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## Conference on ‘Multidisciplinary approaches to nutritional problems’

### Rank Prize Lecture Global nutrition challenges for optimal health and well-being

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Optimal health and well-being are now considered the true measures of human development. Integrated strategies for infant, child and adult nutrition are required that take a life-course perspective to achieve life-long health. The major nutrition challenges faced today include: (a) addressing the pending burden of undernutrition (low birth weight, severe wasting, stunting and Zn, retinol, Fe, iodine and folic acid deficits) affecting those individuals living in conditions of poverty and deprivation; (b) preventing nutrition-related chronic diseases (obesity, diabetes, CVD, some forms of cancer and osteoporosis) that, except in sub-Saharan Africa, are the main causes of death and disability globally. This challenge requires a life-course perspective as effective prevention starts before conception and continues at each stage of life. While death is unavoidable, premature death and disability can be postponed by providing the right amount and quality of food and by maintaining an active life; (c) delaying or avoiding, via appropriate nutrition and physical activity interventions, the functional declines associated with advancing age. To help tackle these challenges, it is proposed that the term ‘malnutrition in all its forms’, which encompasses the full spectrum of nutritional disorders, should be used to engender a broader understanding of global nutrition problems. This term may prove particularly helpful when interacting with policy makers and the public. Finally, a greater effort by the UN agencies and private and public development partners is called for to strengthen local, regional and international capacity to support the much needed change in policy and programme activities focusing on all forms of malnutrition with a unified agenda.

#### **Optimal health and well-being: Global nutrition challenges: Life-course perspective: Integrated strategies for malnutrition**

The health status of developing countries has long been characterised by a predominance of endemic and epidemic infectious diseases. In this context, undernutrition and micronutrient deficiencies, which mostly affect children and women of fertile age, are important as they aggravate the severity and duration of infectious diseases<sup>(1)</sup>. Undernutrition may also increase the incidence of some infections and may potentiate the virulence of some infectious agents<sup>(2,3)</sup>. The enormous scale of the estimated global burden of death and disability currently associated with undernutrition among children <5 years of age is shown in Table 1. In contrast, industrialised countries are usually

characterised by their relative preponderance of disability and death caused by non-communicable chronic diseases. These latter diseases often result from changes in diet and physical activity patterns induced by economic affluence and from degenerative conditions linked to advanced age<sup>(4)</sup>. In these classic characterisations under- and over-nutrition are presented as opposites ends of a spectrum and contrasted against each other in terms of number of deaths or disability-adjusted life years lost and their contingent economic costs. This approach is overly simplistic, which leads to competing research and policy agendas and confusion; it detracts from the need to concentrate on

**Abbreviation:** NRCDC, nutrition-related chronic diseases.

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**Table 1.** Global deaths and disability-adjusted life years (DALY) in children <5 years of age in 2004, showing deaths and disability attributed to micronutrient deficiencies and those attributed to nutritional (anthropometric) status (modified from Black *et al.*<sup>(1)</sup>)

