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EDITORIAL

Sugary Beverages Pose Significant Risks to Cardiovascular and Overall Health

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Abstract

Consumption of added sugar is associated with weight gain and metabolic syndrome, but most importantly with cardiovascular disease (CVD) morbidity and mortality. Sugar-sweetened beverages (SSBs) in the form of soft drinks or sodas constitute a major source of added sugar with its attendant ill effects on health. Of particular concern is the rising consumption of soft drinks among young people. The World Health Organization (WHO) recommends the reduction of free sugars to <10% of total energy intake due to their potential implications in dental caries, weight gain and CVD consequences, however, adherence to this recommendation is generally very low. Non-caloric drinks in the form of artificially sweetened beverages (ASBs) (diet sodas) are popular as alternatives to SSBs. However, these sweeteners may also have various negative, albeit at a lesser degree, health outcomes, including weight gain, obesity, metabolic syndrome, type II diabetes, and CV events. Finally, substantially lower health risks are incurred from 100%

fruit juice consumption compared with SSBs. All these issues are herein reviewed and measures are discussed to lessen the consequences of such an unhealthy dietary behavior. *Rhythmoss 2019;14(3):45-50.*

Key Words: sugary beverages; sugar-sweetened beverages; soft drinks; sodas; colas; added sugars; cardiovascular disease

Abbreviations: ASB = artificially sweetened beverages; CV = cardiovascular; CVD = cardiovascular disease; SSB = sugar-sweetened beverages

Introduction

Dietary behavior shifts to unhealthy habits have been noted over the last 2 decades including greater away-from-home consumption; large increases in total energy from salty snacks, soft drinks, and pizza; and large decreases in energy from low- and medium-fat milk and medium- and high-fat beef and pork.¹ Despite the issuance of dietary guidelines emphasizing these issues and providing guidance to healthy diet and activity, the problem of unhealthy habits remains or seems to be accentuated.^{2,3} Of particular concern is the rising consumption of soft drinks among young people (Table 1).¹ The sugar content of soft drinks is typically 10–15 g per 100 ml or 35–37.5 g per 12-oz serving; sugar-sweetened beverages (SSBs) typically contain 140–150 kcal per 12-oz serving, and they

are the largest source of added sugars in the United States (US) diet (Guideline: Sugars intake for adults and children. Geneva: WHO; 2015: http://apps.who.int/iris/bitstream/10665/149782/1/9789241549028_eng.pdf?ua=1). In the US over the last three decades, high-fructose corn syrup has largely replaced sucrose as the major sweetener in soft drinks.⁴ There is suggestion that the consumption of beverages containing fructose has directly contributed to the obesity epidemic.^{4, 5} There is also considerable evidence that fructose, rather than glucose, is the more harmful sugar component regarding cardiovascular (CV) risk.⁶

Sugar-Sweetened Beverages (SSBs)

According to a systematic review of 30 (15 cross-sectional, 10 prospective, and 5 experimental) publications conducted more than a decade ago, the weight of epidemiologic and experimental evidence indicates that a greater consumption of SSBs is associated with weight gain and obesity.⁷ Similarly, a meta-analysis of 30 trials and 38 cohort studies indicated that among free living people involving ad libitum diets, intake of free sugars or SSBs is a determinant of body weight.⁸ Another meta-analysis of 11 studies (3 for metabolic syndrome and 8 for type 2 diabetes) including 310,819 participants and 15,043 cases of type 2 diabetes, indicated that individuals in the highest quantile of SSB intake (most often 1-2 servings/day) had a 26% greater risk of developing type 2 diabetes than those in the lowest quantile (none or <1 serving/month) (relative risk - RR 1.26).⁹ Among studies evaluating metabolic syndrome, including 19,431 participants and 5,803 cases, the pooled risk ratio (RR) was 1.20. The authors concluded that in addition to weight gain, higher consumption of SSBs is associated with development of metabolic syndrome and type 2 diabetes.⁹

