Announcing "Up to Date in the Science of Sodium"

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Population-wide reductions in dietary salt (sodium) are recommended by a wide range of health and scientific organizations based on comprehensive systematic reviews that demonstrate adverse health effects associated with excess salt consumption, in particular increased blood pressure.[1–25] In 2010, an estimated 1.6 million deaths were attributed to excess dietary salt consumption.[26] The World Health Organization (WHO) recommends that adults should consume <5 g of salt per day with lower amounts for children.[12] The United Nations has also set a target for countries to reduce dietary salt intake by 30% by 2025, in part, to reduce the economic consequences of the evolving epidemic of noncommunicable diseases.[10] The high profile provided by public health efforts to reduce dietary salt has resulted in a vast number of publications on dietary salt.[25] The rapidly growing volume of research makes it challenging, even for focused experts, to stay up to date.

To assist scientists, clinicians, and policy makers in staying on top of the evidence about the effects of dietary salt on disease in humans and the effectiveness and impact of interventions designed to reduce dietary salt intake, an ongoing weekly MEDLINE search was commenced. To date, the results of this MEDLINE search have been summarized and communicated through a weekly online newsletter, the Science of Salt Weekly (available for free at http://www.hypertensiontalk.com/science-of-salt-weekly/). This initiative is funded by the Heart and Stroke Foundation of Canada/Canadian Institutes for Health Research Chair in Hypertension Prevention and Control and the George Institute for Global Health. It is also supported by the World Hypertension League, the WHO Collaborating Centre on Population Salt Reduction, the Pan American Health Organization/WHO Technical Advisory Group on Cardiovascular Disease Prevention through Dietary Sodium, and the World Action on Salt & Health.

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To further enhance the dissemination of the weekly evidence reviews, two alternating narrative summaries of the reviewed articles will soon be published in *The Journal of Clinical Hypertension*—"Up to Date in the Science of Sodium." The first will focus on the relationship between dietary salt and health outcomes and the second on how to achieve dietary salt reduction in populations. The summaries will be published approximately every 2 months.

Articles will be identified by a standardized weekly MEDLINE literature search. (Search terms are summarized in the Table.) This search strategy was adapted from an approach used to conduct Cochrane Collaboration systematic reviews for the development of the WHO dietary salt recommendations.[12,27]

DIETARY SALT AND HEALTH OUTCOMES

A recent challenge in understanding the effects of salt on health outcomes is that low-quality research with discrepant findings has generated unwarranted controversy and publicity,[28] while higher-quality research that aligns with existing evidence has gone largely unnoticed.[29] Accordingly, studies included in the review will be evaluated according to a series of established quality indicators to provide a more objective and balanced interpretation of study conclusions.

The strength of each study design will be assessed using the Cochrane risk of bias tool and a modified Cochrane risk of bias tool developed specifically for a Cochrane review of population-wide interventions to reduce salt (http://bmg.cochrane.org/assessing-risk-bias-included-studies).[30] Evidence derived from adequately powered randomized trials (and overviews of trials) will be weighted more heavily than those from observational studies, which are much more susceptible to confounding. In addition, specific attention will be paid to the methods used for the assessment of dietary salt using criteria developed for the recent Cochrane review of the health impact of dietary salt.[27] Studies will be interpreted in light of the duration of the intervention and magnitude of the salt reduction achieved as well as the most plausible effects of the differences in exposure to salt between groups. For example, interventions of at least 4 weeks are likely necessary to reliably detect maximum effects on blood pressure reduction, and investigations of the effects of salt on "hard" cardio-

TABLE. Medline (Ovid) Search Strategy[a]

Step	Search
1	Exp Sodium Glutamate
2	(monosodium glutamate or msg).tw,kw
3	Exp Sodium Chloride/
4	(salt or sodium).tw,kw
5	1 or 2 or 3 or 4
6	Exp Diet
7	(diet or food or intake).tw,kw
8	6 or 7
9	5 and 8
10	Exp Sodium, Dietary
11	Exp Diet, Sodium-Restricted
12	9 or 10 or 11
13	Limit 12 to animals
14	Limit 12 to (animals and humans)
15	13 not 14
16	12 not 15
17	Limit 16 to English language
18	Limit 17 to year = "2009–Current"

[a]The search was modified to include the kw field code to all text word searches and added sodium intake and NaCl as MeSH terms the week of July 26, 2015.

vascular outcomes likely require at least 12 months of follow-up. Further, the size of the difference in exposure to salt between groups needs to be sufficient to cause the anticipated effect on the selected outcome; therefore, studies with smaller sample sizes, those with small differences in the salt intervention between exposure groups, or studies with imprecise measurements of salt intake may be inadequately powered to address the research question posed. For nonrandomized studies, the quality evaluation will be based on the efforts made to control for potential confounders and the impact of these adjustments on the conclusions drawn. Essentially, research must use methods that produce accurate and reproducible findings to advance scientific understanding.

