided by studies at different points in the life-course. For example, findings from birth cohorts have shown positive associations between perinatal SSB intake and postpartum weight retention among mothers and offspring adiposity.

The majority of RCTs assessing the effects of SSB intake have only evaluated short-term effects on weight change, rather than long-term patterns, owing to the logistical challenges and difficulties in maintaining participant adherence to assigned beverage regimens over time. In our previous meta-analysis of five trials among adults, we found that adding SSBs to the diet in hypocaloric trials statistically significantly increased body weight (weighted mean difference 0.85 kg, 95% CI 0.50–1.20 kg). Similarly, another meta-analysis of seven RCTs found a statistically significant dose-dependent increase in body weight when SSBs were added to participant diets (standardized mean difference 0.28 kg, 95% CI 0.12–0.44 kg). These studies demonstrate that additional calories from SSB intake are not spontaneously compensated for by a reduction in other sources of calories at subsequent meals, which realistically simulates what happens in human populations.

The evidence from hypercaloric trials has been limited to adults. By contrast, studies that reduce SSB consumption (hypocaloric trials) have been conducted among children and adults. Our meta-analysis of hypocaloric trials in children showed a reduction in BMI gain over time when SSB intake was reduced. Of note, more pronounced benefits were observed among children with overweight and obesity compared with lean children. Similar results were observed in a meta-analysis of hypocaloric trials in adults and children that showed an overall benefit of reducing SSB intake on weight that was also more pronounced among participants with overweight and obesity. These findings are consistent with a 2020 trial that found that replacing SSBs with non-caloric beverages reduced body weight among adults with central adiposity. These meta-analyses of hypocaloric trials included many studies with limitations, including small sample size, short duration, lack of blinding and poor adherence. The majority were also effectiveness trials of behaviour modification, which test methods of intervention rather than causal relations. As such, a lack of benefit does not preclude causality but rather that the specific intervention modality might not have been effective in changing behaviours.

Two of the most rigorous RCTs to date, conducted in children and adolescents, have overcome many of the limitations of previous trials. These trials provided strong evidence for a benefit of replacing SSBs with non-caloric options on weight gain. Another meta-analysis of trials in adults found that under isoenergetic conditions where SSBs were replaced with other carbohydrates (isocaloric trials), no changes in body weight were observed. This finding suggests that SSBs contribute to weight change through changes in calories.
**Type 2 diabetes mellitus.** A substantial body of literature has demonstrated that intake of SSBs is associated with a higher risk of T2DM, both through body weight gain and independently through other metabolic pathways. Experimental evidence from RCTs is lacking owing to the high cost of running such trials and other feasibility constraints; however, findings from prospective cohort studies have shown consistent associations. For example, a meta-analysis of 17 prospective cohort studies found that an increase in SSB intake of one serving per day was associated with an 18% higher risk of T2DM (95% CI 9–28%) when estimates that did not adjust for BMI were used in the analysis. When estimates that did adjust for BMI were included, the association was attenuated to 13% (95% CI 6–21%), which suggests that BMI partially mediates the association. Positive associations were also observed between intakes of fruit juice and artificially-sweetened beverages (ASBs) and T2DM risk, although associations were not as strong as those observed for SSBs. This study also estimated that 8.7%
consistent with the literature on weight gain and T2DM, accumulating evidence has also linked intake of SSBs to risk of CVD. For example, a meta-analysis of seven prospective cohort studies found that SSB consumption was associated with a 9% higher risk of CVD when comparing extreme categories of intake (none or less than one per month versus one or more per day) (relative risk (RR) 1.09, 95% CI 1.01–1.18). The association was linear, with each one-serving per day increase in SSB intake associated with an 8% higher risk of CVD (RR 1.08, 95% CI 1.02–1.14). In stratified analysis, each serving per day increment was associated with a 15% higher risk of CHD (RR 1.15, 95% CI 1.09–1.22), whereas no significant association was observed with stroke (RR 1.05, 95% CI 0.95–1.16). These results are consistent with those of a previous meta-analysis that also found a null association with stroke. However, subgroup analyses in that study showed a significant positive association between SSB intake and ischaemic stroke among women (RR 1.33, 95% CI 1.07–1.66), whereas no associations were noted for men or for men or women with haemorrhagic stroke. Similar to studies in T2DM, when estimates were adjusted for BMI, the association between SSB and CHD was somewhat attenuated, suggesting adiposity as a partial mediator.

