Knowledge Generation

Why do we think we know what we know? A metaknowledge analysis of the salt controversy

Ludovic Trinquart,1* David Merritt Johns2 and Sandro Galea1,3

1Department of Epidemiology, 2Department of Sociomedical Sciences, Mailman School of Public Health, Columbia University, New York, NY, USA and 3Boston University School of Public Health, Boston, MA, USA

*Corresponding author. Department of Epidemiology, Mailman School of Public Health, Columbia University, 722 West 168th Street, New York, NY 10032, USA. E-mail: lt2515@columbia.edu

Current address: Cochrane France, Hôpital Hôtel-Dieu, 1 Place du Parvis Notre-Dame, 75004 Paris, France. E-mail: ludovic.trinquart@htd.aphp.fr

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Abstract

Background: Although several public health organizations have recommended population-wide reduction in salt intake, the evidence on the population benefits remains unclear. We conducted a metaknowledge analysis of the literature on salt intake and health outcomes.

Methods: We identified reports—primary studies, systematic reviews, guidelines and comments, letters or reviews—addressing the effect of sodium intake on cerebro-cardiovascular disease or mortality. We classified reports as supportive or contradictory of the hypothesis that salt reduction leads to population benefits, and constructed a network of citations connecting these reports. We tested for citation bias using an exponential random graph model. We also assessed the inclusion of primary studies in systematic reviews on the topic.

Results: We identified 269 reports (25% primary studies, 5% systematic reviews, 4% guidelines and 66% comments, letters, or reviews) from between 1978 and 2014. Of these, 54% were supportive of the hypothesis, 33% were contradictory and 13% were inconclusive. Reports were 1.51 [95% confidence interval (CI) 1.38 to 1.65] times more likely to cite reports that drew a similar conclusion, than to cite reports drawing a different conclusion. In all, 48 primary studies were selected for inclusion across 10 systematic reviews. If any given primary study was selected by a review, the probability that a further review would also have selected it was 27.0% (95% CI 20.3% to 33.7%).

Conclusions: We documented a strong polarization of scientific reports on the link between sodium intake and health outcomes, and a pattern of uncertainty in systematic reviews about what should count as evidence.

Key words: Sodium chloride (dietary), bias (epidemiology), bibliometric analysis, review literature as topic
Background
Universal salt reduction has been the subject of considerable scientific controversy over several decades.\textsuperscript{1,2} Proponents of population-wide reduction in salt consumption note that high sodium intakes increase blood pressure and thus the risk of cerebro-cardiovascular events, and assert that salt reduction policies will produce major public health benefits. The World Health Organization (WHO) recommends reducing sodium intake to \textless 2 g/day in adults.\textsuperscript{3} Opponents of population-based salt reduction argue that the relationship between sodium intake and clinical outcomes is U- or J-shaped and that the harms associated with low sodium intakes may mitigate any potential benefits of blood pressure reductions arising from decreased salt intakes.\textsuperscript{4,5} In a recent report, the United States Institute of Medicine of the National Academies of Science concluded that there is a lack of evidence for benefits of reducing sodium intake to the very low levels recommended by the WHO.\textsuperscript{6}

In many respects, the divide between the uncertainty in the scientific literature about the potential benefits of salt reduction in populations and the certitude expressed by decision makers involved in developing public health policies in this arena is jarring.\textsuperscript{1,7} Whereas several authors involved in the conduct of systematic reviews of the evidence on sodium have argued that the salt hypothesis is a distraction with little empirical grounding,\textsuperscript{8} others have asserted that salt reduction in populations should be a central public health priority in the 21st century.\textsuperscript{9} Assuming that all parties involved have the best interests of science and public health in mind, this controversy raises questions about the production of knowledge in population health science and how that production influences public health practice.\textsuperscript{10}

