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# Frequent Sugar-Sweetened Beverage Consumption and the Onset of Cardiometabolic Diseases: Cause for Concern?

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The incidence of noncommunicable diseases is on the rise and poses a major threat to global public health. This is in parallel to a steady increase in worldwide intake of sugar-sweetened beverages (SSBs) among all age groups. As several studies demonstrated a controversial relationship between SSB consumption and the metabolic syndrome (MetS), this mini-review focuses on links between its intake and (1) MetS, (2) prediabetes/type 2 diabetes mellitus (T2DM), and (3) hypertension. A detailed search for clinical and observational studies published during the past 10 years was conducted using key terms that link SSBs to the MetS, T2DM, and hypertension. Here we excluded all meta-analyses and also literature that solely focused on obesity. The analysis revealed that most epidemiological studies strongly show that frequent SSB intake contributes to the onset of the MetS in the longer term. Some of the findings also show that regular SSB intake can alter glucose handling and insulin sensitivity, thereby contributing to the development of the MetS and T2DM. There is also evidence that frequent SSB intake (and particularly fructose) is linked to hypertension and well-known cardiovascular disease risk factors. However, some studies report on the lack of negative effects as a result of SSB consumption. Because of this discrepancy, we propose that well-designed long-term clinical studies should further enhance our understanding regarding the links between SSB consumption and the onset of cardiometabolic diseases.



**Freeform/Key Words:** cardiometabolic risk, hypertension, metabolic syndrome, sugar-sweetened beverages, type 2 diabetes mellitus

During 2011, the United Nations announced for the first time that noncommunicable diseases pose a greater health risk than infectious diseases in both developed and developing countries [1]. The World Health Organization estimates that noncommunicable diseases result in 38 million deaths annually, with cardiometabolic diseases accounting for ~19 million fatalities [2]. The umbrella term *cardiometabolic diseases* describes both cardiovascular diseases (CVDs) and conditions such as the metabolic syndrome (MetS) and type 2 diabetes mellitus (T2DM). Furthermore, obesity, MetS, and T2DM are all risk factors for the onset of CVD, the current leading cause of global mortality [3]. Beside such risk factors, sugar-sweetened beverage (SSB) intake can also drive CVD onset by promoting hypertension, inflammation, and dyslipidemia [4].

The increased prevalence of cardiometabolic disorders is strongly linked to greater urbanization and the adoption of detrimental lifestyle choices that include sedentary behavior, smoking, and poor dietary preferences. For example, excess sugar consumption has surfaced

Abbreviations: BMI, body mass index; CI, confidence interval; CVD, cardiovascular disease; MetS, metabolic syndrome; SSB, sugar-sweetened beverage; T2DM, type 2 diabetes mellitus.

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as one of the most prominent global dietary changes during the past few decades and is considered a primary driver of cardiometabolic disease onset [5]. In support, a 5-year South African Adult Prospective Urban and Rural Epidemiology cohort study showed an association between higher consumption of added sugars and sucrose-sweetened beverages with increased noncommunicable disease risk factors [6]. It was also recently established that 74% of the 85,451 different edible products (mainly cereals, energy bars, and beverages) on the US market contained added sugars [7]. Here SSBs emerge as a strong culprit with estimates showing that it provides ~46% of added sugars [8]. Nevertheless, there is controversy regarding findings from various studies investigating the relationship between SSBs and the onset of cardiometabolic diseases [9–13]. In light of this, the current mini-review explores the links between SSB intake and the risks for cardiometabolic disease development, focusing on three main aspects: MetS, T2DM, and hypertension.

## 1. Methods

For the present review, three searches for clinical (including all clinical trial phases, clinical studies, controlled clinical trials, randomized controlled trials) and observational studies were performed. Meta-analyses and systematic reviews were not considered for this review process. The term *sugar* is often being used to represent a range of different molecules, and for the purposes of the current review article, it includes sucrose, glucose, fructose, high-fructose corn syrup, and artificial sweeteners. The first search was performed on the link between SSBs and the MetS where we used two keyword combinations: *sugar-sweetened beverages and metabolic syndrome* and *sugar-sweetened beverages and cardiometabolic risk*. The search was performed in PubMed (https://www.ncbi.nlm.nih.gov/pubmed/) and only human studies (written in English) and published within the past decade were selected. This search yielded a total of 12 results.

