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## Editorial

### Conference on ‘Micronutrient malnutrition across the life course, sarcopenia and frailty’

## Micronutrient malnutrition across the life course, sarcopenia and frailty

Micronutrient malnutrition, the deficiency of vitamins or minerals, impacts on physical and mental health, in clinical and general populations, across the life course. In older western populations the high prevalence and impact of micronutrient malnutrition is less well recognised. Low- and middle-income countries are experiencing the ‘double burden of disease’ where malnutrition coexists alongside the non-communicable diseases of aging, obesity, type 2 diabetes and cardiovascular disease. Held in December 2020, the Winter Conference of the Nutrition Society was designed to cover new areas of research and concern in micronutrient malnutrition across the life course. Common themes arising from the conference were: 1) The continuing high prevalence of micronutrient malnutrition across the life-course, in diverse populations, in high, middle and low-income countries. 2) That multiple deficiencies of micronutrients frequently exist. 3) The primary cause of deficiency is poor quality diets, of low diversity, low in micronutrient dense foods. 4) Clinical conditions, medications for common non-communicable diseases, and environmental conditions, interact with and exacerbate the effects of poor diet quality. 5) Understanding of the mechanistic effects of micronutrients is still emerging. 6) Micronutrients are necessary for maintaining immune function, which has importance for the COVID-19 epidemic. 7) Better biomarkers are needed to detect and understand the effects of deficiency. 7) Dietary recommendations need to be updated regularly. Further research is needed in all these areas. Comprehensive public health and government approaches to ensure access and affordability of good quality foods to populations of all ages, particularly during the ongoing COVID-19 epidemic, are crucial.

**micronutrient malnutrition: vitamin and mineral deficiency: sarcopenia: frailty: COVID-19**

### Micronutrient malnutrition

Micronutrient malnutrition, the deficiency of vitamins or minerals, is an important issue impacting on physical and mental health, in clinical and general populations across the life course. Also known as Hidden Hunger, the high prevalence and importance of micronutrient malnutrition is less well recognised in older, western populations whereas low and middle income countries are experiencing the ‘double burden of disease’ where malnutrition, as protein energy malnutrition and micronutrient malnutrition, coexist alongside the non-communicable diseases of aging, obesity, type 2 diabetes and cardiovascular disease<sup>(1,2)</sup>. A number of clinical conditions including bariatric surgery, alcoholism, and a range of gastrointestinal diseases, including malabsorption, also lead to micronutrient malnutrition<sup>(3)</sup>.

Micronutrient malnutrition often accompanies low intakes of both protein and energy and leads to serious

developmental issues in children, affecting cognition, physical function, and growth. At the other end of the life-course, in older adults, recent research shows micronutrient malnutrition leads to decline in physical function, loss of muscle mass and function, cognition, and poor quality of life, so contributing to the diseases of aging, including sarcopenia and frailty<sup>(4–6)</sup>. The effects of micronutrient malnutrition are frequently irreversible, so preventing, identifying and rectifying deficiency of micronutrients is highly important<sup>(7)</sup>.

Vitamins and minerals are crucial for maintaining our metabolism and physiology, and immune function. Deficiencies or sub-optimal nutritional status of micronutrients leads to recognisable clinical symptoms both in children and adults. Many deficiencies such as those of the B vitamins, vitamin C, iron and magnesium lead to fatigue, as well as to poor physical function, particularly in the oldest people in populations<sup>(5, 6)</sup>.

Although good quality diets are important for growth in children and health in adults, of all ages, many societal



and economic issues mean this is not achieved. That micronutrient deficiencies affect about one third of the world's population, persisting despite economic growth such as in South Asia, and are prevalent in high income countries, is a huge concern<sup>(1,8–11)</sup>. Around 45% of deaths among children under 5 years of age are linked to undernutrition, mostly occurring in low- and middle-income countries. A conference to consider the issues of micronutrient malnutrition and how these could be addressed was therefore timely.

### Topics presented during the conference

The conference 'Micronutrient malnutrition across the life course, sarcopenia and frailty', held in December 2020, was designed to cover new and emerging areas of research and concern in relation to micronutrient malnutrition across the life course. Four symposia were arranged on the subjects of; issues of 'population and clinical vitamin and mineral nutrition'; 'micronutrient nutrition in development, health and disease'; 'aging, frailty, sarcopenia, osteoporosis and micronutrients', with the final section designed to address population approaches and solutions for micronutrient malnutrition.

The conference was held remotely and was attended by 295 delegates from 17 countries across Europe, Africa, Asia, Russia and the United States, with overseas speakers providing talks from Europe, the US, Canada and Zambia.

Day one of the conference focused on population and clinical vitamin and mineral malnutrition, as well as micronutrient in childhood development, health and disease<sup>(11)</sup>. Professor Nicola Lowe gave an overview of the global challenges of 'Hidden Hunger', the presence of multiple micronutrient deficiencies, particularly of iron, zinc, iodine and vitamin A. She provided definitions of the 'UN sustainable development goals' that aim to 'end hunger, achieve food security and improve nutrition and sustainable agriculture' but noted how much more needs to be done towards achieving these goals. Whilst supplementation, fortification and biofortification can all deliver benefits, they are not without their limitations so finding a way to sustainably improve the quality of diets in the poorest regions is crucial to meeting the UN Sustainable Development Goals.