Toward the end of contributing to population health epistemology, we examined the patterns of knowledge generation surrounding this controversy. First, we used network analysis to assess the patterns of citations among reports pertaining to the effect of population-level sodium intake on cerebro-cardiovascular disease or all-cause mortality. Second, we assessed the agreement in primary study selection between relevant systematic reviews. By tracking the networks of citations between reports and among researchers co-authoring reports, we aimed to better understand how this controversy has been sustained and to expose beliefs or preferences that shape knowledge production underlying this scientific literature.\textsuperscript{11}

Key Messages
- We documented a strong polarization of scientific reports on the link between sodium intake and health outcomes.
- A majority of the existing papers are supportive of the salt hypothesis but a substantial minority are not.
- Published reports supporting either side of the hypothesis are less likely to cite contradictory papers.
- There was very little consistency in the selection of primary studies in systematic reviews on the topic.

Methods
Selection of reports
We systematically reviewed the literature to include all: (i) reports of primary studies; (ii) systematic reviews; (iii) clinical practice guidelines or consensus statements; and (iv) comments, letters or narrative reviews. We considered as eligible all reports that addressed the effect of sodium intake, or interventions targeting sodium intake, on cerebro-cardiovascular disease or all-cause mortality. Eligible primary studies were randomized trials, cohort studies and case-control studies. Simulation modelling efforts, cost-effectiveness studies and ecological analyses were deemed ineligible.

The last search was conducted in September 2014. We searched MEDLINE, the Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews of Effects, the WHO Institutional Repository for Information Sharing, the US National Guideline Clearinghouse, the National Institute for Health and Care Excellence, the American Heart Association and American Stroke Association statements and guidelines, and the Dietary Guidelines for Americans. We identified primary studies by screening the lists of studies included in the selected systematic reviews. In addition, we screened the reference lists of all reports. For a detailed description of the selection criteria and search strategies, see Web Text 1 (available as Supplementary data at IJE online).

Classification of reports
Two authors (L.T., S.G.) classified each report into one of three categories: supportive of the hypothesis that population-wide reduction of sodium intake results in reduction in cerebro-cardiovascular disease or all-cause mortality; contradictory of this hypothesis; or inconclusive.
primary assessment was based on the conclusion reported in the abstract of the selected reports. If there was no abstract or summary statement about the effect of sodium intake or of interventions targeting sodium intake on cerebro-cardiovascular disease or all-cause mortality, our assessment was based on a review of statements in the full-text report.

Citation network analysis
First, we constructed the network of citations connecting the reports. We identified the citations between the selected reports by using the Web of Science database and by manually screening all selected articles. We counted multiple citations from an article to another as one citation. We constructed a directed acyclic graph in which each node was a report and edges were directed from a citing report to a cited report. We distinguished multiple publications of the same report (whether there was a clear statement that republishing was intentional or not).

Second, we used an exponential random graph (ERG) model to explain the probability of a citation link between two reports, based on publication year, type of report (i.e. primary study, systematic review, guideline and comment, letter or review), journal impact factor and network structure. The model was used to formally test for homophily according to report classification (supportive, contradictory, inconclusive): our hypothesis was that a report would be more likely to cite another report that drew the same conclusion (supportive, contradictory or inconclusive). The interpretation of the results of an ERG model is similar to that of a logistic regression model and we expressed results in terms of odds ratios.

Third, we identified the most influential reports in the citation network by using a random walk approach (see Supplementary data, available at IJE online). We assessed the likelihood that a supportive, contradictory or inconclusive report was among the most influential reports.

Co-authorship network analysis
We identified the authors of each report. First, we produced Lorenz curves showing the cumulative fraction of supportive, contradictory and inconclusive reports against the cumulative fraction of authors. In this analysis, we divided up the authorship credit for a report among all authors (e.g. each author on a three-author report was credited with a third of an authorship).

Second, we constructed an undirected network graph in which each node was an author and edges connected two authors who co-signed at least one report. Node size was proportional to the number of reports written by the author and edge width was proportional to the number of reports co-signed by the two authors.