For the second search, we aimed to establish the link between SSBs and the risk for T2DM. Using the same parameters mentioned previously, the search phrases included *sugar-sweetened beverages and type 2 diabetes* and *sugar-sweetened beverages and prediabetes*. This search yielded a total of 16 results. The third search focused on SSBs and hypertension using the same parameters described previously. Here search terms included *sugar-sweetened beverages and hypertension* and *sugar-sweetened beverages and blood pressure*. The search yielded a total of eight results.

The searches are the latest as of September 2017. The extra literature included in this review was identified separately (not using our systematic review criteria) to demonstrate additional aspects within this field. Although obesity forms a component of MetS, it will not be reviewed in detail as it falls beyond the scope of the current mini-review. During such searches, we observed that there was an overlap with some of the articles as would be predicted because the MetS includes impaired glucose metabolism and increased blood pressure.

## 2. Results

We have structured our results in the same way as the search criteria stipulated in the Methods section of this article.

### *A. SSBs and the MetS/Cardiometabolic Risk*

The literature revealed, at times, contradictory observations in terms of the relationship between SSBs and the MetS. High SSB consumption is considered a risk factor for the onset of the MetS [4], which refers to a cluster of complications that manifest concurrently and serves as a prognostic tool for the future development of T2DM and CVD. Limited clinical and observational trials assess the contribution of SSBs to the MetS. Here some studies do show a

direct correlation [14], whereas in other cases, there is a lack of sufficient evidence to link SSBs to all the comorbidities associated with the MetS [15, 16].

Despite such contradictory findings, most studies thus far completed support a link between SSB intake and the MetS. Here all but one of the studies showed that SSBs promote the risk of developing some or all the components of the MetS [14–24]. In support, Dhingra *et al.* [17] found that the odds of developing the MetS (the mean follow-up period was 4 years) is significantly higher in individuals who consume one or more SSB servings daily [odds ratio,1.44; 95% confidence interval (CI), 1.20 to 1.74). The Prevención con Dieta Mediterránea prospective study also found that the frequent intake of SSBs (>5 servings/wk), artificially sweetened beverages, and natural and bottled fruit juices was associated with an increased risk for the MetS and some of its components [25]. SSB effects are also related to ethnicity; for example, African Americans (28 to 40 years old) who consumed relatively higher SSB amounts (>2 per day), but not moderate dosages, displayed kidney damage as indicated by increased levels of microalbuminuria [26].

De Ruyter *et al.* [27] conducted a small study to establish whether SSB consumption induced weight gain. Here children (4 to 11 years old) of normal weight were assigned to either experimental or control groups in a double-blinded manner and were expected to consume 250 mL SSB or 250 mL artificially sweetened beverage, respectively, on a daily basis. The authors found that body weight, body mass index (BMI), waist circumference, waist-to-hip ratio, and body fat percentage increased significantly in the SSB group compared with the artificially sweetened group after the 18-month intervention period. A substantial increase in body weight and BMI was observed only in the group consuming glucose-sweetened beverages, whereas sucrose- and fructose-sweetened drinks induced changes in the waist circumference and waist-to-hip ratio. Of note, others found a decrease in body weight and BMI in fructose-consuming participants [28], whereas another study also did not support the link between SSB consumption and weight gain [29]. This could possibly be explained by the shorter intervention period (6 months), although the intervention itself was more intense (1 L sucrose-sweetened beverage/d compared with 250 mL/d).

SSB consumption may also trigger effects that occur independently of body weight and energy balance changes. For example, some reported increased low-density lipoprotein cholesterol levels that were induced by the intake of fructose-sweetened beverages [30]. Here metabolites such as triglycerides, fasting blood glucose, and uric acid levels also increased in a dose-dependent manner with SSB intake. Bruun *et al.* [31] reported similar findings (*i.e.*, the daily intake of regular cola for 6 months enhanced circulating uric acid levels in overweight and obese participants). Other cross-sectional studies in adolescents also showed that SSB increased serum uric acid in association with hypertension [32] and pediatric insulin resistance [33]. By contrast, some established that moderate SSB intake did not affect fasting or postprandial cholesterol and triglyceride levels or hepatic insulin clearance [34]. The lack of any effects might be attributed to the short duration of the study (only done over a 2-week period), thus providing a likely explanation why no discernable effects were observed at this relatively early time point.

