Diabetes Management

Sugar-sweetened beverages and Type 2 diabetes: will a reduction in consumption reduce the risk of developing diabetes?



Laura O'Connor[1], Fumiaki Imamura[1] & Nita G Forouhi*[,1]

Context

The number of people with Type 2 diabetes (T2D) is increasing across the globe. By 2035 it is estimated that there will be 592 million people with diabetes worldwide, increasing from 382 million in 2013 [1]. The negative impact of diabetes on the individual's quality of life has long been established [2] and the impact on economic and health resources is a substantial and growing burden [3].

There is high-quality evidence from intervention trials that healthier lifestyles can prevent or delay the onset of T2D [4]. A shift from a nutrient-based approach to one based on foods has been proposed for dietary guidelines [5], with emerging evidence for roles of certain foods in the development of T2D [6–8]. A 'food' item of particular interest is sugar-sweetened beverages (SSBs) [9,10], which, if found to be causally related to T2D, would offer the potential for T2D prevention by reducing or eliminating them from the diet.

SSB is a collective term for soft drinks, fruit juice drinks, cordials, iced teas, sports drinks and other similar beverages, which are sweetened with caloric sugars. It has been estimated that the global consumption of soft drinks has increased from 9.5 gallons per person per year in 1997 to 11.4 gallons in 2010 [11]. Although national surveys from both the USA [12] and UK [13] have reported small decreases in SSB consumption (with the exception of a small increase in men aged ≥19 years in the UK) the contribution of SSBs to free sugar intakes is still high and concerning, as for example, SSBs are listed as the highest individual food contributor to energy intakes (5.3%) in the USA [14] and as one of the major sources of non-milk extrinsic sugar in the UK [13].

Evidence for the association between SSBs & T2D

Probably the first appearance of SSBs in the diabetes literature was in 2004 [15] where higher intake of SSBs was associated with a greater magnitude of weight gain and an increased 14-year risk of T2D in female nurses in the Nurses' Health Study II in

KEYWORDS
• XXX • XXX • XXX • XXX • XXX • XXX

"It has been estimated that the global consumption of soft drinks has increased from 9.5 gallons per person per year in 1997 to 11.4 gallons in 2010."

[1]MRC Epidemiology Unit, University of Cambridge School of Clinical Medicine, Institute of Metabolic Science, Cambridge, UK
*Author for correspondence: Tel.: +44 1223 769145; Fax: +44 1223 330316; nita.forouhi@mrc-epid.cam.ac.uk

Future Medicine part of fsg

the USA. Since then there has been an increasing interest, and strong epidemiological evidence now exists. A meta-analysis of eight studies (six American, one Finnish and one Singaporean) reported a 25% greater risk of developing T2D per 336 g (12 oz) serving per day of SSBs after adjustment for energy intake and BMI (relative risk: 1.25; 95% CI: 1.10–1.42) [16]. We have further contributed to the evidence evaluating 12,403 T2D cases from among a cohort with 3.99 million person years of follow-up from eight European countries in the EPIC-InterAct study [10]. We found that after adjustment for several important confounding factors, as well as energy intake and BMI, one 336 g (12 oz) serving per day higher of SSB consumption was associated with T2D, with a hazard ratio of 1.18 (95% CI: 1.06–1.32). This work provides stronger evidence than the prior meta-analysis, using individual participant data, that even after accounting for factors that may artificially distort observed associations, including other lifestyle and dietary factors, sociodemographic factors and adiposity, there is an independent positive association between habitual consumption of SSBs and the risk of new onset T2D.

"By 2035 it is estimated that there will be 592 million people with diabetes worldwide, increasing from 382 million in 2013."

Further support for the contribution of SSBs to the development of T2D comes more indirectly. Randomized controlled trials (RCTs) that evaluate the short-term effects of defined interventions cannot adequately assess the prolonged cumulative nature of diet in chronic disease risk due to logistics, cost and issues of long-term compliance. Their contribution is nonetheless important as intermediates of the role of SSBs in the development of T2D can be examined, in particular weight gain. Comprehensive meta-analyses of RCTs of SSBs and weight gain in children and adults have been carried out [17]. In children, when SSB consumption was reduced by either school-based or individual-based intervention, BMI reduced concurrently, the weighted mean difference between the intervention and control regimens was -0.12 kg/m^2 (95% CI: -0.22 to -0.02 kg/m^2) over 3–12 months of follow-up. In adults when 600–1000 ml of SSBs were added to diets every day, there were increases in bodyweight, the weighted mean difference between the intervention and control regimens was 0.85 kg (95% CI: 0.50–1.20 kg) over 1–6 months of follow-up.