Evidence from cohort studies also supports a link between SSB intake and risk of the metabolic syndrome, a precursor for cardiometabolic diseases. A review of observational studies and trials among children found consistent evidence that cardiometabolic risk increases as intake of SSBs increases, with strong evidence noted for risk of increased adiposity and dyslipidaemia. Findings from short-term RCTs in adults exploring the effects of SSBs or their constituent sugars on intermediate risk factors for T2DM and CHD provide mechanistic support for the associations observed in epidemiological studies. For example, a meta-analysis...
of 39 RCTS with at least 2 weeks of intervention found that high versus low consumption of SSBs and/or sugar significantly raised serum concentrations of triglycerides (mean difference (MD) 0.11 mmol/l, 95% CI 0.07–0.15 mmol/l), total cholesterol (MD 0.16 mmol/l, 95% CI 0.10–0.24 mmol/l) and LDL cholesterol (MD 0.12 mmol/l, 95% CI 0.05–0.19 mmol/l)\(^a\). Intake of SSBs and/or sugar was also shown to statistically significantly increase blood pressure of participants in studies that were at least 8 weeks in duration (systolic blood pressure, MD 6.9 mm Hg, 95% CI 3.4–10.3 mmol/l; diastolic blood pressure, 5.6 mm Hg, 95% CI 2.5–8.8 mmol/l)\(^a\), consistent with cohort studies that have found positive associations between intake of SSBs and hypertension\(^a\). In a 2-week parallel-arm trial in which participants consumed beverages containing 10%, 17.5% or 25% of energy requirements from high-fructose corn syrup (HFCS) statistically significantly increased serum concentrations of postprandial triglycerides, LDL-cholesterol and uric acid in a linear dose-response manner\(^a\). In a 10-week trial conducted among participants with overweight, a sucrose-rich diet statistically significantly increased postprandial glycaemia, insulinemia and serum concentrations of lipids compared with a diet rich in artificial sweeteners\(^a\). A 3-week crossover trial among healthy-weight men found that consumption of moderate quantities of SSBs resulted in impaired glucose and lipid metabolism, and inflammation\(^a\). In other studies, the results on inflammatory markers have been inconsistent, possibly due to differences in study quality and duration\(^a\). Of note, a 2020 RCT by Ebbeling and colleagues found that replacing SSBs with ASBs or water for 12 months did not affect the triglyceride to HDL-cholesterol ratio or other cardiometabolic risk markers\(^a\). The authors posited that the null findings might have been due to compensatory changes in other dietary sources of carbohydrate, which are typically controlled for along with other measures of diet quality in cohort studies.

**Non-alcoholic fatty liver disease.** Accumulating evidence has linked intake of SSBs with development of non-alcoholic fatty liver disease (NAFLD), owing to metabolism of constituent sugars, particularly fructose moiities from sucrose or HFCS\(^3\). Meta-analyses of a limited number of epidemiological studies support a positive association between intake of SSBs and development of NAFLD in children and adults. Based on 12 studies (one cohort, two case–control and nine cross-sectional), Chen and colleagues found that each one serving per day increase in SSB intake was associated with a 39% higher risk of NAFLD (95% CI 29–50%)\(^4\). Similar findings in previous meta-analyses and qualitative reviews have been reported\(^3\). However, interpretation of these meta-analyses is complicated by the low quality of the included studies.

Meta-analyses of RCTs of fructose, sucrose and HFCS intake have found that among hypercaloric trials, providing excess energy of these sugars in healthy adults can raise intrahepatocellular lipids and serum concentrations of alanine transaminase, a biomarker of liver function\(^7\). However, in isocaloric trials, isocaloric exchange of fructose-containing sugars for other carbohydrates has been found not to induce NAFLD-associated changes, suggesting that the adverse effect of SSBs on the liver might be more attributable to excess calories than fructose\(^7\). Interestingly, isocaloric studies in animals have shown that fructose-fed rats develop features of the metabolic syndrome despite no differences in weight gain between groups and that hepatic steatosis can be induced with calorie restriction in the context of a high-sugar diet\(^7\). Larger, longer and higher-quality observational studies and RCTs on the relationship between SSBs and histopathological changes in NAFLD are required to address key research gaps.