Agreement in primary study selection between systematic reviews
We assessed the agreement between systematic reviews as to which primary studies they included. We assessed which outcomes, which populations and which study designs were used in each study. We estimated the overall probability that, if a primary study was selected in a systematic review, another review would also select it. Finally, we estimated the likelihood that a systematic review included a supportive, contradictory or inconclusive study, respectively. In this analysis, we considered multiple publications of the same report as unique.

Results
Characteristics of reports
We selected 269 distinct reports (Web Figure 1, available as Supplementary data at IJE online). Among these, 68 reported the results of 60 primary studies, 14 reported the results of 10 systematic reviews, 11 reported the conclusions of 9 clinical practice guidelines and 176 were comments, letters or narrative reviews (Table 1). A total of 148 (55%) reports were published in 2011 or after. In all: 146 (54%) of the reports were supportive of the hypothesis that population-wide reduction of sodium intake is associated with reduced cerebro-cardiovascular disease or all-cause mortality; 88 (33%) were contradictory of this hypothesis; and 35 (13%) were inconclusive.

Citation network analysis
Figure 1 shows the complex citation network corresponding to 2156 citations between the 269 reports, with 821.1 million citation paths supporting it. Half of the reports were cited 2 times or less whereas 10% of the reports were cited 25 times or more. Primary studies on average received 22 citations, systematic reviews 19 citations, guidelines 14 citations, and comments, letters, or reviews 4 citations.
The distribution of citations received was similar between the three categories of reports (supportive, contradictory or inconclusive) (Web Figure 2, available as Supplementary data at IJE online). However, according to a multivariate exponential random graph model, reports were 1.51 (95% CI 1.38 to 1.65, \( P < 10^{-4} \)) times more likely to cite a report that drew a similar conclusion (supportive, contradictory or inconclusive), all other variables held constant (Table 2). Lastly, we identified 12 influential reports (Web Figure 3, available as Supplementary data at IJE online). Ten reported the results of primary studies and two of systematic reviews. There was not sufficient evidence for an association between report conclusions and the likelihood of being influential (3%, 7% and 6% in supportive, contradictory and inconclusive reports, respectively, exact \( P \)-value = 0.23).

**Co-authorship network analysis**

We identified 643 distinct authors with a median of 3 authors per report. The production of reports was unbalanced: 25% and 28% of authors produced 75% of contradictory and supportive reports but 41% of authors produced 75% of inconclusive reports (Figure 2). We
Figure 2. Fraction of reports written by the most prolific authors. The Lorenz curves show the cumulative fractions of supportive, contradictory and inconclusive reports against the cumulative fractions of authors. Credit for multi-author reports was divided among co-authors (e.g. each author on a three-author report was credited with a third of an authorship). The production of reports was unbalanced: 25% and 28% of authors produced 75% of contradictory and supportive reports but 41% of authors produced 75% of inconclusive reports, suggesting that few authors making strong arguments either supportive or contradictory of the salt hypothesis dominate the field, whereas authors whose findings are inconclusive appear more heterogeneous.

Table 2. Multivariate model explaining 2156 citation links among 269 reports

<table>
<thead>
<tr>
<th>Terms</th>
<th>Odds ratio (95% confidence interval)</th>
<th>P-value</th>
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<tbody>
<tr>
<td>Structural homophily (within-category citation)</td>
<td>1.51 (1.38–1.65)</td>
<td>&lt;10⁻⁴</td>
</tr>
<tr>
<td>Type of cited report</td>
<td></td>
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<tr>
<td>Comment, letter, review</td>
<td>1</td>
<td></td>
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<tr>
<td>Primary study</td>
<td>9.73 (8.71–10.86)</td>
<td>&lt;10⁻⁴</td>
</tr>
<tr>
<td>Systematic review</td>
<td>6.39 (5.39–11.53)</td>
<td>&lt;10⁻⁴</td>
</tr>
<tr>
<td>Guideline</td>
<td>3.65 (2.93–4.55)</td>
<td>&lt;10⁻⁴</td>
</tr>
<tr>
<td>Difference in publication year between citing and cited report b</td>
<td>0.83 (0.80–0.86)</td>
<td>&lt;10⁻⁴</td>
</tr>
<tr>
<td>Difference in journal impact factor between citing and cited reports c</td>
<td>0.93 (0.89–0.97)</td>
<td>&lt;10⁻²</td>
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Results are expressed in terms of odds ratios. Reports were 1.5 times more likely to cite a report within the same category (i.e. supportive of the hypothesis that sodium intake reduction is beneficial, contradictory of this hypothesis or inconclusive), all other variables held constant. Systematic reviews were 6.4 times more likely to be cited than comments, letters, or reviews.