More importantly, epidemiologic studies have suggested that higher intake of added sugar is associated with CV disease (CVD) risk factors, while prospective studies have associated added sugar intake with CVD mortality. A prospective study of the National Health and Nutrition Examination Survey (NHANES) cohorts (n = 31,147) and NHANES III Linked Mortality cohort (n = 11 733), indicated that among US adults, the adjusted mean percentage of daily calories from added sugar increased from 15.7% in 1988-1994 to 16.8% (p = 0.02) in 1999-2004 and decreased to 14.9% (p < 0.001) in 2005-2010.¹⁰ The majority (71.4%) of adults consumed $\geq 10\%$ of calories from added sugar and $\sim 10\%$ consumed $\geq 25\%$ in 2005-2010. During a median follow-up period of 14.6 years, age-, sex-, and race/ethnicity-adjusted hazard ratios (HRs) of CVD mortality across quintiles of the percentage of daily calories consumed from added sugar were 1.00

(reference), 1.09, 1.23, 1.49, and 2.43 (p < 0.001), respectively. After additional adjustment for sociodemographic, behavioral, and clinical characteristics, HRs were 1.00 (reference), 1.07, 1.18, 1.38, and 2.03 (p = 0.004), respectively. Adjusted HRs were 1.30 and 2.75 (P = 0.004), respectively, comparing participants who consumed 10-24.9% or $\geq 25\%$ calories from added sugar with those who consumed <10% of calories from added sugar. The authors concluded that a significant relationship was observed between added sugar consumption and increased risk for CVD mortality.

Table 1. Sugar Sweetened Beverages (SSBs) and Ingredient List of SSBs

| SSBs | Ingredient List of SSBs / ASBs |
|----------------------------|---|
| sodas / colas * | sugar/raw sugar / brown sugar / |
| energy drinks | cane sugar |
| sports drinks | sucrose (table sugar) / maltose |
| sweetened tea /coffee | glucose |
| fruit juice / juice drinks | lactose |
| flavored milk | syrup / corn syrup / malt syrup / |
| smoothies | maple syrup |
| flavored water | fructose / high-fructose corn syrup |
| non-alcoholic beer/wine | corn sweetener |
| | molasses |
| | dextrose |
| | fruit juice concentrate or nectar |
| | honey |
| | <i>artificial sweeteners:</i> aspartame, |
| | sucralose, saccharin, acesulfame, |
| | neotame, sorbitol, advantame |
| | <i>novel sweeteners:</i> stevia, tomatate |

* N.B.: Diet sodas contain artificial sweeteners

Data from the Framingham Heart Study (N=6730) indicated that SSB intake was associated with a higher incidence of low high-density lipoprotein cholesterol (HDL-C) (hazard ratio-HR: 1.64, p for trend=0.01) and high triglyceride (TG) concentrations (HR: 1.46; p trend=0.009).¹¹ Intake of low-calorie sweetened beverages was associated with a higher incidence of low HDL-C (HR: 1.38, p trend=0.01) and high low-density lipoprotein cholesterol (LDL-C) concentrations (HR: 1.19; p trend=0.01). The authors concluded that SSB intake was associated with changes in HDL-C and TG concentrations and higher risk of dyslipidemia, suggesting that SSB consumption should be limited. Also, high intake of low-calorie sweetened beverages was associated with risk of dyslipidemia. Thus, limiting intake of low-calorie sweetened beverages is also recommended.

A recent cohort study (REGARDS) comprising 13,440 participants (mean age of 63.6 years at baseline; 59.3% men, 68.9% non-Hispanic white, and 70.8% overweight or obese) indicated that mean sugary beverage consumption was 8.4% of total energy (TE)/d (4.4% TE/d from SSBs; 4% TE/d from 100% fruit juice).¹² Among high ($\geq 10\%$ of TE) vs low ($< 5\%$ of TE) sugary beverage consumers, risk-adjusted HRs were 1.44 for coronary heart disease mortality and 1.14 for all-cause mortality. Risk-adjusted all-cause mortality HRs were 1.11 for each additional 12 oz of sugary beverage consumed and 1.24 for each additional 12 oz of fruit juice consumed. In risk-adjusted models, there was no significant association of sugary beverage consumption with coronary disease mortality.

