Evidence does not support the reduction of added sugar intake from all food sources

Ruolin Yan, Chi Bun Chan and Jimmy Chun Yu Louie

We read with interest the Comment article by Kimber Stanhope (Guidelines to lower intake of added sugar are necessary and justified. *Nat. Rev. Cardiol.* **19**, 569–570 (2022))[1], in which she criticized our recent narrative review[2]. We feel that our views were misrepresented and would like to clarify them.

Our original intention was to call for caution regarding the over-extrapolation of results from studies on sugar-sweetened beverages (SSBs), as Dr Stanhope correctly stated[1]. However, we did not intend to exonerate added sugars as being harmless to health. We were pointing out that most, if not all, the available evidence linking added sugars to ill health comes from studies on SSBs. If we follow the principles of evidence-based medicine[3], the appropriate conclusion to draw is that added or free sugars from SSBs are harmful to health — and no more than that. Extrapolating results from SSB studies to demonize all forms of added sugars is not evidence-based but, instead, best guess. Even if it is the most logical line of thought, one should not 'sugar coat' such extrapolation as being evidence-based.

Dr Stanhope also claimed that we did not outline the potential negative consequences of a recommendation to reduce the intake of added or free sugars to <10% of daily energy intake[1]. However, we did point out in our review the possible negative consequences of blanket reductions of added or free sugars in the food supply[2], such as increased exposure to artificial sweeteners in non-low-calorie products[4] and the nutrient dilution effect of a stringent diet that is low in added or free sugars[5], which Dr Stanhope overlooked.

Evidence gathered to inform the World Health Organization (WHO) guidelines demonstrates that both solid and liquid sources of added sugars cause dental caries[6]. However, articles from peer-reviewed journals and the popular media that cite the WHO guidelines generally refer to the guidelines in the context of reducing the risk of being overweight or obese and rarely mention that the WHO itself concluded that the evidence linking added sugar to being overweight or obese was of only moderate to low quality[7]. Indeed, the WHO contradicted this conclusion from the quality-of-evidence assessment and stated that "reducing free sugars intake to less than 10% of total energy" is a strong recommendation. Of note, the quality-of-evidence assessment used by the WHO was based on the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach that Dr Stanhope criticized Erickson and colleagues[8] for using to conclude that the evidence underpinning the WHO guidelines was of low quality.

We looked at the publisher's website for the article reviewing studies from >40 years ago[9] to which Dr Stanhope referred, but we were unable to locate it. Nonetheless, if opposing results can be found only in an article that was published in 1985 (and no newer studies have shown similar findings), perhaps it is appropriate to say that its omission did not drastically affect the conclusion of our review.

In summary, we would like to reiterate that we agree that added or free sugars from SSBs should be reduced, given that the evidence has consistently shown an association between SSBs and ill health[10]. We remain sceptical about the quality of the evidence (if any) on the reduction of added or free sugars from all types of food, especially solid foods, to improve overall health.

There is a reply to this letter by Stanhope, K. L. *Nat. Rev. Cardiol.* https://doi.org/10.1038/s41569-022-00793-8 (2022).

Ruolin Yan, Chi Bun Chan and Jimmy Chun Yu Louie ✉
School of Biological Sciences, Faculty of Science, The University of Hong Kong, Hong Kong, Hong Kong SAR.
✉*e-mail: jimmyl@hku.hk*

https://doi.org/10.1038/s41569-022-00791-w

1. Stanhope, K. L. Guidelines to lower intake of added sugar are necessary and justified. *Nat. Rev. Cardiol.* **19**, 569–570 (2022).
2. Yan, R. R., Chan, C. B. & Louie, J. C. Y. Current WHO recommendation to reduce free sugar intake from all sources to below 10% of daily energy intake for supporting overall health is not well supported by available evidence. *Am. J. Clin. Nutr.* **116**, 15–39 (2022).
3. Akobeng, A. K. Principles of evidence based medicine. *Arch. Dis. Child.* **90**, 837–840 (2005).
4. O, B. Y. S., Coyle, D. H., Dunford, E. K., Wu, J. H. Y. & Louie, J. C. Y. The use of non-nutritive and low-calorie sweeteners in 19,915 local and imported pre-packaged foods in Hong Kong. *Nutrients* **13**, 1861 (2021).
5. Mok, A., Ahmad, R., Rangan, A. & Louie, J. C. Y. Intake of free sugars and micronutrient dilution in Australian adults. *Am. J. Clin. Nutr.* **107**, 94–104 (2018).
6. Moynihan, P. J. & Kelly, S. A. M. Effect on caries of restricting sugars intake: systematic review to inform WHO guidelines. *J. Dent. Res.* **93**, 8–18 (2014).
7. World Health Organization. Guideline: sugars intake for adults and children. *WHO* https://www.who.int/publications/i/item/9789241549028 (2015).
8. Erickson, J., Sadeghirad, B., Lytvyn, L., Slavin, J. & Johnston, B. C. The scientific basis of guideline recommendations on sugar intake: a systematic review. *Ann. Intern. Med.* **166**, 257–267 (2017).
9. Reiser, S. Effect of dietary sugars on metabolic risk factors associated with heart disease. *Nutr. Health* **3**, 203–216 (1985).
10. Qin, P. et al. Sugar and artificially sweetened beverages and risk of obesity, type 2 diabetes mellitus, hypertension, and all-cause mortality: a dose-response meta-analysis of prospective cohort studies. *Eur. J. Epidemiol.* **35**, 655–671 (2020).