Although our focus is on higher grades of evidence than that provided by ecological and cross-sectional studies, which suffer particularly from the inability to determine temporality of association or reverse causation, one ecological study deserves mention. Taking a global perspective, a recent crossnational analysis based on commodity data from 75 countries, including low- and middle-income countries reported an estimated increase of 300 adults with diabetes per 100,000 for each 1% rise in soft drink consumption [11].

Proof of causality

Although there is strong epidemiological evidence, as described above, that SSB consumption is associated with increased incidence of T2D, there is an ongoing debate about implying cause and effect from such findings. Evidence from epidemiological studies is subject to measurement error and residual confounding. Nutritional epidemiology largely relies on participants to self-report what they have consumed. This is open to bias both from changes in dietary habits during survey time in prospective analysis and misreporting of foods consumed including reporting what the participant considers their norm when using retrospective dietary assessment methods. Furthermore, as it is infeasible to follow an individual indefinitely estimates are limited by when dietary assessment is carried out. SSB consumption is also likely to be a marker of other unhealthy dietary patterns and poor behavioral habits making it difficult to pin the association to SSBs alone.

The science of epidemiology has developed theories and tools to account for these concerns and potential biases in interpretation of results. Furthermore, there are criteria that can be used for assessing a causal link, which include strength of association, consistency/repetition, specificity, temporality, dose–response, experimental evidence and biological plausibility [18]. Each of these criteria has been addressed in the association of SSBs and T2D [9]. The studies detailed above [10,16] provide evidence for a significant positive association, which is largely consistent, across a range of populations with heterogeneity of dietary intakes. In terms of specificity, the associations reported have been shown independent of diet, lifestyle, health and other diabetes risk-related characteristics. As the included studies adopted a prospective design, temporality has been demonstrated. Dose–response has been assessed by examining the risk per serving, and also assessed elsewhere using alternative methods [19]. Although experimental

evidence is not directly available as T2D as an end point for an RCT is infeasible (as explained above), RCTs of intermediates including weight gain exists. Biological plausibility is also established with mechanisms both via adiposity and independent of adiposity proposed.

Suggested mechanisms

The association between SSBs and T2D is thought, at least in part, to be mediated by energy intake and adiposity. As a highly palatable product, drinking SSBs may be associated with passive overconsumption of calories that in turn can lead to weight gain. Furthermore, calories consumed in liquid form do not sate to the same extent that those consumed in the form of solid foods do [20]. This can give rise to incomplete compensation for caloric intake from beverages in dietary intake, which may also contribute to weight gain. Many SSBs are also carbonated. Carbon dioxide has been shown to reduce the neural processing of sucrose more than that of artificial sweeteners [21] and may, thus, increase consumption of beverages containing sugar.

Suggested mechanisms independent of adiposity include via glycaemic effects of consuming large amounts of rapidly absorbable sugars and metabolic effects of fructose [9]. Liquid sugars have been shown as a risk factor for the development of impaired glucose homeostasis including insulin resistance [22].

Implications for further research & public health

Further research efforts are needed to investigate the association between SSBs and T2D risk in more depth. For instance, a topical debate is the contribution of naturally occurring sugars as found in fruit juice to free sugar intakes and whether these may also contribute to diabetes onset. To overcome limitations inherent in self-reporting dietary intakes, it would of great interest to identify biomarkers that would provide objective assessment of intake. A proof-of-principle for a biomarker of sugar intake was previously demonstrated [23], and further research is warranted. In terms of mechanisms, more research is needed in particular on whether the body processes liquid sugar differently to solid sugar. Not having the answers to these and other related questions, however, should not detract from the strength of the current evidence for SSBs and T2D. Further research should also focus on assessing appropriate alternatives for hydration and modeling of strategies to reduce SSBs consumption.

