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FREE[JAMA Intern Med.](#) 2016 Aug 1;176(8):1134-45. doi: 10.1001/jamainternmed.2016.2417.

## Association of Specific Dietary Fats With Total and Cause-Specific Mortality.

[Wang DD](#)<sup>1</sup>, [Li Y](#)<sup>2</sup>, [Chiuve SE](#)<sup>3</sup>, [Stampfer MJ](#)<sup>4</sup>, [Manson JE](#)<sup>5</sup>, [Rimm EB](#)<sup>6</sup>, [Willett WC](#)<sup>6</sup>, [Hu FB](#)<sup>6</sup>.

### Author information

### Abstract

**IMPORTANCE:** Previous studies have shown distinct associations between specific dietary fat and cardiovascular disease. However, evidence on specific dietary fat and mortality remains limited and inconsistent.

**OBJECTIVE:** To examine the associations of specific dietary fats with total and cause-specific mortality in 2 large ongoing cohort studies.

**DESIGN, SETTING, AND PARTICIPANTS:** This cohort study investigated 83 349 women from the Nurses' Health Study (July 1, 1980, to June 30, 2012) and 42 884 men from the Health Professionals Follow-up Study (February 1, 1986, to January 31, 2012) who were free of cardiovascular disease, cancer, and types 1 and 2 diabetes at baseline. Dietary fat intake was assessed at baseline and updated every 2 to 4 years. Information on mortality was obtained from systematic searches of the vital records of states and the National Death Index, supplemented by reports from family members or postal authorities. Data were analyzed from September 18, 2014, to March 27, 2016.

**MAIN OUTCOMES AND MEASURES:** Total and cause-specific mortality.

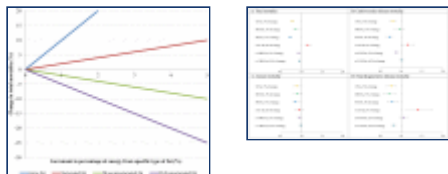
**RESULTS:** During 3 439 954 person-years of follow-up, 33 304 deaths were documented. After adjustment for known and suspected risk factors, dietary total fat compared with total carbohydrates was inversely associated with total mortality (hazard ratio [HR] comparing extreme quintiles, 0.84; 95% CI, 0.81-0.88;  $P < .001$  for trend). The HRs of total mortality comparing extreme quintiles of specific dietary fats were 1.08 (95% CI, 1.03-1.14) for saturated fat, 0.81 (95% CI, 0.78-0.84) for polyunsaturated fatty acid (PUFA), 0.89 (95% CI, 0.84-0.94) for monounsaturated fatty acid (MUFA), and 1.13 (95% CI, 1.07-1.18) for trans-fat ( $P < .001$  for trend for all). Replacing 5% of energy from saturated fats with equivalent energy from PUFA and MUFA was associated with estimated reductions in total mortality of 27% (HR, 0.73; 95% CI, 0.70-0.77) and 13% (HR, 0.87; 95% CI, 0.82-0.93), respectively. The HR for total mortality comparing extreme quintiles of  $\omega$ -6 PUFA intake was 0.85 (95% CI, 0.81-0.89;  $P < .001$  for trend). Intake of  $\omega$ -6 PUFA, especially linoleic acid, was inversely associated with mortality owing to most major causes, whereas marine  $\omega$ -3 PUFA intake was associated with a modestly lower total mortality (HR comparing extreme quintiles, 0.96; 95% CI, 0.93-1.00;  $P = .002$  for trend).

**CONCLUSIONS AND RELEVANCE:** Different types of dietary fats have divergent associations with total and cause-specific mortality. These findings support current dietary recommendations to replace saturated fat and trans-fat with unsaturated fats.

PMID: 27379574 PMCID: [PMC5123772](#) DOI: [10.1001/jamainternmed.2016.2417](#)

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[Martin Mayer](#) 2017 Jan 14 4:27 p.m. [edited](#)

[Reporting and appraising research: a cautionary tale](#)

*Substituting various fats for carbohydrates or saturated fat: an uncertain recipe missing quantitative context and a cautionary example of reporting and appraising research*

Broadly speaking, science is a way of thinking that involves asking answerable questions about phenomena and then systematically and impartially pursuing means to reduce uncertainty about the answer as much as possible. During the pursuit, findings must always be appropriately contextualized to avoid inaccurate, disproportionate, or otherwise mistaken interpretations, as such mistaken interpretations run contrary to the *raison d'être* of scientific inquiry. Unfortunately, confusion about and mistaken or overreaching interpretations of research abound.