A cross-sectional association study of sugary beverage consumption with neuropsychological (n=4276) and magnetic resonance imaging (MRI) (n=3846) markers of preclinical Alzheimer's disease and vascular brain injury in the community-based Framingham Heart Study, indicated that relative to consuming < 1 sugary beverage per day, higher intake of sugary beverages was associated with lower total brain volume, and poorer performance on tests of episodic memory (all $p < 0.01$).¹³ Daily fruit juice intake was associated with lower total brain volume, hippocampal volume, and poorer episodic memory (all $p < 0.05$). Sugary beverage intake was not associated with vascular brain injury in a consistent manner across outcomes. The authors concluded that higher intake of sugary beverages was associated cross-sectionally with markers of preclinical Alzheimer's disease.

The World Health Organization (WHO) recommends the reduction of free sugars to $< 10\%$ of total energy intake due to their potential implications in weight gain and dental caries (www.who.int/elena/titles/guidance_summaries/sugars_intake/en/). Adherence to the WHO recommendations guidelines was generally low in Switzerland, particularly among young adults, and in line with other high-income countries.¹⁴ According to the IDEFICS study, a European multicenter cohort study in children (2-9 years old) from 8 countries, comprising 8308 children (51.4% males), girls had significantly lower intakes of energy, total and free sugars compared with than boys but did not differ in terms of percent of energy from total (23%) or free sugars (18%).¹⁵ There were large variations between countries in average % energy from free sugars (ranging from 13% in Italy to 27% in Germany). Less than 20% of children were within the recommended intake of 10% of energy from free sugars. The food groups that contributed substantially to free sugars intakes were "fruit juices", "soft drinks", "dairy" and "sweets and candies". The authors concluded that the

contribution of free sugars to total energy intake in European children is higher than recommendations. The main food contributors to free sugars intake are sweetened beverages ("fruit juices" and "soft drinks").

Artificially Sweetened Beverages (ASBs)

Non-caloric drinks (diet sodas) are also sweetened beverages, artificially sweetened beverages (ASBs), as they contain non-nutritive sweeteners (NNSs) (Table 1). These artificial sweeteners are popular as alternatives to SSBs. However, these sweeteners are more potent than regular, natural sugars and work by promoting glucagon-like peptide1 (GLP-1) secretion, which then stimulates gastric emptying and increases insulin secretion; epidemiologic studies support the existence of an association between ASB intake and weight gain in children as they may increase appetite and promote greater food consumption.^{16, 17} Studies have found various negative health outcomes associated with NNSs, including weight gain, obesity, metabolic syndrome, type II diabetes, and CV events.¹⁸⁻²⁰

According to the recently published results of the Women's Health Initiative observational study (93,676 postmenopausal women of ages 50-79 years at baseline followed up for a mean of 11.9 years), higher intake of ASB was associated with increased risk of stroke, particularly small artery occlusion subtype, coronary artery disease, and all-cause mortality.²¹ The authors concluded that although requiring replication, these new findings add to the potentially harmful association of consuming high quantities of ASB with these health outcomes.

Fruits and Fruit Juices

A US Health Professionals study indicated that greater consumption of specific whole fruits (e.g. blueberries, grapes, and apples) is significantly associated with a lower risk of type 2 diabetes, whereas greater consumption of fruit juice is associated with a higher risk.²²

A systematic review and meta-analysis of 17 cohort studies indicated that habitual consumption of sugar sweetened beverages was associated with a greater incidence of type 2 diabetes, independently of adiposity.²³ Although artificially sweetened beverages and fruit juice also showed positive associations with incidence of type 2 diabetes, the findings were likely to involve bias.