Model fit: AIC = 12037 and BIC = 12098 (smaller is better).

The model included an edges term, which measures the structural density of citations. The estimated log-odds of any citation occurring was \( \hat{\beta} = -1.74 \) [standard error (SE) 0.10]. Thus, the probability of a citation was \( \frac{1}{1 + \exp(1.74)} = 15.0\% (95\% CI 12.7\%–17.5\%) \).

b Odds ratio associated with a difference of 5 years in publication year.

c Odds ratio associated with a difference of 10 in journal impact factor.
classified 337 authors as being supportive, 178 as being contradictory and 128 as being inconclusive. The network of co-authorship showed a strong clustering, with few collaborations between authors holding different positions (homophily index –0.67) (Figure 3).

Figure 3. Co-authorship network graph with 643 authors. Each node is an author and two nodes are connected when the corresponding authors co-signed at least one manuscript. Node colour indicates author classification (supportive, contradictory, inconclusive). Node size is proportional to the number of reports the corresponding author signed. Edge width is proportional to the number of reports the corresponding authors co-signed. Networks were drawn using the Harel-Koren Fast Multiscale algorithm. Disconnected network diagrams correspond to authors that never collaborated on manuscripts; in particular, diagrams at the bottom correspond to authors co-authoring a single report. However, the overall pattern showed a strong clustering of co-authorship, with few collaborations between authors holding different positions.

Agreement in primary study selection between systematic reviews

Overall, the 10 systematic reviews included a total of 48 different primary studies (Figure 4). We identified six potentially eligible studies that were included in none of the systematic reviews and seven additional primary studies that were published after the date of last search of the most recent systematic review. There was poor agreement in primary study selection between the 10 systematic reviews (Web Figure 4A, available as Supplementary data at IJE online). The estimated probability that, if a study was selected by a review, a further review would also have selected it was 27.0% (95% CI 20.3% to 33.7%). The 48 selected studies had a wide range of study designs: 52% were cohort studies and 27% were randomized trials. Of note, the estimated probability that, if a randomized trial was selected by a review, a further review would also have selected it was 15.0% (95% CI 7.2% to 22.9%). The studies included different populations: 35% were conducted in general population and 17% in heart failure population (Web Figure 4B, C). Across the 54 potentially eligible studies, the impact of sodium intake on all-cause mortality was reported in 33 (61%) studies, on cardiovascular mortality in 15 (28%), on cardiovascular diseases in 25 (46%) and on stroke in 21 (39%) (Web Figure 4D). In all, the average likelihood that a systematic review included a primary study was lower for primary studies that reached a contradictory rather than a supportive conclusion (22.6%, 30.7% and 25.5% for contradictory, supportive and inconclusive reports, respectively, $P = 0.18$) (Figure 4). Among the 10 systematic reviews, 4 reached a supportive conclusion, 3 reached a contradictory conclusion and 3 were inconclusive. On average, supportive systematic reviews were more likely to select supportive primary studies than other reviews (43.7% vs 23.0%, $P < 0.001$),
contradictory systematic reviews were more likely to select contradictory primary studies (41.5% vs 14.4%, \(P < 0.001\)) and inconclusive systematic reviews were more likely to select inconclusive primary studies (89.7% vs 5.3%, \(P < 0.001\)).