**SSBs and gout.** Regular consumption of SSBs and fructose-containing sugars has also been associated in epidemiological studies with hyperuricaemia and gout. For example, a meta-analysis of three prospective cohort studies found a twofold higher risk of gout comparing the highest with the lowest intake of SSBs (RR 2.08, 95% CI 1.40–3.08)\(^4\). A dose–response association was also observed, with each serving per week increase in intake of SSBs associated with a 4% higher risk of gout (RR 1.04, 95% CI 1.02–1.07). In this study, a positive yet weaker association was observed between intake of fruit juice and gout, whereas no association was observed for intake of whole fruit\(^4\). These findings are consistent with cross-sectional studies linking SSB intake to hyperuricaemia\(^3\) and with RCTs that have demonstrated increases in serum concentrations of uric acid with intake of SSB or fructose\(^2\).

**SSBs and cancer.** Intake of SSBs might increase the risk of certain cancers through excess adiposity and cardiometabolic perturbations. Obesity, insulin resistance and T2DM are established risk factors for different cancers\(^3\). However, the epidemiological evidence for an association between SSB intake and the risk of cancer is limited and conflicting, which has precluded international health authorities from drawing firm conclusions\(^6\). This inconsistency is also reflected in meta-analyses and reviews. The most up-to-date meta-analysis, including 27 prospective cohort and case–control studies, found a positive association between SSB intake and breast cancer (RR 1.14, 95% CI 1.01–1.30) and prostate cancer (RR 1.18, 95% CI 1.10–1.27) and also between fruit juice intake and prostate cancer (RR: 1.03, 95% CI: 1.01–1.05), when comparing extreme categories of intake (as defined in the individual studies)\(^3\). A subgroup analysis also found a stronger association between SSB intake and the risk of premenopausal breast cancer, compared with the risk of postmenopausal breast cancer. A tendency also existed for positive associations between SSB intake and the risks of colorectal cancer and pancreatic cancer\(^3\). Associations were not observed between SSB intake and bladder or renal cell cancers.

Among the studies included in this meta-analysis\(^4\), the NutriNet-Santé study in a large French cohort found a positive association between SSB intake and overall cancer risk and breast cancer risk, with a stronger association with the risk of premenopausal breast...
cancer compared with postmenopausal breast cancer\(^6\). No associations were observed with prostate cancer or colorectal cancer risk, possibly owing to the limited number of cases as noted by the authors. In the Melbourne Collaborative Cohort Study, statistically significant positive associations were observed between SSB intake and postmenopausal breast cancer and colorectal cancer\(^8\). A positive association between SSB intake and postmenopausal breast cancer was also observed in the Seguimiento Universidad de Navarra (SUN) cohort in Spain\(^9\). In contrast, no associations were observed between sugary beverage (SSB or fruit juice) consumption and combined and site-specific (breast, prostate, colorectal) cancers associated with excess adiposity in the Framingham Offspring Cohort\(^10\). However, in a subgroup analysis, a positive association was observed between SSB consumption and cancer risk among participants with central adiposity\(^10\). A meta-analysis of food groups and risk of colorectal cancer found no association with SSBs\(^11\), which is consistent with an analysis in the California Teacher’s Study\(^12\). The evidence regarding SSBs and weight gain or type 2 diabetes mellitus (T2D) from cohort studies to be of low or moderate quality\(^20,34\). Meta-analyses using GrADe have typically rated the evidence on and a well-designed cohort study can simulate a trial when relevant confounders are accounted for\(^15\). Subgroup analysis using GrADe has typically rated the evidence on and a well-designed cohort study can simulate a trial when relevant confounders are accounted for\(^15\). Subgroup analysis using GrADe has typically rated the evidence on and a well-designed cohort study can simulate a trial when relevant confounders are accounted for\(^15\). Subgroup analysis using GrADe has typically rated the evidence on and a well-designed cohort study can simulate a trial when relevant confounders are accounted for\(^15\).

Although heterogeneity exists across these studies due to differences in population characteristics, study design and analysis strategies, the majority were adjusted for BMI. This fact suggests that pathways other than body weight gain might be implicated in the associations. Given the diverse aetiologies of site-specific cancers, additional research is warranted that explores intake of SSB by cancer type and in different ethnic groups, in which associations between SSB and cancer might vary\(^6\).