Competing interests
The authors declare no competing interests.

Reply to: 'Evidence does not support the reduction of added sugar intake from all food sources'

Kimber L. Stanhope

I thank Drs Yan, Chan and Louie for their Correspondence (Evidence does not support the reduction of added sugar intake from all food sources. *Nat. Rev. Cardiol.* https://doi.org/10.1038/s41569-022-00791-w (2022))[1] on my Comment article (Guidelines to lower intake of added sugar are necessary and justified. *Nat. Rev. Cardiol.* **19**, 569–570 (2022))[2]. The authors feel that their views were misrepresented and the purpose of their letter was to clarify them.

They state that the intention of their review[3] was not to exonerate added sugars as being harmless to health. My Comment article did not suggest that this was their intention. However, on the basis of the final sentence of their abstract — "We argue the current public health recommendations to encourage the reduction of both solid and liquid forms of free sugar intake (e.g., sugar reformulation programs) should be revised due to the overextrapolation of results

from [sugar-sweetened beverages] SSBs studies"[3] — I did conclude that their review, and the other two articles that I discussed, sent the implicit message that consumers should be sceptical about the recommendations to reduce their consumption of added sugar. I stand by that conclusion and also by my firm belief that such a message is harmful to consumers and likely to exacerbate the incidence of dental caries and the epidemic of metabolic disease.

As I previously stated[2], there are three clinical dietary intervention studies conducted by Reiser and Hallfrish that demonstrated that added sugar in solid food increases cardiometabolic risk factors compared with a carefully matched starch diet. These studies have generated ten publications. They are among the most well-controlled diet studies that have ever been conducted, with participants consuming half of their standardized, eucaloric meals while being monitored at a clinical research centre. The most likely reason that the findings from these studies have not been replicated is expense. Clinical research centres with dietary kitchens are no longer subsidized by the NIH, so these studies are now far more expensive to conduct. However, the research groups of John Bantle and Arne Astrup have each conducted two studies that demonstrated detrimental health effects of dietary interventions that were high in added sugar from both solid food and beverages. Also, five recent dietary intervention studies have demonstrated that the restriction of free and added sugar from both solid food and beverages reduced the levels of liver fat and other risk factors. Would these same results have been generated if only SSBs had been restricted and the participants had been allowed to eat their usual amount of ice cream, cake, cookies, candy and pastry? Given that sugars in solid food make up about 58% of the average added sugar intake in the USA, perhaps not. Indeed, it is interesting to compare the results of the latest of these sugar-restriction studies[4] with those of a study in which the intervention consisted solely of reducing the consumption of SSBs[5]. In both studies, the interventions were 12 weeks long and the participants were adults who were overweight or obese and had non-alcoholic fatty liver disease. For the trial that focused only on the reduction of SSBs, the participants had a decrease in liver lipid levels compared with the control group, but there were no other significant differences between the groups[5]. For the trial that focused on the reduction of both sources of free sugar, the intervention group had reduced steatosis and fibrosis score, HOMA-IR (Homeostatic Model Assessment for Insulin Resistance) score, and circulating triglyceride, total cholesterol, C-reactive protein and tumour necrosis factor levels compared with the control group[4].

In summary, there are clinical data to show that the consumption of added sugar in solid food increases cardiometabolic risk factors. There are also data to show that increased consumption of added sugar from both solid and liquid sources increases risk factors and that decreased consumption of added sugar from both solid and liquid sources decreases risk factors. Therefore, it is more than my "best guess" that the risk of harm would be greater than the likelihood of benefit if the WHO and US dietary guidelines were revised to recommend solely a reduction in free and added sugar from SSBs. Such a revision might better meet the principles of evidence-based medicine, but I do not believe that it would meet the 'do no harm' axiom of the health-care profession.

