Institution: University of East Anglia

Unit of Assessment: 6 - Agriculture, Veterinary and Food Science

Title of case study:

Micronutrients and health: Refining dietary requirements and addressing deficiencies to ensure future food security

1. Summary of the impact

Although an adequate micronutrient intake and status is necessary for health and deficiency disease prevention, an excess dietary intake may have deleterious effects on health. Our impact has been to inform, stimulate and move forward our understanding of micronutrient requirements across the human lifecycle. Our activities have led to the development of WHO, EU and national nutrient intake recommendations which have had a significant impact on public health policies and initiatives which address food security.

We provided specialist expertise to the WHO Guidance Expert Advisory Group for assessing the effects of potassium and sodium intakes on human health. As a result, WHO has developed its first dietary guideline on intakes of potassium (adults and children) and sodium (children) for cardiovascular health.

Our original research in micronutrients including iron, zinc and fluoride and our systematic review approach have generated the evidence required for deriving nutritional recommendations, exemplified by our contribution to European dietary reference values (DRVs). These are used by member states to produce national health policies, guidelines and nutrient intake recommendations.

2. Underpinning research

The underpinning research for this case has further established the micronutrient requirements for optimising human health, including studies on the absorption of minerals (bioavailability), on micronutrient interactions, and on establishing the best biomarkers to monitor micronutrient status in the body. The research spans a continuous period of 30 years, with some of the earlier work carried out by Fairweather-Tait at the Institute of Food Research (one of the partner Institutes of the Norwich Research Park) and subsequent work from 2005 (Hooper) and 2007 (Fairweather-Tait, Collings) at UEA.

In order to establish dietary requirements for different population groups, and to assess the impact of implementation, information on micronutrient intake, bioavailability, and the relationship with health end-points is required. From 2007-2012, UEA was one of the main driving forces leading the EURopean RECommendations Aligned (EURRECA) Network of Excellence, funded by the European Commission to develop scientific outputs ('tools') to harmonise European micronutrient recommendations. Deriving such values in a transparent, systematic way is challenging. To explore the relationship between micronutrient status and health, it is important to understand which markers of micronutrient status can be relied on and under what circumstances. A critical piece of our research was to provide detailed data from randomised controlled trials to establish sensitive biomarkers of status associated with particular levels of intake (research references 1-2) and these contributed to our development of a comprehensive methodology framework to assess which biomarkers reflect changes in nutritional status in different population groups (research references 3-6).

Our systematic review and meta-analysis (research reference 7) integrated the available high quality research on potassium and health. Prior to this work, the evidence on the potential beneficial effect of increased potassium intake on blood pressure and cardiovascular disease risk was inconsistent. Specifically, our meta-analysis showed that increased potassium resulted in a decrease in blood pressure and that the greatest impact was achieved when potassium intake was 90–120 mmol/day.

To inform the development of a WHO global guideline on sodium, our BMJ meta-analysis quantified dose-response relationships and showed that reducing sodium intake to <2 g/day

resulted in significant and clinically relevant decreases in blood pressure (systolic blood pressure was reduced by 3.47 mmHg, diastolic blood pressure by 1.81 mmHg) (research reference 8). This is now the WHO recommended intake for adults. This research also underpinned the first WHO guideline on sodium intake for children which is based on the adult intake of 2 g/day, but adjusted downwards based on the relative energy requirements of children.

Key UEA researchers:

- **Susan Fairweather-Tait**, Professor of Nutrition (mineral metabolism) at UEA since 2007, was principal investigator on all of the micronutrient clinical studies, led the EFSA reports and the EURRECA work on iron and selenium
- **Lee Hooper**, Senior Lecturer (systematic reviews) at UEA since 2005, led on the development of systematic review methodologies that would be applicable to nutrition research and was a core member of the WHO guidelines committee
- **Rachael Collings**, Research Associate at UEA 2008-2012, EURRECA led the literature reviews, data analysis and drafted manuscripts

