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VIEWPOINT

New evidence relating to the health impact of reducing salt intake

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Abstract This paper is a Position Statement from an 'ad hoc' Scientific Review Subcommittee of the PAHO/WHO Regional Expert Group on Cardiovascular Disease Prevention through Dietary Salt Reduction. It is produced in response to requests from representatives of countries of the Pan-American Region of WHO needing clarification on two recent publications casting doubts on the appropriateness of population wide policies to reduce salt intake for the prevention of cardiovascular disease. The paper provides a brief background, a critical appraisal of the recent reports and explanations as why the implications have been mis-interpreted. The paper concludes that the benefits of salt reduction are clear and consistent, and reinforces the recommendations outlined by PAHO/WHO and other organizations worldwide for a population reduction in salt intake to prevent strokes, heart attacks and other cardiovascular events.

Strong and consistent evidence shows that a diet high in salt is harmful to health and that reducing its intake is among the most cost effective possible means to reduce disease risk [1–5]. Excess dietary salt causes an increase in blood pressure, the leading risk for premature death in the developed and developing world. In addition, a high dietary salt intake is strongly associated with stroke and cardiovascular outcomes [6], gastric cancer, loss of calcium in urine and the ensuing risks of calcium-containing kidney stones and osteoporosis [7]. There are also strong associations and a pathophysiological basis for high dietary sodium intake to contribute to obesity [8].

Recently two highly publicized reports have been used by public and scientific media to suggest that high dietary

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sodium intake does not adversely affect health [9,10]. The critical appraisal that follows seeks to put these studies in the broader scientific and methodological context, and shows that these studies do not form a rational basis upon which to make changes to existing public health efforts to reduce population dietary salt intake.

The background to these studies is fifty years of intensive animal and human research that has seen a vast array of studies conducted on dietary sodium intake and health [1–5]. The human research program has been particularly extensive including migration studies, cross sectional studies, cohort studies, randomized trials and meta-analyses and has involved hundreds of thousands of individuals. Like most research programs it is comprised of pieces of work of varying quality and significance and the interpretation of any one project requires careful consideration of both its individual strengths and weaknesses and the broader scientific context. When taken overall, the message is very clear – salt causes high blood pressure and vascular disease. This consensus is widely accepted by national and international governmental, scientific and health organizations.

Discovering truth in science is dependent upon two key aspects of research design – precision and validity. Precision describes the capacity of a piece of work to determine exactly what is going on by controlling for random errors (the play of chance) and mostly it relates to the size of the studies done. Small projects provide poor precision and are at high risk of turning up findings just by chance, or missing real effects because the study was unlucky. Even then science compromises because to be absolutely precise is usually impractical. So we settle on the notion that 'truth' is defined by studies that have a 90% chance of picking up a real effect if it does exist (90% power) and only a one in 20 change of showing a chance positive finding that isn't really there ($p = 0.05$). It is very important to look at every study in this context and to interpret the reported findings in light of what the study was actually able to show.

Validity describes a different concept, that of controlling for systematic (or non-random) errors and truly understanding the cause and effect relationship. Confounding of associations is a particular problem in nutritional epidemiology and has been a major cause of the debate in the salt field. Caution is required in interpreting the findings reported by cohort studies with very close examination of the mechanisms that the researchers have put in place to control for potential confounding factors and the extent to which these methods are likely to have been successful. In particular, if the observed effects in the observational data do not fit with what the results of the unconfounded randomized trials they need to be treated with extreme caution.