Recently, the European Prospective Investigation into Cancer and Nutrition-Netherlands (EPIC-NL) study indicated that compared with no consumption, pure fruit juice consumption up to 7 glasses/week - but not consumption of ≥ 8 glasses - was significantly associated with reduced risk of CVD and coronary artery disease,

with hazard ratios (HRs) from 0.83 to 0.88.²⁴ Consumption of 1-4 and 4-8 glasses/week was significantly associated with lower risk of stroke with HR of 0.80 and 0.76, respectively. Associations did not differ considerably between low and high fruit consumers. The highest three quintiles of fruit consumption (≥ 121 g/d) were significantly associated with lower incidence of CVD, with HR of 0.87 and 0.88. The authors concluded that, although favourable associations of moderate pure fruit juice consumption with CVD were observed, for now, consumption of whole fruit should be preferred because the evidence of the health benefits of fruit is more conclusive.

Other investigators suggest that, although fruit juices may not be as harmful as SSBs, their consumption should be moderated in children and adults, especially for reasons of body weight control.²⁵ Indeed, evidence from systematic reviews and meta-analyses of health effects of 100% fruit juice remains inconclusive, but most studies show no association with chronic ill effects, except for an increased risk of caries in children and small increases in long-term weight gain, possibly inconsequential in normal-weight individuals.²⁶ On the other hand, a protective effect of citrus fruit juice against ischemic stroke was reported by a prospective cohort study.²⁷ A meta-analysis of 19 trials (n=618) suggested that fruit juice had a borderline significant effect on reducing diastolic blood pressure, but had no effect on total cholesterol, HDL-C, LDL-C concentrations or systolic blood pressure.²⁸ Another meta-analysis of 12 trials (n=412) indicated no overall effect of fruit juice on fasting glucose and insulin concentrations.²⁹ Thus, the current body of evidence suggests that there are substantially lower health risks from 100% fruit juice consumption compared with SSBs.^{25,26}

On the other hand, a recent prospective study of 27,842 men (mean age 51 years), indicated that higher intakes of total vegetables, total fruits, and fruit juice were each significantly associated with lower odds of moderate or poor subjective cognitive function after controlling for major nondietary factors and total energy intake.³⁰ The association with total fruit intake was weaker after further adjusting for major dietary factors. In this model, the multivariate odds ratios (OR) for vegetable intake (top vs bottom quintile) were 0.83, *p* trend <0.001 for moderate cognitive function and 0.66, *p* trend <0.001 for poor cognitive function. For orange juice, compared to <1 serving/mo of intake, daily consumption was associated with a substantially lower odds of poor cognitive function (0.53, *p* trend <0.001). Higher consumption of vegetables and fruits 18 to 22 years before cognitive function

assessment was associated with lower odds of poor cognitive function independent of more proximal intake.³⁰

One important aspect in determining the risk or benefit of fruits and fruit juices relates to the type and degree of processing of these nutrients. A systematic review of 10 meta-analyses of cohort studies and randomized controlled trials that linked fruit consumption with the risk of chronic disease and metabolic deregulation showed that the degree of processing influences the health effects of fruit-based products.³¹ Particularly, fresh and dried fruits appeared to have a neutral or protective effect on health, 100% fruit juices had intermediary effects, and high consumption of canned fruit and sweetened fruit juice was positively associated with the risk of all-cause mortality and type 2 diabetes, respectively. The authors concluded that the degree of food processing will need to be considered in future epidemiological studies and randomized controlled trials in order to adjust official recommendations for fruit consumption.

Finally, sugar-containing foods in their natural form, like whole fruit, are nutritious, high in fiber, and low in glycemic load. Contrariwise, refined, concentrated sugar consumed in large amounts swiftly leads to increased blood glucose, insulin levels, and triglycerides, increases inflammatory mediators and oxygen radicals, with the attendant risk for diabetes, CV disease and other chronic diseases. The American Academy of Pediatrics (AAP),³² the US Dietary Guidelines for Americans 2015-2020,² and the Robert Wood Johnson Foundation Healthy Eating Research program have published policy statements on how much daily 100% fruit juice is recommended for children and adults.²⁶ They emphasize that consuming water and whole fruit is preferred to 100% fruit juice which contains less dietary fiber than whole fruit; when consumed in excess, 100% fruit juice may contribute extra calories. These guidelines recommend that 100% fruit juice intake should be limited to one 240-mL serving/d.