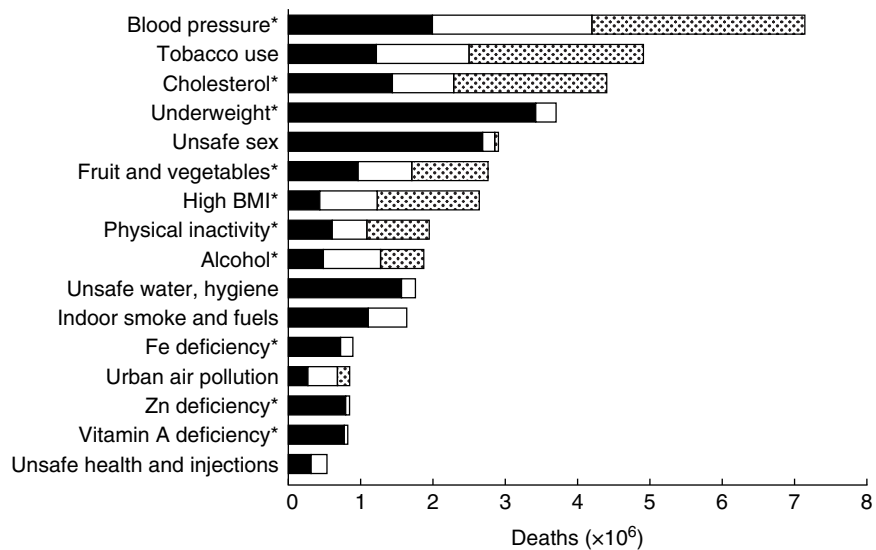
Condition	Deaths (n)	Percentage of <5 years deaths	Disease burden ( $\times 10^3$ DALY)	Percentage of <5 years DALY
Vitamin A deficiency	667 771	6.5	22 668	5.3
Zn deficiency	453 207	4.4	16 342	3.8
Fe deficiency	20 854	0.2	2 156	0.5
Iodine deficiency	3 619	0.03	2 614	0.6
<b>Measure</b>				
Underweight*	1 957 530	19.0	81 358	18.7
Stunting	1 491 188	14.5	54 912	12.6
Wasting*	1 505 236	14.6	64 566	14.8
Severe wasting*†	449 160	4.4	25 929	6.0
IUGR–low birth weight	337 047	3.3	13 536	3.1
Total of stunting, severe wasting and IUGR–low birth weight*‡	2 184 973	21.4	90 962	21.2

IUGR, intrauterine growth restriction.

\*Includes deaths (138 739) and DALY (14 486 400) directly attributed to 'protein–energy malnutrition'.

†Included in wasting.

‡Total takes into account the joint distribution of stunting and severe wasting.



**Fig. 1.** Global deaths attributable to sixteen leading risk factors. (■) High mortality, developing countries; (□), low mortality, developing countries; (▨), developed countries; \*nutrition-related risks. (Modified from Uauy & Solomons<sup>(4)</sup>.)

solving the existing problems in which undernutrition and nutrition-related chronic diseases (NRC) are intertwined<sup>(5,6)</sup>.

Epidemiological and nutrition transitions have now been documented in most countries in the world making NRC the main cause of death and disability globally. These transitions have resulted in increased life expectancy as a result of a combination of falling neonatal deaths, increased infant and child survival and extended longevity of adults. The appearance of these transitions underscores the need to see the effects of nutrition on health and well-being as a continuum across the lifespan with multiple interlocking consequences<sup>(7–9)</sup>. As more of the population

reach older ages greater emphasis needs to be placed on NRC, many of which, to an important extent, originate in early life. The prevention of diabetes, heart disease and cancer was not considered as relevant in developing countries until recently<sup>(10–12)</sup> as these diseases were considered to be diseases of affluence. However, both on an absolute and age-adjusted basis these diseases are becoming progressively more important in developing countries<sup>(10,13)</sup>. The most common risk factors responsible for global deaths according to the extent of socio-economic development are summarised in Fig. 1. It is clear that most nutrition-related risk factors for chronic disease are common in both developing and developed countries, perhaps

with the only exception of underweight and specific nutrient deficiencies. High prevalence of chronic conditions in later life not only increases the burden of disease but will also affect the allocation of financial resources, and thus potentially undermine a country's capacity to address nutritional problems in early life.

In the face of this global scenario it is time to re-examine the many faces of malnutrition and address them with a common agenda that recognises the full spectrum of nutrition-related death and disability. Before addressing what are considered to be the key global challenges for nutrition scientists a case will be made for the expansion of the basic definition of malnutrition to one that encapsulates malnutrition in all its forms.

### Malnutrition in all its forms

In the new global nutrition environment it is clear that the basic definition of malnutrition is not sufficient, and that there is a need for a new definition that encompasses underweight and overweight, wasting and stunting, micronutrient deficiencies and NRC. Underweight is defined by a low weight-for-age, yet a child may be underweight because she or he is wasted (low weight-for-height) or stunted (low height-for-age) or both. Conversely, a child may be stunted but overweight for his or her length. Within the underweight category, wasted and stunted children must be considered separately since they need to be approached differently in their treatment and follow up. The fact that among the undernourished as defined by stunted linear growth there exist many who are of normal weight for their length and some who are overweight for their length<sup>(14)</sup> can no longer be ignored. Importantly, since length is not systematically assessed in defining nutritional status of populations<sup>(15)</sup> it is possible that the prevalence of undernutrition may currently be overestimated and the problem of excess body fat stores neglected. It follows that if the aim is to tackle malnutrition in all its forms, length must be systematically measured and assessed in all children.