In addition to ethnicity, sex is also a factor that may account for the different observations discussed. In support, a recent prospective study by Kang and Kim [35] showed increased MetS parameters were associated with frequent consumers of soft drinks (>4 servings/wk), but only in females and not in men. Together, the bulk of epidemiological data strongly indicates that frequent SSB intake is linked to the MetS, with potentially serious long-term effects on overall health and well-being (Table 1).

### *B. SSBs and Prediabetes/T2DM*

Epidemiological studies reported that regular SSB consumption, in some cases as little as two SSB servings per week, is linked to a greater risk for the development of T2DM (36, 37). The negative effects of SSB consumption may also further exacerbate the already impaired glucose metabolism underlying T2DM [38]. As most studies used specific intervals of SSB

**Table 1. SSB Consumption and Risk of MetS**

| Author | Cohort/Location | Participants | | | Average Follow-up Period |
|---|---|---|---|---|---|
| | | N | Age (Mean/ Range), y | Sex | |
| Barrio-Lopez *et al.* (14) | SUN Project; Spain | 8157 | 36 | M and F | 6 y |
| Khosravi-Boroujeni *et al.* (15) | Iran | 1752 | 39.4 ± 14.2 (F); 41.6 ± 16.7 (M) | M and F | Cross-sectional study |
| Chan *et al.* (16) | Taiwan | 2727 | 12–16 | M and F | Cross-sectional study |
| Wang *et al.* (18) | QUALITY study, Canada | 633 | 8–10 | M and F | 8 y |
| Hernandez-Cordero *et al.* (19) | Mexico | 240 | 18–45 | F | 9 mo |
| Mattei *et al.* (20) | Costa Rica | 1872 | 49–70.3 | M and F | Cross-sectional study |
| Denova-Gutierrez *et al.* (21) | Mexico | 8307 | 20–70 | M and F | Cross-sectional study |
| Loh *et al.* (22) | Malaysia | 873 | 13 | M and F | Cross-sectional study |
| Dhingra *et al.* (17) | Framingham Offspring study; United States | 6039 | 46–66 | M and F | Cross-sectional study |
| Duffey *et al.* (23) | CARDIA study; United States | 2774 | 25 ± 3.6 (at start) | M and F | 20 y |
| Ambrosini *et al.* (24) | Raine study; Australia | 1433 | 14 (at start) | M and F | 14 y |
| Ferreira- Pêgo *et al.* (25) | PREDIMED; Spain | 1868 | M: 55–80 F: 60–80 (at start) | M and F | |
| Kang and Kim (35) | KoGES | 5797 | 40–69 | | 10 y |

consumption (lowest: <1 SSB per month; highest: ≥1 SSB per day), Fagherazzi *et al.* [5] designed a model to describe the continuous correlation between SSB consumption and T2DM development. These findings revealed that the consumption of SSB (0 to 1000 mL/wk) is directly related to a greater T2DM risk (relative risk, 1.3; 95% CI, 1.03 to 1.66) [39]. Moreover, the 14-year prospective Framingham study showed an association between increased insulin resistance and a higher risk of developing prediabetes with regular SSB intake but not for