Continuing with the topic of Hidden Hunger Professor Mairead Kiely talked about the profound effects of deficiencies of vitamin D, iron and iodine during pregnancy, highlighting the importance of maternal micronutrient status on neonatal outcomes, and subsequent lifelong health and wellbeing<sup>(12)</sup>. Deficiencies of these micronutrients exist within high as well as low income countries. Interactions between maternal micronutrient status and obesity are also important. Prof Kiely noted the challenges include how to rectify deficiencies, and development of standardised screening methods with sufficient sensitivity and specificity. Also, implementation of treatments and public health prevention strategies are required to improve overall nutritional status of women of reproductive age, and their children.

Professor Paul Kelly, gave his Keynote Lecture from Lusaka, and continued to address the issue of Hidden Hunger, suggesting that one cause may be the condition of environmental enteropathy that leads to malabsorption of nutrients<sup>(10)</sup>. Environmental enteropathy, previously known as tropical enteropathy, also referred to as environmental enteric dysfunction, is an asymptomatic disorder of small intestinal structure and function. This is very highly prevalent in many disadvantaged populations. This is likely caused by the very high pathogenic burden in children and adults living in insanitary environments. New research using transcriptomic techniques suggests that damage to the epithelial cells of the gut mucosa has effects on nutrient transporters and enzymes responsible for nutrient absorption, so leading to impaired digestion and absorption nutrients including zinc<sup>(10)</sup>.

### *Clinical conditions*

In terms of clinical risk of micronutrient malnutrition, Associate Professor Christophe Matthys focused on the risks of developing vitamin and mineral deficiencies after bariatric surgery, as a result of the anatomical changes that influence nutrient digestion and absorption. Affected micronutrients include malabsorption of the fat-soluble vitamins A, D, E, and K, which in turn affect other nutrients, such as calcium<sup>(13)</sup>. Post-surgical conditions frequently identified are bone loss, osteoporosis, and anaemia. However, current success in rectifying these conditions is limited.

### *Micronutrients, immune health and susceptibility to COVID-19*

Micronutrients are also involved in maintaining immune resilience conferring protection against viral diseases<sup>(14)</sup>. With the advent of the COVID-19 epidemic the importance of micronutrients and a micronutrient rich diet in maintaining optimal immune function, particularly during aging, has come to the fore. Professor Philp Calder spoke on the relevance of micronutrient malnutrition to the ongoing coronavirus epidemic of COVID-19. He discussed the substantial evidence for the roles of vitamin D, zinc and selenium, noting that other micronutrients are also important, although research to date is limited<sup>(14)</sup>.

### *New research on micronutrients and mechanisms of action*

Two presentations focused on recent research on magnesium and vitamin E, that has identified their mechanisms of action in supporting human health. Although it has been long been known that vitamin E is essential for successful outcome of pregnancy, the molecular mechanisms involved have only recently identified by Professor Maret Traber. Using experiments with zebrafish studies she identified how vitamin E is involved in neurogenesis and cognition in neonates<sup>(15)</sup>. Her findings were that sufficient vitamin E prevents lipid peroxidation, secondary deficiencies of choline, betaine and thiols, such as glutathione, as well as energy dysregulation; changes



which would otherwise lead to malformations and mortality<sup>(15)</sup>.

Magnesium is an essential ion required for activity of more than 300 enzymes. Dr Jeroen De Baaij discussed the relationships between recently discovered hereditary mutations in magnesium channels that lead to hypomagnesaemia, as well as to that resulting from certain commonly prescribed medications in older age<sup>(16)</sup>. These medications include loop or thiazide diuretics, prescribed for treatment of hypertension, or proton pump inhibitors, used to treat gastroesophageal reflux disease. Dr De Baaij concluded that both mutations and medications impact on magnesium status by reducing gastrointestinal absorption or resorption by the kidney and share common molecular mechanisms.

#### *Micronutrients, non-communicable diseases and conditions of aging*

Three presentations focused on micronutrients, their deficiencies, and their relevance to aging, and the conditions of frailty, sarcopenia and osteoporosis. The importance of micronutrients in relation to the onset of sarcopenia, the loss of strength, function or low skeletal muscle mass was discussed by Prof Sian Robinson<sup>(5)</sup>. She noted that while there is some consistency across studies for the roles of antioxidant nutrients, B vitamins and magnesium, as yet, the data are inconsistent. However, given that low intakes of micronutrients are common in older populations research, is needed to understand their role in muscle health. Professor Lisette de Groot, reviewed the evidence for the role of nutritional concerns in aging-related disorders, with a focus on deficiencies of vitamins D and B<sub>12</sub>, and low intakes of protein; highlighting that healthy dietary patterns are also important in older age<sup>(6)</sup>.