Acute wasting is an important form of malnutrition and requires particular attention, especially within the context of emergencies caused by famine (acute and chronic) and conflict. Acute wasting is associated with child survival since it has a direct impact on resistance to infection. Effective treatment and control of acute wasting are essential if hunger and mortality in children is to be reduced in accordance with the internationally-agreed Millennium Development Goals<sup>(16)</sup>.

Micronutrient deficiencies also form part of the broader definition of malnutrition. Poor quality of diets can lead to inadequate intakes or deficiencies in one or more micronutrients and, where possible, an attempt should be made to determine the common underlying dietary causal factors. For example, epidemiological risk analysis indicates that Fe and Zn deficiencies frequently occur together; similarly, vitamin A deficit is observed in infants and mothers subsisting on single staple foods (cereals or tubers). Integrating findings in this manner, and examining the need for changes in dietary patterns rather than

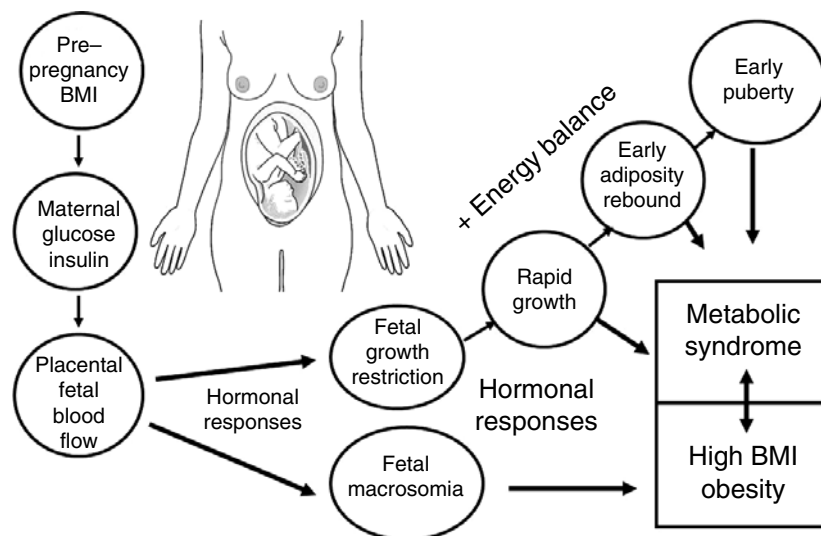
targeting individual nutrients, may provide more sustainable long-term solutions<sup>(9,17)</sup>.

Finally, at the other end of the spectrum, any new definition of malnutrition must now also include NRC. These chronic diseases commonly presenting in adults are related to long-term patterns of diet and physical activity. Prevention for these conditions therefore starts with the achievement of optimal fetal and infant growth and continues throughout the life course with the promotion of healthy diets and active living<sup>(8)</sup>. It must be remembered that the pre-clinical conditions associated with ageing such as loss of muscle and skeletal mass and loss of cognitive functions are not obligatory states, and their impact may be substantially attenuated by dietary, physical activity and social interventions. The ultimate goal is what has been termed the 'compression of morbidity'<sup>(18)</sup>, meaning that ideally individuals should live the majority of their lives free of the disabilities of acute and chronic illnesses and impaired function, and extend their longevity towards the upper limits of the human lifespan.

Reductionist approaches to nutrition have to date provided good service and important knowledge has been gained on the effects of specific nutrients at the molecular, cellular, organ and whole-body level. However, this approach will not necessarily bring early provision of coherent guidance to policy makers to achieve better population health and well-being. If the gap between present knowledge and population nutritional status and health is to be bridged it will be necessary to use integrated approaches to address malnutrition in all its forms with a life-course perspective<sup>(19)</sup>. Such approaches are also more likely to attract the interest of the public and policy makers, and thus effective action nationally and globally will be brought closer. Agreeing on a definition of malnutrition in all its forms will encourage more widespread usage and hopefully contribute to developing a common agenda for action.