**Table 1. Continued**

| Range of SSB Intake/d | Elevated Risk Factors of MetS | *P* Value for Trends | Confounder Adjustment |
|---|---|---|---|
| 0–2.4 servings | BP; WC; TAG | BP ($P < 0.001$); WC ($P < 0.001$); TAG ($P = 0.016$) | Yes |
| <1/wk to >3/wk | DBP in females | $P < 0.05$ | Yes |
| 0/d; 1–500 mL/d and >500 mL/d | WC; TGs; SBP in males | Metabolic risk cluster (*P*-trend < 0.038); SBP males ($P = 0.043$) | Yes |
| Median SSB intake 146 mL/d | HOMA-IR; SBP; WC | In overweight children, HOMA-IR (increase) ($P = 0.009$); SBP ($P = 0.001$); in children with impaired glucose tolerance, SBP higher by (>1.4 mm Hg); WC ($P < 0.001$) | Yes |
| 418 ± 11 mL/d | No elevated risk factors observed | NA | No |
| None to ≥1 serving /d | WC; TGs; higher odds of MetS | WC ($P \leq 0.001$); TGs ($P \leq 0.001$); MetS ($P = 0.009$) | Yes |
| None to >2 servings/d | Prevalence of MetS higher in obese subjects; increased TGs; reduced HDL | 26.65 obese people had MetS; 0.49-mmol/L increase in TGs/additional SSB consumption; 0.39-mmol/l decrease in HDL/additional SSB consumption | Yes |
| 110–190 mL/d | Elevated TGs; FBG; insulin; insulin resistance; low HDL-C | None were statistically significant | Yes |
| <1 to ≥2 servings/d | Increased prevalence of MetS; obesity; WC; fasting glucose; blood pressure; TGs; HDL | Increased MetS (OR, 1.48; 95% CI, 1.30–1.69); Obesity (OR, 1.31; 95% CI, 1.02–1.68); WC (OR, 1.30; 95% CI, 1.09–1.56); fasting glucose (OR, 1.25; 95% CI, 1.05–1.48); BP (OR, 1.18; 95% CI, 0.96–1.44); TGs (OR, 1.25; 95% CI, 1.04–1.51); HDL (OR, 1.32; 95% CI, 1.06–1.64) | Yes |
| Average intake over 7 y | WC; TG; LDL; hypertension | WC ($P < 0.001$); TGs ($P = 0.033$); LDL ($P = 0.018$); hypertension ($P = 0.023$) | Yes |
| None to >1.3 servings/d | BMI; obesity risk; TGs; HDL | Girls consuming >1.3 servings/d had increased BMI and obesity risk (*P*-trend ≤ 0.001); girls and boys consuming >1.3 servings/d show increased TGs (*P*-trend ≤ 0.03); boys show reduced HDL (*P*-trend < 0.04) | |
| <1 to >5/wk | | | Yes |
| <1 to >5/wk | BMI; fasting glucose; blood pressure; TGs; HDL | Females consuming >4 servings/wk showed increased BMI ($P = 0.0095$); systolic blood pressure ($P = 0.0086$); fasting glucose ($P = 0.0150$) | Yes |

Abbreviations: BP, blood pressure; CARDIA, coronary artery risk development in young adults; CI, confidence interval; DBP, diastolic blood pressure; F, female; FBG, fasting blood glucose; HDL, high-density lipoprotein; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, HOMA-IR, homeostatic model assessment–insulin resistance; KoGES, Korean Genome and Epidemiology Study; LDL, low-density lipoprotein; M, male; NA, not applicable; OR, odds ratio; QUALITY, Quebec Adipose and Lifestyle Investigation in Youth; SBP, systolic blood pressure; SUN, Seguimiento Universidad de Navarra; TAG, triacylglycerol; TG, triglyceride; WC, waist circumference.

**Table 2. SSB Consumption and Risk of T2DM**

| Author | Cohort/Location | Participants | | | Average Follow-up Period |
|---|---|---|---|---|---|
| | | N | Age (Mean/ Range), y | Sex | |
| De Koning *et al.* (42) | HPFS; United States | 40,389 (2680 developed diabetes) | 40–75 | M and F | 20 y |
| Fagherazzi *et al.* (5) | E3N study; France | 66,118 | 52.6 ± 6.6 | F | 14 y |
| The InterAct Consortium (37) | EPIC database; 8 European countries | 11,684 | 41–62 | M and F | 16 y |
| Lofvenborg *et al.* (10) | ESTRID study; Sweden | 2864 | 45.2–71.8 | M and F | 5 y |
| Maki *et al.* (43) | | 43 (n = 21 for SSB) | 53.8 ± 2.1 | M and F | 14 wk |
| Palmer *et al.* (39) | Black Women's Health Study, United States | 43,960 | 29–49 | F | 10 y |
| Sakurai *et al.* (41) | Japan | 2037 | 35–55 | M | 7 y |
| Teshima *et al.* (44) | Mihama Diabetes Prevention Study; Japan | 93 | 40–69 | M and F | 3.6 ± 0.2 y |
| Odegaard *et al.* (36) | Singapore | 43,580 | 45–74 | M and F | 5.7 y |

