The role of bias in nutrition research

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Typical recipe of nutrition research

- Mostly non-randomized designs with impossible-to-control confounding, also many low-quality, small trials
- Large measurement error
- Cherry-picking among multiple hypotheses
- Post-hoc analyses
- Selective reporting
- P<0.05 is enough
- No registration
- Limited data sharing
- Strong beliefs (+cultural, religious, personal views)
- White hat bias
- Strong financial interests from Big Food
A systematic cookbook review

• Open a popular cookbook
• Randomly check 50 ingredients
• How many of those have been assessed for association with increased or decreased cancer risk in the scientific literature?
Associated with cancer risk

- veal, salt, pepper spice, flour, egg, bread, pork, butter, tomato, lemon, duck, onion, celery, carrot, parsley, mace, sherry, olive, mushroom, tripe, milk, cheese, coffee, bacon, sugar, lobster, potato, beef, lamb, mustard, nuts, wine, peas, corn, cinnamon, cayenne, orange, tea, rum, raisin
Schoenfeld and Ioannidis, Am J Clin Nutr 2013
Vibration of effects and the Janus phenomenon: any result is possible
Some countries are even worse (PNAS, 2013)

US studies may overestimate effect sizes in softer research

Daniele Fanelli\textsuperscript{a,1} and John P. A. Ioannidis\textsuperscript{b,c,d,e}

**Fig. 1.** Magnitude of effect sizes of primary studies relative to the summary effect size in their respective meta-analysis, partitioned by geographical
Correlation between daily intake of specific nutrients

Ioannidis et al. Science Translational Medicine 2009
Bradford Hill Criteria: 50 years’ celebration

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Do they work?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strength</td>
<td>Mostly no, possibly even opposite</td>
</tr>
<tr>
<td>Consistency</td>
<td>Mostly yes</td>
</tr>
<tr>
<td>Specificity</td>
<td>Mostly no</td>
</tr>
<tr>
<td>Temporality</td>
<td>Yes, but rarely documented</td>
</tr>
<tr>
<td>Biological gradient</td>
<td>Unclear</td>
</tr>
<tr>
<td>Plausibility</td>
<td>Mostly no, possibly detrimental</td>
</tr>
<tr>
<td>Coherence</td>
<td>Unclear how to operationalize</td>
</tr>
<tr>
<td>Experiment</td>
<td>Yes</td>
</tr>
<tr>
<td>Analogy</td>
<td>Mostly no, possibly detrimental</td>
</tr>
</tbody>
</table>

Ioannidis, Statistics in Medicine, 2016
Observational epidemiology versus efforts to replicate effects in randomized trials

• Five out of the 6 most-cited claims of observational studies were refuted within a decade (Ioannidis, JAMA 2005)

• 52 of 52 major epidemiological claims not validated in randomized trials (Stan Young et al, 2011)
Contradicted and Initially Stronger Effects in Highly Cited Clinical Research

John P. A. Ioannidis, MD

Context Controversy and uncertainty ensue when the results of clinical research on the effectiveness of interventions are subsequently contradicted. Controversies are most prominent when high-impact research is involved.

Objectives To understand how frequently highly cited studies are contradicted or find effects that are stronger than in other similar studies and to discern whether specific characteristics are associated with such refutation over time.

Design All original clinical research studies published in 3 major general clinical journals or high-impact-factor specialty journals in 1990-2003 and cited more than 1000 times in the literature were examined.

Main Outcome Measure The results of highly cited articles were compared against subsequent studies of comparable or larger sample size and similar or better controlled designs. The same analysis was also performed comparatively for matched studies that were not so highly cited.