3. References to the research

(UEA authors in bold) {citation count from Scopus on 21/11/13}

1. Establishing optimal selenium status: results of a randomized, double-blind, placebo-controlled trial
   Hurst R, Armah CN, Dainty JR, Hart DJ, Teucher B, Goldson AJ, Broadley MR,Motley AK, **Fairweather-Tait SJ**
   Am J Clin Nutrition **2010** 91:923-31 {39}
   doi: 10.3945/ajcn.2009.28169
2. Plasma hepcidin concentrations significantly predict interindividual variation in iron absorption in healthy men
   Roe MA, **Collings R**, Dainty JR, Swinkels DW, **Fairweather-Tait SJ**
   Am J Clin Nutrition **2009** 89:1088-91 {35}
   doi:10.3945/ajcn.2008.27297
3. The absorption of iron from whole diets: a systematic review
   Collings R, **Harvey LJ**, **Hooper L**, **Hurst R**, Brown TJ, Ansett J, King M, **Fairweather-Tait SJ**
   Am J Clin Nutrition **2013** 98:65-81 {0}
   doi: 10.3945/ajcn.112.0506094
4. Effect of iron intake on iron status: a systematic review and meta-analysis of randomized controlled trials
   Casgrain A, **Collings R**, **Harvey LJ**, **Hooper L**, **Fairweather-Tait SJ**
   Am J Clin Nutrition **2012** 96:768-80 {3}
   doi: 10.3945/ajcn.112.040626
5. EURRECA's approach for estimating micronutrient requirements
   Matthys C, van 't Veer P, de Groot L, **Hooper L**, Cavelaars AE, Collings R, Dhonukshe-Rutten R, **Harvey LJ**, Casgrain A, Rollin F, Contor L
   Int J Vitam Nutr Res **2011** 81:256-63 {14}
   doi: 10.1024/0300-9831/a000071
6. Assessing potential biomarkers of micronutrient status by using a systematic review methodology: methods
   Hooper L, Ashton K, **Harvey LJ**, Decsi T, **Fairweather-Tait SJ**
   Am J Clin Nutrition **2009** 89:1953S-1959S {32}
   doi: 10.3945/ajcn.2009.27230A
7. Effect of increased potassium intake on cardiovascular risk factors and disease: systematic review and meta-analyses
   Aburto NJ, Hanson S, Gutierrez H, **Hooper L**, Elliott P, Cappuccio FP
   BMJ **2013** 346:f1378 {3}
   doi: 10.1136/bmj.f1378

8. Effect of lower sodium intake on health: systematic review and meta-analyses
Aburto NJ, Ziolkovska A, **Hooper L**, Elliott P, Cappuccio FP, Meerpohl JJ
BMJ **2013** 346:f1326 {9}
doi: 10.1136/bmj.f1326

Funding for the research:
EU FP6: EURopean RECommendations Aligned (EURRECA) Network of Excellence 2007 - 2012; total value €12.2million, UEA budget €1.04million

EFSA: total value £102K

4. Details of the impact

Micronutrients play a central part in metabolism and in the maintenance of tissue function. Micronutrient deficiencies adversely affect the health of a large proportion of the world population and according to the WHO, over 1.3 million children die each year because of micronutrient deficiencies in three critical micronutrients that are most limiting in the diet (iron, zinc, and vitamin A). Inadequate micronutrient intake and status is also a problem in industrialised countries especially in relation to iron. In sharp contrast, an excess intake of particular micronutrients is associated with an increased risk of chronic disease, exemplified by the association between dietary sodium intake and cardiovascular disease.

WHO Guidelines: We provided core expertise in systematic review methodology and meta-analysis for the WHO Guidance Expert Advisory Group to assess the scientific data on the effects of potassium and sodium intakes on human health. On the basis of the research in (7), WHO developed its first guideline for potassium intake. This new guideline (corroborating source A) states that:

> *'adults and children without compromised renal handling of potassium should increase their potassium intake from food and that adults should consume >90 mmol potassium/d for beneficial effects on blood pressure and risk of related cardiovascular disease'.*

WHO recommends that this is adjusted downwards for children, based on their relative energy requirements.

Our WHO committee work and BMJ meta-analysis (research reference 8) has also informed the revision and update of the WHO guidelines for sodium (corroborating source B) which states:

> *'WHO recommends a reduction in sodium intake to reduce blood pressure and risk of cardiovascular disease, stroke and coronary heart disease in adults. WHO recommends a reduction to <2 g/day sodium (5 g/day salt)'.*

and established a new WHO guideline for children, which states:

> *'WHO recommends a reduction in sodium intake to control blood pressure in children. The recommended maximum level of intake of 2 g/day sodium in adults should be adjusted downward based on the energy requirements of children relative to those of adults'.*

European Food Standards Authority (EFSA) work: There is no uniform approach for establishing micronutrient recommendations, and the large variations across Europe create confusion among consumers, food producers and policy-makers. The EFSA is the EU authority that provides independent scientific advice on risk assessment associated with the food chain.