diet-type beverages [40]. In addition, ethnicity, sex, and age may influence the interplay between SSB intake and the onset of T2DM [41] (Table 2).

Daily SSB intake for 6 months also increased ectopic fat accumulation (liver, skeletal muscle, visceral depots) [29], whereas another study reported that replacement of SSBs with artificially sweetened beverages decreased intrahepatic fat over a 12-week period [45]. As ectopic fat accumulation is linked to insulin resistance and T2DM, this may represent early signs of longer-term damaging effects elicited by regular SSB intake. A 4-week observational study in which healthy participants received SSB supplementation showed a metabolic adaptation with a shift toward carbohydrates, increasing glycolytic and lipogenic gene expression that is likely the cause of altered glucose metabolism [46]. Similarly, a cross-sectional observational study showed altered glucose homeostasis following consumption of SSB vs consumption of dairy products [43]. A prediction-type study found that a 10% to 12% reduction in SSB consumption would lower new cases of diabetes, coronary heart disease, and myocardial infarctions [9]. Of note, this reduction is projected to have the most impact on African Americans, especially those who fall within the lower-income bracket [9]. Despite some contradictory studies, the collective data at present provide robust evidence that SSB intake plays a central role in the onset of T2DM.

### *C. SSBs and Hypertension/Blood Pressure*

Obesity, MetS, and T2DM are all risk factors for the onset of CVD, the leading cause of global mortality [3]. Besides such risk factors, SSB intake can also drive the onset of CVD by promoting hypertension, inflammation, and dyslipidemia [4]. For example, Kim *et al.* [47] found that daily SSB consumption (≥1 to <3 servings) is linked to an increased risk for developing hypertension (odds ratio, 1.43; 95% CI, 0.93 to 2.20) (refer to Table 3). Some studies show that SSB intake specifically elevates systolic blood pressure [32, 48], whereas others found that it raised diastolic blood pressure [53]. However, one such study [32] was criticized as the published adult norms were directly applied to an adolescent cohort (54). A pooled

**Table 2. Continued**

| Mean SSB Intake/d | Risk of T2DM | *P* Value for Trend | Confounder Adjustment |
|---|---|---|---|
| 887 mL/d | HR, 1.25 (95% CI, 1.11–1.39) vs nonconsumers | <0.01 | Yes |
| 328.3 mL/d | HR, 1.34 (95% CI, 1.05–1.71) vs nonconsumers | 0.0002 | Yes |
| <1 glass/mo to ≥1 glass/d | HR, 1.22 (95% CI, 1.09–1.38) increase with one serving of SSB | 0.86 | Yes |
| None to >2 servings/d | OR increased to 2.39 (95% CI, 1.39–4.09); 20% increase with each additional serving | Not available | Yes |
| 2160 ± 91.7 kcal/d | SSB consumption is associated with less favorable values for T2DM risk | Not available | Yes |
| <1 to ≥2/d | Incident rate ratio was 1.51 (95% CI, 1.31–1.75) vs fruit juice | 0.002 | Yes |
| 0 to ≥1 serving/d | HR, 1.34 (0.72– 2.36), ≥ 1 serving/d vs rare/never | 0.424 | Yes |
| No intake to daily intake | OR, 3.26 (95% CI, 1.17–9.06) vs no SSB intake | 0.001 | No |
| None to 2–3 servings/wk | RR, 1.42 (95% CI, 1.25–1.62) vs no SSB intake | *P*-trend < 0.0001 | Yes |

