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Martin Mayer

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

Wang DD. JAMA Intern Med. 2016. [4 comments](#)[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-----

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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

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.)

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Treating Influenza With Neuraminidase Inhibitors: What Is the Evidence?

Louie JK. JAMA Intern Med. 2015. [1 comment](#)

Martin Mayer 2017 Jan 02 11:32 a.m. [edited](#)

The new online format of *JAMA Internal Medicine* no longer shows the comments that were submitted and posted for this article (one from Peter Doshi and Tom Jefferson, and one from me). The comments to which I refer are not the same as the above-noted comments that were

published as Letters to the Editor (though Doshi and Jefferson did also publish a Letter to the Editor). The comments to which I refer are available [here](#) for interested readers.

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Nonfasting Mild-to-Moderate Hypertriglyceridemia and Risk of Acute Pancreatitis.

Pedersen SB. JAMA Intern Med. 2016. [1 comment](#)

Martin Mayer 2016 Dec 11 3:32 p.m. 3 of 3 people found this helpful

Cut the fat: Putting the risks of hypertriglyceridemia into context

A brief response to "Nonfasting mild-to-moderate hypertriglyceridemia and risk of acute pancreatitis"

In their article, Pedersen and colleagues present findings from their prospective cohort study on hypertriglyceridemia and its association with both acute pancreatitis and myocardial infarction.¹ With a median follow-up of 6.7 years (interquartile range, 4.0 to 9.4 years) among 116,550 "white individuals of Danish descent from the Danish general population"^{1(p1835)} selected randomly from two similar prospective studies (the Copenhagen City Heart Study and the Copenhagen General Population Study), this is a sizable study with respectable follow-up, even if generalizability of the findings might be at least somewhat limited. They rightly note "there is no consensus on a clear threshold above which triglycerides are associated with acute pancreatitis,"^{1(p1835)} and others have highlighted important issues with the evidence base.² Pedersen and colleagues also cite a review³ on triglycerides and cardiovascular disease, but here too the evidence is not entirely clear; the review only concludes evidence "is increasing"^{3(p633)} and recommends high-intensity statin therapy. The review also considers the future potential of add-on triglyceride-lowering therapy for those already on a statin, pointing to two ongoing trials of ω -3 fatty acids ([REDUCE-IT](#) and [STRENGTH](#)). However, the currently-available evidence - particularly that with patient-relevant outcomes - does not support such a strategy for ω -3 fatty acids or other agents that can substantially lower triglycerides (such as fibrates and niacin).^{2,4,5}

Even if their study reflects an underlying truth, Pedersen and colleagues unfortunately demonstrate a relative inattention to absolute risks and the implications thereof. They devote a small amount of text to absolute risks and report absolute numbers in the figures, but they repeatedly state their findings show "high risk" for acute pancreatitis, a perspective seemingly driven by the magnitude of the hazard ratios (HRs). In their concluding statements, they even remark: "Mild-to-moderate hypertriglyceridemia at 177 mg/dL (2 mmol/L) and above is associated with high risk of acute pancreatitis in the general population, with HRs higher than for myocardial infarction."^{1(p1841)}

When caring for individual patients, relative metrics such as HRs are most useful when appropriately applied to corresponding baseline absolute risks. Conversely, disproportionate focus on relative metrics or failure to adequately contextualize relative metrics with corresponding absolute risks is considerably less informative and can contribute to a distorted sense of reality. Even if one accepts research findings as being likely reflective of an underlying truth, one must always carefully appraise absolute risks to gain a finer appreciation of the quantitative implications of the research findings. This practice is still useful even if one finds weaknesses in methodology, as one can simply consider the estimates increasingly uncertain in a manner qualitatively proportional to the weaknesses in methodology. A tool customized for this study is available [here](#) (TinyURL: <http://tinyurl.com/JAMAIMhypertrigcalctool>).

According to their own data, comparing the lowest triglyceride level group (<89 mg/dL or <1 mmol/L) to the highest triglyceride level group (≥ 443 mg/dL or ≥ 5 mmol/L), one finds an absolute risk difference (ARD) for acute pancreatitis of 0.93% over 10 years if using the absolute numbers reported in Figure 1 to estimate absolute risks, and an ARD of 2.05% over 10 years (95% confidence interval [CI], 0.73% to 4.99%) if using the absolute risk in the lowest triglyceride level group and the multivariable-adjusted HR estimate for the highest triglyceride level group (HR 8.7; 95% CI, 3.7 to 20). Repeating this for myocardial infarction, one finds an ARD of 5.6% over 10 years or an ARD of 5.08% (95% CI, 3.00% to 7.73%) over 10 years. This demonstrates at least one reason why it is important to put relative metrics into context: Although the HRs for acute pancreatitis may be "higher than for myocardial infarction",^{1(p1841)} the absolute risks and absolute risk differences are higher for myocardial infarction. Additionally, it is more informative to provide risk estimates in absolute terms than in relative terms. Indeed, as aforementioned, absolute risks give better insight into what research might mean for a patient if one accepts the findings as being

reflective of an underlying truth. Unfortunately, *The New York Times*' coverage of the study exacerbates the issue, with the only attempt to contextualize the relative metrics being a quote from one of the study's authors. (Such mishandling of evidence is not uncommon in the media, but that is not the focus of this commentary. Including *The New York Times*' coverage is not meant to single them out as uniquely bad or good in this regard; it simply serves as an example.) It is ultimately a disservice to say the risk of pancreatitis was 770% higher in patients with triglycerides ≥ 443 mg/dL (≥ 5 mmol/L) compared to patients with triglycerides < 89 mg/dL (< 1 mmol/L) without contextualizing such a metric with absolute risks. More technically, and as discussed in the [tool](#), HRs are also not quite the same as relative risks.

Lastly, while management was not a focus Pedersen and colleagues' article, sensible lifestyle changes should be emphasized wherever poor lifestyle factors exist. As for interventions beyond lifestyle changes, a medication that can reduce cardiovascular risk – such as a statin – might be instituted after shared decision-making concerning a person's cardiovascular risk estimate; importantly, however, a person's cardiovascular risk estimate is *not* dependent on triglyceride levels, and pharmaceutical intervention targeted at lowering triglycerides *per se* is *not* clearly supported by currently-available evidence examining cardiovascular, pancreatic, or other patient-relevant outcomes.

References

- (1) Pedersen SB, Langsted A, Nordestgaard BG. Nonfasting mild-to-moderate hypertriglyceridemia and risk of acute pancreatitis. *JAMA Intern Med.* 2016 Dec 1;176(12):1834-1842. doi: 10.1001/jamainternmed.2016.6875.
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- (5) Keene D, Price C, Shun-Shin MJ, Francis DP. Effect on cardiovascular risk of high density lipoprotein targeted drug treatments niacin, fibrates, and CETP inhibitors: meta-analysis of randomised controlled trials including 117,411 patients. *BMJ.* 2014 Jul 18;349:g4379. doi: 10.1136/bmj.g4379. (Note about this reference: Although the title implies focus on HDL as a therapeutic target, this study nevertheless provides meaningful insight into whether there is any cardiovascular or mortality benefit from adding either niacin or a fibrate to statin therapy, and both these agents can substantially lower triglycerides.)

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