**Discussion**

Based on a systematic review of the literature, we documented a strong polarization of scientific reports on the link between sodium intake and clinical outcomes in populations, and a pattern of uncertainty in published systematic reviews. We found, first, that a majority of existing reports were supportive of the hypothesis but that a substantial minority were not. Second, we found substantial citation bias, where published reports preferentially cited previous reports that reached a similar conclusion. Third, the literature in the field was dominated by a few reports and by a few prolific authors, who each hold and repeat particular positions. Fourth, there was very little consistency in the selection of primary studies in systematic reviews, further compounding the challenges the field faces in achieving resolution.

Uncertainty is an important motivator of scientific work. However, it also tends to stifle action, particularly in fields such as public health where practitioners frequently are confronted by problems for which there is little relevant research evidence. The mandates of public health require decision makers to act in the absence of certitude in many, if not most, cases. Given the prominence of population-wide salt reduction as a cornerstone of global health policies to curb cardiovascular disease mortality, the case of salt reduction represents a particularly important example for examining how evidence and uncertainty inform, or do not inform, public health practice. Several modelling studies have concluded that the effects of reducing dietary salt intake on cardiovascular disease mortality, as mediated through blood pressure, would be considerable.\(^{17-19}\) However, we found that the published literature bears little imprint of an ongoing controversy, but rather contains two almost distinct and disparate lines of scholarship, one supporting and one contradicting the hypothesis that salt reduction in populations will improve clinical outcomes.

We first mapped the salt controversy by connecting reports, through a citation network, in a dialogue of
supportive, contradictory and inconclusive statements. We found evidence of homophily on citation patterns, where authors who had a pro or con point of view were 50% more likely to cite papers with their point of view than the other point of view. We also mapped the controversy by re-attaching the statements to their authors and found marked clustering in existing networks of scientists. We interpret these findings as reflecting the sustained divide between opposing groups of scientists who differ in their interpretation of the data about whether population-wide salt reduction will improve population health. Part of the observed pattern may be explained by direct as well as co-author and collaborative self-citations. The data are consistent with a picture where a few authors and a few key papers dominate the literature. These authors and publications make strong arguments either supportive or contradictory of the salt hypothesis. Those scientific voices whose findings are inconclusive appear more heterogeneous and are situated mainly on the outskirts of the dispute.

Previous studies have shown how citation practices can be biased towards positive, statistically significant findings or distorted by the amplification or avoidance of evidence. Several authors have also discussed the selective citation of studies that support a given hypothesis or idea (viewpoint citation or unbalanced citation). To our knowledge, our analytical approach is novel as it allows an empirical quantification of such polarization. Our application around the debate about reducing salt intake echoes other scientific controversies, such as the dispute around electronic cigarettes. It could be applicable to different areas of scientific controversy, and our analysis is intended to encourage such empirical investigations; it would be interesting to compare patterns of polarization for other controversial or, conversely, strongly consensual topics.

The citation bias we found was paralleled by considerable variation in the inclusion of primary evidence in systematic reviews addressing the effect of sodium intake on cardiovascular outcomes. We found that if a primary study was selected by a review, the chance that another review would also have selected it was less than a third; this probability was lower for randomized trials. This is a level of disagreement that goes beyond differences in selection criteria across reviews. This finding reflects ongoing uncertainty and disagreement about what should count as evidence. Some have previously questioned the role of randomized trials as the source of definitive evidence, and a recent review of the methodological quality of observational studies relating sodium to cardiovascular outcomes found that methodological defects, considered to have the potential to alter the direction of association, affected all 26 observational studies (except for one which showed a null association). Systematic reviews have the potential to provide the highest level of evidence. However, meta-analysts must cast a dispassionate eye over the literature. In our analysis, we found that the variation in the inclusion of primary evidence directly influenced the conclusions of systematic reviews and that the inclusion or exclusion of specific studies shaped the secondary evidence. This variation threatens the validity of the syntheses and reinforces existing uncertainty about the science that sustains the dispute. These findings have implications for the translation of conflicting, uncertain evidence into public health policy. Both the misuse of uncertainty and the exaggeration of certainty can shape the outcomes of public health decision-making processes.

