

## Impact case study (REF3)

<b>Institution:</b> University of East Anglia		
<b>Unit of Assessment:</b> 6 – Agriculture, Food and Veterinary Sciences		
<b>Title of case study:</b> Shaping new national and international policy and guidance on sodium (salt) in our food		
<b>Period when the underpinning research was undertaken:</b> 2009 - 2013		
<b>Details of staff conducting the underpinning research from the submitting unit:</b>		
<b>Name(s):</b>	<b>Role(s) (e.g. job title):</b>	<b>Period(s) employed by submitting HEI:</b>
Dr Lee Hooper	Reader in Research Synthesis, Nutrition & Hydration	2005 to Present
<b>Period when the claimed impact occurred:</b> January 2014 to 2020		
<b>Is this case study continued from a case study submitted in 2014?</b> Yes		
<b>1. Summary of the impact</b>		
<p>High sodium (salt) intake raises blood pressure and raised blood pressure causes death and morbidity from cardiovascular disease (CVD). Lee Hooper at the University of East Anglia delivered the first systematic reviews of randomised controlled trials assessing effects of sodium reduction on long-term blood pressure and CVD outcomes. One of these reviews, published in 2013, underpins the 2012 World Health Organization guidelines, which have shaped public health policy on sodium intake worldwide. Sodium intake fell by 191mg per person per day in 47 countries whose guidelines explicitly cite UEA research or the resulting WHO guidance, compared to 45mg per person per day (<math>p=0.0045</math>) in the other 143 countries. These changes have led to significant reductions in salt intake, prevented stroke-related disability and saved tens of thousands of lives annually.</p>		
<b>2. Underpinning research</b>		
<b>Effects of sodium on blood pressure and health</b>		
<p>According to British Heart Foundation figures, 18% of all deaths and 55% of all cardiovascular disease globally can be attributed to raised blood pressure. Consuming high levels of sodium (from processed foods high in salt, or by adding salt to our food in cooking or at table) makes blood vessels less flexible, increasing blood pressure, and ultimately increasing the risk of stroke and heart attacks, major causes of ill-health, life-changing disability and death. The Global Burden of Disease study calculated that in 2017 alone high sodium intake led to three million deaths worldwide. It also calculated that in the same year 70 million years of healthy life were lost due to ill-health, life-changing disability or early death (DALYs) due to high blood pressure caused or exacerbated by excessive sodium intake (over 3g/d).</p>		
<b>Previous research into the effects of dietary salt on blood pressure</b>		
<p>Despite widespread debate about the role of high salt intakes in contributing to high blood pressure, worldwide individual intakes of sodium increased between 1990 and 2010, to a mean global sodium consumption equivalent to more than 10g of salt per person per day (or 4g of sodium per person per day). Previous research on the health effects of eating more sodium raised concern about this but was contradictory. Evidence of a positive linear relationship between sodium intake and blood pressure came from ecological studies, but the precise nature of that relationship proved difficult to isolate from other factors associated with modern life (such as population density, smoking, physical activity and body weight). Causality was unclear to those charged with making public health policy.</p>		
<p>Hooper carried out a series of initial systematic reviews (SRs) but realized that there were methodological problems. Addressing these Hooper pioneered development of new systematic review methodologies applicable to nutrition research within the Cochrane Collaboration. She also became an editor of the Cochrane Heart Group and a member of the Cochrane Nutrition Advisory Board. This work underpinned expanded and updated reviews, which Hooper conducted from</p>		

2009 while at UEA, on the effects of salt reduction on blood pressure and cardiovascular disease (R1, R2).

Meta-analysis of six RCTs of long-term effects suggested that reducing sodium intake cut the risk of all-cause mortality by a third in general populations but was underpowered in establishing statistical significance. These estimates were consistent with the predicted effects on clinical events attributable to the blood pressure reduction achieved, suggesting that basing health effect estimates on blood pressure changes was appropriate (R1, R2).