Wang and colleagues recently published an article in *JAMA Internal Medicine* investigating various patterns of fat intake on total and cause-specific mortality. Their article speaks to the above and will add tangibility to the above considerations; it therefore serves as an instructive example to be considered in some detail, but the concepts considered herein are certainly more broadly applicable.

Read the rest [here](http://blogs.bmj.com/bmjebmspotlight/2016/10/03/reporting-and-appraising-research-a-cautionary-tale/) (<http://blogs.bmj.com/bmjebmspotlight/2016/10/03/reporting-and-appraising-research-a-cautionary-tale/>).

*Note: I edited this post on September 14, 2017 to update all URLs hyperlinking to my original commentary due to a rebranding of the website on which my blog post appears. I did not make any other changes. The original post appears below in its original form for the sake of completeness and transparency of the record.*

-----Begin original post from January 14, 2017-----

### **Reporting and appraising research: a cautionary tale**

*Substituting various fats for carbohydrates or saturated fat: an uncertain recipe missing quantitative context and a cautionary example of reporting and appraising research*

Broadly speaking, science is a way of thinking that involves asking answerable questions about phenomena and then systematically and impartially pursuing means to reduce uncertainty about the answer as much as possible. During the pursuit, findings must always be appropriately contextualized to avoid inaccurate, disproportionate, or otherwise mistaken interpretations, as such mistaken interpretations run contrary to the *raison d'être* of scientific inquiry. Unfortunately, confusion about and mistaken or overreaching interpretations of research abound.

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**Dong Wang** 2017 Feb 11 5:52 p.m. edited

Reply to Martin Mayer, MS, PA-C

Authors: Dong D. Wang, MD, ScD and Frank B. Hu, MD, PhD

From the Departments of Nutrition (DDW and FBH) and Epidemiology (FBH), Harvard T. H. Chan School of Public Health, Boston, MA; The Channing Division for Network Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA (FBH)

We agree with Mr. Mayer that 'well-designed, well-executed randomized controlled trials (RCTs)' can provide strong evidence for the causal effect between dietary fatty acids and mortality. However, because of multiple methodological limitations, e.g., poor compliance and high drop-out rate, decades-long RCTs testing effects of dietary interventions on hard endpoints, such as cardiovascular disease (CVD) incidence and mortality, are extremely difficult to conduct [1]. High cost and ethical considerations are additional challenges for conducting such a RCT. Further, the notion that RCTs are 'confounding-free' is only held when there are low rates of drop out and high degree of compliance. In most large-scale long-term RCTs, biases may occur after baseline randomization due to differential adherence to assigned treatment regimens, differential loss to follow-up, and other differences between comparison groups [2]. In addition, our findings based on prospective cohorts are consistent with effects of replacing saturated fatty acid (SFA) by polyunsaturated fatty acid (PUFA) on both blood lipids

[3] and cardiovascular disease [4] from RCTs. Thus, in most situations, large prospective cohort studies of hard clinical endpoints, when well designed and interpreted in the context smaller RCTs on intermediate endpoints such as blood lipids, can provide the best available evidence to inform dietary recommendations. One such example is trans fat. Large epidemiologic studies like ours found a consistent positive association between trans fat intake and risk of cardiovascular disease. Meanwhile, small RCTs found that trans fatty acids increase total and LDL cholesterol. The combination of these two types of evidence has led to the policies that result in food labeling and banning in the food supply [5].

Citing Nissen and Ioannidis' attacks on methodological issues of nutritional epidemiology [6, 7], Mr. Mayer questioned the validity of the food frequency questionnaires (FFQs) in assessing dietary intakes. However, Nissen and Ioannidis' viewpoints and Mr. Mayer's question simply reflect lack of understanding of the basic methodology of nutritional epidemiology and human nutrition research. In contrary to Mr. Mayer's claim, our food frequency questionnaires (FFQs) have been demonstrated to be a useful and valid dietary assessment instrument to measure long-term usual dietary intake in well-conducted epidemiological studies [1, 8]. The validity of our FFQs against multiple-day diet records and biomarkers in the validation studies has been extensively documented [8]. For example, the correlations between energy-adjusted intakes assessed by the 1986 FFQ and the mean of multiple weighed 1-week dietary records collected in 1980 and 1986, corrected for variation in the records, were 0.67 for total fat, 0.70 for SFA, 0.69 for MUFA, and 0.64 for PUFA. [8] Correlations increased when the mean of 3 FFQs (1980, 1984, and 1986) was used; for example, for SFAs the correlation was 0.95. The correlation between dietary fatty acid intake assessed by the FFQ and the composition of fatty acids in adipose tissue were 0.51 for TFA, 0.35 for LA, and 0.48 for long-chain n-3 PUFA in NHS, [9] and 0.29 for TFA, 0.48 for LA, and 0.47 for EPA in HPFS. Moreover, adjustment for total energy intake, along with use of cumulative average intake calculated from many repeated FFQs, further dampens the measurement errors and improves the validity [8].