### Mortality

Consistent with the literature on clinical outcomes, evidence has shown a link between SSB intake and mortality. Our previous analysis in the Nurses’ Health Study (NHS) and Health Professional Follow-Up study (HPFS) found a positive dose–response association between SSBs and mortality that was largely driven by CVD mortality, with stronger associations observed among women than among men\(^13\). Consuming two or more SSBs per day was associated with a 31% higher risk of death from CVD (RR 1.31, 95% CI 1.15–1.50) than consuming none or less than one SSB per month\(^13\). A 2021 meta-analysis of six cohort studies found an 8% higher risk of CVD mortality per one serving per day increment in SSB (RR 1.08, 95% CI 1.04–1.13)\(^16\). In 2019, the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study, found that each additional serving per day of SSBs was associated with an 11% higher risk of all-cause mortality (RR 1.11, 95% CI 1.03–1.19)\(^14\). However, no association was observed for CHD mortality, possibly owing to the limited number of cases. Positive associations between SSB intake and mortality have also been found in the UK Biobank\(^3\) and the Western New York Exposures and Breast Cancer (WEB) Study\(^7\). In a 2020 study in Mexico, an estimated 6.9% (95% CI 5.4–8.5%) of adult deaths were attributable to SSBs, representing 40,842 excess deaths per year\(^7\). Similarly, based on NHANES data for 2012, an estimated 7.4% of all cardiometabolic-related deaths in the US were attributable to intake of SSBs\(^7\).

### Causality and strength of the evidence

The majority of evidence considered in this review was obtained from meta-analyses and systematic reviews, which provide overall summaries of the evidence. Meta-analyses of trials and prospective cohort studies are increasingly used to inform dietary recommendations, public policies and clinical practice guidelines, under-scoring the importance of quality and transparency in evidence synthesis. Best practices for meta-analysis require that authors conduct individual assessments of study quality, followed by an overall grading of the strength of the meta-evidence. The methods used to grade the evidence are critical, as findings are often used to guide recommendations or next steps in policy action. Multiple grading tools, which differ in how they rate evidence (particularly with respect to observational studies) are in common use [BOX 2]. This variation has led to some confusion regarding the strength of the evidence linking SSBs to weight gain and cardiometabolic outcomes. Given the constraints of RCTs in nutritional epidemiology, and the need for well-designed cohort studies of hard end points that are not feasible in trials (such as incident T2DM), evidence rating tools that support a variety of combinations of study designs will be the most informative for evidence grading in nutrition research.

### Underlying biological mechanisms

The leading biological mechanisms that link SSBs to weight gain include decreased satiety after consumption of SSBs than after consumption of solid food, and an incomplete compensatory reduction in energy intake\(^1\).
This model is supported indirectly by short-term feeding trials in healthy adults showing that consumption of SSBs leads to greater energy intake and weight gain than consumption of ASBs. Some evidence has also been provided by a limited number of studies in healthy adults showing that isocaloric consumption of liquid sugars leads to greater energy intake and weight gain than consumption of solid food. These studies suggest that calories consumed in the form of liquid beverages might not be satiating and might not be able to suppress intake of calories from foods consumed in subsequent meals to the level needed to maintain energy balance. Findings from studies in animals are consistent with this observation. However, the underlying mechanisms of this lack of compensatory response remain unknown. Fructose in SSBs is thought to potentially promote weight gain through inducing reductions in resting energy expenditure and through the induction of leptin resistance; however, further studies are needed to elucidate these pathways. Early introduction of SSBs might be particularly detrimental in children, as it might promote sweet taste preference.

**Sugar addiction.** Interest is growing in sugar addiction as a putative driver of excessive SSB intake. Consumption of sugar has been shown to release endogenous opioids in the nucleus accumbens, a primary site for reinforced behaviours in the brain, and to activate the dopaminergic reward system. Rats with intermittent access to sugar show the same decrease in levels of dopamine D2 receptor mRNA in the nucleus accumbens that occurs in morphine and cocaine addiction, and demonstrate characteristics of addiction such as escalation of intake, withdrawal and cravings. These findings suggest that sugary foods and beverages are potentially rewarding and can trigger addictive-like behaviours, which might be responsible for over-consumption. However, a variety of reviews on this topic are conflicting and findings in humans are less consistent than findings from studies in animals. Intake of sugars containing glucose and fructose has also been shown to induce the metabolic syndrome in mice in the absence of taste, probably due to over-consumption owing to post-ingestive reward signals. Whether these findings are applicable to humans is unknown.