A position paper of the European Society for Pediatric Gastroenterology, Hepatology and Nutrition Committee on Nutrition recommends that sugar should preferably be consumed as part of a main meal and in a natural form as human milk, milk, unsweetened dairy products, and fresh fruits, rather than as SSBs, fruit juices, smoothies, and/or sweetened milk products.³³ Free sugars in liquid form should be replaced by water or unsweetened milk drinks.

Measures

As mentioned, the World Health Organization (WHO) recommends the reduction of free sugars to <10% of total energy intake (www.who.int/elena/titles/guidance_summaries/sugars_intake/en/). In 2016, the US Food and Drug Administration (FDA) mandated the labeling of added

sugar content on all packaged foods and beverages (www.fda.gov/food/food-labeling-nutrition/changesnutrition-facts-label). Recently (2019), a validated microsimulation model (US IMPACT Food Policy model) indicated that implementing the US FDA added sugar labeling policy could generate substantial health gains and cost savings for the US population.³⁴ Also recently, a Science Advisory was issued by the American Heart Association (AHA) describing innovative approaches to developing a healthy and sustainable food system; the elements of this advisory concerning SSBs are listed in Table 2. Similar suggestions have been made by the WHO (www.who.int/elena/bbc/ssbs_childhood_obesity/en/).

Conclusion

One may conclude with two scientific statements from societies across the Atlantic. A scientific statement from the AHA about added sugars and CVD risk in children indicates “Associations between added sugars and increased CVD risk factors among US children are present at levels far below current consumption levels. Strong evidence supports the association of added sugars with increased CVD risk in children through increased energy intake, increased adiposity, and dyslipidemia. The committee found that it is reasonable to recommend that children consume ≤ 25 g (100 cal or ≈ 6 teaspoons) of added sugars per day and to avoid added sugars for children < 2 years of age. Although added sugars most likely can be safely consumed in low amounts as part of a healthy diet, few children achieve such levels, making this an important public health target”.³⁵ This is in line with the European recommendation that “sugar should preferably be consumed as part of a main meal and in a natural form as human milk, milk, unsweetened dairy products, and fresh fruits, rather than as SSBs, fruit juices, smoothies, and/or sweetened milk products. Free sugars in liquid form should be replaced by water or unsweetened milk drinks”.³³

Table 2. Measures and Approaches for a Healthier Food System Concerning Sugary Beverages

- Implement nutrition standards for food and beverages in schools that may beneficially influence diet and weight
- Provide incentives for vegetables/fruits and restrictions of SSB for healthier diets and reduced CVD
- Restrict SSB marketing to youth that may reduce childhood obesity
- Ban sales of SSBs on government property, in schools and in hospitals
- Set local (e.g. worksite) healthy food procurement policies that restrict SSBs

- Increase pricing/taxing of SSBs and decrease pricing/taxing of healthier products
- Product (food and menu) labeling
- Healthy default choices, e.g. no SSBs in children’s meals
- Mobile health apps / Online shopping strategies to promote healthier purchases / Gaming to improve children’s dietary intake
- Community campaign to reduce SSBs (shown to reduce purchases of SSBs)
- Children should consume ≤ 25 g (100 cal or ≈ 6 teaspoons) of added sugars per day / avoid added sugars for children < 2 years of age
- Sugar should preferably be consumed as part of a main meal and in a natural form as human milk, milk, unsweetened dairy products, and fresh fruits, rather than as SSBs, fruit juices, smoothies, and/or sweetened milk products
- 100% fruit juice intake should be limited to one 240-mL serving/d
- Free sugars in liquid form should be replaced by water or unsweetened milk drinks

