

# The associations between dietary sodium and atherosclerosis: are the methods used accurate and reproducible?

Norman R. C. Campbell  \*

Department of Medicine, Physiology and Pharmacology and Community Health Sciences, Libin Cardiovascular Institute of Alberta, University of Calgary, 9th Floor, 1403-29th Street NW, Calgary, Alberta T2N 2T9, Canada

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We read with interest the article by Wuopio *et al.* on the associations between dietary sodium and atherosclerosis.<sup>1</sup> The results are consistent with the known causal and linear association between dietary sodium and blood pressure and the moderately strong causal and linear association between dietary sodium and cardiovascular events in meta-analyses of randomized controlled trials.<sup>2</sup>

Wuopio *et al.* assessed dietary sodium using a spot urine sample with a Kawasaki estimating equation (spot urine method) and also with a food frequency questionnaire (FFQ).<sup>1</sup> Wuopio *et al.* suggest that false or altered disease associations with the spot method are unproven and reference two select validation studies (one of which has been highly critiqued for lack of scientific rigour and mainstream scientific organizations consider to confirm a lack of validity and the other which was not analysed by the recommended Bland Altman plot method).<sup>1,2</sup> Wuopio *et al.* also suggest that the Kawasaki formula is good enough to estimate salt intake at a population level even though their analysis did not assess validation, or dietary salt using a recommended standard and their analysis was based on estimated sodium intake at the individual level.<sup>1</sup>

Spot urine samples with estimating equations have for over a decade repeatedly been recommended not to be used to assess an individual's salt consumption by major international health and scientific organizations.<sup>2</sup> In systematic reviews of validation studies, the spot method has a very large random and systematic error and the estimating equations have been shown in two large databases to cause altered outcome associations (blood pressure and death) compared to dietary sodium assessed by the recommended standard of multiple non-consecutive 24 h urine collections.<sup>2</sup> The estimating equations cause spurious outcome associations with dietary sodium as they are complex equations with

variables that strongly and independently predict most health outcomes (i.e. age, gender, body mass index, creatinine). The estimating equations have disease associations independent of the sodium. The use of quartile analyses does not avoid the altered disease associations with spot urine equations as the systematic errors are larger as sodium consumption both increases and decreases from mean intake levels. The large random error of the spot method also results in a lack of reproducibility of disease associations.<sup>2</sup>

The World Hypertension League, International Society of Hypertension and Resolve to Save Lives (RTSL) with the support of 21 additional health and scientific organizations stated very clearly 'It is strongly recommended to not conduct, fund, or publish research studies that use spot urine samples with estimating equations to assess individuals' sodium (salt) intake in association with health outcomes'.<sup>2</sup>

A prior consortium of health and scientific organizations also commissioned a systematic review of the assessment of dietary sodium with FFQs.<sup>3</sup> In the assessed studies, there was poor agreement between FFQs and 24 h urine sodium, only one study reported the recommended Bland Altman plot to assess validation, and the studies reported nonsignificant to low correlation coefficients ( $r \leq 0.36$ ). The consortium authors made a recommendation not to use FFQs to assess dietary sodium.<sup>3</sup>

Major non-governmental and governmental organizations have expressed concerns that weak research methods prone to spurious results are a major cause of controversy about the benefits of reducing dietary sodium.<sup>2</sup> Researchers, reviewers, editors and funders need to insist on high-quality reproducible research methods to advance scientific knowledge on the impact of dietary sodium on health. Studies with weak methods prone to spurious results that are not reproducible do not advance scientific understanding and need to be discouraged. Although the results of the study by Wuopio *et al.* confirm conventional expectations, that does not validate their use of unreliable methods nor confirm their findings.

\* Corresponding author. Tel: 001 403 560 6418, Email: [ncampbel@ucalgary.ca](mailto:ncampbel@ucalgary.ca)

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## Lead author biography

Dr Campbell is a Professor Emeritus of Medicine, Community Health Sciences and Physiology and Pharmacology and a member of the Libin Cardiovascular Institute of Alberta and O'Brien Institute of Public Health at the University of Calgary. Dr Campbell is currently a senior consultant to RTSL (to save 100 million lives), and to several national and international governmental programs to reduce dietary salt and to control hypertension. Dr Campbell has over 550 peer-reviewed manuscripts and over 500 national/international invited presentations.

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**Conflict of interest:** Dr Campbell reports personal fees from Resolve to Save Lives (RTSL), the Pan American Health Organization, and the World Bank outside the submitted work; and is an unpaid member of World Action on Salt, Sugar and Health and an unpaid consultant on dietary sodium and hypertension control to numerous governmental and non-governmental organizations. Dr Campbell chaired the International Consortium for Quality Research on Dietary Sodium/Salt (TRUE) which

is an unpaid voluntary position. Dr Campbell was on the Medical Advisory Board of Switch Health (2022–2023) and was a one-time reviewer of a joint Novartis Canada Alberta Health Services collaborative project to treat dyslipidemia. All the honoraria from Switch Health and Novartis Canada have been donated to the University of Calgary to support a community cardiovascular disease prevention recognition award.

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