### Commission to underpin new World Health Organization (WHO) guidance and policy

The Cochrane reviews (including R1 & R2) were followed by a systematic review commissioned by the World Health Organization (WHO) to ensure that WHO guidance on sodium intake was based on the most comprehensive, up-to-date high-quality summary of the evidence (R3). Hooper provided substantial intellectual input into the review protocol, search strategies and methodology as an External Resource Person to the WHO Nutrition Guidance Expert Advisory Group (NUGAG) Subgroup in Diet and Health. The review quantified dose-response relationships and showed that reducing sodium intake to less than 2g per person per day (5g salt) resulted in significant and clinically relevant falls in blood pressure (systolic blood pressure was reduced by 3.47 mmHg, diastolic blood pressure by 1.81 mmHg). Hooper and her colleagues found high quality evidence that reducing sodium intake reduces blood pressure and has no adverse effect on blood lipids, catecholamine levels, or renal function in adults. Moderate quality evidence showed that reducing sodium intake reduces blood pressure in children. Lower sodium intakes were shown to be associated with a reduced risk of stroke and fatal coronary heart disease in adults (R3). Taken together with the strong established link between high blood pressure, cardiovascular disease and death these observations mean that most people were likely to benefit from reducing sodium intake.

### 3. References to the research

- R1** Reduced dietary salt for the prevention of cardiovascular disease. Taylor, R.S., Ashton, K.E., Moxham, T., **Hooper, L.**, and Ebrahim, S. Cochrane Database of Systematic Reviews, **2011**, (7). DOI: 10.1002/14651858.CD009217 Cited 156 times to 31<sup>st</sup> Jan 2021 in Pablon (not logged in Google Scholar)
- R2** Reduced Dietary Salt for the Prevention of Cardiovascular Disease: A Meta-Analysis of Randomized Controlled Trials (Cochrane Review). Taylor, R.S., Ashton, K.E., Moxham, T., **Hooper, L.**, and Ebrahim, S. *American Journal of Hypertension*, **2011**, 24(8), 843-53. DOI: 10.1038/ajh.2011.115. Cited 179 times to 31<sup>st</sup> Jan 2021 in Pablon, 352 times on Google Scholar
- R3** Effect of lower sodium intake on health: systematic review and meta-analyses. Aburto, N.J., Ziolkovska, A., **Hooper, L.**, Elliott, P., Cappuccio, F.P., and Meerpohl, J.J. *British Medical Journal*, **2013**, 346, f1326. DOI: 10.1136/bmj.f1326. Cited 606 times to 31<sup>st</sup> Jan 2021 on Pablon, 1007 times on Google Scholar. R3 was funded by the World Health Organization.

### 4. Details of the impact

The review commissioned by the WHO (R3) has informed WHO global guidance. Public policy change through the translation of UEA research has been delivered in 47 countries saving lives.

#### Driving changes to WHO guidance on sodium intake for adults and children

The updated, expanded systematic review commissioned by WHO formed the scientific basis of WHO sodium guidance for adults and children released in 2012. At page 11 it states “*This guideline is based on a review of the epidemiologic literature, including three new systematic reviews conducted by WHO (49-51). One review included a reanalysis of data of a fourth systematic review (36, [R1])*”. The WHO references 49-51 cited in this quotation were published as R3 in 2013. Not only did this WHO guidance set out recommended daily salt intakes for adults, based on the results of R3, but it contained the first ever WHO recommended intake for children

and was a springboard to influencing international sodium intake goals (discussed below). The WHO guidelines were completed in the previous REF period but influenced changes in policy and practice for many nations occurring throughout the current REF period. On the back of this work, as well as being an editor of the Cochrane Heart Group and leading WHO systematic reviews on health effects of dietary fats, Hooper became and has continued to be a core member of the WHO NUGAG subgroup on diet and health.

### **Influencing International sodium intake goals: General**

As global sodium intakes in 2010 were double the safe limits suggested by **R3**, a target for reduction in mean population sodium intake was included in the WHO Global Action Plan for the Prevention and Control of Noncommunicable Diseases 2013–2020. Citing 2012 WHO guidance driven by UEA research, this reduction was declared essential to enabling a 25% reduction in premature mortality from non-communicable diseases by 2025. The recommendation was endorsed by the World Health Assembly in May 2013 and agreed for collective action by all member states.