Based on the evidence for SSB consumption and weight gain, it is widely accepted that public health strategies to reduce SSB consumption are needed. The evidence for the association of SSBs and T2D independent of adiposity adds considerable weight to the argument and highlights the urgency of developing and introducing such strategies.

Taxation has been proposed as one means of reducing the intake of unhealthy food products. This, in turn, would lower healthcare costs, as well as generate revenue that can be used for health programs. SSBs have been proposed as a specific target for such a policy. Modeling approaches for the potential benefits and effectiveness of SSB taxation have shown that a tax of 20% on SSBs could reduce the prevalence of obesity in the UK by 1.3% [24]. There is a further suggestion that taxation of SSBs could avert 4.2% of prevalent overweight/obesity and 2.5% of incident T2D in India from 2014 to 2023, in both urban and rural populations [25]. Despite such economic–epidemiologic modeling, there is as yet no agreement to push a tax forward, and this remains a hotly debated issue amid calls from some quarters demanding absolute proof of a cause–effect relationship. For reasons described herein, providing such cast-iron proof is currently near impossible. Considering the abundance of evidence and support for the fulfillment of criteria for causal inference as outlined above, in the absence of absolute proof a 'best intentions/no harm' approach could be justified.

Moving upstream from policies targeted at the level of the individual and to tackling the food environment opens up other plausible strategies, including limiting portion sizes and clear front of pack labeling, even considering a health warning on the sugar content of certain drinks. Engagement with industry is also pertinent and the 'responsibility deal' in England [26] is a step in the right direction.

Conclusion

In conclusion, there is robust evidence of a strong and consistent association between the habitual consumption of SSBs and the development of T2D, both through effects on adiposity, and independently of it. By implication, there is also accumulating evidence that a reduction in consumption of SSBs will reduce the risk of new onset T2D. Although there are questions still to

> "...there is robust evidence of a strong and consistent association between the habitual consumption of sugar-sweetened beverages and the development of Type 2 diabetes..."

be answered, these should not impede actions to reduce intake of SSBs given the strength of the current body of evidence.

Financial & competing interests disclosure

The authors acknowledge funding from the Medical Research Council Epidemiology Unit (MC_UU_12015/5). The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

No writing assistance was utilized in the production of this manuscript.

References

1 International Diabetes Federation. *IDF Diabetes Atlas* (*6th Edition*). International Diabetes Federation, Brussels, Belgium (2013).

2 Rubin RR, Peyrot M. Quality of life and diabetes. *Diabetes Metab. Res. Rev.* 15(3), 205–218 (1999).

3 American Diabetes Association. Economic costs of diabetes in the U.S. in 2012. *Diabetes Care* 36(4), 1033–1046 (2013).

4 Gillies CL, Abrams KR, Lambert PC *et al.* Pharmacological and lifestyle interventions to prevent or delay Type 2 diabetes in people with impaired glucose tolerance: systematic review and meta-analysis. *BMJ* 334(7588), 299 (2007).

5 Mozaffarian D, Ludwig DS. Dietary guidelines in the 21st century – a time for food. *JAMA* 304(6), 681–682 (2010).

6 The Interact Consortium: Association between dietary meat consumption and incident Type 2 diabetes: the EPIC-InterAct study. *Diabetologia* 56(1), 47–59 (2013).

7 Sluijs I, Forouhi NG, Beulens JW *et al.* The amount and type of dairy product intake and incident Type 2 diabetes: results from the EPIC-InterAct Study. *Am. J. Clin. Nutr.* 96(2), 382–390 (2012).

8 O'Connor LM, Lentjes MA, Luben RN, Khaw KT, Wareham NJ, Forouhi NG. Dietary dairy product intake and incident Type 2 diabetes: a prospective study using dietary data from a 7-day food diary. *Diabetologia* 57(5), 909–917 (2014).

9 Malik VS, Hu FB. Sweeteners and risk of obesity and Type 2 diabetes: the role of sugar-sweetened beverages. *Curr. Diab. Rep.* doi:10.1007/s11892-012-0259-6 (2012) (Epub ahead of print).