### Global nutrition challenge 1: addressing the pending burden of undernutrition and micronutrient deficits

Undernutrition, as assessed by abnormal anthropometric measures, and micronutrient deficiencies are frequently interrelated. For example, the disease outcome diarrhoea is associated with vitamin A and Zn deficiencies as well as stunting. In contrast, certain micronutrient deficiencies such as iodine and Fe may occur in children with normal somatic growth, which is further complicated by the fact that the consequences of certain micronutrient deficiencies may in fact be dependent on their effects on growth. For example, approximately half the effect of Zn deficiency is mediated by stunting; the rest is a direct effect on morbidity and mortality, probably as a result of impaired immune function<sup>(1)</sup>. Analyses of the population attributable risk of malnutrition should therefore consider the effects of not only single but also combined micronutrient deficits together with other measures of malnutrition such as somatic growth.



**Fig. 2.** Life-course approach to prevention of chronic disease in adult life. (○), The critical steps to achieve healthy growth and long-term health; (□), the end points that define increased risk. High BMI and metabolic syndrome interact in defining risk for chronic disease in adult life.

While the risks related to suboptimal breast-feeding (optimal breast-feeding based on WHO recommendations<sup>(20)</sup> is exclusive breast-feeding from birth to 6 months of life and continued breast-feeding complemented with appropriate micronutrient dense foods after 6 months) may in part be associated with micronutrient deficiencies resulting from inadequate dietary intake by the infant, they are more importantly a result of the role of breast milk in preventing infections. The disease burden attributed to suboptimal breast-feeding cannot be added to that of undernutrition without considering their joint effects; however, it is nonetheless appropriate to consider breast-feeding practices as one of the most important modifiable risk factors for infectious disease in infants. Effective interventions are also available to reduce stunting, micronutrient deficiencies and child deaths. If implemented at scale, they would reduce disability-adjusted life years and child deaths by about one-quarter in the short term<sup>(16,21,22)</sup>.

Systematic reviews of available evidence on the effectiveness of interventions published in the *Lancet* series on maternal and child undernutrition indicate that breast-feeding counselling and vitamin A and Zn fortification or supplementation have the greatest potential to reduce the burden of child morbidity and mortality<sup>(21)</sup>. The reviews also suggest that enhancing complementary feeding via nutrition counselling for food-secure populations and nutrition counselling, food supplements and/or conditional cash transfers in food-insecure populations could also substantially reduce stunting in the short term. Elimination of stunting, however, will require long-term investments to improve education, economic status and empowerment of women. The evidence base in the systematic reviews for maternal health is weaker, but there is some evidence that nutrition interventions such as Fe and folate supplements and targeted balanced energy and protein supplementation may make a difference to maternal health and birth outcomes. Collectively, the anthropometric and micronutrient

deficiencies examined in the recent *Lancet* series on maternal and child undernutrition accounted for approximately 30% of total deaths and disease burden in children <5 years of age, which equates to approximately 9% of the total global disease burden in all ages<sup>(1)</sup>. This enormous pending burden highlights the need for immediate and concerted efforts to implement known effective actions.

### Global nutrition challenge 2: prevention of diet-related chronic disease with a life-course perspective

The excessive segmentation and specialisation of human nutrition into energy, macronutrients and micronutrients and of clinical sciences into newborn medicine, paediatrics, adolescent health, adult health and geriatrics has been a barrier to integrating the various stages of development in human health<sup>(23)</sup>. A common denominator for an integrated view is a systematic 'life-course' approach<sup>(8)</sup>. A complex but compelling and highly-relevant relationship (schematically presented in Fig. 2) has been revealed between the processes of undernutrition and poor growth in fetal life or early infancy and metabolic and malignant disease consequences in adult life<sup>(19,24)</sup>.

