

nary artery disease remain relevant to the study of cardiovascular and metabolic diseases.

The authors also raise concern for potential overadjustment bias. The authors point out that statistical adjustment in regression models for effects that may be on the causal pathway between fitness and a cardiovascular outcome may inappropriately diminish that relationship. The underlying question of our report (and fundamental hypothesis for this work) was whether objective point assessments of fitness in young adulthood (not necessarily sustained physical activity) provide long-lasting benefit independent of cardiometabolic risk factors. We had sufficient power to explore multiple adjustments in our models. The adjustments used in this work were similar in scope to those reported in earlier work in CARDIA⁵ and used in a variety of other epidemiologic investigations.

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1. Möhlenkamp S, Lehmann N, Breuckmann F, et al; Marathon Study Investigators; Heinz Nixdorf Recall Study Investigators. Running: the risk of coronary events: prevalence and prognostic relevance of coronary atherosclerosis in marathon runners. *Eur Heart J*. 2008;29(15):1903-1910.
2. Puri R, Nicholls SJ, Shao M, et al. Impact of statins on serial coronary calcification during atheroma progression and regression. *J Am Coll Cardiol*. 2015;65(13):1273-1282.
3. Criqui MH, Denenberg JO, Ix JH, et al. Calcium density of coronary artery plaque and risk of incident cardiovascular events. *JAMA*. 2014;311(3):271-278.
4. Shah RV, Murthy VL, Colangelo LA, et al. Association of fitness in young adulthood with survival and cardiovascular risk: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. *JAMA Intern Med*. 2016;176(1):87-95.
5. Lee CD, Jacobs DR Jr, Hankinson A, Iribarren C, Sidney S. Cardiorespiratory fitness and coronary artery calcification in young adults: The CARDIA Study. *Atherosclerosis*. 2009;203(1):263-268.

Corporate Funding of Nutrition Research and Unjustified Conclusions

To the Editor In her Viewpoint about corporate funding of food and nutrition research, Dr Nestle criticizes the food industry and scientists who associate with it.¹

Dr Nestle claims that scientists who receive industry-derived research grants “often fail to realize that food-industry funding may affect their work...”^{1(p13)} She cites newspaper articles that “illustrate the concerns about biases introduced by industry funding.”^{1(p13)} She also cites reports^{2,3} showing that there are relatively few studies funded by industry whose results are contrary to the funders’ interest and discusses her work on the subject including reference to her Food Politics blog.⁴

The study by Massougbdji et al² also determined that the quality of the methods of the studies reviewed did not explain

the orientation of the authors’ conclusions, nor was there any relationship between the source of funding and the overall quality of the studies examined. The study by Lesser et al³ did not examine any aspect of the studies that were reviewed other than funding source. The newspaper stories did not describe any flaw in the research of the scientists profiled. In addition, the authors of a great number of the presumably tainted industry-sponsored studies discussed on the blog written by Dr Nestle⁴ explicitly stated that the funding source was not involved in the design, conduct, data analysis and interpretation, or manuscript preparation. Although Dr Nestle also states that the quality of dietary advice is adversely affected by the source of research funds, many believe that the real problem is the overall poor quality of nutrition research.⁵ Before guilt by association is established, criticisms by Dr Nestle deserve much more analysis.

It would certainly be helpful, if not essential, for Dr Nestle or others to show that industry-funded studies have more design flaws, inappropriate analyses, or unjustified conclusions relative to similar studies funded by other sources. Furthermore, in addition to financial conflicts of interest, there are non-financial conflicts resulting from career self-interest or unbounded intellectual passion that can be just as worrisome. Conflicts of interest in science can affect anyone, and are relevant to proponents of any point of view.

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Additional Information: Dr Kahn served as the Chief Scientific and Medical Officer of the American Diabetes Association.

1. Nestle M. Corporate funding of food and nutrition research: science or marketing. *JAMA Intern Med*. 2016;176(1):13-14.
2. Massougbdji J, Le Bodo Y, Fratu R, De Wals P. Reviews examining sugar-sweetened beverages and body weight: correlates of their quality and conclusions. *Am J Clin Nutr*. 2014;99(5):1096-1104.
3. Lesser LI, Ebbeling CB, Gozner M, Wypij D, Ludwig DS. Relationship between funding source and conclusion among nutrition-related scientific articles. *PLoS Med*. 2007;4(1):e5.
4. Nestle M. Food Politics Blog. <http://www.foodpolitics.com/>. Accessed March 2, 2016.
5. Ioannidis JP. Implausible results in human nutrition research. *BMJ*. 2013;347:f6698.