Results Of 49 highly cited original clinical research studies, 45 claimed that the intervention was effective. Of these, 7 (16%) were contradicted by subsequent studies, 7 others (16%) had found effects that were stronger than those of subsequent studies, 20 (44%) were replicated, and 11 (24%) remained largely unchallenged. Five of 6 highly cited nonrandomized studies had been contradicted or had found stronger effects vs 9 of 39 randomized controlled trials (P = .008). Among randomized trials, studies with contradicted or stronger effects were smaller (P = .009) than replicated or unchallenged studies although there was no statistically significant difference in their early or overall citation impact. Matched control studies did not have a significantly different share of refuted results than highly cited studies, but they included more studies with “negative” results.

Conclusions Contradiction and initially stronger effects are not unusual in highly cited research of clinical interventions and their outcomes. The extent to which high citations may provoke contradictions and vice versa needs more study. Controversies are most common with highly cited nonrandomized studies, but even the most highly cited randomized trials may be challenged and refuted over time, especially small ones.

JAMA. 2005;294:218-228
Some highly-cited contradicted findings

• Vitamin E and cardiovascular mortality (two large prospective cohorts and one trial of 2,002 subjects claimed large decreases in mortality)
• Flavonoids decrease cardiovascular mortality by 80%
• Low-fat diet dramatically decreases colorectal cancer, heart disease, stroke, and breast cancer
• Beta-carotene is highly effective in preventing against cancer and heart disease
• Fruit intake diminishes breast cancer risk by up to 90%
Resistance to refutation

Persistence of Contradicted Claims in the Literature

Athina Tatsioni, MD
Nikolaos G. Bonitsis, MD
John P. A. Ioannidis, MD

Some research findings that have received widespread attention in the scientific community, as proven by the high citation counts of the respective articles, are eventually contradicted by subsequent evidence. A number of such high-profile contradictions pertain to differences between nonrandomized and randomized studies. For example, the effect of vitamin E on cardiovascular disease prevention has been the center of a major debate in clinical research over the last two decades. Vitamin E is known to have antioxidant activity, and a long list of citations in the preclinical literature on antioxidants suggested that these agents may be beneficial for cancer and cardiovascular disease. Two highly cited publications suggested in the 1990s that vitamin E might decrease cardiovascular disease risk by almost half in men and in women. However, subsequent randomized trials showed no benefit or even suggested increased harm. Several other highly prominent contradictions have also been recorded pertaining to the effects of other dietary components and hormones. The prominent refutation of the epidemiological studies has sparked considerable controversy for observational epidemiology in general.

Such debate offers opportunities to study what happens to the scientific literature when a highly prominent claim is refuted. How quickly are such beliefs abandoned? Is there still literature citing the contradicted studies despite their refutation? What counterarguments are there?

Context Some research findings based on observational epidemiology are contradicted by randomized trials, but may nevertheless still be supported in some scientific circles.

Objectives To evaluate the change over time in the content of citations for 2 highly cited epidemiological studies that proposed major cardiovascular benefits associated with vitamin E in 1993; and to understand how these benefits continued being defended in the literature, despite strong contradicting evidence from large randomized clinical trials (RCTs). To examine the generalizability of these findings, we also examined the extent of persistence of supporting citations for the highly cited and contradicted protective effects of beta-carotene on cancer and of estrogen on Alzheimer disease.

Data Sources For vitamin E, we sampled articles published in 1997, 2001, and 2005 (before, early, and late after publication of refuting evidence) that referenced the highly cited epidemiologic studies and separately sampled articles published in 2005 and referencing the major contradicting RCT (HOPE trial). We also sampled articles published in 2006 that referenced highly cited articles proposing benefits associated with beta-carotene for cancer (published in 1981 and contradicted long ago by RCTs in 1994-1996) and estrogen for Alzheimer disease (published in 1996 and contradicted recently by RCTs in 2004).

Data Extraction The stance of the citing articles was rated as favorable, equivocal, and unfavorable to the intervention. We also recorded the range of counterarguments raised to defend effectiveness against contradicting evidence.

