

## CORRESPONDENCE OPEN



# Response to comment on “Relation of fruit juice with adiposity and diabetes depends on how fruit juice is defined: a re-analysis of the EFSA draft scientific opinion on the tolerable upper intake level for dietary sugars” by Chen et al. 2023

© The Author(s) 2023

*European Journal of Clinical Nutrition* (2023) 77:1178–1179; <https://doi.org/10.1038/s41430-023-01323-6>

**TO THE EDITOR:**

We would like to thank Martínez et al. for their insightful comments [1] and for bringing to our attention the publication of the final version of the European Food Safety Authority (EFSA)'s Scientific Opinion on the Tolerable Upper Intake Level for dietary sugars [2]. We appreciate that the authors have included the EPIC-InterAct study [3] in the final version to reflect the totality of evidence and have concluded on fruit juice in general, rather than specifically on 100% fruit juice, to address the issue of misclassification. However, we note that an analysis separated by fruit juice type (100% fruit juice vs. non-specified fruit juice) is still missing. Although EFSA combined the analyses for 100% fruit juice and total fruit juice (including sugar-sweetened fruit juice) due to the similarity in their content of free sugars [2], this approach may not provide an accurate picture of the risk associated with each juice type. Large evidence syntheses of randomized controlled trials and prospective cohort studies have shown that the impact of fructose-containing sugars on cardiometabolic outcomes may depend on the food source [4, 5]. For example, harm is observed for sugar-sweetened beverages while benefit is observed for fruit. The beneficial nutrients and bioactive compounds found in natural fruit are often retained in 100% fruit juice but are either absent or present in only small amounts in fruit drinks. These nutrients and bioactive compounds may counteract any effect of free sugars in 100% fruit juice for cardiometabolic outcomes. For example, a recent systematic review and meta-analysis of controlled trials demonstrated that 100% fruit juice when providing less than 10% of calories decreased body weight and BMI, while fruit drinks increased body weight, BMI and body fat [6]. Similarly, systematic reviews and meta-analyses of prospective cohort studies have also demonstrated a benefit at low to moderate doses, showing a U-shaped association between 100% fruit juice intake and various cardiometabolic outcomes including hypertension [7], metabolic syndrome [4] and cardiovascular event risk [8]; however, this was not the case for non-specified fruit juice. Therefore, we emphasize the importance of conducting a stratified analysis by fruit juice type [9].

Martínez et al. also identified the low number and heterogeneity of the included studies as barriers to conducting a quantitative analysis. While we agree that more studies are needed to improve the certainty of the evidence, two studies

are considered sufficient to perform a quantitative meta-analysis [10]. We addressed some of the heterogeneity by conducting separate analyses for children and adults, pooling only data that assessed the same outcomes (e.g., incident abdominal obesity was reported separately from change in body weight) and adjusting for the study period (e.g., studies including data on change in BMI over a study period different than 1-year were adjusted to per 1-year). We also provided separate conclusions based upon these populations and endpoints. Although EFSA's final version of the scientific opinion on fruit juice has greatly improved from the draft version, our comprehensive and granular analysis based on fruit juice type provides additional information that is not present in EFSA's final version. Therefore, our perspective piece should be seen as complementing EFSA's scientific opinion and not detracting from it. Our study stands as a more comprehensive analysis of the work done by EFSA when relating to fruit juice type and adiposity and diabetes outcomes.

Victoria Chen<sup>1,2</sup>, Tauseef A. Khan<sup>1,2</sup>, Laura Chiavaroli<sup>1,2,3</sup>,  
Amna Ahmed<sup>1,2</sup>, Danielle Lee<sup>1,2</sup>, Cyril W. C. Kendall<sup>1,2,4</sup> and  
John L. Sievenpiper<sup>1,2,3,5,6</sup>✉

<sup>1</sup>Department of Nutritional Sciences, Temerty Faculty of Medicine, University of Toronto, Toronto, ON, Canada. <sup>2</sup>Toronto 3D Knowledge Synthesis and Clinical Trials Unit, Clinical Nutrition and Risk Factor Modification Centre, St. Michael's Hospital, Toronto, ON, Canada. <sup>3</sup>Li Ka Shing Knowledge Institute, St. Michael's Hospital, Toronto, ON, Canada. <sup>4</sup>College of Pharmacy and Nutrition, University of Saskatchewan, Saskatoon, SK, Canada. <sup>5</sup>Division of Endocrinology and Metabolism, Department of Medicine, St. Michael's Hospital, Toronto, ON, Canada. <sup>6</sup>Department of Medicine, Temerty Faculty of Medicine, University of Toronto, Toronto, ON, Canada.  
✉email: john.sievenpiper@utoronto.ca

**DATA AVAILABILITY**

All data generated or analyzed during this study are included in this published article.