Abbreviations: CI, confidence interval; ESTRID, Epidemiological Study of Risk Factors for LADA and Type 2 Diabetes; E3N, Etude Epidémiologique auprès des femmes de la Mutuelle Générale de l'Education Nationale; F, female; HPFS, Health Professionals Follow-up Study; HR, hazard ratio; M, male; OR, odds ratio; RR, relative risk.

analysis of three prospective cohorts (Nurses' Health Studies I and II and the Health Professionals Follow-up Study; total N > 220,000) supports the notion that there is a higher incidence of hypertension among those consuming ≥1 SSB serving/d compared with nonconsumers (RR, 1.13; 95% CI, 1.09 to 1.17) [50]. Interestingly, the association between carbonated drinks and hypertension was also significantly stronger compared with noncarbonated ones for all three cohorts, whereas the consumption of cola-containing SSBs also indicated a robust link to hypertension compared with noncola ones (Nurses' Health Study I; Health Professionals Follow-up Study). Other prospective studies provide additional evidence for an association between regular SSB intake and the development of hypertension [24], whereas some demonstrated that blood pressure can be successfully lowered by decreasing SSB consumption [49]. In support, some showed beneficial effects of artificial sweetener consumption (erythritol) on reducing arterial stiffness and antihypertensive effects in the context of T2DM [55]. Although most studies detect a positive association between SSB consumption and hypertension, the adjusted risk is not always significant [17, 24], and it is therefore essential that more robust interventional studies be initiated to confirm such findings.

The International Study of Macro/Micro-Nutrients and Blood Pressure found that participants consuming >1 SSB serving/d exhibited statistically significant increases in systolic and diastolic blood pressures [48]. They also discovered that the mean energy intake was lower in nonconsumers compared with those who consumed ≤1 SSB serving/d and even significantly lower in those who consumed >1 SSB serving/d. These participants also displayed a higher BMI vs nonconsumers (30.2 vs 28.4 kg/m$^2$) [48]. In support, others found a significantly higher risk for hypertension with increasing SSB intake (especially in females); that is, hazard ratios for new-onset hypertension were 1.01 (95% CI, 0.99 to 1.03; 1 to 4 SSB/mo), 1.06 (95% CI, 1.03 to 1.08; 2 to 6 SSB/wk), and 1.13 (95% CI, 1.09 to 1.17; ≥1 SSB/d) vs those who consumed ≤1 SSB/mo [50]. Furthermore, Sayon-Orea *et al.* [51] identified 1308

**Table 3. SSB Consumption and Risk of Hypertension**

| Author | Cohort/Location | Participants | | | Average Follow-up Period |
|---|---|---|---|---|---|
| | | N | Age (Mean/ Range), y | Sex | |
| Brown *et al.* (48) | INTERMAP; United States, United Kingdom | 2696 | 48.8–50.8 | M and F | 3 y |
| Chen *et al.* (49) | PREMIER; United States | 810 | 25–79 | M and F | 18 mo |
| Cohen *et al.* (50) | NHS I, NHS II and HPFS; United States | 223,891 | 39–52 (NHS I); 31–40 (NHS II); 42–63 (HPFS) | F (NHS I); F (NHS II); M and F (HPFS) | 38 y (NHS I); 16 y (NHS II); 22 y (HPFS) |
| Green *et al.* (11) | Cohort used from Framingham; United States | 5107 | 40.8–53.9 (combined) | M and F | |
| Sayon-Orea *et al.* (51) | SUN; Spain | 1308/13,843 | 36.4 | M and F | 8.1 y |
| Souza *et al.* (52) | Brazil | 559 | 9–16 | M and F | Once off study |
| Kim *et al.* (47) | NHANES; South Korea | 3044 | ≥19 | M and F | Cross-sectional study |
| Nguyen *et al.* (32) | NHANES; United States | 4867 | 12–18 | M and F | Cross-sectional study |

new hypertension cases in their 6-year follow-up Seguimiento Universidad de Navarra Study and established that increased SSB consumption was associated with 26% higher odds of developing hypertension—this association was especially strong in women.