Results For the 2 vitamin E epidemiological studies, even in 2005, 50% of citing articles remained favorable. A favorable stance was independently less likely in more recent articles, specifically in articles that also cited the HOPE trial (odds ratio for 2001, 0.65 [95% confidence interval, 0.01-0.19; P <.001] and the odds ratio for 2005, 0.06 [95% confidence interval, 0.02-0.24; P <.001], as compared with 1997), and in general/International medicine vs specialty journals. Among articles citing the HOPE trial in 2005, 41.4% were unfavorable. In 2006, 62.5% of articles referencing the highly cited article that had proposed beta-carotene and 61.7% of those referencing the highly cited article on estrogen effectiveness were still favorable; 100% and 96%, respectively, of the citations appeared in specialty journals; and citations were significantly less favorable (P=.001 and P=.009, respectively) when the major contradicting trials were also mentioned. Counterarguments defending vitamin E or estrogen included diverse selection and information biases and genuine differences across studies in participants, interventions, interventions, and outcomes. Favorable citations to beta-carotene, long after evidence contradicted its effectiveness, did not consider the contradicting evidence.

Conclusion Claims from highly cited observational studies persist and continue to be supported in the medical literature despite strong contradictory evidence from randomized trials.


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Resistance to refutation

**Figure 2.** Standardized Citation Counts for the Most Highly Cited Article on Effectiveness of Beta-Carotene in Cancer Prevention and Effectiveness of Estrogen in Alzheimer Dementia Prevention

- **Effectiveness of Beta-Carotene in Cancer Prevention**
  - Highly cited beta-carotene article (published in 1981)
  - All articles in same journal published in 1991

- **Effectiveness of Estrogen for Prevention of Dementia**
  - Highly cited estrogen article (published in 1996)
  - All articles in same journal published in 1996
The current situation for RCTs of lifestyle, non-regulated interventions: many, but fragmented = not very reliable

Call to improve transparency of trials of non-regulated interventions

The public and clinicians require transparent, quality evidence for all interventions. Trials of non-regulated interventions are common, and efforts to improve their registration and publication compared with drug trials are overdue, say Rafael Dal-Ré, Michael Bracken, and John Ioannidis
What have we learnt from several thousands of trials of nutrition?

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Registered interventional trials in ClinicalTrials.gov*</th>
<th>Sample of randomised trials published in 2013 (indexed in PubMed)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>% (95% CI)</td>
</tr>
<tr>
<td>Behaviour</td>
<td>7195</td>
<td>5.1 (5.0 to 5.3)</td>
</tr>
<tr>
<td>Diet or nutrition</td>
<td>4375</td>
<td>3.1 (3.0 to 3.2)</td>
</tr>
<tr>
<td>Exercise</td>
<td>2835</td>
<td>2.0 (2.0 to 2.1)</td>
</tr>
<tr>
<td>Physiotherapy</td>
<td>586</td>
<td>0.4 (0.4 to 0.5)</td>
</tr>
<tr>
<td>Surgery</td>
<td>3096</td>
<td>2.2 (2.1 to 2.3)</td>
</tr>
<tr>
<td>Acupuncture</td>
<td>88</td>
<td>0.1 (0.0 to 0.1)</td>
</tr>
<tr>
<td>Any of the above†</td>
<td>13225</td>
<td>9.5 (9.3 to 9.6)</td>
</tr>
<tr>
<td>Other non-regulated</td>
<td>4083</td>
<td>2.9 (2.8 to 3.0)</td>
</tr>
<tr>
<td>Total non-regulated</td>
<td>17308</td>
<td>12.4 (12.2 to 12.6)</td>
</tr>
<tr>
<td>Total regulated</td>
<td>122431</td>
<td>87.6 (87.4 to 87.8)</td>
</tr>
<tr>
<td>Total</td>
<td>139739</td>
<td>—</td>
</tr>
</tbody>
</table>

*Based on a search in ClinicalTrials.gov with “NOT (drug OR device OR biologic OR imaging OR diagnostic OR vaccine OR radiation)” on 16 August 2014.
†Less than the sum of the listed specific categories because some trials compared interventions belonging to more than one category.
Big data meets public health