The authors do suggest potential negative consequences of reducing free and added sugar consumption to less than 10% of daily energy, and these concerns consist of increased exposure to artificial sweeteners and nutrient dilution. The data suggesting that exposure to artificial sweeteners might promote obesity and metabolic diseases in humans are almost exclusively from epidemiology studies. The conclusions from these studies might be subject to the 'reverse causality' phenomenon, whereby associations exist because individuals with prediabetes or diabetes mellitus or who are overweight or obese might choose to consume artificial sweeteners to reduce their blood glucose level or their risk of weight gain, and not because artificial sweeteners increase blood glucose level or cause weight gain[6]. Of note, the various artificial and non-nutritive sweeteners have different chemical structures that lead to different digestion and uptake patterns in the gut and so are likely to have different metabolic effects in the human body[7]. Therefore, long-term randomized controlled trials will have to be conducted on the individual sweeteners because the results for one sweetener cannot be extrapolated to others. These studies are mainly lacking, but those that have been performed suggest that the consumption of artificial or non-nutritive sweeteners might promote body weight loss and do not elevate blood glucose levels[8,9]. Clearly the evidence does not support revising the WHO and US dietary guidelines to avoid increased exposure to artificial sweeteners.

As reviewed by Louie and colleagues, the majority of the studies do not support the suggestion that reduced consumption of added sugar leads to nutrient dilution; instead, they show the opposite[10]. However, the paper cited by the authors[1] suggests that holding free sugar to <5% of daily energy is associated with nutrient dilution compared with the 5–10% level. This observation is not surprising because the group consuming <5% of daily energy as free sugar had a significantly higher proportion of dieters than the other groups and consumed the least energy. When adjusted for energy intake, this group had higher intake of fibre, vitamin A, vitamin E, magnesium, potassium and zinc than the other five groups[10]. Therefore, I do not agree that nutrient dilution is a potential negative consequence of reducing the consumption of added sugar that justifies revising the WHO and US dietary guidelines.

Kimber L. Stanhope
Department of Molecular Biosciences, School of Veterinary Medicine, University of California – Davis, Davis, CA, USA.
e-mail: klstanhope@ucdavis.edu
https://doi.org/10.1038/s41569-022-00793-8

1. Yan, R., Chan, C. B. & Louie, J. C. Evidence does not support the reduction of added sugar intake from all food sources. *Nat. Rev. Cardiol.* https://doi.org/10.1038/s41569-022-00791-w (2022).
2. Stanhope, K. L. Guidelines to lower intake of added sugar are necessary and justified. *Nat. Rev. Cardiol.* **19**, 569–570 (2022).
3. Yan, R. R., Chan, C. B. & Louie, J. C. Y. Current WHO recommendation to reduce free sugar intake from all sources to below 10% of daily energy intake for supporting overall health is not well supported by available evidence. *Am. J. Clin. Nutr.* **116**, 15–39 (2022).
4. Khodami, B. et al. Effects of a low free sugar diet on the management of nonalcoholic fatty liver disease: a randomized clinical trial. *Eur. J. Clin. Nutr.* **76**, 987–994 (2022).
5. Campos, V. et al. Sugar- and artificially sweetened beverages and intrahepatic fat: a randomized controlled trial. *Obesity (Silver Spring)* **23**, 2335–2339 (2015).
6. Gallagher, A. M. et al. Low-calorie sweeteners in the human diet: scientific evidence, recommendations, challenges and future needs. A symposium report from the FENS 2019 conference. *J. Nutr. Sci.* **10**, e7 (2021).
7. Magnuson, B. A., Carakostas, M. C., Moore, N. H., Poulos, S. P. & Renwick, A. G. Biological fate of low-calorie sweeteners. *Nutr. Rev.* **74**, 670–689 (2016).
8. Rogers, P. J. et al. Does low-energy sweetener consumption affect energy intake and body weight? A systematic review, including meta-analyses, of the evidence from human and animal studies. *Int. J. Obes. (Lond.)* **40**, 381–394 (2016).
9. Nichol, A. D., Holle, M. J. & An, R. Glycemic impact of non-nutritive sweeteners: a systematic review and meta-analysis of randomized controlled trials. *Eur. J. Clin. Nutr.* **72**, 796–804 (2018).
10. Louie, J. C. & Tapsell, L. C. Association between intake of total vs added sugar on diet quality: a systematic review. *Nutr. Rev.* **73**, 837–857 (2015).

Acknowledgements
The author thanks Bettina Hieronimus (Institute for Physiology and Biochemistry of Nutrition, Max Rubner-Institut, Germany) and Desiree Sigala (Department of Molecular Biosciences, School of Veterinary Medicine, University of California, Davis, CA, USA) for discussion, insight and editing before submission

Competing interests
K.L.S. has received honoraria for speaking from numerous organizations (since 2016: American Diabetes Association, Columbia University, Harvard School of Medicine, Swedish Medical Center and University of Missouri) and from CrossFit for serving as academic organizer of a 2017 conference and lead author of the conference summary report.