CVD = cardiovascular disease; SSB = sugar sweetened beverage
 * Items were compiled from the AHA Science Advisory,³⁶ the European Society for Pediatric Gastroenterology, Hepatology and Nutrition Committee on Nutrition³³ and other sources²⁶

References

1. Nielsen SJ, Siega-Riz AM, Popkin BM. Trends in energy intake in U.S. between 1977 and 1996: similar shifts seen across age groups. *Obes Res* 2002;10:370-8.
2. USDHHS. U.S. Department of Health and Human Services and U.S. Department of Agriculture. 2015–2020 Dietary Guidelines for Americans. 8th Edition. December 2015. Available at <http://health.gov/dietaryguidelines/2015/guidelines> /2015-2020 Dietary Guidelines for Americans. US Department of Health and Human Services. 2015.
3. Manolis AS. You Are What You Eat, Hence Curtail Saturated and Trans Fats, Free Sugars and Salt. *Rhythmos* 2016;11:28-38.
4. Bray GA, Nielsen SJ, Popkin BM. Consumption of high-fructose corn syrup in beverages may play a role in the epidemic of obesity. *Am J Clin Nutr* 2004;79:537-43.
5. Elliott SS, Keim NL, Stern JS, Teff K, Havel PJ. Fructose, weight gain, and the insulin resistance syndrome. *Am J Clin Nutr* 2002;76:911-22.
6. Brown CM, Dulloo AG, Montani JP. Sugary drinks in the pathogenesis of obesity and cardiovascular diseases. *Int J Obes (Lond)* 2008;32 Suppl 6:S28-34.
7. Malik VS, Schulze MB, Hu FB. Intake of sugar-sweetened beverages and weight gain: a systematic review. *Am J Clin Nutr* 2006;84:274-88.

