Institution: Imperial College London

Unit of Assessment: 02 Public Health, Health Services and Primary Care

Title of case study: Improving Cardiovascular Health through International Recommendations on Population Intakes of Sodium and Potassium

1. Summary of the impact (indicative maximum 100 words)

Research by Professor Elliott and colleagues at Imperial College on worldwide salt and potassium intakes, their relationships to blood pressure, and co-authored systematic reviews and meta-analyses of their effects in adults and children on blood pressure and cardiovascular disease – and potential adverse effects – has played an instrumental role in developing international guidelines and public policy on sodium reduction strategies. Furthermore, published primary research has influenced US Centers for Disease Control and Prevention (CDC) strategies for population-wide monitoring of sodium intakes in the USA. This work has thus had impact on policies for sodium reduction and monitoring of sodium intakes worldwide.

2. Underpinning research (indicative maximum 500 words)

Key Imperial College London researchers:
Professor Paul Elliott, Professor of Epidemiology and Public Health (1995-present)
Dr Ian Brown, PhD student, then Postdoctoral Researcher (2006-2011)
Dr Queenie Chan, Researcher (2000-present)
Dr Ioanna Tzoulaki, Lecturer (2006-present)

Professor Elliott and colleagues have provided long standing academic leadership of INTERSALT and INTERMAP studies (1, 2) examining the relationships of sodium and potassium intakes (and other nutrients) with blood pressure. In the INTERSALT study, 24-hour urinary sodium collections (the 'gold standard' measurement of sodium intake) were obtained from more than 10,000 men and women aged 20 to 59 years from 52 different population groups across 32 countries. This study created the largest set of standardized data on 24-hour urinary sodium samples in the world. The INTERMAP study obtained 24-hour urinary sodium collections from men and women aged 40 to 59 years from 17 population groups in 4 countries: China, Japan, the United Kingdom, and the United States. Both studies were led jointly by Professor Elliott (Imperial College London from 1995) and Northwestern University Chicago. In 1996 analyses of the INTERSALT study, led by Imperial College researchers, provided updated estimates of the size of associations of sodium intake to blood pressure both within and across the 52 populations studied, including significant associations of sodium intake with the rise of blood pressure with age (key to determining the high prevalence of raised blood pressure and hypertension at older ages) (1). In addition to 24-hour urine collections, the INTERMAP study collected blood pressure readings and multiple 24-hour dietary recalls. Except in China, where sodium urine values were higher, the INTERMAP study reported, in 2003, similar findings to that of the INTERSALT study with respect to 24-hour urinary sodium excretions (Stamler J, Elliott P, Chan Q. INTERMAP Appendix Tables. *J Hum. Hypertens*. 2003; 17:759–775). Results for US adults indicate that 24-hour urinary sodium excretions were well in excess of the limits recommended in the *Dietary Guidelines for Americans* 2010*,* averaging 4.2 g of sodium per day in men and 3.3 g in women. In the UK, averages were 3.7 g of sodium per day in men and 2.9 g in women.

Professor Elliott and Dr Brown drew heavily on this evidence in their analysis of sodium intakes worldwide (3) for the World Health Organization (WHO) Forum and Technical Meeting on Reducing Salt Intakes in Populations held in Paris, 2006 (http://www.who.int/dietphysicalactivity/reducingsaltintake_EN.pdf). It showed that in the vast majority of populations, salt intake is well above recommended levels; it was argued that simple and cost-effective public health initiatives, in tandem with efforts by the food industry, have the potential to lower salt consumption and consequently lower cardiovascular disease burden and increase life expectancy. The paper published in the peer-reviewed literature in 2009 (3) was a distillation of the original technical report for WHO presented at the WHO meeting in 2006 by

Professor Elliott (http://www.who.int/dietphysicalactivity/Elliot-brown-2007.pdf).

WHO published guidelines on sodium and potassium intakes in adults and children in 2012, according to procedures laid down in the *WHO Handbook for guideline development.* This includes identification of priority questions and outcomes, and retrieval, assessment and synthesis of the evidence according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology. These systematic reviews were planned and refined in meetings of the Nutrition Guidance Expert Advisory Group (NUGAG) Subgroup on Diet and Health (Geneva, March 2011 and Seoul, November 2011) including definition of the scientific questions and design of the supporting meta-analyses. Professor Elliott was an invited expert at these meetings providing specialist subject-matter knowledge and provided substantial intellectual input to, and co-authored, the subsequent peer-reviewed publications in *BMJ* (4,5), the substance of which formed the scientific basis of the guidelines.

Imperial College research, funded by the US CDC, has additionally influenced work by CDC to develop a national strategy for monitoring sodium intakes in the US population. The 'gold standard' for monitoring sodium intakes via biomonitoring of 24-hr urine collections is expensive and burdensome to participants. Imperial College-led research (in collaboration with INTERSALT investigators) has shown that analysis of spot (casual) urine may be a viable low-cost and less burdensome alternative to 24-hr urine collections (6).