**Glycaemic load.** Consumption of SSBs might also promote weight gain through adverse effects on metabolism, through their ability to induce rapid spikes in blood levels of glucose and insulin. In general, SSBs have moderate-to-high glycaemic index values, which in combination with the large quantities consumed contribute to a high dietary glycaemic load. Diets with a high glycaemic load might promote weight gain by raising the postprandial ratio of serum concentrations of insulin to glucagon, resulting in increased hunger and decreased energy expenditure. Individuals with increased central adiposity are more likely to have high insulin secretion in response to sugar consumption; thus, reducing glycaemic load among this group might have the most pronounced benefits on metabolism.

SSBs contribute to the development of cardiometabolic diseases and some cancers, in part through weight gain, but also through independent metabolic effects of glucose and fructose contained in constituent sugars. Through their contribution to a high glycaemic load diet, SSBs can promote insulin resistance, exacerbate inflammatory biomarkers, and have been associated with increased risk of T2DM and CHD. Habitual consumption of diets with a high glycaemic load might also influence cancer risk via hyperinsulinaemia and activation of the insulin-like growth factor axis. Studies in animals have suggested that the

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**Fig. 3 | Biological mechanisms for sugar-sweetened beverage intake and development of obesity, cardiometabolic risk and related chronic diseases.** Biological mechanisms linking intake of sugar-sweetened beverages (SSBs) to the development of obesity, intermediate cardiometabolic risk factors (such as non-alcoholic fatty liver disease, hypertension, insulin resistance, inflammation and dyslipidaemia) and related chronic diseases (the metabolic syndrome, type 2 diabetes mellitus (T2DM), cardiovascular disease and cancer). Mechanisms that promote weight gain and obesity include: an incomplete compensatory reduction in food intake in response to liquid calories provided by SSBs; hyperinsulinaemia induced by rapid absorption of glucose; and potential activation of the dopaminergic reward system in the brain. Obesity increases cardiometabolic risk and is associated with the development of related chronic diseases. Elevated risk of these outcomes also occurs independently of weight gain through the development of risk factors precipitated by adverse glycaemic effects and fructose metabolism in the liver. Excess fructose ingestion promotes uric acid production, hepatic de novo lipogenesis, accumulation of visceral adipose tissue (VAT) and ectopic lipid deposition, and can lead to the development of gout and non-alcoholic fatty liver disease. HFCS, high-fructose corn syrup. Adapted from Ref. \[CC BY 4.0 (https://creativecommons.org/ licences/by/4.0/).\]
metabolic effects of glucose might be partly driven by
the conversion of glucose to fructose in the liver\(^{102}\). Thus, fructose might have a role in how diets with a high
glycaemic load induce metabolic effects\(^{26}\).

**Fructose.** Fructose is consumed from SSBs as a com-
ponent of sucrose or HFCS and is thought to contribute to
cardiometabolic risk through its metabolic fate in the
liver. The absorption of fructose in the gut is enhanced
in the presence of glucose and this effect accounts for
the rapid and complete absorption of both monogly-
cerides when ingested as sucrose or HFCS, as found
in SSBs. Uptake of glucose in the liver is tightly regu-
lated; however, the hepatic uptake and metabolism of
fructose, which occurs through first-pass metabolism
via fructokinase, is unregulated\(^{104}\). When consumed
in moderation, fructose is converted to glucose, lac-
tate and fatty acids in the liver for use as metabolic
substrates\(^{104}\). However, when fructose is consumed in
excess, an increase in hepatic de novo lipogenesis occurs
that can lead to atherogenic dyslipidaemia and insulin
resistance. The amount of fructose needed to increase
blood lipid levels is debated; however, consuming HFCS-
sweetened beverages containing 10–25% of total daily
calorie requirements has been shown to produce nota-
ble linear increases in postprandial triglycerides. This
finding suggests a dose–response relationship between
fructose consumption and increases in triglycerides\(^{35}\).
Increased concentrations of lipid in the liver can upregu-
late the production and secretion of VLDL, which leads
to increased circulating levels of triglycerides. Excess
intake of fructose has also been associated with the
production of small dense LDL-C particles, resulting
from increased levels of VLDL-induced lipoprotein
remodelling\(^{106,107}\). Some studies have shown that intake of
fructose can promote the accumulation of visceral adi-
pose tissue and ectopic lipid deposition in humans\(^{106-109}\).
The metabolism of fructose in the liver can also deplete
intracellular ATP in hepatocytes, which can lead to
an increase in uric acid production. These fructose-
induced alterations to hepatic metabolism have implic-
cated SSBs in the development of NAFLD and other
metabolic complications\(^{110}\), possibly through cellular
energy homeostasis and mitochondrial oxidative stress\(^{40}\).
Studies in animals have suggested that fructose met-
alism is largely responsible for the effects of SSBs on
cardiometabolic diseases\(^{111,112}\).