The epidemiology of the early origins of adult disease<sup>(25)</sup> and the concept of early-life programming based on a persistence of a nutrient-conserving metabolic pattern throughout the lifespan, emphasise health over disease in the relationship of nutrition, early growth, metabolic imprinting and vulnerability to chronic disease<sup>(26)</sup>. The postulate of the 'developmental origins of health and disease' hypothesis is that the early environment programmes metabolism, organ growth and functional development in an irreversible manner even after the original deprivation has been resolved. Programming may be explained by

structural changes in organs induced during early development, or by epigenetic modifications that permanently modify the patterns of gene expression, which in turn affect organ function at later stages in the life course. These changes are associated with permanent changes in physiology and/or structure that will predispose individuals to obesity and other NRCd in later life.

The relationship between low birth weight and later occurrence of central obesity, insulin resistance, type 2 diabetes, hypertension and CVD has been documented in a number of epidemiological studies conducted mostly in industrialised countries<sup>(27–29)</sup>, and in follow-up studies of historic cohorts from transitional countries<sup>(30)</sup>. In most developing regions low birth weight, and underweight and stunting in young children, coexists with overweight and obesity in older children, adolescents and the adult population<sup>(31,32)</sup>. Thus, the ‘developmental origins of health and disease’ hypothesis may be most relevant to present and future public health in these countries.

Analyses of the five existing cohort studies from developing countries (India, Guatemala, South Africa, Brazil and the Philippines) have recently been reported<sup>(30)</sup>. These cohorts were established in 1975–90 and with some interruptions subjects have been followed to the present. In India, Guatemala and Brazil birth weight was found to be positively associated with BMI at age 25–30 years, yet with a stronger association for lean mass than for fat mass. The links between birth weight and later occurrence of NRCd have proven more difficult to elucidate and the results are not fully consistent across studies. However, the studies differ widely in the extent of early malnutrition, the presence and extent of recovery of growth and of accelerated growth at various life stages and in the final nutritional status in terms of residual stunting, underweight and/or overweight. These factors are likely to be responsible for the observed differences in outcomes across studies. In the case of subjects from south and south-east India the susceptibility to insulin resistance and cardiovascular risks is even higher than in the population from other developing countries. This finding is explained by their particular malnutrition phenotype, in which low-birth-weight babies have increased visceral adiposity and insulin resistance even before overweight and obesity can be established based on current Western criteria<sup>(33,34)</sup>.

The other maladaptive nutritional situation of fetal life with an adverse prognosis for long-term health is macrosomia (birth weight of >4000 g). This excessive intrauterine growth is a result of excess fuel availability leading to higher insulin levels, generally as the result of gestational hyperglycaemia in the mothers<sup>(35)</sup>. Cohort studies of infants who are macrosomic have shown that high birth weight and overweight in infancy is also a risk factor for diabetes in later life<sup>(36,37)</sup>.

The importance of the existence and timing of a period of rapid childhood growth in potentiating the relationship between fetal undernutrition and later chronic disease is a matter of current debate<sup>(38,39)</sup>, partly because of the recent changes in the environment in terms of progressive increased prevalence of risk factors for obesity as opposed to the subtle effects observed in the older historic cohorts. A systematic review has identified sixteen studies that have

presented data on the role of rapid childhood growth as a possible determinant of obesity in adulthood, thirteen of which have reported significant associations, although the lack of standardisation between studies is also noted, making interpretation difficult<sup>(40)</sup>. The extent to which rapid infant growth represents a risk may depend on whether it occurs in the context of recovery from fetal growth restriction and results in normalisation of body weight and length, or whether excess growth is predominantly ponderal with constrained linear gain, thus leading to excess weight for length<sup>(29,41)</sup>.

The age of the adiposity rebound (age at which the BMI increases after its childhood nadir) is another period in which childhood growth seems to be critical for later life<sup>(42)</sup>. On average this BMI increase normally happens between 5 and 7 years of age, an earlier adiposity rebound is associated with increased fatness later in life<sup>(43)</sup>. This relationship is illustrated by the fact that adults whose adiposity rebound occurred by 4–8 years of age have a six times higher risk of being obese (BMI > 27 kg/m<sup>2</sup>) than those who had their adiposity rebound after 6.2 years of age<sup>(44)</sup>. Similar adverse consequences of early adiposity rebound have been reported for risks of glucose intolerance, diabetes and hypertension<sup>(45–47)</sup>. However, there is some uncertainty as to whether the negative effect of an early adiposity rebound is independent of early-life BMI or BMI percentile crossing<sup>(48,49)</sup>.

