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Commentary

Commentary: Salt and the assault of opinion on evidence

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The meta knowledge analysis by Trinquart and colleagues¹ shows a clear polarization of the literature on salt reduction. Most authors publish, cite, review and conclude systematically in favour of the salt hypothesis, but many others systematically cluster against it. The two groups have little communication between them. When IJE invited commentaries on the paper from leading scientists, that polarization was immediately evident. One scientist whom I admire declined our invitation saying that 'the paper ... is rubbish ... there doesn't seem to be any realization that the majority of those papers that are against salt reduction are funded by the food or salt industry, just like the tobacco industry did (or still does for that matter) for cigarettes ... I wouldn't want to have anything to do with it'. Bruce Neal² kindly agreed to write a commentary, but he also focused eventually on the point that the food industry is standing behind the unconvinced and concluded that 'a balanced assessment of the multiple strands of evidence ... raises important questions about the reasoning of the non-believers'. Conversely, Martin O'Donnell and colleagues³ argued that the evidence on salt reduction (from moderate to low levels) is inconclusive, so apparently they are among those non-believers. They even argued³ that believers should be drastically extradited from guidelines, and suggest excluding from the guideline development process everybody who has ever expressed an opinion on salt. Anyone left out there?

Several major issues are confounded in this controversy. There are potentially millions of lives jeopardized, and the Damoclean moral argument is that whoever is wrong may be dooming those people to death intentionally or unintentionally. Then there is also my personal pet topic: the industry distorts the evidence in its favour, and as an academic and public health researcher I want to rise to the occasion and defend the community against corporate greed. At the same time, there are also clearly strong academic opinions here and allegiance, confirmation and other academic bias can sometimes be worse than financial allurement. Trinquart and colleagues have meta-analysed the network of the published evidence plus the published comments and interpretations on the evidence, but this published corpus is just the selective end product of a long manipulative process. How that primary evidence and its comments and interpretations have accumulated is akin to sausage making (hmm, talking about sausages, another hot public health debate). It gives me pause when I wonder how it is decided what studies are done, how they are conducted, how they are analysed, how they are reported, how they are interpreted, how they are seen by reviewers and editors and rejected unless they fit to their world view and what changes in analyses, results, must-cite references and interpretation are potentially imposed by the editors and reviewers as a condition for publication. Sometimes I wonder whether published observational epidemiology is simply reflecting a power-weighted vote count of the opinions of epidemiologists. What does a risk ratio of 1.3 mean? Perhaps it means that those who believe in the risk factor have 1.3-fold more powerful opinions than those

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who don't believe in the risk factor. In this (hypothetical) nightmare situation, risk ratios are accurate measures of epidemiologists' net bias.⁵

Systematic reviews cannot settle this conundrum after the fact. Even systematic reviews of randomized trials can reach almost any conclusion the reviewers believe in. For example,6 an overwhelming 185 meta-analyses of antidepressants for depression were published over 7 years, 79% of which had industry involvement; 54 of the 55 meta-analyses with industry authors expressed no caveats about the antidepressants, whereas half of those without industry involvement expressed caveats and negative statements in their abstracts. Academic allegiance can be equally selective. Selection of eligible studies is one mechanism by which meta-analyses can reach different conclusions, but there are many more tools that can shape the conclusions: selection of meta-analysis model, choice of outcomes, outcome definitions, eligible follow-up and more. Even with identical summary results, different conclusions may still emerge, depending on what one wants to highlight most: the certainty or the uncertainty, the benefits or the harms. Guidelines, by being a step further than reviews in the evidence sausage making, have multiple additional places where bias can creep in and this can lead even more frequently to heated debates.

As I am demonstrating the grand power of uncertainty and bias, I wonder if people think that I have been funded by the salt industry and should be burned to the stake as a non-believer. I have not been funded, please spare my life. Plus I do confess that I do think that too much salt is bad for your health, amen. However, I also don't know what would be the relative effectiveness of various interventions that might try to reduce excess salt intake in real life. Even if salt kills people, will having a moustache-carrying minister of health or some erudite public health officials broadcast 'cut down on salt' suffice to save lives? I doubt it. I also lament the lack of some pivotal long-term pragmatic randomized trials to answer questions in the contested borderland between believers and non-believers. I hate being a believer or a non-believer, I went into science because I did not want just to have to believe.

Will such randomized trials be immune from belief systems? Not necessarily; the design, conduct, analysis choices, outcome ascertainment and, foremost, the interpretation can still be affected. But degrees of freedom in reaching self-fulfilling conclusions are fewer. Even when multiple large randomized trials refute a hypothesis, the hypothesis often maintains its retinue of followers who continue citing it. Sometimes, like in the case of betacarotene, believers continue to cite the original claim with no mention of the randomized trials, as if they had never happened. On other occasions, as in the case of vitamin E for prevention of cardiovascular disease and estrogen for dementia, believers attack the randomized trials, finding a zillion problems with them. A wrong opinion is like an epidemic that is difficult to eradicate. 10 But stronger evidence will hopefully help contain these epidemics of opinion.

Conflict of interest: None.

References

- 1. Trinquart L, Merritt D, Galea, S. Why do we think we know what we know? A meta knowledge analysis of the salt controversy. *Int J Epidemiol* 2016.
- 2. Neal B. This issue.
- 3. O'Donnell et al. This issue.
- PLoS Medicine editors. Making sense of non-financial competing interests. PLoS Med 2008;5:e199.
- Ioannidis JP. Why most published research findings are false. PLoS Med 2005;2:e124.
- Ebrahim S, Bance S, Athale A, Malachowski C, Ioannidis JP.
 Meta-analyses with industry involvement are massively published and report no caveats for antidepressants. *J Clin Epidemiol* 2015, Sep 21. doi: 10.1016/j.jclinepi.2015.08.021. [Epub ahead of print.]
- 7. Ioannidis JP. Meta-research: the art of getting it wrong. *Res Synth Methods* 2010;1:169–84.
- Grilli R, Magrini N, Penna A, Mura G, Liberati A. Practice guidelines developed by specialty societies: the need for a critical appraisal. *Lancet* 2000;355:103–06.
- Tatsioni A, Bonitsis NG, Ioannidis JP. Persistence of contradicted claims in the literature. JAMA 2007;298:2517–26.
- Greenberg SA. How citation distortions create unfounded authority: analysis of a citation network. BMJ 2009; 339:b2680.