One study compared blood pressures in adolescents from 20 public schools in Brazil [52], and after adjusting for confounding factors, they found higher systolic blood pressure and diastolic blood pressure values for youngsters consuming SSBs. Others investigated the effects of the monosaccharides glucose, fructose, and sucrose on blood pressure. Here they showed that fructose and glucose triggered opposite effects, with fructose resulting in increased blood pressure due to increased total peripheral resistance, unlike glucose [56]. The impact of varying SSB doses within this context is best demonstrated by focusing on studies aiming to lower consumption. For example, a reduction of 1 SSB serving/d resulted in a decrease of 2 and 1.2 mm Hg in systolic and diastolic blood pressures, respectively [49].

## 3. Discussion

Long-term epidemiological studies provide sufficient evidence to prove a positive association between SSB and weight gain and the eventual risk for developing MetS [4]. However, it is important to also consider studies (limited number) that report negative or neutral results with SSB intake. Here the lack of standardization of measurements used to assess obesity can make it difficult to interpret and compare the results of various published studies [57]. For example, although some only measured weight gain, others determined BMI, waist-to-hip ratio, and skinfold thickness (all markers of obesity).

SSBs are energy dense, and their consumption is associated with excessive caloric intake and subsequent weight gain [58], and such changes can induce cardiometabolic perturbations. For example, SSB drinkers—especially young African Americans—are more likely to consume salty and sweet snacks [59]. In a study on the Australian population, SSBs contributed

**Table 3. Continued**

| Maximum SSB Intake | Mean Systolic Pressure (mm Hg) After High SSB Intake | Mean Diastolic Pressure (mm Hg) After High SSB Intake | *P* Value for Trend | Confounder Adjustment |
|---|---|---|---|---|
| 306 mL/d (United States)<br>66 mL/d (United Kingdom) | 122.5 mm Hg | 75.5 mm Hg | <0.001 | Yes |
| 310.5 ± 351.9 mL/d | 133.2 mm Hg | 85.0 mm Hg | 0.57 (SBP); 0.01 (DBP) | Yes |
| 354.8 mL/d | >140 mm Hg (HPFS) | >90 mm Hg (HPFS); HR, 1.13 (95% CI, 1.09–1.17) ≥1 serving/d vs <1/mo | Not stated | Yes |
| 354.8 mL/d (7 servings/wk) | 54.6% increase in SBP vs normal weight | 59.7% increase in DBP vs normal weight | <0.001 | Yes |
| ≥354.8 mL/d (≥ 7 servings/wk) | HR, 1.33 (95% CI, 1.08–1.68) vs no SSB consumption | | 0.007 | Yes |
| +709.6 mL/d (+2 servings/d) | 102.6 mm Hg | 58.8 mm Hg | 0.01 (SBP); 0.04 (DBP) | Yes |
| None to 6 times/d | SSBs 3 times/d associated with 1.74 times higher prevalence of hypertension (95% CI, 1.00–3.01) | | 0.05 | Yes |
| 0 to >36 oz/d | Data not shown | Data not shown | 0.03 (SBP); 0.09 (DBP) | Yes |

Abbreviations: CI, confidence interval; DBP, diastolic blood pressure; F, female; HPFS, Health Professionals Follow-up Study; HR, hazard ratio; M, male; NHANES, National Health and Nutritional Examination Survey; NHS, Nurses' Health Study; PREMIER, a randomized trial to determine the effects of multi-component lifestyle interventions on blood pressure; SBP, systolic blood pressure.

to the highest added sugar intake, causing more than half of the total population to exceed the free sugar intake norms set by the World Health Organization [60]. Alarmingly, this effect was predominantly observed in children and adolescents. Epidemiological studies are not sufficient to establish causality between SSB consumption and the development of cardiometabolic diseases. For this reason, there is a great need for clinical intervention studies to support existing findings. Clinical studies may also help reveal plausible molecular mechanisms—a necessary step in establishing causality between SSB consumption and cardiometabolic pathophysiology [61]. These findings may provide some insights into the mechanisms at play and may help explain why some failed to detect changes in body weight. Unfortunately, there are limited clinical findings available regarding SSB intake and the onset of cardiometabolic diseases, and most of the available studies have some drawbacks as reviewed before [62].