3. References to the research (indicative maximum of six references)

(1) Elliott, P., Stamler, J., Nichols, R., et al. for the INTERSALT Cooperative Research Group. (1996). INTERSALT revisited: further analyses of 24 hour sodium excretion and blood pressure within and across populations. *BMJ,* 312, 1249-53. DOI. Times cited: 372 (as at 8th November 2013 on ISI Web of Science). Journal Impact Factor: 17.21.

(2) Stamler, J., Elliott, P., Dennis, B., et al. (2003). INTERMAP: background, aims, design, methods, and descriptive statistics (nondietary). *Journal of Human Hypertension*, 17(9), 591–608. DOI. Times cited: 112 (as at 7th November 2013 on ISI Web of Science). Journal Impact Factor: 2.81.

(3) Brown, I.J., Tzoulaki, I., Candeias, V., Elliott, P. (2009). Salt intakes around the world: implications for public health. *Int J Epidemiol*, 38(3), 791-813. DOI. Times cited: 125 (as at 7th November 2013 on ISI Web of Science). Journal Impact Factor: 6.98.

(4) Aburto, N.J., Ziolkovska, A., Hooper, L., Elliott, P., Cappuccio, F.P., Meerpohl, J.J. (2013). Effect of lower sodium intake on health: systematic review and meta-analyses. *BMJ,* 346, f1326 DOI. Times cited: 8 (as at 7th November 2013 on ISI Web of Science). Journal Impact Factor: 17.21.

(5) Aburto, N.J., Hanson, S., Gutierrez, H., Hooper, L., Elliott, P., Cappuccio, F.P. (2013). Effect of increased potassium intake on cardiovascular risk factors and disease: systematic review and meta-analyses. *BMJ,* 346, 1378. DOI. Times cited: 2 (as at 7th November 2013 on ISI Web of Science). Journal Impact Factor: 17.21.

(6) Brown, I.J., Dyer, A.R., Chan, Q., Cogswell, M.E., Ueshima, H., Stamler, J., Elliott, P., on behalf of the INTERSALT Co-Operative Research Group.(2013). Estimating 24-Hour Urinary Sodium Excretion From Casual Urinary Sodium Concentrations in Western Populations. The INTERSALT Study. *Am J Epidemiol,* 177(11), 1180–1192. DOI. Times cited: 3 (as at 7th November 2013 on ISI Web of Science). Journal Impact Factor: 4.78.

Key funding:

- US National Institutes of Health (NIH)/National Heart, Lung & Blood Institute (1995-2004, £986,500; 2004-2009, £703,200; 2009-2014, £1,573,034), Principal Investigator (PI) P. Elliott INTERMAP Study: international cooperative study of macronutrients and blood pressure.
- US NIH/National Heart, Lung & Blood Institute (2007-2012, £1,079,810; 2012-2015, £884,584), PI, P Elliott, Metabolomics measured urinary metabolites, diet and blood pressure, 17 population samples: INTERMAP.
- US CDC (2010-2011, £77,158) PI P Elliott, Assessing the use of spot (casual) urine specimens

to estimate population mean 24-hr sodium excretion: INTERSALT project.

4. Details of the impact (indicative maximum 750 words)

Impacts include: health and welfare, public policy and service
Main Beneficiaries include: public, government and public policy makers

Since the publication of WHO recommendations and guidelines on sodium intake in 2003 (as part of WHO Technical Report Series 916) and 2007 (*Prevention of Cardiovascular Disease*), Imperial College researchers and others have published a significant body of scientific evidence concerning sodium intakes in adults and children worldwide (research ref. 6), and the associated risks of high blood pressure and cardiovascular disease. In response to the new research, Member States and international partners requested WHO to review the guidelines on sodium intake for adults, and also for the first time to generate a guideline on sodium intake for children. At the same time, guidelines for potassium intakes for adults and children were requested as there were none previously.

The 2012 WHO guidelines [1, 2] have set the world standards on sodium and potassium intakes in both adults and children, and are a template being used by governments, policy makers and industry for reductions in sodium and increases in potassium intakes worldwide [3, 4]. Both guidelines cite Imperial College-led research. The guidelines recommend a reduction in sodium intake to <2 g/day sodium (5 g/day salt) in adults to reduce the worldwide burden of high blood pressure, heart disease and stroke, and a reduction in sodium intake to control blood pressure in children (intake to be based on the energy requirements of children relative to those of adults) [1]. For potassium, WHO recommends an increase in potassium intake from food to reduce blood pressure and risk of cardiovascular disease, stroke and coronary heart disease in adults with a suggested potassium intake of at least 90 mmol/day (3510 mg/day); and an increase in potassium intake from food to control blood pressure in children (intake to be based on the energy requirements of children relative to those of adults) [2].