Recently, it has been proposed that, at least in women, puberty may correspond to a critical period for the development of certain cancers<sup>(50)</sup>. In a cohort of women born in Finland during the early 1930s women whose mothers had larger pelvic diameters (iliac crests) had a higher risk of breast and ovarian cancer, especially if those mothers also had an early menarche. The authors have proposed that the larger diameters of the pelvic bones may result from a higher exposure to oestrogens during puberty, an effect that may persist throughout life and might impact on cell differentiation of breast and ovarian tissue of female fetuses while *in utero*. They conclude that the maternal sex-hormone profile that initiates ovarian and breast cancer may be the product of poor nutrition and growth in early childhood followed by catch-up pre-pubertal growth.

Overall, there is good evidence that growth trajectory is relevant in the aetiology of later chronic disease<sup>(51)</sup>. Whether the sequence is underweight-to-overweight or overweight-to-overweight, the consequence of malnutrition in early life is an increased risk of the burden of chronic disease during adolescence and adulthood. This outcome creates a second burden in societies simultaneously disposed to high rates of poor fetal growth, and supports the need to have appropriate definitions of malnutrition and carefully-designed research on the life-course consequences of early growth patterns. This research can serve as a framework to uncover the most effective measures to promote individual and public health in order to reduce future morbidity and disability. Such an approach will not only lead to better health and wellbeing, but ultimately may halt the progression of the escalating economic costs of malnutrition to beyond a level that society can afford to provide in an equitable manner.

### Global nutrition challenge 3: nutrition for optimal health and well-being across the lifespan (healthy ageing)

Increased longevity in human subjects must surely rank as one of the great biosocial and biomedical triumphs of the modern era. Declining fertility together with increased longevity has meant that all countries are experiencing growth in the absolute number, and in many countries also in the proportion, of older individuals in the population. UN estimates project that by the year 2050 individuals aged  $\geq 60$  years will represent 22% of the world's population, or about two billion individuals (a rise from 10% or 600 million individuals in 2000)<sup>(52)</sup>. Of particular importance is the growth in the population of the proportion of the oldest old. The world's population of individuals aged  $\geq 80$  years is projected to more than triple in the period 2000–50, from 1.2% (73 million individuals) to 4.3% (400 million individuals)<sup>(52)</sup>. However, while increased longevity is a triumph, it is also likely to be one of the great global challenges for human health<sup>(53)</sup>.

With the growing size of the cohort of older individuals, identifying interventions that promote good health in later life becomes increasingly desirable, especially in countries with limited resources to devote to the care of older individuals in poor health. The Madrid International Plan of Action on Ageing provides a framework for the multi-sectoral efforts that are needed to encourage active and healthy ageing<sup>(54)</sup>. This Plan of Action on Ageing emphasises the importance of adequate nutrition throughout the life course and of national food policies that recognise older individuals as potentially vulnerable. Global perturbations in food costs, especially of staple crops such as rice and wheat, are also likely to have a dramatic effects on food security<sup>(55)</sup>.

Compared with research commitments and policy initiatives in younger age-groups, national-level actions designed to have an impact on the nutrition and health of older individuals have been limited until relatively recently. This situation may be the result of a variety of factors, such as negative images of ageing, concepts that health promotion and disease prevention in old age are not worthwhile and the research community's relative neglect of many of the common problems of old age. The reality of demographic change should force a reconsideration of many of these factors and it is becoming clear that a multidisciplinary national level approach is required that fully integrates population ageing and the needs of older individuals into all areas of public policy, including health, housing, economic development and transport.