**Uric acid production.** Fructose is the only sugar known to
increase hepatic uric acid production. Hyperuricaemia
is a precursor to gout\(^{113,114}\) and both gout and hyperuri-
casia have been associated with hypertension, T2DM
and CVD\(^{15,115}\). The development of hyperuricaemia has
been shown to precede the onset of obesity and T2DM.
Furthermore, hyperuricaemia might mediate the asso-
ciation between SSB intake and hypertension, possibly
through the induction of renal disease, endothelial
dysfunction and activation of the renin–angiotensin
system\(^{115}\). Excess production of uric acid has also been
linked to a reduction in nitric oxide levels in endothelial
cells, which might partially explain the link between
fructose-containing beverages and CHD\(^{115}\).

**Alternative beverages**

As public health measures continue to call for reduc-
tions in intake of SSBs to prevent weight gain and
cardiometabolic diseases, interest is growing in alterna-
tive beverages. Among these, ASBs have attracted the
most attention.

**ASBs.** Despite containing few calories and no sugar,
some cohort studies among adults have found positive
associations between intake of ASBs and weight gain and
the risks of T2DM and CVD\(^{14,41,117}\), which has obscured
dietary guidance. Interpretation of findings from these
studies is complicated, due to potential residual con-
 founding by unmeasured or poorly measured factors
linked to ASB intake. Reverse causation is also a con-
cern in these studies, since individuals with obesity
or with other risk factors for T2DM, such as elevated
blood glucose or insulin levels, might switch from SSBs
to ASBs and this scenario might drive spurious positive
associations\(^{118,119}\). Although it is difficult to address these
biases in statistical analyses, studies with repeated assess-
ments of diet are less prone to reverse causation, as they
enable changes in intake over time to be examined\(^{120}\).
These types of studies have shown marginal statistically
non-significant associations between ASBs and weight
and cardiometabolic outcomes\(^{22,23,121-123}\).

Substitution analyses in cohort studies have shown
inverse associations with weight gain, T2DM and mor-
tality when SSBs are replaced with ASBs\(^{24,73,124,125}\). These
findings are consistent with those of short-term trials
in different populations including healthy children,
and adults with and without overweight and obesity
that have shown modest benefits on body weight and
metabolic risk factors when SSBs are replaced with
ASBs\(^{126,127}\). However, a number of biological mechanisms
have been proposed that might link ASBs to weight gain
and adverse cardiometabolic health. For example, the
intense sweetness of artificial sweeteners might condi-
tion towards a taste preference for sweets. Furthermore,
ASBs stimulate sweet taste receptors and can activate the
cephalic phase insulin response (CPIR). ASBs might also
stimulate the release of gut hormones. In addition, neural
responses to ASBs might exert a food reward response.
Moreover, ASB consumption might modulate appetite
regulation. Finally, ASBs might cause alterations in the
gut microbiota\(^{47}\). Although intriguing, these mecha-
nisms are not well understood and different types of
artificial sweeteners might elicit different physiological
effects\(^{128}\). For example, saccharine and sucralose seem-
ingly stimulate the CPIR, whereas aspartame and stevia
do not\(^{124}\). A 2019 RCT in adults with overweight or obe-
sity illustrated modest reductions in weight with intake
of sucralose, modest weight gain with saccharine and
no effect on weight with intake of aspartame or stevia,
relative to sucrose\(^{124}\). Although the findings need to be
replicated, this study suggests that some of the inconsis-
tency observed in the epidemiological evidence might be
due to combined effects of different artificial sweeteners.
Given that ultra-processed foods might increase
weight gain independently of calories\(^{18}\), the processing
of both SSBs and ASBs could potentially be implicated in
obesity, although this hypothesis requires investigation.
Further studies are needed to better understand the effects of individual sweeteners and the consequences of consuming ASBs over the life-course. Based on the current evidence, consumption of ASBs in place of SSBs could be a helpful strategy to reduce cardiometabolic risk, with the ultimate goal of switching to water or other healthful beverages.