By pointing out that our study population was 'exclusively health care professionals with noteworthy exclusion criteria', Mr. Mayer questioned the generalizability of our findings. However, the effect estimates represent the underlying physiological mechanisms relating fatty acid intake to mortality that are generally applicable to other populations. In addition, for the estimated effect of substituting SFA by PUFA, the hazard ratio (HR) of CVD mortality in our study (0.72, 95% CI, 0.65-0.80) is similar to the HR of coronary death (0.74, 95% CI, 0.61-0.89) estimated from a pooled analysis including 11 cohorts with diverse sociodemographic characteristics, which further support the generalizability of our findings [10]. Because our study intended to mimic a primary prevention setting, we excluded participants with major chronic diseases, including CVD, cancer and diabetes, at baseline. In contrary to Mr. Mayer's assertion, applying these exclusion criteria, our study produced more generalizable findings to inform dietary recommendations for primary prevention of disease outcomes in the general population.

Mr. Mayer criticized our use of HR, a ratio measure, and claimed only reporting HRs is 'considerably less informative and can contribute to distorted appraisal of research findings'. These assertions are unfounded. Both ratio and difference measurements have their own merits and usefulness. Difference measures are measures of the public health and clinically relevant effect of exposure, whereas relative measures are measures of the biological strength of the association between an exposure and disease outcome. Therefore, reporting HRs is compatible with the objective of our study, i.e., to examine the associations of specific dietary

fats with total and cause-specific mortality. From a technical perspective, HR is the default outputs estimated by the multiplicative Cox proportional hazards model, the most robust and widely applied statistical model for time-to-event data. It is important to note that HRs can be compared across different studies and populations, whereas difference measures are difficult to compare because of different baseline risk in different populations.

In summary, our study provided strong evidence because of the solid study design, such as many repeated measurements of diet, validated measurement methods and high follow-up rates over decades, and sophisticated statistical analysis, i.e., extensive adjustment for a large number of potential confounding factors. Our findings are consistent with other high-quality evidence from both observational cohort studies and RCTs [3, 4, 10] and meet multiple key Bradford-Hill criteria, including the strength and consistency of the evidence, biological plausibility, temporal relationships and experimental evidence on intermediate biomarkers.

Conflict of interest: None

## Reference

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**[Lydia Maniatis](#)** 2017 Feb 14 06:13 a.m.

"Our findings are consistent with ... biological plausibility...." "Plausibility" is quite a low and rather subjective bar; an argument against outright rejection, not an argument in support of...

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**[Martin Mayer](#)** 2017 Mar 08 6:24 p.m. [edited](#)

**Reply to Dong D. Wang, MD, ScD and Frank B. Hu, MD, PhD**

**Author: Martin Mayer, MS, PA-C**

**Conflict of interest: None**

I sincerely appreciate the reply from Drs. Wang and Hu, including the time they took to read my original commentary on their study and the time they took to compose a response. However, their reply ultimately does not resolve the issues I present in [my original commentary](#), and I am concerned they may mistakenly believe I am attempting to dismiss entirely the field of nutritional epidemiology or the potential benefits of a sound diet; neither of these are true, and

nothing herein or in [my original commentary](#) should be construed as a suggestive, definitive, or *de facto* exoneration or dismissal of various patterns of fat intake or dietary composition. Such impressions would suggest having missed the central thrust behind my original commentary, namely (1) researchers should always endeavor to provide balanced and objective qualitative and quantitative context for their research findings, and (2) those reading research articles should consider these issues during evidence appraisal, synthesis, translation, and application. Nevertheless, and even though I am a strong advocate for healthy lifestyles (including a sound diet), I stand by [my original commentary](#), and I respond [here](#) in a point-by-point fashion.

(Post edited after original posting to update the link to my reply, as it was not displaying correctly.)

*Note: I edited this post and my full reply to Wang and Hu on September 14, 2017 to update all URLs hyperlinking to my original commentary due to a rebranding of the website on which my blog post appears. I did not make any other changes to this post (I even include the originally-present parenthetical note about editing the original post due to issues with how my reply was displaying) or my full reply. The original post appears below in its original form for the sake of completeness and transparency of the record, as does the original link to my full reply to Wang and Hu.*

-----Begin original post from March 8, 2017-----

## **Reply to Dong D. Wang, MD, ScD and Frank B. Hu, MD, PhD**

**Author: Martin Mayer, MS, PA-C**

**Conflict of interest: None**

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