In Reply Dr Kahn requests evidence that nutrition research funded by food companies is of lesser quality than studies funded by independent agencies or performed by investigators with non-financial conflicts of interest. Concerns about such issues are relatively recent; few published studies address them directly. Instead, concerns about industry sponsorship of nutrition research derive from comparisons with the results of studies of funding by tobacco, chemical, drug, or medical device companies. This research typically finds industry-sponsored studies to report results more favorable to the products of the sponsor than studies not funded by industry. It identifies subtle rather than substantive differences in the quality of this research; industry-

funded studies are more likely to underreport unfavorable results and interpret neutral results more positively.¹ When results are negative, they are less likely to be published.²

Between March 2015 and March 2016, I identified 166 industry-funded nutrition research studies and posted and discussed them on my blog.³ Of these, 154 reported results favorable to the interest of the sponsor; only 12 reported contrary results. The few studies systematically examining the influence of industry funding on nutrition research tend to confirm results obtained from other industries. For example, a systematic review comparing industry-funded and nonindustry-funded trials of probiotics in infant formula reported no association of funding source with research quality. Industry-funded studies, however, seemed more likely to report favorable conclusions unsupported by the data.⁴

Dr Kahn states that sponsored studies often specify that the funder had no role in the study. Only recently have some journals required such statements, and I am unaware of research on the extent of this practice or authors' adherence to it. Among the 166 industry-funded studies that I reviewed, few disclosed involvement of a sponsor.

Dr Kahn asks whether industry funding is any more biasing than career self-interest or intellectual passion. Unlike industry funding, self-interest and passions are intrinsic to every scientist who conducts research, are a matter of public record, cannot be eliminated, and have not been shown to consistently bias research results in the same ways as industry funding.⁵ Fortunately, nutrition societies and research institutions are developing policies to manage financial relationships with industry.⁶ Such policies hold promise for preventing financial conflicts of research in nutrition research.

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1. Lundh A, Sismondo S, Lexchin J, Busuioic OA, Bero L. Industry sponsorship and research outcome. *Cochrane Database Syst Rev*. 2012;12:MR000033.
2. Rising K, Bacchetti P, Bero L. Reporting bias in drug trials submitted to the Food and Drug Administration: review of publication and presentation. *PLoS Med*. 2008;5(11):e217.
3. Nestle M. Food Politics Blog. <http://www.foodpolitics.com/>. Accessed March 2, 2016.
4. Mugambi MN, Musekiwa A, Lombard M, Young T, Blaauw R. Association between funding source, methodological quality and research outcomes in randomized controlled trials of synbiotics, probiotics and prebiotics added to infant formula: a systematic review. *BMC Med Res Methodol*. 2013;13:137.
5. Bero L. What is in a name? Nonfinancial influences on the outcomes of systematic reviews and guidelines. *J Clin Epidemiol*. 2014;67(11):1239-1241.
6. Charles Perkins Centre. Engagement with Industry Guidelines 2015. University of Sydney, 2015. <https://intranet.sydney.edu.au/perkins/research-support/engaging-with-industry.html>. Accessed March 2, 2016.

Mixed Diagnoses and Mixed Messages

To the Editor The pragmatic, randomized clinical trial of delayed antibiotic prescribing strategies reported by de la Poza Abad and colleagues¹ combined antibiotic-inappropriate diagnoses (acute bronchitis) and diagnoses for which antibiotics might be appropriate (rhinosinusitis, pharyngitis). Combining and randomizing patients with diagnoses that should and should not receive antibiotics limits the interpretability and applicability to clinical practice of the trial.

In the main analyses of de la Poza Abad and colleagues,¹ the investigators adjusted the main outcomes—symptom severity and duration—for antibiotic use, rather than using an intent-to-treat approach based on randomization alone. This unusual analytic choice effectively compares all subjects who did not take antibiotics to each other and separately compares all subjects who did take antibiotics to each other across the study arms. Because such analyses control away a key step (use of antibiotics) on the causal pathway between random assignment and study outcomes, the results should not be interpreted as measuring the complete effects of each prescribing strategy on symptom severity and duration.

Beyond these problems with the design and analysis, we advocate against delayed antibiotic prescriptions for the following reasons.²

First, there are reasonably clear guidelines about which patients do and do not benefit from treatment with antibiotics.³ Second, delayed antibiotic prescriptions are microbiologically nonsensical: patients with a viral illness will have that viral illness 3 days later. Third, delayed antibiotic prescriptions ignore the natural history of most acute respiratory infections. The sore throat from acute viral pharyngitis lasts about 5 days; symptoms from the common cold last 2 weeks; the cough from acute bronchitis averages 3 weeks.

Fourth, delayed antibiotic prescriptions send mixed messages to patients and clinicians, effectively telling patients, “You don’t need an antibiotic, but here’s one anyway.” Such waffling contributes to confusion about whether antibiotics can treat viral illnesses.⁴

Fifth, delayed antibiotic prescriptions place the burden of clinical decision-making on patients but without giving them an evidence-based rationale for taking an antibiotic at all. This is abdication of good decision-making, not shared decision-making.

In attempting to address the threat of antibiotic-resistant bacteria—which is serious and real—we have lost focus on individual patients. By using a delayed antibiotic prescribing strategy, clinicians would be prescribing a medication that for most patients is more likely to harm than to help.⁵

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