Nutritional epidemiology in practice: learning from data or promulgating beliefs?1–3

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The world can be a scary place. Bad things sometimes happen to us and our loved ones, and few things are scarier than cancer. When we are facing frightening things, a sense of controllability can ease our fears (1). But experience and empirical evidence tell us that things are often more seemingly random and less predictable and controllable than we commonly think (2). Before Benjamin Franklin’s scientific investigation of lightning and invention of the lightning rod, lightning was a terrifying, seemingly random and uncontrollable, and often deadly occurrence. People sought explanations and control: they found those explanations in divine provenance and perceived control in the ringing of church bells. Unfortunately, ringing church bells does not actually dissuade lightning and often led to the deaths of bell ringers who ascended the bell towers in the midst of storms (3).

One author described cancer as the result of a “lottery-like accumulation of stochastic mutations” (4). Faced with such a lottery that none of us voluntarily enter, we grasp desperately for signs of controllability. Would it not be wonderful if food itself, the daily sustenance that we all take and one of our greatest pleasures, offered such controllability? For centuries, we have sought causes and cures for cancer, and food has been a prime candidate in that search (5). Has this search and our collective conflict of interest in wanting to reduce our fear potentially affected our interpretation and reporting of research results, leading to bias in the scientific record? Are we like church-bell ringers in a storm?

John Ioannidis has been a pioneer in creatively finding the skeletons in the epistemologic closet of the biomedical research community. In this issue of the Journal, he and Jonathan Schoenfeld do so again with the provocative and innovative flair we have come to expect (6). They raise an important question in nutritional epidemiology by asking, “Is everything we eat associated with cancer?” As they noted in the Discussion, analyzing all nutrient-cancer interactions would be impossible. Yet, by selecting 50 ingredients from a cookbook, they ensured that the analysis would be relevant to common, familiar foods, including specific dairy products, meats, vegetables, and spices and even tea and rum. This method of selecting the subject of review was just as innovative as the question at hand. They found that almost three-fourths of the articles they reviewed concluded that there was an increased or decreased risk of cancer attributed to various foods, with most evidence being at least nominally significant. It appears, then, that according to the published literature almost everything we eat is, in fact, associated with cancer. However, Schoenfeld and Ioannidis proceeded to show that biases exist in the nutrient-cancer literature. The fidelity of research findings between nutrients and cancer may have been compromised in several ways. They identified an overstating of weak results (most associations were only weakly supported), a lack of consistent comparisons (inconsistent definitions of exposure and outcomes), and possible suppression of null findings (a bimodal distribution of outcomes, with a noticeable lack of null findings).

Although Schoenfeld and Ioannidis (6) showed that biases exist in the nutrient-cancer literature, it is unclear what causes these breaches in scientific objectivity. Bias is not new to the field of science. Antoine-Laurent Lavoisier in the 1700s wrote about bias and its clouding of scientific findings, stating, “Imagination, on the contrary, which is ever wandering beyond the bounds of truth, joined to self-love and that self-confidence we are so apt to indulge, prompt us to draw conclusions which are not immediately derived from facts; so that we become in some measure interested in deceiving ourselves” (7). White hat bias, confirmation bias, and publication bias can lead to self-deception (8, 9). White hat bias, defined by Cope and Allison as “bias leading to distortion of research-based information in the service of what may be perceived as ‘righteous ends,’” may be a factor in the overstatement of research findings (8). In addition, overstatement of results can be influenced by confirmation bias, in which the overstated results match preconceived views and hypotheses, leading to acceptance of the results even if the results are weak or nonsignificant (9). When results are null, publishing can be difficult and can lead to publication bias in which significant findings are more likely to be published, further distorting our view of what is known (9). When results are presented in a biased manner, the distorted results are disseminated to the public through lay media (10).

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First published online December 5, 2012; doi: 10.3945/ajcn.112.052472.
The implications of Schoenfeld and Ioannidis’ analysis may be important for nutritional epidemiology even more broadly. Numerous food ingredients are thought to have medicinal properties that are not sufficiently supported by current knowledge—for example, coffee “curing” diabetes (11). These distortions can also be used to demonize foods, as shown by the longstanding presumption that dietary cholesterol in eggs contributes to heart disease (12). Causative relations between various foods and diseases likely do exist, but the evidence for many relations is weak, although conclusions about these relations are stated with the certainty one would expect only from the most strongly supported evidence.

Important steps to improve the fidelity of research reporting include the following: increased use and improvement of clinical trial (13) and observational study (14) registries; making raw data publicly available (15); making supporting documentation such as protocols, consent forms, and analytic plans publicly available (16); and mandating the publication of results from human (or animal) research supported by taxpayer funds. As Schoenfeld and Ioannidis (6) highlighted, comprehensive approaches to improve reporting of nutrient-disease outcomes could go a long way toward decreasing repeated sensational reports of the effects of foods on health. However, none of these debiasing solutions address the fundamental human need to perceive control over feared events. Although scientists may have ulterior motives for looking for nutrient-disease associations, the public is always the final audience. It is therefore imperative that we spend less time repeating weak correlations and invest the resources to vigorously investigate nutrient-cancer and other disease associations with stronger methodology, so that we give the public lightning rods instead of sending them up the bell tower.

The authors have no conflicts of interest to disclose. The contents of this editorial are solely the responsibility of the authors and do not necessarily represent the opinions of any organization with which they are affiliated.