Human well-being could benefit from large-scale data if large-scale noise is minimized

By Muin J. Khoury1 and John P. A. Ioannidis2

In 1854, as cholera swept through London, John Snow, the father of modern epidemiology, painstakingly recorded the locations of affected homes. After long, laborious work, he implicated the Broad Street water pump as the source of the outbreak, even without knowing that a Vibrio organism caused cholera. Today, Snow might have crunched Global Positioning System information and disease prevalence data, solving the problem within hours (1). That is the potential impact of “Big Data” on the public’s health. But the promise of Big Data is also accompanied by claims that “the scientific method itself is becoming obsolete” (2), as next generation computers, such as IBM’s Watson (3), sift through the digital world to provide predictive models based on massive information. Separating the true signal from the gigantic amount of noise is neither easy nor straightforward, but it is a challenge that must be tackled if information is ever to be translated into societal well-being.

The term “Big Data” refers to volumes of large, complex, linkable information (4). Beyond genomics and other “omic” fields, Big Data includes medical, environmental, financial, geographic, and social media information. Most of this digital information was unavailable a decade ago. This swell of data will continue to grow, stoked by sources that are currently unimaginable. Big Data stands to improve health by providing insights into

From validity to utility, Big Data can improve tracking and response to infectious disease outbreaks, discovery of early warning signals of disease, and development of diagnostic tests and therapeutics.

For non-genomic associations, false alarms due to confounding variables or other biases are possible even with very large-scale studies, extensive replication, and very strong signals (9). Big Data’s strength is in finding associations, not in showing whether these associations have meaning. Finding a signal is only the first step.

Even John Snow needed to start with a plausible hypothesis to know where to look, i.e., choose what data to examine. If all he had was massive amounts of data, he might well have ended up with a correlation as spurious as the honey bee-marijuana connection. Crucially, Snow “did the experiment.” He removed the handle from the water pump and dramatically reduced the spread of cholera, thus moving from correlation to causation and effective intervention.

How can we improve the potential for Big Data to improve health and prevent disease? One priority is that a stronger epidemiological foundation is needed. Big Data analysis is currently largely based on convenient samples of people or information available on the Internet. When associations are probed between perfectly measured data (e.g., a genome sequence) and poorly measured data (e.g., administrative claims health data), research accuracy is dictated by the weakest link. Big Data are observational in nature and are fraught with many biases such as selection, confounding variables, and lack of generalizability. Big Data analysis may be embedded in epidemiologically well-characterized and representative populations. This epide-
##Death by food: it can all kill you

###FOOD GROUPS AND MORTALITY

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Relative risks from nonlinear dose-response analysis of 12 predefined food groups and all-cause mortality according to servings per day¹</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Associations by food group</th>
<th>Servings per day</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Inverse association</td>
<td></td>
</tr>
<tr>
<td>Whole grains (30 g/d)</td>
<td>1.00</td>
</tr>
<tr>
<td>Vegetables (80 g/d)</td>
<td>1.00</td>
</tr>
<tr>
<td>Fruit (80 g/d)</td>
<td>1.00</td>
</tr>
<tr>
<td>Nuts (28 g/d)</td>
<td>1.00</td>
</tr>
<tr>
<td>Legumes (100 g/d)</td>
<td>1.00</td>
</tr>
<tr>
<td>Fish (100 g/d)</td>
<td>1.00</td>
</tr>
<tr>
<td>Positive association</td>
<td></td>
</tr>
<tr>
<td>Eggs (55 g/d)</td>
<td>1.00</td>
</tr>
<tr>
<td>Red meat (85 g/d)</td>
<td>1.00</td>
</tr>
<tr>
<td>Processed meat (30 g/d)</td>
<td>1.00</td>
</tr>
<tr>
<td>Sugar-sweetened beverages</td>
<td>1.00</td>
</tr>
<tr>
<td>(250 mL/d)</td>
<td></td>
</tr>
<tr>
<td>Inverse and positive association</td>
<td></td>
</tr>
<tr>
<td>Dairy (200 g/d)</td>
<td>1.00</td>
</tr>
<tr>
<td>No association</td>
<td></td>
</tr>
<tr>
<td>Refined grains (30 g/d)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

