Commentary: Evidence on salt and blood pressure is consistent and persuasive

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Alderman’s paper\textsuperscript{1} gives a selected and unbalanced account on salt and blood pressure, and reaches unsound conclusions. Time and again when the totality of evidence has been scrutinized by independent expert committees, they have concluded that the average sodium consumption at the population level is too high, that reductions to no more than 100 mmol sodium/day (6 g salt/day) is desirable, and that public health benefits would accrue.\textsuperscript{2–5} Alderman obliquely notes these recommendations, but quickly dismisses them as ‘… dogma…’ without any attempt at specific refutation. These recommendations have received wide acceptance among professional organizations and government departments responsible for protecting the health of the public.\textsuperscript{6,7} but they have been opposed by powerful commercial interests among the salt manufacturers (represented by the Salt Institute in the US) and some food companies.\textsuperscript{8,9} Alderman’s argumentation lends justification to the ‘do nothing’ position of the Salt Institute and others at the expense of substantial potential gains in public health.\textsuperscript{10,11}

Randomized Clinical Trials and Evidence from Clinical Practice and Anthropology

The evidence on salt and blood pressure comes from animal and clinical studies, clinical trials, epidemiological and anthropological findings.\textsuperscript{12} In discussing randomized controlled trials, Alderman focuses on findings from two meta-analyses,\textsuperscript{13,14} ignores a third\textsuperscript{15} and concludes that ‘… a large (50–75%) reduction in sodium intake …’ produces on average a ‘… modest …’ fall in blood pressure, ‘… with wide individual variation…’. In so doing, he is silent on the crucial matter of varying quality among the many trials in these meta-analyses,\textsuperscript{16} including varying adherence of participants to counselling for salt intake reduction, leading to underestimation of true effects on blood pressure. Correspondingly, he is silent on the recently published results of the DASH-Na trial\textsuperscript{17} which crucially illuminate this issue. The DASH-Na trial differed from most in two key respects. It was a feeding study with all food supplied to participants to achieve very high adherence, and its design provided for three levels of sodium—higher (141 mmol/day), intermediate (106 mmol/day), lower (64 mmol/day)—as verified by analyses of 24-hour urine samples. For hypertensive participants eating usual American fares, lower compared to higher sodium produced an 8 mmHg fall in systolic blood pressure (SBP), considerably greater than the estimates (4 and 6 mmHg) in the two cited meta-analyses. Crucially, in terms of salt and population-wide adverse blood pressure levels, for non-hypertensive DASH-Na participants (SBP/diastolic blood pressure [DBP] 120–139/80–89 mmHg, i.e. normal but not optimal, and high-normal blood pressures), lower versus higher sodium (again, 77 mmol/day lower) produced a 5.5 mmHg fall in SBP (7 mmHg in African-Americans, 4 mmHg in other groups), versus 1.6 and 1.2 mmHg in the two meta-analyses. For all DASH-Na participants, lower versus higher sodium reduced SBP/DBP 6.7/3.5 mmHg, versus about 3/2 from the meta-analyses. Further, the effect on blood pressure of salt reduction in the DASH-Na trial was greater for lower versus intermediate sodium than for intermediate versus higher sodium: –4.6 versus –2.1 mmHg SBP, for sodium lower by 42 and 35 mmol/day, respectively. This is a finding seminal for public policy recommendations.

Alderman also fails to mention the unique double-blind randomized controlled trial of reduced sodium intake in newborns done in The Netherlands in the early 1980s before no-added-salt baby feeds were widely available.\textsuperscript{18} With a reduction in sodium intake by about two-thirds, SBP at 6 months was significantly lower by 2.1 mmHg. At follow-up 15 years later, the reduced sodium group continued to have lower blood pressures than the ‘usual’ (high) sodium group, despite no further intervention since infancy.\textsuperscript{19}

In addition, Alderman ignores evidence from clinical practice, for example, on the beneficial effects of the low-sodium rice diet of Kempner used to treat malignant hypertension in the 1940s, and the antihypertensive effects of thiazide diuretics, which promote sodium excretion.\textsuperscript{12}

Also relevant are the findings among chimpanzees,\textsuperscript{20} cited all too-briefly by Alderman. With stepwise addition of up to 15 g salt/day to their usual low-sodium diets, SBP rose 26 mmHg over a 20-month period, with rapid reversal when the added salt was removed.