**REFERENCES**

- Martínez S, Turck D, Craciun I, Vinceti M. Comment on “Relation of fruit juice with adiposity and diabetes depends on how fruit juice is defined: a re-analysis of the EFSA draft scientific opinion on the tolerable upper intake level for dietary sugars” by Chen et al. 2023. *Eur J Clin Nutr.* 2023.
- EFSA Panel on Nutrition Novel Foods and Food Allergens, Turck D, Bohn T, Castenmiller J, de Henauw S, Hirsch-Ernst KI, et al. Tolerable upper intake level for dietary sugars. *EFSA J.* 2022;20:e07074.

Received: 2 May 2023 Revised: 25 July 2023 Accepted: 27 July 2023  
Published online: 18 October 2023

- Romaguera D, Norat T, Wark PA, Vergnaud AC, Schulze MB, van Woudenberg GJ, et al. Consumption of sweet beverages and type 2 diabetes incidence in European adults: results from EPIC-InterAct. *Diabetologia*. 2013;56:1520–30.
- Semnani-Azad Z, Khan TA, Blanco Mejia S, de Souza RJ, Leiter LA, Kendall CWC, et al. Association of major food sources of fructose-containing sugars with incident metabolic syndrome: a systematic review and meta-analysis. *JAMA Netw Open*. 2020;3:e209993.
- Choo VL, Vigiouliouk E, Blanco Mejia S, Cozma AI, Khan TA, Ha V, et al. Food sources of fructose-containing sugars and glycaemic control: systematic review and meta-analysis of controlled intervention studies. *BMJ*. 2018;363:k4644.
- Chiavarioli L, Cheung A, Ayoub-Charette S, Ahmed A, Lee D, Au-Yeung F, et al. Important food sources of fructose-containing sugars and adiposity: a systematic review and meta-analysis of controlled feeding trials. *Am J Clin Nutr*. 2023;117:741–65.
- Liu Q, Ayoub-Charette S, Khan TA, Au-Yeung F, Blanco Mejia S, de Souza RJ, et al. Important food sources of fructose-containing sugars and incident hypertension: a systematic review and dose-response meta-analysis of prospective cohort studies. *J Am Heart Assoc*. 2019;8:e010977.
- Zurbau A, Au-Yeung F, Blanco Mejia S, Khan TA, Vuksan V, Jovanovski E, et al. Relation of different fruit and vegetable sources with incident cardiovascular outcomes: a systematic review and meta-analysis of prospective cohort studies. *J Am Heart Assoc*. 2020;9:e017728.
- Clemens R, Drewnowski A, Ferruzzi MG, Toner CD, Welland D. Squeezing fact from fiction about 100% fruit juice. *Adv Nutr*. 2015;6:236s–43s.
- Deeks J, Higgins J, Altman D. Chapter 10: analysing data and undertaking meta-analyses. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al, editors. *Cochrane handbook for systematic reviews of interventions* version 6.3. Cochrane; 2022. [www.training.cochrane.org/handbook](http://www.training.cochrane.org/handbook).

## AUTHOR CONTRIBUTIONS

VC, TAK, LC, AA, DL, CWCK and JLS interpreted the data. VC and TAK drafted the manuscript. TAK and JLS provided supervision. All authors critically revised the manuscript and approved the final version of the manuscript.

## FUNDING

This work was supported by the Canadian Institutes of Health Research (funding reference number, 129920) through the Canada-wide Human Nutrition Trialists' Network (NTN). The Diet, Digestive tract, and Disease (3-D) Centre, funded through the Canada Foundation for Innovation (CFI) and the Ministry of Research and Innovation's Ontario Research Fund (ORF), provided the infrastructure for the conduct of this project. VC was funded by a University of Toronto Department of Nutritional Sciences Fellowship. TAK was funded by a Toronto 3D Postdoctoral Fellowship Award. AA was funded by a Toronto 3D MSc Scholarship Award. DL was funded by a St. Michael's Hospital Research Training Centre MSc Scholarship Award. JLS was funded by a Diabetes Canada Clinician Scientist Award.