The recently recognised syndrome or condition of osteosarcopenic adiposity was discussed by Professor Jasminka Ilich<sup>(17)</sup>. Osteosarcopenic obesity refers to the concurrent conditions of osteoporosis or osteopenia, accompanied by sarcopenia, as well as obesity. Low grade chronic inflammation is associated with osteosarcopenic obesity, and micronutrient status, with several vitamins and minerals interacting with chronic inflammation. The micronutrients with established roles in bone physiology, maintenance of both health, and prevention of osteoporosis include; calcium, vitamin D, magnesium, vitamin K and potassium. Prof Ilich concluded that although current research is limited, calcium, magnesium, phosphorus, sodium, and vitamins D and K, likely have roles in the condition of osteosarcopenic obesity.

#### *Population approaches to addressing micronutrient malnutrition*

The final symposium of the conference covered measures used to address issues relating to micronutrient deficiency, and this included the approaches to development and setting of dietary reference values that provide guidance on the daily intake of micro and macro nutrients required to meet the needs of the majority of the

population. Professor Hilary Powers, summarised how dietary recommendations are developed and implemented<sup>(18)</sup> and Professor Ann Prentice highlighted that policy decisions and the practice of public health nutrition need to be based on “solid evidence developed through rigorous research studies where objective measures are used to determine their relevance”<sup>(19, 20)</sup>. Prof Prentice also noted the relevance of sexual dimorphism on recommendations for micronutrients as they are influenced by body size or macronutrient intake. She also noted that while many of the original recommendations were based on limited evidence, more recent clinical data are now available for sex, ethnicity and lifestyle factors which will allow guidelines for more specific population groups to be developed in future.

#### **Common themes, concepts and areas for future research arising from the conference**

Common themes arose from the conference which included issues associated with micronutrient malnutrition in diverse situations; from low to high income countries, in clinical as well as general populations, and in children as well as older aged people.

Despite the long recognition of malnutrition in all its forms, large sectors of populations in low, mid and high income countries experience micronutrient deficiency and its physiological and metabolic effects<sup>(1,2,8,9,21)</sup>. Although comprehensive dietary recommendations and guidelines exist, across the globe as large sectors of our populations do not reach them<sup>(21)</sup>. In many low- and middle-income countries the situation has been exacerbated by the COVID-19 epidemic. Even in the UK, vulnerable sectors of the population include adults over 65 years, those in low income groups and in Care Homes. The UK National Diet and Nutrition survey has identified that<sup>(22)</sup> only 20% of people over 75 years consume 5 portions of fruits and vegetables or more, and in care homes 40% have blood concentrations of vitamin C indicative of scurvy, as do 4% of free-living adults. The prevalence of vitamin D deficiency is also high, being 40% in care homes and 15% in free-living older adults<sup>(22)</sup>.

It is clear that micronutrient malnutrition is a primary cause of poor health across the life course as well as contributing to the onset of conditions of aging, and the primary cause is diets of poor quality with low dietary diversity. However, micronutrient malnutrition also results from diseases that impact on their absorption or utilisation, such as those of the gastrointestinal tract. Interactions with medical treatments such medications administered for non-communicable diseases or bariatric surgery are also important<sup>(13,16)</sup>. Micronutrient deficiency also compromises immune function, increasing susceptibility to COVID-19 infection and mortality.

The majority of micronutrient deficiencies do not exist alone with individuals frequently subject to one or more deficiencies; even in the UK 48% of those over 50 years of age have at least one micronutrient deficiency<sup>(21)</sup>. Given the physiological interactions between these nutrients greater understanding of the multiple micronutrient

deficiencies is needed, as are the interactions between obesity, medications and the environment<sup>(10)</sup>. Although much of our understanding of the physiological mechanisms of micronutrients for maintaining health was elicited some time ago, the newer research for vitamin E and magnesium presented, indicates there remains more to learn<sup>(15,16)</sup>.

The conference also highlighted that dietary guidelines need to be updated regularly due to new evidence of the importance and mechanisms of action of micronutrients, and their deficiencies, on health. It was agreed that better biomarkers are needed to detect and understand the effects of deficiency, and high-quality studies using robust scientific methods are needed to support development of dietary guidelines.

The direct and indirect costs of micronutrient malnutrition on health and social care in older populations, as well as on childhood growth and cognition, are huge and it is important to rectify this situation. The solutions to micronutrient deficiency include provision and access to diets of high diversity and high-quality, that include consumption of micronutrient dense foods, to all sectors of populations. However, micronutrient malnutrition exists for many socioeconomic reasons. To quote Professor Lowe, “addressing inequalities within the food system must be central to developing a sustainable, cost effective strategy for improving food quality that delivers benefit to the hardest to reach and marginalised communities”. Comprehensive public health and government approaches are needed to ensure access and affordability of good quality foods to populations of all ages. This is even more important during the ongoing the COVID-19 epidemic.

Ailsa Welch

Department of Epidemiology and Public Health,  
Norwich Medical School, University of East Anglia,  
Norwich, NR4 7TJ, UK

Corresponding author: Professor Ailsa A Welch,  
email: [a.welch@uea.ac.uk](mailto:a.welch@uea.ac.uk)

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