While summaries of both high- and low-quality studies will be included in the "Up to Date in the Science of Sodium" review, the focus will be on those meeting key quality criteria applicable to the scientific question being addressed. As in the Cochrane risk of bias tool, outcomes reported from nonrandomized intervention studies will be viewed with greater skepticism and the comparative findings of unadjusted and adjusted effect estimates will be carefully reviewed such that the effects of potential confounders and measurement error are fully considered. Studies in which co-interventions were used alongside salt reduction (eg, other nondrug interventions, antihypertensive drugs, diuretics) will also be interpreted cautiously as it will be hard to reliably isolate the discrete effects of salt reduction alone, as compared with the other components of the intervention.

Observational study designs associating salt intake with disease outcomes are weaker sources of causal inference but are still often utilized for public health decision-making in the absence of adequate evidence from randomized controlled trials. Of the various types of observational studies, prospective cohort designs will be considered as stronger studies, presuming there is careful measurement of exposures and outcomes, comprehensive exploration and adjustment of relevant confounders, and adequate statistical power.[27] The inclusion of blood pressure as a covariate is generally not appropriate in studies assessing the effects of salt on hard outcomes because blood pressure lies on the causal pathway. For observational studies, assessment of exposure to salt intake should be done with at least one 24-hour urine collection, although assessments spanning multiple days are preferable. The use of spot urine to estimate 24-hour intake is highly problematic in assessing the causal association between exposure to salt and the development of disease, in part because of the dynamic nature of natriuresis, which is subject to significant changes throughout the day, according to time of day, posture, activity, and meals. Accordingly, spot urine collections may be misleading, depending on the conditions under which they were collected. Spot urine samples also often rely on equations that include other powerful predictors of risk such as creatinine, age, and sex to estimate 24-hour sodium excretion. Finally, studies that include people with established disease may be subject to confounding by reverse causation (whereby sicker individuals may be more likely to improve their dietary patterns yet still retain an elevated risk for long-term adverse outcomes), sometimes resulting in spurious J- or U-shaped associations.

The adverse health outcomes of primary interest will be total cardiovascular disease, stroke, coronary heart disease, all-cause mortality, bone diseases, and cancer. Hypertension will be viewed as a substantive health outcome because 18% of global deaths, 7% of global disability, and 10% of healthcare costs are attributed to increased blood pressure.[23,31] Surrogate indicators will also be included, such as markers of kidney function, endothelium-dependent dilation, aortic pulse wave velocity, markers of bone metabolism, renal stones, weight gain and obesity, and heart rate.

THE PRACTICALITIES OF ACHIEVING LARGE-SCALE REDUCTIONS IN DIETARY SALT CONSUMPTION

The second focus of the "Up to Date in the Science of Sodium" review will be on studies exploring the practicalities of how to reduce dietary salt in populations or other large groups of individuals. The robustness of these studies will also be assessed using a modified Cochrane risk of bias tool developed specifically for a Cochrane review of population-wide interventions to reduce salt.[30] Implementation studies that seek to achieve population-wide dietary salt reduction will be of particular interest, as will studies that capture data about specific population groups such as children, the elderly, or ethnic minorities. The setting of such

studies will vary but may be defined by national, regional, or local geography or specific institutional setting such as schools, hospitals, childcare centers, or the workplace.

Studies assessing the implementation of salt reduction programs may directly address salt intake of the population by examining salt-related consumer knowledge, attitudes, or behaviors or indirectly by reducing the salt content of foods. In the latter case, salt reduction programs based on pricing, food procurement, food labeling, food reformulation, or food advertising will all be of interest. In general, the primary outcome for these studies will be population dietary salt consumption although other outcomes of interest may include changes in the salt content of foods; improvements to knowledge, attitudes, or behaviors; and the introduction of regulations or policies. Implementation studies conducted exclusively in people with disease will be considered less relevant to public health because of uncertainty about generalizability.

DISCUSSION

This regular publication will provide a systematic and up-to-date critical appraisal of all studies that examine the relationship between dietary salt and health or assess the impact of strategies designed to achieve population dietary salt reduction. The publication is expected to be a valuable resource for researchers, clinicians, and policy makers. In addition to providing a balanced and objective assessment of the evidence, the authors plan to highlight advances in the methods for assessing salt intake and conducting studies designed to determine the effects of dietary salt on health outcomes.

In tandem with these reports in *The Journal of Clinical Hypertension*, an international consortium of health and scientific organizations has formed to consider standards for human dietary salt research, based on concerns that low-quality research has been generating unwarranted controversy.[28] This consortium is expected to report recommendations in 2016, which will be incorporated as quality indicators for this review process. Stay up to date on a critical and evolving area of scientific and public health research by looking for "Up to Date in the Science of Sodium" in the *Journal* later this year (2015).

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