## COMPETING INTERESTS

VC has received research support from a University of Toronto Department of Nutritional Sciences Fellowship, the Toronto 3D Knowledge Synthesis and Clinical Trials foundation and Banting and Best Diabetes Centre. TAK has received research support from the Canadian Institutes of Health Research (CIHR), the International Life Science Institute (ILSI), and National Honey Board. He has received honorarium from Calorie Control Council Annual meeting and Arab Beverage Association for invited talks. He has received funding from the Toronto 3D Knowledge Synthesis and Clinical Trials foundation. LC was a Mitacs-Elevate post-doctoral fellow jointly funded by the Government of Canada and the Canadian Sugar Institute (Sep 2019–Aug 2021). AA has received research support from the Toronto 3D Knowledge Synthesis and Clinical Trials foundation. DL has received research support from a University of Toronto Department of Nutritional Sciences Graduate Student Fellowship, University of Toronto Fellowship in Nutritional Sciences, Dairy Farmers of Canada Graduate Student Fellowship, and St. Michael's Hospital Research Training Centre MSc Award. CWCK has received grants or research support from the Advanced Food Materials Network, Agriculture and Agri-Foods Canada (AAFC), Almond Board of California, Barilla, Canadian Institutes of Health Research (CIHR), Canola Council of Canada, International Nut and Dried Fruit Council, International Tree Nut Council Research and Education Foundation, Loblaw Brands Ltd, the Peanut Institute, Pulse Canada and Unilever. He has received in-kind research support from the Almond Board of California, Barilla, California Walnut Commission, Kellogg Canada, Loblaw Companies, Nutrartis, Quaker (PepsiCo), the Peanut Institute, Primo, Unilever, WhiteWave Foods/Danone. He has received travel support and/or honoraria from the

Barilla, California Walnut Commission, Canola Council of Canada, General Mills, International Nut and Dried Fruit Council, International Pasta Organization, Lantmannen, Loblaw Brands Ltd, Nutrition Foundation of Italy, Oldways Preservation Trust, Paramount Farms, the Peanut Institute, Pulse Canada, Sun-Maid, Tate & Lyle, Unilever and WhiteWave Foods/Danone. He has served on the scientific advisory board for the International Tree Nut Council, International Pasta Organization, McCormick Science Institute and Oldways Preservation Trust. He is a founding member of the International Carbohydrate Quality Consortium (ICQC), Executive Board Member of the Diabetes and Nutrition Study Group (DNSG) of the European Association for the Study of Diabetes (EASD), is on the Clinical Practice Guidelines Expert Committee for Nutrition Therapy of the EASD and is a Director of the Toronto 3D Knowledge Synthesis and Clinical Trials foundation. JLS has received research support from the Canadian Foundation for Innovation, Ontario Research Fund, Province of Ontario Ministry of Research and Innovation and Science, Canadian Institutes of Health Research (CIHR), Diabetes Canada, American Society for Nutrition (ASN), International Nut and Dried Fruit Council (INC) Foundation, National Honey Board (U.S. Department of Agriculture [USDA] honey "Checkoff" program), Institute for the Advancement of Food and Nutrition Sciences (IAFNS; formerly ILSI North America), Pulse Canada, Quaker Oats Center of Excellence, The United Soybean Board (USDA soy "Checkoff" program), The Tate and Lyle Nutritional Research Fund at the University of Toronto, The Glycemic Control and Cardiovascular Disease in Type 2 Diabetes Fund at the University of Toronto (a fund established by the Alberta Pulse Growers), The Plant Protein Fund at the University of Toronto (a fund which has received contributions from IFF), and The Nutrition Trialists Network Research Fund at the University of Toronto (a fund established by an inaugural donation from the Calorie Control Council). He has received food donations to support randomized controlled trials from the Almond Board of California, California Walnut Commission, Peanut Institute, Barilla, Unilever/Upfield, Unico/Primo, Loblaw Companies, Quaker, Kellogg Canada, Danone, Nutrartis, Soylent, and Dairy Farmers of Canada. He has received travel support, speaker fees and/or honoraria from ASN, Danone, Dairy Farmers of Canada, FoodMinds LLC, Nestlé, Abbott, General Mills, Nutrition Communications, International Food Information Council (IFIC), Calorie Control Council, International Sweeteners Association, International Glutamate Technical Committee, Phynova, Arab Beverages Association, and Brightseed. He has or has had ad hoc consulting arrangements with Perkins Coie LLP, Tate & Lyle, and Inquis Clinical Research. He is a former member of the European Fruit Juice Association Scientific Expert Panel and former member of the Soy Nutrition Institute (SNI) Scientific Advisory Committee. He is on the Clinical Practice Guidelines Expert Committees of Diabetes Canada, European Association for the study of Diabetes (EASD), Canadian Cardiovascular Society (CCS), and Obesity Canada/Canadian Association of Bariatric physicians and Surgeons. He serves as an unpaid member of the Board of Trustees and formerly served as an unpaid scientific advisor for the Carbohydrates Committee of IAFNS. He is a Director at Large of the Canadian Nutrition Society (CNS), founding member of the International Carbohydrate Quality Consortium (ICQC), Executive Board Member of the Diabetes and Nutrition Study Group (DNSG) of the EASD, and Director of the Toronto 3D Knowledge Synthesis and Clinical Trials foundation. His spouse is an employee of AB InBev.

## ADDITIONAL INFORMATION

**Correspondence** and requests for materials should be addressed to John L. Sievenpiper.

**Reprints and permission information** is available at <http://www.nature.com/reprints>

**Publisher's note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.



**Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons license, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons license and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this license, visit <http://creativecommons.org/licenses/by/4.0/>.

© The Author(s) 2023