¹ Values are risk ratios (95% CIs). NA, not applicable.
With one hazelnut per day you will live one year longer
If you eat that many hazelnuts each day, your life expectancy exceeds 100 years.
If you drink three cups of coffee every day you will live 12 years longer.
Exposure-wide assessment of death risk: almost nothing for diet

Correlation between smoking (cotinine) and other exposures

Patel and Ioannidis, JAMA 2014
Each correlation interdependency globe includes 317 environmental exposures represented by the nodes around the periphery of the globe. Pairwise correlations are depicted by edges (lines) between the node of interest (arrowhead) and other nodes. Correlations with absolute values exceeding 0.2 are shown (strongest 10%). The size of each node is proportional to the number of edges for a node, and the thickness of each edge indicates the magnitude of the correlation.
Field-specific specificity or lack thereof: Placing results in the context of their entire field

Patel and Ioannidis, JECH 2014
Exposure-outcome-wide association study (250 exposures, 86 outcomes)

Patel et al (in preparation)
Nutrients are associated with most outcomes

Patel et al (in preparation)
What to do (at a minimum)

• Clarify which analyses are not pre-specified
• Use pre-registration when appropriate
• Perform additional large, simple trials with long follow-up (they will be mostly “negative”)
• Fit the research agenda to small/tiny effects (abandon designs where noise overwhelms the signal)
• Share publicly all data by default
• Share in advance protocols (when protocols exist)
• Disclose financial and non-financial conflicts
• Limit or control involvement of stakeholders with conflicts
The Importance of Potential Studies That Have Not Existed and Registration of Observational Data Sets

John P. A. Ioannidis, MD, DSc

Knowing the complete results of all conducted studies on a question of interest is important to avoid publication and selective outcome reporting biases and to obtain a reliable picture of the evidence. However, in practice, few analyses through the main analyses would require little time, yet preparing a manuscript requires considerable effort, so scientists ponder whether it is worth it. They weigh the perceived importance and priority of the question, the statistical significance of any (quickly obtained) results, and other evidence circulating at the time. The possibility that multiple studies could have existed should also provide an independent testing the result of the 3 and...
Levels of registration

- Level 0: no registration
- Level 1: registration of dataset
- Level 2: registration of protocol
- Level 3: registration of analysis plan
- Level 4: registration of analysis plan and raw data
- Level 5: open live streaming
Table 1. Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study (enrolled in 1985-1988): initial results and postintervention period results

<table>
<thead>
<tr>
<th></th>
<th>RR (95% CI), beta-carotene</th>
<th>RR (95% CI), alpha-tocopherol</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-death</td>
<td>1.08 (1.01-1.16)</td>
<td>1.18 (1.03-1.36)</td>
</tr>
<tr>
<td>Lung cancer</td>
<td></td>
<td>1.02 (0.95-1.09)</td>
</tr>
<tr>
<td>All-death</td>
<td></td>
<td>0.68 (0.53-0.88)</td>
</tr>
<tr>
<td>Prostate cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention to 4/1993 (68)</td>
<td>1.08 (1.01-1.16)</td>
<td>1.18 (1.03-1.36)</td>
</tr>
<tr>
<td>Postintervention</td>
<td></td>
<td></td>
</tr>
<tr>
<td>to 4/1999 (69)</td>
<td>1.06 (0.94-1.20)</td>
<td>0.88 (0.76-1.03)</td>
</tr>
<tr>
<td>to 4/2001 (69)</td>
<td>1.07 (1.02-1.12)</td>
<td>1.01 (0.96-1.05)</td>
</tr>
<tr>
<td>to 12/2009 (70)</td>
<td>1.02 (0.99-1.05)</td>
<td>1.04 (0.96-1.01)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.02 (0.98-1.05)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.97 (0.89-1.05)</td>
</tr>
</tbody>
</table>