Since August 2013, this recommendation, alongside WHO guidance, has gone on to underpin professional and governmental sodium guidance in 47 countries and regions (**S1**). For example, European Society of Cardiology and European Society of Hypertension 2018 hypertension guidelines state “*Salt restriction to <5g/d is recommended*” (*Evidence class 1 Level A*) as their first lifestyle recommendation for those with hypertension or high-normal blood pressure (**S2**, referencing **R2 & R3** plus 2 other SRs). The Pan-African Society of Cardiology Taskforce on Hypertension recommends as one of its ten recommendations to “*Invest in population-level interventions for preventing hypertension, such as reducing salt intake and obesity levels....*” citing “*High-quality evidence in nonacutely ill adults shows that reduced sodium intake reduces BP [blood pressure]...*” (**S3**, referencing **R3**).

UEA analysed data on sodium intake both before and after 2013 across 190 countries, using data from nationally representative surveys wherever possible. This confirms that concerted efforts including WHO guidance and support (leading to national and professional guidance, policy, education and campaign packages) have reduced sodium intake from a mean of 3.63 g/d (SD 0.8) worldwide in 2004-2012 to 3.55 g/d (SD 0.8) per person since 2013 (**S4**).

### **Greater reductions in salt intake in countries incorporating reviews and/or WHO guidance compared to those who have not**

Forty seven of 190 countries had national or professional body sodium guidance citing Hooper’s systematic reviews (**R1, R2, R3**) and/or 2012 WHO guidance based on **R3** (**S4**). Falls in national adult sodium intake were on average 146mg/d greater in the 47 citing countries (-191mg/d, 95% CI -355 to -28), than in non-citing countries (-45mg/d, 95% CI -80 to -11),  $p=0.0045$  (**S4**), providing highly significant evidence of a link.

### **Influencing International sodium intake goals: Case Studies and Modelling**

#### i) Changes to US guidelines, sodium intake and health

UEA research and/or resulting new WHO guidance are cited in ten major US guidelines on dietary intakes of sodium published since 2013, including guidance by the American Heart Association, Academy of Nutrition and Dietetics, National Academies of Sciences (US Dietary Reference Intake for Sodium) and American Academy of Paediatrics (all referenced in **S1**). For example, the American College of Cardiology/American Heart Association Task Force states “*Best proven non-pharmacological interventions: Reduced intake of dietary sodium, optimal goal is <1500mg/d but aim for at least a 1000mg/d reduction in most adults*” (**S5**, referencing **R3** plus one other SR).

US National Health and Nutrition Examination Survey (NHANES) data suggest US sodium intakes fell by 0.06g/d or 2% from 2011-2 to 2015-6 (**S6 & S7**). Although this seems a small reduction, modelling estimates that these reductions are associated with reductions of 12,600 US deaths each year and 207,000 DALYs annually (UEA calculations, see below and **S8**). Sodium reductions in children were even greater (0.12g/d over the same period). If sustained into adulthood these falls would lead to more significant health benefits.

ii) Changes to Japanese guidelines, sodium intakes and health

Dietary Reference Intakes for Japanese (2015) set daily recommended intakes for sodium based on a compromise between the WHO guideline recommendations and current Japanese sodium intakes, to ensure health benefits and a realistic sodium goal. “*The 2013 WHO guideline for the general population strongly recommends achieving a dietary salt intake goal of 5 g/day ... the DG [dietary goal] for sodium was set at the median of 5 g/day and the current intake (the median intake from the 2010 and 2011 NHNS)*” (S9)]. The 5g/d goal comes directly from R3.