The government of Chile provides a good example of a national-level nutrition intervention aimed at promoting healthy ageing and preserving health and function in later life. The Programme of Complementary Feeding for the Older Population is a package of actions which, since 1998, has been providing micronutrient-fortified foods to individuals aged  $\geq 70$  years registered at Primary Health Centres. The recommended serving size (50 g/d) of these fortified foods provides 50% of the daily micronutrient requirements and 20% of the daily energy requirements of older individuals<sup>(56)</sup>. In collaboration with the Ministry

of Health in Chile, a cluster randomised trial is currently being conducted in Santiago to determine the cost-effectiveness of the Programme of Complementary Feeding for the Older Population and a specially-designed resistance training exercise class for older individuals<sup>(57)</sup>, which could serve as blueprints for similar interventions in other nations.

In order to reflect on the level of the UK government's actions in social and health policy to support older individuals, the cost of healthy living for older individuals in England has recently been estimated<sup>(58)</sup>. Using conclusions of expert reviews and published research, the best evidence on the needs for healthy living for individuals aged  $\geq 65$  years (without major disability) in England, was derived for nutrition, physical activity, housing, psychosocial relations and social inclusion, mobility, medical care and hygiene. This knowledge was translated into presumptively acceptable ways of living, and the corresponding minimal personal costs were assessed from low-cost retailers or, where unavoidable, from national data on the expenditure of low-income older individuals. The minimum income requirements for healthy living for this population in England were found to be 50% greater than the state pension, and even appreciably greater than the official minimum income safety level. The results suggest that inadequate income currently could be a barrier to healthy living for older individuals in England. In 2007 the cost of the defined healthy diet represented 25% of the total weekly budget for older individuals. Increasing food costs, without concomitant increases in social support, is likely to create further strains on household budgets and may also affect food security for older individuals.

It is evident, however, that there is tremendous variation between individuals in the extent of age-related changes in health and function. This disparity has led some researchers to propose a distinction between 'usual' and 'successful' ageing, or ageing well<sup>(59)</sup>. While there is a growing body of evidence to support the role of genetic constitution in some aspects of healthy ageing, such as risk of Alzheimer's disease<sup>(60)</sup> and age-related macular degeneration<sup>(61)</sup> and physiological responses to exercise<sup>(62)</sup>, it is also clear that nutrition and lifestyle factors across the life course are crucially important. For example, in a pan-European study adherence to four healthy lifestyle characteristics, i.e. consumption of a Mediterranean-style diet, moderate alcohol intake, regular physical activity and not smoking, was shown to increase the chance of survival over 10 years by  $>50\%$ <sup>(63)</sup>. Such a regimen can be promoted by public health nutrition professionals and does not depend on access to high-tech medical care or large financial resources.

Interestingly, a recent Finnish cohort study has shown that maintenance of healthy public health nutrition variables (healthy body weight, low cholesterol, low blood pressure and regular physical activity) are also associated with lower risk of incident dementia<sup>(64)</sup>. This finding highlights the possible role of nutrition in the prevention of cognitive decline and dementia, a role first proposed 25 years ago<sup>(65)</sup>. The number of individuals with age-related cognitive impairment is rising dramatically in the UK<sup>(66)</sup> and globally<sup>(67)</sup>, and the prevention and treatment of

dementia is one of the major global challenges for health in which nutrition may have an important role to play.

A mass of epidemiological evidence linking nutrient supplementation to cognitive function and dementia has been published over the past 25 years, but unfortunately it has largely not been corroborated by the clinical trials that have been conducted in older individuals. Indeed, a series of Cochrane and other systematic reviews have concluded that there is no evidence of an effect of supplementation with various B-vitamins<sup>(68,69)</sup> or vitamin E<sup>(70)</sup> on cognitive health in later life. However, two sets of candidate nutrients, the B-vitamins and the *n*-3 long-chain PUFA, remain influential on the nutrition and cognitive function research agenda<sup>(71)</sup>.