**Fruit juice.** Whether 100% fruit juice is an acceptable replacement for SSBs has also been a question of great interest. Fruit juice is often perceived as healthful, as most juices contain some vitamins and nutrients. However, some fruit juices contain similar amounts of calories and sugar to SSBs from the natural sugars present in fruit. Findings from cohort studies in the USA suggest that intake of fruit juice is associated with weight gain and the risk of T2DM, while the opposite has been shown for whole fruit. This finding can be explained by differences in the food matrix and effects on absorption. Sugars in juice are absorbed more quickly than those in whole fruit, owing in part to the fibre content of whole fruit, which slows the rate of absorption. The rapid absorption of liquid fructose from juice, combined with the large volumes that are sometimes consumed, can lead to increased concentrations of fructose in the liver and could drive de novo lipogenesis and the production of lipids. High intake of fruit juice has been associated with a higher risk of mortality compared with low intake. However, some benefits of fruit juice on cardiometabolic risk have also been reported. Further research on fruit juice is warranted, which should consider different types of juices that are consumed in different countries, as their nutrient profiles and sugar contents probably differ.

**Water, tea and coffee.** Water is free of sugar and calories and is considered the optimal beverage for hydration. In an analysis of the Harvard cohorts, we found that replacing one serving per day of SSBs with water was inversely associated with weight gain and risk of T2DM. With the growing demand for water, different types of sparkling and flavoured options (some containing artificial sweeteners) are now available, which might help habitual SSB consumers switch to water. Ensuring access to potable water and limiting use of plastic bottled water for both environmental and health reasons will be important initiatives when promoting water intake in place of SSBs.

A number of studies have shown that moderate consumption (two to five cups per day) of regular or decaffeinated coffee or tea is associated with decreased risk of T2DM and CVD, which is probably owing to the myriad of bioactive compounds in these beverages. In a substitution analysis, we found that replacing one serving per day of SSBs with coffee (decaffeinated and caffeinated; whether the coffee was sweetened was not specified) was associated with a 17% lower risk of T2DM. Provided there are no contraindications and that the use of caloric sweeteners and creamers is limited, coffee and tea can be healthful alternatives to SSBs. Certain groups such as pregnant women and children should consume caffeine-containing beverages with caution, as little is known about their effects in children, and excess caffeine could be harmful during pregnancy.

**Policies**

Based on the current evidence, national and international organizations recommend limiting intake of SSBs. The WHO, and US and Canadian dietary guidelines recommend an upper limit of 10% of total energy from all added sugar or free sugar; this recommendation is supported by numerous medical associations. Consistent with these recommendations, a number of public policies have been identified to help change SSB consumption patterns. The most common include SSB taxation, banning of sales and vending in schools, government restrictions on marketing unhealthy foods or beverages to children, public health education campaigns and front-of-package warning labels.

Several countries as well as some US cities have implemented excise taxes on SSBs as a strategy to curtail intake and generate revenue. In 2014, Mexico implemented a 10% excise tax (that is, 1 peso per litre) on SSBs, which sparked global interest. Two years after implementation, a 7.6% reduction in sales of SSBs was observed, while sales of untaxed beverages such as water increased by 2.1%. Based on modelled data, the potential effect of the tax was estimated to have prevented ~200,000 people from developing obesity and to have saved International $980 million in health-care costs between 2013 and 2022 (REF). Berkeley, California, was the first US city to implement a penny per ounce excise tax on SSBs.
comparing trends before and 1 year after tax implementation, a 9.6% reduction in sales of SSBs was observed while sales of untaxed beverages increased by 3.5%\textsuperscript{149}. A meta-analysis of studies evaluating SSB taxes found that taxation resulted in decreases in sales, purchasing and consumption of taxed beverages\textsuperscript{147,148}. More recently in 2018, the UK implemented a tiered tax on SSBs, based on sugar content (£0.24 per litre for drinks containing 2 g total sugar per 100 ml, and £0.18 per litre for drinks containing between 5 g and <8 g total sugar per 100 ml) that was designed to incentivize reformulation. Analyses of soft drink sugar content and sales illustrate the intended benefits following reformulation\textsuperscript{148,149}. Compared with pre-tax trends, 1 year after implementation there was no change in the volume of soft drinks purchased but the quantity of sugar purchased in these beverages decreased by 30 g per household per week\textsuperscript{150}. This finding suggests that a tiered tax might reduce sugar intake without harming industry sales. Whether these early benefits of SSB taxes will continue and translate into improvements in health will be important factors to monitor.