Particularly since chimpanzees and humans have 95+% genes in common, these data highlight the findings on dietary salt from anthropology and evolutionary biology—findings bypassed by Alderman. During 70 million years of mammalian and primate evolution, and 4–15 million years of hominoid and hominid evolution leading to Homo sapiens, and—for Homo sapiens—tens of thousands of years of evolution as a nomadic food gatherer and hunter, until 6000–8000 years ago when agriculture and animal husbandry were invented, our predecessors knew nothing about salt as a food additive.\textsuperscript{21} Evolving on a low salt diet of no more than 20–40 mmol sodium/day, generally in warm climates (e.g. Africa), our species became—and remains...
—exquisitely adapted for the physiological conservation of the limited salt naturally present in foods, i.e. for salt retention, not for excretion of a chronically excessive intake 10–20+ times physiological need (8–10 mmol/day).2 Thus, when Alderman talks about current intake ‘... between 100 and 200 ... ’ mmol sodium/day and its ‘... uniformity across all dietary, cultural, environmental and hereditary circumstances ...’, he one-sidedly ignores human prehistory, unscientifically equates levels of current sodium intake (100 and 200 mmol/day) that are not uniform in their effects on blood pressure and, by implying that present-day usual = normal = optimal, infers that current intake relates positively to worldwide increasing life spans, without specifying whether he means 100 or 200 mmol (or what level) sodium per day. For example, in Japan (erroneously cited by Alderman in support of this concept), public health efforts have led to decreasing salt intake from levels as high as 400 mmol/day, a change associated with declines in stroke mortality (from levels originally highest in the world) of 80–90%, which have made an important contribution to Japan’s recent emergence as the country with highest population life spans.

**Observational Studies of Salt and Blood Pressure**

The same problems prevail in Alderman’s account of the observational data from epidemiology. Thus, he cites studies on the Kuna Indians and Italian nuns to cast doubt on evidence that salt plays a role in the change in blood pressure that accompanies migration. Counter examples are not mentioned, including findings on the Qash’qai nomads of Iran22 and six Solomon Islands population samples, where only one, the Lau, had prevalent high blood pressures.23 In contrast with the other five population samples that consumed low salt diets, the Lau cooked their food in brackish water from a Pacific inlet, hence had higher salt intake. Neither of Alderman’s examples directly involved migration, in contrast to data from China, Africa, and elsewhere. For example, when the Luo in Kenya moved from their rural villages to Nairobi, the move was accompanied by a rapid rise in blood pressure associated with higher urinary sodium:potassium ratio and higher body weight.24

The senior of us (JS) has déjà vu in reading Alderman’s arguments, since all of them are repeats 30–40 years later of assertions put out, with support from special commercial interests, to undermine the conclusion that dietary cholesterol-saturated fat plays a key aetiological role in producing epidemic atherosclerotic disease through its major adverse influences on serum lipids, etc. The immediate argument about ‘exceptional’ populations was a favourite then too—there were Eskimos in the Arctic, Masai in Africa and others. These ‘exceptions’ died on the vine as the aetiological issue became fully resolved. Particularly against this background, it is relevant to note that an exception tests the rule; it does not refute it. An exception may have many roots. It may reflect the fact that the exposure (e.g. high lipid intake) may be necessary to produce the effect (e.g. high serum cholesterol on average), but it may in certain circumstances not be sufficient, given that multiple factors are at work causatively. Or, an exception may be due to flawed data, or to lack of statistical power due to small sample size, i.e. it really is not an exception at all. Again, Alderman does not come to grips with such basic issues.

Correspondingly, Alderman’s discussion of INTERSALT findings25,26 is critically flawed, repeating his previously published incorrect assertions despite our written communications setting the record straight.27 Thus, he continues to claim that INTERSALT found no association between sodium and blood pressure when analyses were restricted to 48 population samples (excluding four low sodium population samples). In fact, the highly significant within-population association between urinary sodium excretion and SBP across all 52 population samples was virtually unchanged when the four low-sodium populations were excluded (N = 9343 instead of 10 074),27,28 and the association between sodium excretion and upward slope of blood pressure with age found across 52 population samples persisted across 48 samples.25 Alderman also states that ‘the notion that pressure rises with age ... is in no way a genuine observation.’ Though the INTERSALT data were cross-sectional, there is repeated evidence from many longitudinal population studies of a genuine rise of blood pressure with age.29,30

Adjusted INTERSALT estimates26 are quantitatively similar to the DASH-Na feeding trial results for influences of sodium on the blood pressure of individuals. Particularly in view of the much larger effects in the chimpanzee experiments and in the ecological analyses of INTERSALT, estimating effects of 100 mmol less sodium/day on upward slope of blood pressure from age 25 to age 55, it is reasonable to infer that there is also a large decades-long influence operating from early in life—a concept supported by the findings of the Rotterdam study of infants.