As noted in section 2, the WHO guidelines were developed by the Nutrition Guidance Expert Advisory Group (NUGAG) Subgroup on Diet and Health (Geneva, March 2011 and Seoul, November 2011) with substantial intellectual input from Professor Elliott and other subject-matter experts, using the WHO evidence-informed guideline development procedures and the Grading of Recommendations Assessment, Development and Evaluation (GRADE) criteria. The guidelines drew on results of systematic reviews and meta-analyses undertaken by WHO staff and their consultants working with the subject matter experts, including Professor Elliott. Meetings of NUGAG and its subject-matter experts including Professor Elliott were held to agree on study design and inclusion/exclusion criteria for the supporting meta-analyses, which were subsequently published in the peer-reviewed literature (research refs. 4, 5). These publications in *BMJ* (2013) provided the science-base for both guidelines; as noted in the *BMJ* papers "*WHO agreed with the publication of this systematic review in a scientific journal as it serves as the background evidence review for updating the WHO guideline on sodium intake for adults and for the establishment of a guideline on sodium intake in children [for establishing the WHO guideline on potassium intake] and should therefore be widely available*." The author contributions state that Professor Elliott and colleagues "*provided substantial intellectual input on research methods and interpretation of results. All authors read, provided input on, and agreed the final draft of the manuscripts*" (research ref 4, p8; 5, p7).

WHO Member States have agreed a target 25% reduction in premature mortality from Non-Communicable Diseases (NCDs) by 2025 through enactment of 9 voluntary targets, including a global target of 30% relative reduction in mean population intake of salt/sodium by 2025. The report adopting the *Global Monitoring Framework and Voluntary Global Targets for the Prevention and Control of NCDs* dated 27 May 2013, following the *2011 Political Declaration of the United Nations High Level Meeting on NCDs*, cites the WHO sodium guideline [3; page 43] and both the sodium and potassium guidelines as relevant WHO tools to achieve the targets [3; page 47]. A joint technical meeting convened by WHO and The George Institute for Global Health was held in

Sydney, Australia, in March 2013 (attended by Professor Elliott as a subject-matter expert and Chair of session) to agree methods to take forward salt reduction and iodine fortification strategies in public health. The report of that meeting [4] cites both the WHO sodium and potassium guidelines, based on the work of WHO staff, Professor Elliott and colleagues, as key documents "*to help develop and guide national policies [on sodium and potassium] and public health nutrition programmes*".

Imperial College-led research has also influenced US CDC efforts underpinning the US government strategy for monitoring population-wide sodium intakes. Thus our demonstration of the use of spot urines as a valid, low-cost alternative to 24-hr urine collections for monitoring population sodium intakes (research ref. 6) has had impact on the US CDC approach to use of biomarkers for monitoring sodium intakes in the US population [5, page 13; 6]. INTERMAP and INTERSALT are cited by CDC as being among the top ten resources on sodium reduction and biomarkers [5, page 14 and 15]. CDC's own research using INTERSALT equations developed by Imperial College (research ref. 6) concludes "*[INTERSALT] equations could be used with a single spot urine specimen to monitor temporal trends in population mean sodium intake among young US adults... as part of a national surveillance system critical to evaluating US efforts to reduce sodium intake*" [6]. CDC is now taking this forward in its approach to evaluating sodium intakes in the US population. Specifically it is using spot urines collected in the National Health and Nutrition Examination Survey (NHANES) to examine trends over time in sodium intakes in the US adult population [7].

5. Sources to corroborate the impact (indicative maximum of 10 references)

[1] WHO. *Guideline: Sodium intake for adults and children* (2012). http://www.who.int/nutrition/publications/guidelines/sodium_intake_printversion.pdf (archived on 8th November 2013)

[2] WHO. *Guideline: Potassium intake for adults and children* (2012). http://www.who.int/nutrition/publications/guidelines/potassium_intake_printversion.pdf (archived on 8th November 2013)

[3] Sixty-sixth World Health Assembly. WHA66.10. Follow-up to the Political Declaration of the High-level Meeting of the General Assembly on the Prevention and Control of Non-communicable Diseases, 2013 http://apps.who.int/gb/ebwha/pdf_files/WHA66/A66_R10-en.pdf (archived on 8th November 2013)

[4] Salt reduction and iodine fortification strategies in public health. Report of a joint technical meeting convened by World Health Organization (WHO) and The George Institute for Global Health in collaboration with the International Council for the Control of Iodine Deficiency Disorders Global Network, Sydney, Australia, March 2013. Geneva, World Health Organization (WHO), 2013 (in press).

[5] U.S. CDC Sodium Reduction Toolkit: http://www.cdc.gov/dhdsp/toolkit/Bio-Package/data/resources/Biomarkers%20Transcript.pdf (archived on 8th November 2013)

[6] Cogswell, M.E., Wang, C.Y., Chen, T.C., Pfeiffer, C.M., Elliott, P., Gillespie, C.D., Carriquiry, A.L., Sempos, C.T., Liu, K., Perrine, C.G., Swanson, C.A., Caldwell, K.L., Loria, C.M. (2013). Validity of predictive equations for 24-h urinary sodium excretion in adults aged 18-39 y. *Am J Clin Nutr*, 98(6), 1502-1513. DOI.

Contact to corroborate impact on US CDC policy:
[7] Senior Scientist, Epidemiology & Surveillance Branch, Division for Heart Disease and Stroke Prevention, National Center for Chronic Disease and Health Promotion, U.S. Centers for Disease Control and Prevention (CDC).