RR, relative risk; CI, confidence interval
Risk factors and interventions with statistically significant tiny effects

George CM Siontis¹ and John PA Ioannidis¹,²*

¹Clinical Trials and Evidence-Based Medicine Unit and the Clinical and Molecular Epidemiology Unit, Department of Hygiene and Epidemiology, University of Ioannina School of Medicine, Ioannina, Greece and ²Stanford Prevention Research Center, Department of Medicine, Stanford University School of Medicine, Stanford, USA.

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Accepted 19 May 2011

Background Large studies may identify postulated risk factors and interventions with very small effect sizes. We aimed to assess empirically a large number of statistically significant relative risks (RRs) of tiny magnitude and their interpretation by investigators.

Methods RRs in the range between 0.95 and 1.05 were identified in abstracts of articles of cohort studies; articles published in NEJM, JAMA or Lancet; and Cochrane reviews. For each eligible tiny effect and the respective study, we recorded information on study design, participants, risk factor/intervention, outcome, effect estimates, P-values and interpretation by study investigators. We also calculated the probability that each effect lies outside specific intervals around the null (RR interval 0.97–1.03, 0.95–1.05, 0.90–1.10).

Results We evaluated 51 eligible tiny effects (median sample size 112,786 for risk factors and 36,021 for interventions). Most (37/51) appeared in articles published in 2006–10. The effects pertained to nutrition (n = 19), genetic and other biomarkers (n = 8), correlates of health care (n = 8) and diverse other topics (n = 16) of clinical or public health importance and mostly referred to major clinical outcomes. A total of 15 of the 51 effects were >80% likely to lie outside the RR interval 0.97–1.03, but only 8 were >40% likely to lie outside the RR interval 0.95–1.05 and none was >1.7% likely to lie outside the RR interval 0.90–1.10. The authors discussed at least one concern for 23 effects (small magnitude n = 19, residual confounding n = 11, selection bias n = 1). No concerns were expressed for 28 effects.

Conclusions Statistically significant tiny effects for risk factors and interventions of clinical or public health importance become more common in the literature. Cautious interpretation is warranted, since most of these effects could be eliminated with even minimal biases and their importance is uncertain.
A manifesto for reproducible science

Marcus R. Munafò¹,²*, Brian A. Nosek³,⁴, Dorothy V. M. Bishop⁵, Katherine S. Button⁶, Christopher D. Chambers⁷, Nathalie Percie du Sert⁸, Uri Simonsohn⁹, Eric-Jan Wagenmakers¹⁰, Jennifer J. Ware¹¹ and John P. A. Ioannidis¹²,¹³,¹⁴

Improving the reliability and efficiency of scientific research will increase the credibility of the published scientific literature and accelerate discovery. Here we argue for the adoption of measures to optimize key elements of the scientific process: methods, reporting and dissemination, reproducibility, evaluation and incentives. There is some evidence from both simulations and empirical studies supporting the likely effectiveness of these measures, but their broad adoption by researchers, institutions, funders and journals will require iterative evaluation and improvement. We discuss the goals of these measures, and how they can be implemented, in the hope that this will facilitate action toward improving the transparency, reproducibility and efficiency of scientific research.
Disclosures in Nutrition Research
Why It Is Different

Nutrition research is among the most contentious fields of science. Although the totality of an individual's diet has important effects on health, most nutrients and foods individually have ambiguously tiny (or non-existent) effects. Substantial reliance on observational data for which causal inference is notoriously difficult also limits the clarifying ability of nutrition science. When the data are not clear, opinions and conflicts of interest between financial and nonfinancial may influence research articles, editorials, guidelines, and laws. Therefore, disclosure policies are an important safeguard to help identify potential bias. In this Viewpoint, we contend that current norms for disclosure in nutrition science are inadequate and propose that greater transparency is needed, including a broader definition of what constitutes disclosure-worthy information.