Alderman cites two of his own studies31,32 to imply that reduced sodium intakes may be harmful, but fails to cite subsequent letters to the editor and articles that have been highly critical of both studies. The first of his studies followed up treated hypertensive patients who had been instructed to refrain from excess salt intake for 5 days prior to plasma rennin activity measurement. Their urinary sodium excretion was then used—in a way that was obviously flawed methodologically—as an index of their usual salt intake. Sodium excretion in the lowest quartile was unusually low (reflecting likely under-collection), and results could have been further biased by the fact that those with the highest risk may have reduced their sodium intake more extensively (i.e. reverse causality).33,34 The second of Alderman’s studies gave follow-up data from the NHANES-1 study, but was fatally flawed because of inadequacies of measurement of sodium consumption at baseline.35–38 Alderman, citing a further analysis of the MRFIT data, which (unlike his study) reported no association between sodium intake and subsequent mortality,39 claims (with no supportive data) that the study showed a ‘tendency for those consuming the least sodium to have the highest coronary heart disease event rates’. Alderman then cites a recent Finnish study that found significant direct—not inverse—associations between urinary sodium excretion and subsequent coronary heart disease, cardiovascular and all-cause mortality, with adjusted hazard ratios (men and women combined) of 1.56 (95% CI : 1.15–2.12), 1.36 (95% CI : 1.05–1.76) and 1.22 (95% CI : 1.02–1.47), respectively per 100 mmol sodium.40 The paper included a sub-group analysis that stratified the population by gender and weight, thus reducing statistical power: for normal-weight men, hazard ratio for cardiovascular disease mortality was 1.23 (95% CI : 0.76–1.98) per 100 mmol sodium, while for overweight men it was 1.44 (95% CI : 1.02–2.04). Alderman claims that these findings
imply that only obese people are at risk from high sodium intake, a claim refuted by the author,\(^4\) in answer to a letter to the editor by Alderman on this very point. As Alderman then notes, the associations between sodium intake and mortality are likely to have been diluted because sodium estimates were based on only a single 24-hour measurement of urinary excretion. In the light of this point, Alderman’s argument—against a significant positive overall relation of sodium intake to mortality in this population—is further flawed.

Finally, Alderman raises issues about the safety of sodium reduction, based on results of small short-term studies with very large manipulations in sodium intake. However, he fails to cite articles highly critical of this position, indicating that the metabolic changes are not seen with longer-term, moderate sodium reduction.\(^28,34,42\)

**Conclusions**

By ignoring the overwhelming scientific consensus on this issue, Alderman appears to condone the ‘do nothing’ approach favoured by some elements of the food industry (who have much to gain commercially from the status quo). Alderman calls for a long-term randomized trial of sodium reduction with a focus on cardiovascular morbidity and mortality. But for reasons of costs and practicality (including sample size, problems of blinding and confounding) such a trial is not being seriously considered by any responsible agency, governmental or non-governmental, national or international. It will never be done. Instead, as with many matters in public health (e.g. on dietary lipid and atherosclerotic disease) and in other walks of life, reasoned decisions need to be taken based on the weight of evidence to hand.\(^6\) For sodium and blood pressure, as attested by many independent scientific reviews, the evidence from animal studies, clinical trials and epidemiological observation is strong, consistent and persuasive. Recent analysis demonstrates both the potential health and economic benefits of adopting a population approach to sodium reduction.\(^11\) The proponents of the ‘do nothing’ approach have no case for the status quo as the preferred public health option. In fact, the body of scientific knowledge affords no basis for valid debate; efforts to promote the idea that there is a scientifically grounded ‘controversy’ in this area—as in the area of tobacco and disease—are scientifically unsound and detrimental to health. With his faulted methodological thrust involving a heterogeneous mix of errors and omissions, Alderman has no trouble coming to conclusions about salt and blood pressure which are contrary to repeated expert group reviews, and supportive of the position adopted by special commercial interests.

**References**

Commentary: Salt, blood pressure and public policy

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The ‘salt hypothesis’ is that higher levels of salt in the diet lead to higher levels of blood pressure, increasing the risk of cardiovascular disease. The corollary is a public health recommendation for a drastic cut in the level of dietary salt, by a factor of two or more. The salt hypothesis and its public health corollary have a number of highly visible advocates, both individual and corporate.

Alderman1 provides an incisive review of the evidence from epidemiological studies, as well as experiments on humans and animals. He concludes that existing data do not support draconian restrictions on salt intake. He even cites some studies showing that a marked reduction in salt levels will do more harm than good, while properly noting the limitations in such data. Results depend on making the proper adjustments, but statistical science offers only the most general guidelines as to which adjustments should be made and which should not.

Alderman also mentions two remarkable and little-known natural experiments—the San Blas Indians and the Italian nuns—which demonstrate that the link between dietary salt and blood pressure is weak at best. The San Blas study is cross-sectional rather than longitudinal, which perhaps weakens the force of the data.

What would be the health effects of cutting salt intake in half? To settle the question, Alderman points out that long-term clinical trials would be needed, measuring primary endpoints of mortality and morbidity rather than intermediate endpoints like blood pressure. Others have reached similar conclusions about the state of the evidence and its policy implications,2,3 as does our own review.4

We examined4 the summary data published by INTERSALT;5 if anything, these data contradict the salt hypothesis. The data cover 52 centres scattered around the world—ranging from two Indian tribes in Brazil, through Chicago and Warsaw to Kenya and Beijing. As Alderman notes, however, such ecologic comparisons are especially prone to confounding.