EFSA reports - our pathway to impact: As a result of the EURECCA work, UEA was awarded two tenders, where we were commissioned to collate all scientific data from which DRVs may be derived for six trace elements (magnesium, potassium, fluoride, chromium, manganese, and molybdenum).The submitted reports are:

> *Preparation of an evidence report identifying health outcomes upon which Dietary Reference Values could potentially be based for magnesium, potassium and fluoride*. (2012) Brown T, Mullee A, Collings R, Harvey L, Hooper L, Fairweather-Tait S.
> Final report CT/EFSA/NDA/03 Lot 3, University of East Anglia
> (http://www.efsa.europa.eu/fr/supporting/pub/283e.htm)
>
> *Preparation of an evidence report identifying health outcomes upon which Dietary Reference Values could potentially be based for chromium, manganese and molybdenum.* (2012) Mullee A, Brown T, Collings R, Harvey L, Hooper L, Fairweather-Tait S.

Final report CT/EFSA/NDA/03 Lot 2, University of East Anglia (http://www.efsa.europa.eu/fr/supporting/pub/284e.htm)

The reports included detailed systematic searches and reviews of studies relating to these micronutrients and used methodologies developed as part of the EURRECA project. These focussed on primary studies in humans, and reported on the dose-response relationship between intakes of the nutrients within the physiological (dietary) intake range and health outcomes, upon which DRVs may be based.

EFSA opinions - impact on the formulation of Dietary Reference Values for micronutrients: The reports are now the research base behind the EFSA DRV Minerals Working Group's strategy to issue opinions (the scientific committee's consensus documents) on Dietary Reference Values for the population of the European Union. Of the six micronutrients reviewed in our EFSA-funded work, detailed draft opinions have significantly advanced policy and have already been released by the EFSA committee on two micronutrients, molybdenum and fluoride (corroborating sources C and D). The other EFSA opinions will be released in the 2013-14 period.

Our expertise in this area is also having impact on the development of micronutrient nutrition policy/guidelines by individual nations. One example is the Nordic countries, who collectively set their nutritional recommendations and dietary guidelines. Professor Fairweather-Tait was appointed to the international Reference Group for the development of the NNR5 guidelines as a result of her micronutrient expertise and involvement with developing the methodologies for EURRECA (http://www.slv.se/en-gb/Startpage-NNR/Reference-group/).

Micronutrient deficiencies - impact on food security: The world is facing a potential crisis in terms of food security. The challenge is to produce and supply enough safe and nutritious food in a sustainable way for a growing global population, which is projected to reach 9 billion by 2050. Micronutrient deficiencies are a significant public health problem in developing countries and Fairweather-Tait's EURRECA work has informed the development of an international biofortification programme, HarvestPlus, partly funded by the Bill and Melinda Gates foundation. HarvestPlus is helping to develop breeding of staple foods that are a better source of micronutrients, and works with key international stakeholders in micronutrient research, including Fairweather-Tait. In order to define targets for the level of zinc needed in biofortified rice or wheat to have an impact on health, HarvestPlus was informed by the findings from a workshop organised by EURRECA on intake-status-health relationships, and the systematic review of biomarkers of zinc status. HarvestPlus is now developing two key staples for the Indian sub-continent, rice and wheat, biofortified with optimal levels of zinc (final report, corroborating source E).

5. Sources to corroborate the impact

WHO Guidelines:

A. *Potassium intake for adults and children*. Geneva, World Health Organisation, 2012
Research reference 7 in section 3 above underpins this source.

B. *Sodium intake for adults and children*. Geneva, World Health Organisation, 2012
Research reference 8 in section 3 above underpins this source.

EFSA OPINIONS (the scientific committee's consensus documents):

C. *EFSA Scientific Opinion on Dietary Reference Values for molybdenum* - Released for public consultation in May 2013
Reference to UEA tender Ref D (Mullee *et al.* 2012) on p.18.

D. *EFSA Scientific Opinion on Dietary Reference Values for fluoride* - Released for public consultation in May 2013

HarvestPlus:

E. *Human Zinc Requirements*. Report of the HarvestPlus Consultation on Physiological and Dietary Zinc Requirements. July 24th 2012. Maryland, USA
References to UEA/EURRECA inputs to the consultation on pp.4-5.