Sodium intake, tracked by the Japanese National Health and Nutrition Survey, fell by 0.26g/d or 8.7%, between 2010 and 2016 (S10). Modelling suggests that these changes reduced annual deaths by 6300 in Japan, and annual DALYs by 77,000 (UEA calculations, see below and S8).

iii) Changes to European guidelines, sodium intakes and health

The additional sodium reductions associated with European guidance (above and S4) have reduced annual deaths by an estimated 21,200 annually in European Union countries citing the systematic reviews and/or WHO guidance, and DALYs by 279,000 annually (estimated by UEA modelling based on national sodium intake data, S8).

iv) Modelling deaths and DALY reduction due to changes in sodium intake

Modelling is presented in S8. Summarising to assess effects of sodium reductions across the world on mortality and disability adjusted life years (DALYs) assumed that sodium intake of 2g/d would eliminate health risk from superfluous sodium (as calculated by R3 and cited in WHO guidance). As mean global adult sodium intake was 3631mg/d in 2007 (S4), reduction of 1631mg/d was needed to eliminate excess deaths related to sodium intake. The additional fall of **146mg/d** in those countries citing UEA research is the equivalent of **9%** of this excess sodium. With respect to deaths The Global Burden of Disease Study 2017 suggests that globally the age-standardised proportion of deaths associated with diet is 22%, of which sodium contributes approximately 23%, so excess sodium underlies 5% of deaths globally (2.5 million deaths). Nine percent of this 5% of deaths is **0.45% of deaths** (225,000 deaths annually, S8). A similar calculation for DALYs estimates that if we could reduce sodium intake by 146mg/d across the world we would avoid an extra 4.8million DALYs annually (S8). Calculations for Europe, Japan and Europe are presented above.

**5. Sources to corroborate the impact**

- S1** Impacts of sodium systematic reviews and resulting WHO guidance Stage 1. **Tracking guidelines that make use of Hooper’s systematic reviews and related WHO guidance.** *UEA analysis documenting salt/sodium guidelines citing Hooper’s SRs or WHO guidance (late 2012 to mid-2020).*
- S2** 2018 ESC/ESH Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Cardiology (ESC) and the European Society of Hypertension (ESH). Reference: Williams, B., Mancia, G., Spiering, W., et al. *European Heart Journal*, 2018, 39(33):3021-104. DOI: 10.1093/eurheartj/ehy339 (p.3056) (References 255 (R2) & 258 (R3)).
- S3** Roadmap to Achieve 25% Hypertension Control in Africa by 2025. Dzudie A, Rayner B, Ojji D, Schutte AE, Twagirumukiza M, Damasceno A, et al. *Global Heart*. 2018;13(1):45-59. DOI: 10.1016/j.ghheart.2017.06.001 (p 57, Reference 29 (R3)).
- S4** Impacts of sodium systematic reviews and resulting WHO guidance Stage 2. **Tracking changes in sodium intake and the relationship with guidelines that make use of Hooper’s systematic reviews and related WHO guidance.** *UEA analysis documenting associations between countries having guidelines, and having guidelines citing Hooper’s SRs or WHO guidance and degree of population sodium reduction.*
- S5** 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary: A Report of the American College of Cardiology/American Heart

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Association Task Force on Clinical Practice Guidelines. Reference: Whelton, P.K., Carey, R.M., Aronow, W.S., et al. Hypertension, 2018, 71(6):1269-324. DOI: 10.1161/HYP.0000000000000066 (p.1285, table 15).

- S6** US Department of Agriculture Agricultural Research Service. Nutrient Intakes from Food and Beverages: Mean Amounts Consumed per Individual, by Gender and Age, What We Eat in America, NHANES 2011-2012. (p. 5).
- S7** US Department of Agriculture Agricultural Research Service. Nutrient Intakes from Food and Beverages: Mean Amounts Consumed per Individual, by Gender and Age, What We Eat in America, NHANES 2015-2016. (p. 5).
- S8** Impacts of sodium systematic reviews and resulting WHO guidance Stage 3. **Relating sodium reduction to health outcomes** (mortality and disability adjusted life years, DALYs). *UEA analysis assessing effects of additional sodium reduction associated with salt/sodium guidelines citing Hooper's SRs or WHO guidance and national mortality and DALY load.*
- S9** Ministry of Health, Labour and Welfare. Dietary Reference Intakes for Japanese (2015) (pp 203-.204).
- S10** The trends in total energy, macronutrients and sodium intake among Japanese: findings from the 1995–2016 National Health and Nutrition Survey. Saito A, Imai S, Htun NC, Okada E, Yoshita K, Yoshiike N, et al. Br J Nutr. 2018;120(4):424-34. DOI: 10.1017/S0007114518001162.