

Editor, *American Journal of Clinical Nutrition*

Re: Fructose overconsumption causes dyslipidemia and ectopic lipid deposition in healthy subjects with and without a family history of type 2 diabetes

Editor,

The recent study by Le et al. (1) contains justification and experimental design weaknesses that have become the unfortunate hallmarks of contemporary fructose research. It is useful to be reminded of the following points for perspective when reading their account of the effects of fructose overconsumption on dyslipidemia and ectopic lipid disposition:

Bray's celebrated hypothesis from 2004 stated that high fructose corn syrup (HFCS) is uniquely responsible for obesity—that is, beyond its caloric contribution (2). The hypothesis was based on a graphical correlation between increased HFCS use and rising rates of obesity. It is not widely appreciated that there was a downturn in HFCS consumption beginning in 1999 (3) that invalidated Bray's hypothesis, since obesity rates continued to escalate to the present day.

Second, contemporary fructose experimentation is characterized by a) testing of pure sugars (fructose or glucose) in isolation rather than in combination (fructose + glucose) as they are encountered in foods or in added nutritive (caloric) sweeteners; and b) testing of exaggerated levels, exceeding daily human population mean intakes (4) by 2- to 5-fold in human test subjects and by 6-fold in rodent studies. This applies to the authors' own test diet (fructose *supplement* at 35% of energy) as well as to those cited in the paper as examples of the untoward effects of fructose on lipid metabolism (9-11, 13-14 in (1)).

And third, the study was confounded by an unusual experimental arm that was both higher in fructose *and* one-third higher in calories than the control. As the authors point out, this made the study extraordinarily difficult to interpret, since it was not possible to determine whether observed effects were due to energy overconsumption or to unique metabolic effects of fructose.

The study of Le et al. may indeed become a useful mechanistic study the authors say they intended, but it does not remotely model real-world diets and should not be used to predict outcomes in human populations.

References

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4. Marriott BP, Cole N, Lee E. National estimates of dietary fructose intake increased from 1977 to 2004 in the United States. *J Nutr* 2009;139:1228S-1235S.