High levels of homocysteine are a known risk factor for vascular disease in mid-life<sup>(72)</sup> and older age<sup>(73)</sup>, and interestingly have also been shown to be associated with cognitive function in later life<sup>(74)</sup>. A small clinical trial that randomised 276 individuals aged  $\geq 65$  years at baseline to receive either a daily supplement containing 1000  $\mu\text{g}$  folate, 500  $\mu\text{g}$  vitamin B<sub>12</sub> and 10 mg vitamin B<sub>6</sub> or a placebo for 2 years has demonstrated marked reductions in homocysteine in the intervention group, but no difference between trial arms in cognitive function at the end of the intervention<sup>(75)</sup>. However, the recent publication of a larger clinical trial<sup>(76)</sup> that randomised 818 individuals aged 50–70 years at baseline to receive either 800  $\mu\text{g}$  folic acid or placebo daily for 3 years has revitalised the hypothesis. The intervention was found to result in a 26% decrease in homocysteine levels, and the authors reported a beneficial effect of folic acid supplementation on three of the five cognitive domains under investigation. As background work for an ongoing trial investigating the effect of vitamin B<sub>12</sub> supplementation on central and peripheral nerve function and cognitive health (the Older People and Enhanced Neurocognitive function Study), an analysis of individual participant data from the available published clinical trials investigating B-vitamin supplementation and cognitive function is currently being undertaken, which will hopefully provide more information on the potential role of these nutrients in cognitive health in later life.

Epidemiological evidence for an association between *n*-3 long-chain PUFA consumption and cognitive function is similarly intriguing. A systematic review has identified four cohort studies reporting associations between *n*-3 long-chain PUFA and cognitive health<sup>(77)</sup>. All four studies have suggested a positive impact of increased *n*-3 long-chain PUFA consumption (either as fish or as total *n*-3 long-chain PUFA) on risk of impaired cognitive function or incidence of dementia. More recently, follow up of 210 surviving males in the Zutphen Elderly Study has demonstrated that among men aged 70–89 years at baseline fish consumption is associated with a slower rate of cognitive decline over 5 years<sup>(78)</sup>. Finally, follow up of 899 men and women in the Framingham Heart Study with a mean age of 76 years at baseline has demonstrated that individuals with the highest levels of plasma phosphatidylcholine-DHA have a decreased risk of incident dementia over 9 years<sup>(79)</sup>.

While the case for *n*-3 long-chain PUFA in healthy cognitive ageing is building, a Cochrane review has found no published randomised controlled trials investigating the

effect of *n*-3 long-chain PUFA supplementation on cognitive function among healthy older adults<sup>(80)</sup>. One recent clinical trial randomised 174 participants with mild-to-moderate Alzheimer's disease and a mean age of 74 years to receive either 2.3 g *n*-3 long-chain PUFA or placebo daily for 6 months<sup>(81)</sup>. No difference was found in the rate of decline in cognitive function between the study groups at the end of the 6-month intervention, but in a subgroup of thirty-two participants with very mild cognitive function loss at baseline the rate of cognitive decline in the intervention arm was found to be slower than that in the placebo arm. While these results are exciting, they must be confirmed by larger studies. A randomised controlled trial, the Older People And *n*-3 Long chain polyunsaturated fatty acid Study<sup>(82)</sup>, is currently investigating the effect of 0.7 g *n*-3 long-chain PUFA supplementation daily (which equates to about two portions of oily fish per week) for 2 years on a cohort of >860 healthy adults aged 70–79 years at baseline. The results of the trial are due in early 2009. To meet the global challenge of ageing, considerably greater attention is clearly needed to help define cost-effective public health nutrition interventions to maintain health and function in later life.

## Conclusions

The following conclusions are proposed in order to meet the global nutrition challenges for optimal human health and well-being in the new millennium:

1. agree to use the term 'malnutrition in all its forms' as a description that encompasses the full spectrum of nutritional disorders when interacting with policy makers and members of the public;
2. develop integrated prevention and control strategies for infant, child and adult undernutrition, and nutrition-related chronic disease throughout the life course;
3. reconsider the concept of dietary quality and optimal growth beyond immediate survival, particularly in relation to life-long health. There remains a critical need to define what is meant in practice by 'adequate food', considering not only quantity of energy but also overall diet quality;
4. address optimal nutrition for healthy aging based on emerging evidence of the impact of nutrition and physical activity interventions on age-related functional and health decline;
5. call for a greater effort by the UN agencies, private and public development partners and other organisations to develop and/or strengthen local, regional and international leadership capacity to support the much-needed change in policy and programme activities, focusing on malnutrition in all its forms with a unified agenda.

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