Although science has been acutely alert to potential financial conflicts of interest in recent decades, much less attention has been paid to other potential conflicts—particularly biases that are embedded in long-held beliefs that resist re-examination when new data become available. It has previously been suggested that these conflicts of interest may be more powerful than financial consideration. Our findings support a strong bias towards the status quo and the absence of a genuine scientific conversation where each side engages the other. The citation patterns underlying this particular debate suggest that the scientific community is not engaged in a collaborative effort to arrive at a data-informed consensus on the matter and instead appears to be divided into two silos. This pattern is worrisome when one considers how such a division may be perpetuated as future generations of researchers are brought up in one or another ‘tradition’, rendering the gap between the two ‘sides’ of the argument ever more difficult to bridge. In recognition of this problem, at least in the abstract, Osborne et al. proposed to give a central place to collaborative argumentation in the scientific educational process, to help students learn to argue based on available evidence and develop insight into how and why we know what we know. Such an approach might contribute to greater clarity around difficult problems such as salt consumption and public health if a commitment to collaborative argumentation in science can be made.

Our analyses have limitations. First, we may have been missed some relevant reports, despite our search of a range of databases. In particular, we searched comments, letters and narrative reviews in MEDLINE only. We did not consider material from conferences, although some conference proceedings appeared in abstracts that we selected. In fact, we manually screened the reference lists of all reports. Consequently, it is unlikely that a relevant report, if cited, was left out of our claim-specific citation network. Second, our classification of reports as supportive, contradictory or inconclusive was based on conclusions that others may
interpret differently. However, we used explicit criteria for classification that was performed in duplicate by independent reviewers. As a consequence, the classification process was burdensome; natural language processing methods, especially supervised machine learning classification, may be used to reduce the amount of human review required to assess each article, so that the analysis method could be applied to a wider array of topics. Last but not least, previous content in order to criticize its validity or reframe its meaning to divert its implications. Third, citation does not mean endorsement and we did not assess if the cited reports were qualified either positively or negatively by the citing reports. The claim-specific citation network may be affected either positively or negatively by the citing reports. The claim-specific citation network may be affected by other biases. For example, reports may have cited previous content in order to criticize its validity or reframe its meaning to divert its implications. Last but not least, we do not here intend to ‘take sides’ in the salt debate: we neither endorse nor oppose the central hypothesis at hand. Our intention in this article was not to be part of the debate, and our findings should not be used to fuel it. Instead we aimed to better understand the production of scholarship underlying the controversy and, on the basis of a systematic review and quantitative analyses, to try to lay bare and begin to unravel the challenges underlying the dispute.

Supplementary Data
Supplementary data are available at IJE online.

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Authors’ contributions
L.T. and S.G. contributed to the conception and design, to the acquisition of data, and to the analysis and interpretation of data. D.M.J. contributed to the analysis and interpretation of data. L.T. and S.G. drafted the article and D.M.J. revised it critically for important intellectual content. All authors approved the version to be published.

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References
Commentary: Accepting what we don’t know will lead to progress

Martin O’Donnell,1,2* Andrew Mente2 and Salim Yusuf2

1Clinical Research Facility, NUI Galway, Galway, Ireland and 2Population Health Research Institute, McMaster University, Hamilton, ON, Canada

*Corresponding author. HRB-Clinical Research Facility, Newcastle Rd, NUI Galway, Galway, Ireland. E-mail: martin.odonnell@nuigalway.ie

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Sodium intake in most Western countries is a mean of about 4 g/day (equivalent to 10 g salt/day) with regional variations in mean intake.1 Lowering sodium intake to < 2.0–2.4 g/day in the entire population is recommended by some, but not all, guidelines.2,3 The World Health Organization (WHO) recommends a 30% reduction in salt intake in all adult populations, with a target sodium intake of < 2 g/day (5 g/day salt).3 These recommendations do not take into account the marked variations in the mean intakes between populations and that within each population there are also variations. The controversy about sodium intake arises from the disconnection between objective evaluation of the evidence and the pressures to advocate for public health interventions, even when key data are lacking.4 It also stems from differences in