HHS Public Access

Author manuscript

Circulation. Author manuscript; available in PMC 2016 July 21.

Published in final edited form as:

Circulation. 2015 July 21; 132(3): e23–e24. doi:10.1161/CIRCULATIONAHA.115.015526.

Reply to Michel Lucas' and Robert Hoenselaar's comments

Maryam S Farvid, Ph.D.[1,2], **Ming Ding, MS**[1], **An Pan, Ph.D.**[3], **Qi Sun, MD, ScD**[1,4], **Stephanie E Chiuve, ScD**[1,5], **Lyn M Steffen, Ph.D., MPH, RD, FAHA**[6], **Walter C Willett, MD, DrPH**[1,4,7], and **Frank B Hu, MD, Ph.D.**[1,4,7]

[1]Department of Nutrition, Harvard School of Public Health, Boston, MA, USA

[2]Department of Community Nutrition, Faculty of Nutrition Sciences and Food Technology, Shahid Beheshti University of Medical Sciences, Tehran, Iran

[3]School of Public Health, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

[4]Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA

[5]Division of Preventive Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA

[6]Division of Epidemiology and Community Health, University of Minnesota School of Public Health, Minnesota, MN, USA

[7]Department of Epidemiology, Harvard School of Public Health, Boston, MA. USA

Reply

We appreciate Michel Lucas' and Robert Hoenselaar's comments on our meta-analysis of linoleic acid and coronary heart disease (CHD) events.[1] Lucas pointed out that evidence from epidemiologic studies including our meta-analyses contradicts the assertion that higher consumption of n-6 polyunsaturated fats (PUFAs) is harmful. Despite theoretical concern about n-6 PUFAs' potential pro-inflammatory and thrombogenic properties, evidence from human studies to support a positive association between intakes of these fatty acids and biomarkers of inflammation or risk of cardiovascular disease (CVD) or cancer is limited. To the contrary, epidemiologic studies and randomized clinical trials have documented beneficial effects of replacing saturated fat with n-6 PUFAs on blood lipids and CVD risk. We agree with Lucas that the n-6/n-3 ratio is not be particularly meaningful because both types of fatty acids are essential and confer health benefits and there is little evidence that the ratio per se is related to health outcomes.

Hoenselaar argued that "Effects found were largely driven by results from 2 cohorts: the Nurses' Health Study (NHS) and the Health Professional Follow-Up Study (HPFS)." To address this issue, in sensitivity analysis, we tested the influence of an individual study on

Corresponding author: Frank B Hu, Address: Department of Nutrition, Harvard T. H. Chan School of Public Health, Boston, MA 02115, frank.hu@channing.harvard.edu.

Disclosures: None

the results. By systematically removing one study at a time, the summary relative risks (RRs) for CHD events for highest versus lowest categories of linoleic acid (LA) intake did not change materially. The summary RR was 0.89 (95% confidence interval (95% CI) = 0.81–0.98) after excluding data from NHS and 0.85 (95% CI = 0.77–0.93) after excluding data from HPFS. We found stronger association after excluding Malmo Diet and Cancer Cohort Study (MDC) (RRs=0.81, 95% CI = 0.75–0.88). Similar results were observed for LA and CHD deaths (after excluding NHS: RR = 0.83, 95% CI= 0.73–0.94; after excluding HPFS: RR=0.80, 95% CI = 0.70–0.92; and after excluding MDC: RR = 0.77, 95% CI = 0.67–0.87) (All data included in this meta-analysis were presented in supplemental tables S1–4 of our paper). Similar results were found for an increment of 5% energy from LA and risk of either CHD events or CHD deaths after removing one study at a time. Updated dietary data during follow-up and large number of individuals followed for a long time and high rates of follow-up distinguished NHS and HPFS from other cohorts.[2]

Stronger associations for LA and either CHD events or CHD deaths were observed in categorical analyses (i.e., highest versus lowest categories) than continuous analyses. We used the median intake of LA in each tertile or quintile to calculate the RRs for each 5% energy from LA. Because the cutpoints for the categories of LA differed somewhat across different studies, the estimates from the categorical analyses were more approximate, while the estimates from continuous analyses were more comparable across studies and hence, more accurate.

Via direct investigator communication, we had a unique opportunity to evaluate the association between LA intake and CHD morbidity and mortality in the largest and most complete systematic review and meta-analysis to date. Based on a funnel plot and Begg's test, no significant publication bias was noted. Also, these robust inverse associations were not dependent on an individual study. Overall, our results are consistent with an earlier pooled analysis of the primary individual data from 11 cohort studies on LA and CHD risk[3] as well as a meta-analysis of randomized clinical trials, which showed a 10% lower CHD risk (RR = 0.90, 95% CI = 0.83–0.97) for each 5% energy increment in PUFA intake.[4] Although different dietary sources of LA might affect the relation between LA and CHD events, the cardioprotective effects of specific foods high in LA was not the subject of this meta-analysis and should be addressed in future work.

References

1. Farvid MS, Ding M, Pan A, Sun Q, Chiuve SE, Steffen LM, Willett WC, Hu FB. Dietary linoleic acid and risk of coronary heart disease: a systematic review and meta-analysis of prospective cohort studies. Circulation. 2014; 130:1568–78. [PubMed: 25161045]
2. Willett WC. Dietary fats and coronary heart disease. J Intern Med. 2012; 272:13–24. [PubMed: 22583051]
3. Jakobsen MU, O'Reilly EJ, Heitmann BL, Pereira MA, Bälter K, Fraser GE, Goldbourt U, Hallmans G, Knekt P, Liu S, Pietinen P, Spiegelman D, Stevens J, Virtamo J, Willett WC, Ascherio A. Major types of dietary fat and risk of coronary heart disease: a pooled analysis of 11 cohort studies. Am J Clin Nutr. 2009; 89:1425–32. [PubMed: 19211817]
4. Mozaffarian D, Micha R, Wallace S. Effects on coronary heart disease of increasing polyunsaturated fat in place of saturated fat: a systematic review and meta-analysis of randomized controlled trials. PLoS Med. 2010; 7:e1000252. [PubMed: 20351774]