An assessment of the metabolic health of 5107 individuals from the Framingham Heart Study Offspring and third-generation cohorts showed that, irrespective of weight, SSB consumers were at a higher risk for the onset of metabolic abnormalities such as hypertension, insulin resistance, high fasting glucose and triglycerides, and lower high-density lipoprotein cholesterol levels [11]. Aerberli *et al.* [63] explained that higher glucose consumption stimulates an intensified insulin response to promote the deposition of subcutaneous fat, thereby increasing the BMI. By contrast, fructose (and sucrose to some extent) possesses a lower glycemic load and does not trigger the release of insulin to the same degree as glucose. Thus, the activity of lipoprotein lipase is reduced and the deposition of visceral fat is favored, resulting in an increase in waist circumference and waist-to-hip ratio (also concluded by Stanhope *et al.* [30]). Waist circumference and waist-to-hip ratio are markers of

abdominal obesity—a key feature of the MetS—indicating that SSB consumption can elicit detrimental consequences even if it does not always reflect in overall body weight.

Some studies also provide insight into the effects on glucose handling; for example, some found that SSB intake attenuated insulin sensitivity [43]. Moreover, participants consuming glucose- or fructose-sweetened drinks display elevated fasting blood glucose levels [30, 63]. This is a noteworthy result considering that such beverage intake elicited no effects on fasting insulin levels. Here glucose consumption resulted in a spike in insulin levels [30], whereas it decreased in response to fructose intake. Indeed, individuals consuming either glucose- or fructose-sweetened beverages for 10 weeks displayed a ~17% decrease in insulin sensitivity with fructose consumption, explaining the rise in fasting blood glucose levels associated with fructose intake [30]. Of note, the adverse effects of SSBs are mainly attributed to the fructose component as it has been suggested to upregulate lipid production, leading to increases in liver fat content [30, 64]. The lack of negative effects observed with diet-type beverages in some of the studies may possibly result due to its effect on gut hormones (*e.g.*, glucagon-like peptide 1) that promote insulin secretion [65].

After careful examination of the available clinical studies, it is clear that SSB consumption does trigger metabolic perturbations together with the development of obesity. Here some of the findings show that frequent SSB consumption can alter hepatic insulin sensitivity and fat accumulation, thereby contributing to the development of the MetS and T2DM. SSB intake is also linked to dyslipidemia, higher uric acid levels, and inflammation (known CVD risk factors) [4]. Although none of the clinical studies support a link between SSB consumption and the onset of hypertension, there is some support for a link between SSB intake and inflammation. For example, some observed higher C-reactive protein levels of young men consuming SSB for a 3-week period [28, 63].

SSB consumption has been widely studied in different ethnic groups as well as varying age groups. The consumption of SSB is closely linked to socioeconomic class, with poorer communities displaying relatively higher intakes compared with their more affluent counterparts. For example, the Native American Indian population exhibits a relatively high prevalence of obesity and T2DM, and here it was reported that a significant percentage of Navajo girls and boys consumed SSBs (86% and 93%, respectively) [66]. Together these studies show that SSB intake not only is detrimental to the adult population but extends to adolescents as well and that its effects may vary depending on ethnicity.

## 4. Conclusion

Recent data show that SSB consumption has increased globally, thus putting many at risk for the onset of weight gain, T2DM, hypertension, CVD, and other chronic illnesses. The mechanisms whereby such diseases progress are closely linked to insulin resistance, pancreatic $\beta$-cell dysfunction, visceral adiposity, dyslipidemia, and inflammation. The current mini-review evaluated recent literature (past decade) and shows that SSB consumption worsens the risk for MetS, T2DM, and CVD onset. However, there are limitations; for example, many do not take the sex and/or ethnicity of participants into account, although it is evident that such factors may contribute to the complexity of the results. The short-term nature of numerous studies is also a problem as long-term effects can therefore only be projected or predicted. Together these data highlight the need for (1) well-designed basic and clinical studies to obtain a clearer picture, (2) further research into the molecular mechanisms underlying the development of such debilitating conditions, and (3) increased roll-out of educational programs to inform the general public of the harmful effects of high SSB intake.

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