Recently JAMA published an article by Stolarz-Skrzypek and colleagues [10]. This cohort study examined urinary sodium excretion in relation to hypertension and fatal and non-fatal outcomes and concluded that low sodium diets increased cardiovascular disease and should not be recommended on a population basis. The key problem with this trial is residual confounding. The data from the Stolarz-Skrzypek's study show that the group consuming low salt diets were very different from the group consuming high salt in many more ways than just their level of salt consumption. They had higher levels of many known risks for CVD that would be expected to result in a poor outcome regardless of their salt intake – the lowest educational attainment, higher baseline systolic blood pressure, older age and higher total cholesterol. While the investigators sought to adjust for these confounders statistical models mostly fail to achieve full correction for such imbalances. The very large changes produced by statistical adjustment in this study are a cause for concern because this suggests that confounding was substantial and that under-correction may therefore also have been substantial. Similar imbalances were a feature of 2 previous cohort studies by Alderman and Cohen et al. and statistical adjustment in that case resulted in the conclusion of no significant relationship between high dietary salt and adverse outcomes [11,12]. In the examples of Alderman and Cohen, the data was from a cohort derived from the NHANES in the United States, and notably two studies by different groups of investigators examining salt consumption using NHANES data refuted their findings, confirming high salt intake was associated with cardiovascular disease [13,14].

The lower sodium excretion group in the Stolarz-Skrzypek study also had lower urinary creatinine, urinary potassium, and urine volumes suggesting concurrent illness or non adherence to the collection of the full 24 h urine sample. In diverse research studies poor adherence, even to placebo, is a strong marker of bad outcomes [15,16]. The Stolarz-Skrzypek data are also unusual in that lower sodium intake is almost always also associated with a higher potassium intake and excretion because the main mechanism for reducing dietary sodium is to eat unprocessed foods that are high in potassium (such as vegetables and fruits) [17].

In addition to major concerns about validity, the study had very limited precision. The study population was young with a low cardiovascular disease event rate and the conclusions were based on just a small number of events. Statistical power was negligible and there is a very high risk of this being a spurious finding. When the study of Stolarz-Skrzypek is included in an updated meta analysis of all the prospective cohort studies addressing this question the overall finding is that high dietary sodium is associated with an increased incidence of stroke with a corresponding trend toward higher total cardiovascular events [18].

The second, more recent report derives from the Cochrane Collaboration and examined the impact of high dietary salt consumption on death and disability in a meta analysis of randomized controlled trials [9]. The overview found no strong evidence that salt reduction through individual dietary advice reduced all-cause mortality or CVD morbidity in normotensive persons or hypertensive patients. The media have widely misreported the findings and a false sense of controversy has been broadcast, confusing the public on important health messages. The key issue here was the study power. The overview simply did not have large enough numbers of people studied, long enough trials or large enough reductions in dietary salt to adequately assess the question being addressed. The study also separated trials of people with normal blood pressure and those with high blood pressure further limiting the studies statistical power. Another major limitation of this study is their decision to truncate follow-up in the TOHP studies to just the trial period [19]. Extended follow-up

documented a significant reduction in cardiovascular events over the long-term (not evident in the trial phase alone) [19]. In contrast to the media reports, the Cochrane meta analysis results were absolutely consistent with large reductions in death and disability from lower salt diets with clear effects of salt reduction on blood pressure that were exactly in line with what would have been anticipated.

A further limitation of the Cochrane overview was the decision to include a trial done in people with severe heart failure on very high doses of diuretic. This is an inappropriate group in which to study the effects of salt reduction, since the high doses of diuretic will have left many already substantially salt depleted. The adverse findings in this study are therefore not entirely unsurprising and the small size of the study also makes the findings prone to the play of chance. Interestingly, repeating the Cochrane meta analysis and combining the studies of people with normal and high blood pressure together results in an overall estimate of effect showing a substantive reduction in cardiovascular events [20].

Perhaps as important as the science which overwhelmingly supports the health and economic benefits of reducing dietary salt is the media attention and controversy it has generated. Many headlines have been generated that confuse the public and health care professionals. The new studies should not deter efforts to reduce dietary salt and do not change our understanding, regarding the adverse impact of salt on health. In conclusion, the benefits of salt reduction are clear and consistent, the recent studies do not indicate that salt does not affect hypertension or CVD, their publication does not change the priorities outlined by PAHO/WHO and worldwide for a population reduction in salt intake to prevent heart attacks and strokes.

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