In the USA and Canada, the nutritional facts labels on packaged foods and beverages were recently revised (with respective compliance dates in 2021 and 2022) to require the added sugar (USA) and total sugar (Canada) content of packaged products to be displayed, with percentage daily values to help consumers meet sugar recommendations. Different types of front of package labels have been implemented in different countries, including traffic light labelling in the UK, the Nutri-Score in France, the star system in Australia and New Zealand, the Nordic keyhole in Norway, Denmark and France, the star system in Australia and New Zealand, and consumption of taxed beverages\textsuperscript{147}. More recently in 2018, the UK implemented a tiered tax on SSBs, based on sugar content (£0.24 per litre for drinks containing 2 g total sugar per 100 ml, and £0.18 per litre for drinks containing between 5 g and <8 g total sugar per 100 ml) that was designed to incentivize reformulation. Analyses of soft drink sugar content and sales illustrate the intended benefits following reformulation\textsuperscript{148,149}. Compared with pre-tax trends, 1 year after implementation there was no change in the volume of soft drinks purchased but the quantity of sugar purchased in these beverages decreased by 30 g per household per week\textsuperscript{150}. This finding suggests that a tiered tax might reduce sugar intake without harming industry sales. Whether these early benefits of SSB taxes will continue and translate into improvements in health will be important factors to monitor.

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To change SSB consumption patterns, a combination of policies across different levels of governance is needed, together with widespread public health education to serve as an important step in changing social norms surrounding beverage habits. A key priority for researchers and policymakers will be the continued evaluation of these policies in relation to short-term behaviour changes and clinical outcomes to ensure their effectiveness over time.

Conclusions

SSBs are consumed on a global scale, with intake levels above recommendations in many high-income countries and on the rise in LMICs. Based on the available evidence from prospective cohort studies that assessed long-term outcomes, as well as RCTs that assessed intermediate risk factors, strong evidence exists for an aetiological relationship between intake of SSBs and weight gain, and risk of T2DM, CHD and/or NAFLD. The evidence for other conditions, including stroke and specific types of cancer, is less consistent and further research is warranted. Although specific thresholds for intake of SSBs have not been identified as most observations are from dose–response analyses, clinically important weight gain and risk of attendant cardiometabolic conditions are associated with intake of SSBs at commonly consumed levels, such as one serving per day.

SSBs might promote weight gain through multiple mechanisms, including incomplete compensation for liquid calories by reductions in food intake at subsequent meals, hyperinsulinaemia induced by the rapid absorption of large amounts of sugar and possibly through neural pathways of food addiction. These beverages are thought to increase T2DM and cardiometabolic risk through weight gain. In addition, SSBs act independently of weight gain through a high glycaemic load and the unique metabolic effects of excess fructose in the liver, which has been linked to accumulation of visceral adipose tissue and ectopic lipid deposition, gout and NAFLD. Various policies and regulatory strategies to reduce intake of SSBs are in place or are being considered in several countries. Continued evaluation of these policies is needed in order to gauge their effectiveness over time. In addition, more and higher quality trials are required to identify new strategies or combinations of actions that are effective in reducing SSB intake at the individual and population level. Although policies targeting SSBs should not be considered a ‘magic bullet’ for obesity prevention, they can be effective in shifting consumption levels or social norms, which are important public health goals.

Key areas for which future research is warranted include examining the effects of different sugars on health outcomes over a broad range of doses, investigating the health effects of sugar consumed in solid form compared with liquid form and further elucidating biological mechanisms of energy compensation and sugar addiction. Important research gaps also exist regarding suitable alternative beverages, including the health effects of consuming ASBs over the life-course, examination of different types of juices and ensuring global access to potable water.

In the coming years, as the world grapples with rising obesity and chronic disease burdens alongside infectious diseases, such as the COVID-19 pandemic that has been worsened by obesity, there will be an urgent need for coordinated actions across all sectors of society to prioritize obesity prevention. These efforts should focus on nutrition policies and regulatory strategies aimed at improving overall diet quality, creating healthier food environments and reducing health disparities. Given the strength and consistency of the evidence across different populations and increased consumption patterns associated with nutrition transitions, SSBs present a clear target for policy action. With the high intake levels across the globe, reducing consumption of SSBs remains an important step in improving diet quality, which could have a measurable effect on weight control and in improving global health.

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Author contributions
The authors contributed equally to all aspects of the article.

Competing interests
V.S.M. is on a pro bono retainer for expert support for litigations related to sugar-sweetened beverages and has served as a consultant for the City of San Francisco for a case related to health warning labels on soda. There are no other financial or personal conflicts of interest to disclose that are related to the content of this paper. F.B.H. declares no competing interests.

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