Financial conflicts of interest have received substantial attention in nutrition science, particularly conflicts of interest involving the food industry, and for good reason. Food represents a huge market so it is logical that the food industry will try to promote its products and influence the scientific literature and opinion making. Major distortion may sometimes ensue for both the gathering of evidence and its interpretation. A financial disclosure registry may be helpful in understanding how the scientific literature, public policy, and individual and population dietary preferences might be affected. At the same time, the parochial view that accepting funding from the food industry (post facto) automatically blames the results is outdated.

Industry sponsorship is not the only form of financial conflict of interest germane to nutrition science. Some indirect financial gains may also be important. Many nutrition scientists and experts write books about their opinions and diet preferences. Given the interest of the public in this topic, books about nutrition, diets, and weight loss often appear on best-selling lists, even though often offer little to no evidence to support their frequently bold claims. Financial conflicts of interest can also appear in unexpected places. For example, many not-for-profit nutrition initiatives require considerable donor money to stay solvent. Public visibility through the scientific literature and its reiteration through press releases, other media coverage, and social media magnification can be critical in this regard.

Another aspect involves nonfinancial conflicts of interest. Allegiance bias and preference for favorite theories are prevalent across science and can affect any field of study. It is almost unavoidable that a scientist eventually will form some opinion that goes beyond the data, and they should. Scientists are likely to defend their work, their own discoveries, and the theories that they proposed or espoused. Nutrition scientists are faced with an additional challenge. Every day, they must make numerous choices about what to eat while not allowing those choices to affect their research. Most of them also have been exposed to various dietary norms from their family, culture, or religion. These norms can sometimes be intertwined with core values, absolutist metaphysical beliefs, or both. For instance, could an author who is strongly adherent to some religion conclude that a diet-related prescription of his or her religion is unhealthy as not to be worthwhile?

Advocacy and activism have become larger aspects of the work done by many nutrition researchers, and one should be viewed as conflicts of interest that need to be disclosed. These endeavors often spring from some of the noblest intentions and can lead to invaluable contributions to society and public health in particular. However, advocacy and activism are also orthogonal to a key aspect of the scientific method, which is to not take sides preemptively or based on belief or partnership. Examples of white hat bias (bias that distorts scientific evidence in support of a perceived righteous end such as better human health) have been reported. Therefore, it is important for nutrition researchers to disclose their advocacy or activist work as well as their dietary preferences if any are relevant to what is presented and discussed in their articles. This is even more important for dietary preferences that are specific, circumscribed, and adhered to strongly. For example, readers should know if an author is strongly adherent to a vegan diet, the Atkins diet, a gluten-free diet, a high animal protein diet, specific brands of supplements, and so forth if these dietary choices are discussed in an article. The types of articles in which relevant disclosure should be expected include original research, reviews, and opinion pieces (such as editorials).

Such disclosure should not be seen as an admission of lack of integrity. To the contrary, disclosure strengthens the perceived integrity of the author. Moreover, some disclosures may end up being advantageous depending on future research findings. For example, it might be advantageous for a scientist who is not adherent to a vegan diet to disclose that fact if the topic is related to plant-based diets.
Concluding comments

- Most current evidence on nutrition at the population level is hopelessly biased and unreliable
- Bias should be taken for granted
- In the current environment, the literature is shaped primarily by the biases of scientists, reviewers, editors (often the same people) and sponsors (often heavily conflicted ones)
- Many things need to change in the nutrition agenda before some minimal credibility can be claimed
- Nutrition is extremely important for health; nutrition science deserves better
Special thanks

Daniele Fanelli
Steve Goodman
Shanil Ebrahim
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