10 The Interact Consortium. Consumption of sweet beverages and Type 2 diabetes incidence in European adults: results from EPIC-InterAct. *Diabetologia* 56(7), 1520–1530 (2013).

11 Basu S, Mckee M, Galea G, Stuckler D. Relationship of soft drink consumption to global overweight, obesity, and diabetes: a cross-national analysis of 75 countries. *Am. J. Public Health* 103(11), 2071–2077 (2013).

12 Kit BK, Fakhouri TH, Park S, Nielsen SJ, Ogden CL. Trends in sugar-sweetened beverage consumption among youth and adults in the United States: 1999–2010. *Am. J. Clin. Nutr.* 98(1), 180–188 (2013).

13 National Diet and Nutrition Survey. Headline results from Years 1 and 2 (combined) of the Rolling Programme (2008/2009–2009/10) (2011). http://webarchive.nationalarchives.gov.uk/20130402145952/https://www.gov.uk/government/publications/national-diet-and-nutrition-survey-headline-results-from-years-1-and-2-combined-of-the-rolling-programme-2008-9-2009-10

14 National Cancer Institute. Mean Intake of Energy and Mean Contribution (kcal) of Various Foods Among US Population, by Age, NHANES 2005–2014 (2006). http://appliedresearch.cancer.gov/diet/foodsources/energy/table1b.html

15 Schulze MB, Manson JE, Ludwig DS *et al.* Sugar-sweetened beverages, weight gain, and incidence of Type 2 diabetes in young and middle-aged women. *JAMA* 292(8), 927–934 (2004).

16 Malik VS, Popkin BM, Bray GA, Despres JP, Willett WC, Hu FB. Sugar-sweetened beverages and risk of metabolic syndrome and TYPE 2 diabetes: a meta-analysis. *Diabetes Care* 33(11), 2477–2483 (2010).

17 Malik VS, Pan A, Willett WC, Hu FB. Sugar-sweetened beverages and weight gain in children and adults: a systematic review and meta-analysis. *Am. J. Clin. Nutr.* 98(4), 1084–1102 (2013).

18 Hill AB. The environment and disease: association or causation? *Proc. Royal Soc. Med.* 58, 295–300 (1965).

19 Fagherazzi G, Vilier A, Saes Sartorelli D, Lajous M, Balkau B, Clavel-Chapelon F. Consumption of artificially and sugar-sweetened beverages and incident Type 2 diabetes in the Etude Epidemiologique aupres des femmes de la Mutuelle Generale de l'Education Nationale-European Prospective Investigation into Cancer and Nutrition cohort. *Am. J. Clin. Nutr.* 97(3), 517–523 (2013).

20 Drewnowski A, Bellisle F. Liquid calories, sugar, and body weight. *Am. J. Clin. Nutr.* 85(3), 651–661 (2007).

21 Di Salle F, Cantone E, Savarese MF *et al.* Effect of carbonation on brain processing of sweet stimuli in humans. *Gastroenterology* 145(3), 537–539 e533 (2013).

22 Wang J, Light K, Henderson M *et al.* Consumption of added sugars from liquid but not solid sources predicts impaired glucose homeostasis and insulin resistance among youth at risk of obesity. *J. Nutr.* 144(1), 81–86 (2014).

23 Tasevska N, Runswick SA, McTaggart A, Bingham SA. Urinary sucrose and fructose as biomarkers for sugar consumption. *Cancer Epidemiol. Biomarkers Prev.* 14(5), 1287–1294 (2005).

24 Briggs AD, Mytton OT, Kehlbacher A, Tiffin R, Rayner M, Scarborough P. Overall and income specific effect on prevalence of overweight and obesity of 20% sugar sweetened drink tax in UK: econometric and comparative risk assessment modelling study. *BMJ* 347, f6189 (2013).

25 Basu S, Vellakkal S, Agrawal S, Stuckler D, Popkin B, Ebrahim S. Averting obesity and Type 2 diabetes in India through sugar-sweetened beverage taxation: an economic-epidemiologic modeling study. *PLoS Med.* 11(1), e1001582 (2014).

26 Department of Health. Public health responsibility deal. https://responsibilitydeal.dh.gov.uk