8. Te Morenga L, Mallard S, Mann J. Dietary sugars and body weight: systematic review and meta-analyses of randomised controlled trials and cohort studies. *Bmj* 2012;346:e7492.
9. Malik VS, Popkin BM, Bray GA, et al. Sugar-sweetened beverages and risk of metabolic syndrome and type 2 diabetes: a meta-analysis. *Diabetes Care* 2010;33:2477-83.
10. Yang Q, Zhang Z, Gregg EW, et al. Added sugar intake and cardiovascular diseases mortality among US adults. *JAMA Intern Med* 2014;174:516-24.
11. Haslam D, Peloso G, Herman M, et al. Beverage Consumption and Longitudinal Changes in Lipid Concentrations and Incident Dyslipidemia in U.S. Adults: The Framingham Heart Study (P18-017-19). *Curr Dev Nutr* 2019;3.
12. Collin LJ, Judd S, Safford M, Vaccarino V, Welsh JA. Association of Sugary Beverage Consumption With Mortality Risk in US Adults: A Secondary Analysis of Data From the REGARDS Study. *JAMA Netw Open* 2019;2:e193121.
13. Pase MP, Himali JJ, Jacques PF, et al. Sugary beverage intake and preclinical Alzheimer's disease in the community. *Alzheimers Dement* 2017;13:955-64.
14. Chatelan A, Gaillard P, Kruseman M, Keller A. Total, Added, and Free Sugar Consumption and Adherence to Guidelines in Switzerland: Results from the First National Nutrition Survey menuCH. *Nutrients* 2019;11.
15. Graffe MIM, Pala V, De Henauw S, et al. Dietary sources of free sugars in the diet of European children: the IDEFICS Study. *Eur J Nutr* 2019.
16. Brown RJ, de Banate MA, Rother KI. Artificial sweeteners: a systematic review of metabolic effects in youth. *Int J Pediatr Obes* 2010;5:305-12.
17. Swithers SE. Artificial sweeteners are not the answer to childhood obesity. *Appetite* 2015;93:85-90.
18. Nettleton JA, Lutsey PL, Wang Y, et al. Diet soda intake and risk of incident metabolic syndrome and type 2 diabetes in the Multi-Ethnic Study of Atherosclerosis (MESA). *Diabetes Care* 2009;32:688-94.
19. Swithers SE. Artificial sweeteners produce the counterintuitive effect of inducing metabolic derangements. *Trends Endocrinol Metab* 2013;24:431-41.
20. Vyas A, Rubenstein L, Robinson J, et al. Diet drink consumption and the risk of cardiovascular events: a report from the Women's Health Initiative. *J Gen Intern Med* 2015;30:462-8.
21. Mossavar-Rahmani Y, Kamensky V, Manson JE, et al. Artificially Sweetened Beverages and Stroke, Coronary Heart Disease, and All-Cause Mortality in the Women's Health Initiative. *Stroke* 2019;50:555-62.
22. Muraki I, Imamura F, Manson JE, et al. Fruit consumption and risk of type 2 diabetes: results from three prospective longitudinal cohort studies. *Bmj* 2013;347:f5001.
23. Imamura F, O'Connor L, Ye Z, et al. Consumption of sugar sweetened beverages, artificially sweetened beverages, and fruit juice and incidence of type 2 diabetes: systematic review, meta-analysis, and estimation of population attributable fraction. *Bmj* 2015;351:h3576.
24. Scheffers FR, Boer JMA, Verschuren WMM, et al. Pure fruit juice and fruit consumption and the risk of CVD: the European Prospective Investigation into Cancer and Nutrition-Netherlands (EPIC-NL) study. *Br J Nutr* 2019;121:351-59.
25. Guasch-Ferre M, Hu FB. Are Fruit Juices Just as Unhealthy as Sugar-Sweetened Beverages? *JAMA Netw Open* 2019;2:e193109.
26. Auerbach BJ, Dibey S, Vallila-Buchman P, Kratz M, Krieger J. Review of 100% Fruit Juice and Chronic Health Conditions: Implications for Sugar-Sweetened Beverage Policy. *Adv Nutr* 2018;9:78-85.
27. Joshipura KJ, Ascherio A, Manson JE, et al. Fruit and vegetable intake in relation to risk of ischemic stroke. *Jama* 1999;282:1233-9.
28. Liu K, Xing A, Chen K, et al. Effect of fruit juice on cholesterol and blood pressure in adults: a meta-analysis of 19 randomized controlled trials. *PLoS One* 2013;8:e61420.
29. Wang B, Liu K, Mi M, Wang J. Effect of fruit juice on glucose control and insulin sensitivity in adults: a meta-analysis of 12 randomized controlled trials. *PLoS One* 2014;9:e95323.
30. Yuan C, Fondell E, Bhushan A, et al. Long-term intake of vegetables and fruits and subjective cognitive function in US men. *Neurology* 2019;92:e63-e75.
31. Fardet A, Richonnet C, Mazur A. Association between consumption of fruit or processed fruit and chronic diseases and their risk factors: a systematic review of meta-analyses. *Nutr Rev* 2019;77:376-87.
32. Heyman MB, Abrams SA. Fruit Juice in Infants, Children, and Adolescents: Current Recommendations. *Pediatrics* 2017;139.
33. Fidler Mis N, Braegger C, Bronsky J, et al. Sugar in Infants, Children and Adolescents: A Position Paper of the European Society for Paediatric Gastroenterology, Hepatology and Nutrition Committee on Nutrition. *J Pediatr Gastroenterol Nutr* 2017;65:681-96.
34. Huang Y, Kypridemos C, Liu J, et al. Cost-Effectiveness of the US Food and Drug Administration Added Sugar Labeling Policy for Improving Diet and Health. *Circulation* 2019;139:2613-24.
35. Vos MB, Kaar JL, Welsh JA, et al. Added Sugars and Cardiovascular Disease Risk in Children: A Scientific Statement From the American Heart Association. *Circulation* 2017;135:e1017-e34.
36. Anderson CAM, Thorndike AN, Lichtenstein AH, et al. Innovation to Create a Healthy and Sustainable Food System: A Science Advisory From the American Heart Association. *Circulation* 2019;139:e1025-e32.