1 Introduction

> *"Men and women have the right to live their lives and raise their children ... free from hunger."*
> *(United Nations Millennium Declaration)*

Hunger is a scourge of humanity since times immemorial – and until our present days. At the dawn of the new millennium (2000-2002) more than 850 million people worldwide were undernourished (FAO 2004a). Given a total population of 6 billion[2] people this means that one out of seven people is suffering from hunger. While this situation is appalling and while only episodes of acute hunger and not the more prevalent chronic hunger receive broader attention, the problem is generally acknowledged and the task is now rather to move from political commitment and the setting of goals to action and the achievement of actual outcomes (Sanchez and Swaminathan 2005; von Braun et al. 2004). And action is indeed imperative, because the unacceptability of hunger is also underlined in numerous human rights declarations, international conventions and resolutions (c.f. section 2.5.2). Still, since Malthus (1798) established the connection between the level of the means of subsistence (like food) and the preventive and positive checks on population growth (like early marriages and famines, respectively), human ingenuity in increasing the means of subsistence has so far mostly succeeded in avoiding the deadly mechanism of outright famines that Malthus envisioned otherwise. In our times, science has brought about great progress in ensuring food security for millions of people: the Green Revolution, with the introduction of high-yielding crop varieties and the more intense use of inputs like irrigation and agro-chemicals, has helped to avoid widespread starvation and impede famines, especially in Asia.

However, much larger numbers of people suffer from a different, stealthier form of hunger than simple lack of sufficient quantities of foodstuffs: micronutrient malnutrition, or "hidden hunger", is caused by a lack of food of sufficient dietary quality (Kennedy et al. 2003). While often providing enough calories, monotonous diets based on cereals and other starchy staple foods frequently fail to deliver sufficient quantities of essential minerals and vitamins like iodine, iron, zinc and vitamin A (Demment et al. 2003).[3] The resulting micronutrient deficiencies can have devastating consequences for the life, health and well-being of the affected individuals: premature death, blindness, cretinism, weakened immune system, stunting, reduced productivity, fatigue and lack of drive.[4] In many countries the dimension of these deficiencies attains proportions that make micronutrient malnutrition to a public health problem of primary concern – with concomitant effects on productivity and overall welfare of the affected societies (FAO 2004a; MI/UNICEF 2004; UN-SCN 2004; WHO 2002, World Bank 1994). In total, more than two-thirds of the world population – for the most part women and children – suffer from at least one micronutrient deficiency: 4-5 billion people are iron deficient (WHO 2003a), 2 billion are iodine deficient, about 150 million are vitamin A deficient (UN-SCN 2004) and as many as 3 billion people are at risk of zinc deficiency (Hotz and Brown 2004) (Figure 1). Given these large figures and the general agreement on the individually debilitating and

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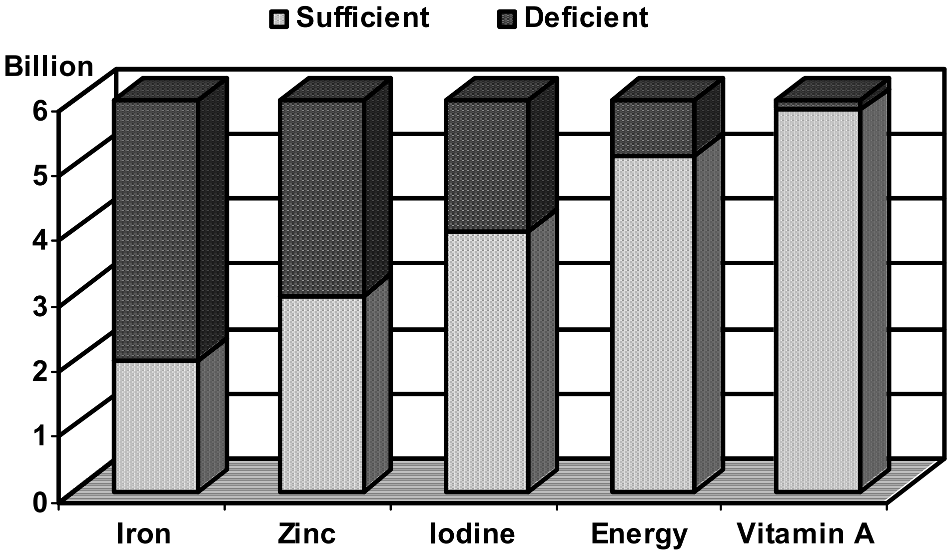
[2] To avoid misunderstandings, in this study "billion" is used in its US notation, i.e. 1 billion = 1,000,000,000.

[3] Incidentally, the Green Revolution is partly blamed for this situation as its primary focus was increasing the quantity of food but not its quality or diversity (Demment et al. 2003; Welch and Ross 2000).

[4] While above I have stated that humankind has mostly succeeded in preventing general and widespread famines, I should perhaps add that Malthus (1798) has also counted "unwholesome" food as a secondary cause of other positive checks on population growth (like poor health and epidemics).

economically damaging effects of micronutrient malnutrition, focussing public attention and research on this more subtle form of malnutrition is certainly warranted (Black 2003).

Figure 1. Number of people suffering from malnutrition worldwide



Source: WHO (2002); UN-SCN (2004); Hotz and Brown (2004).

In the long run, economic development and rising incomes of the poor can be expected to help solving the problem of malnutrition and ill health – but the reverse may also be true, namely that reducing malnutrition can boost economic growth (Strauss and Thomas 1998; WHO 2001a), especially in very poor countries that may be caught in a poverty trap (Sachs et al. 2004). In either case, relying on economic growth alone will not be sufficient to meet the challenge of halving malnutrition in the near future (Behrman et al. 2004; FAO 2005a; World Bank 2006). To do so, a balanced strategy – including micronutrient interventions – is necessary to accelerate reductions in malnutrition (Haddad et al. 2003). To address the problem of micronutrient deficiencies directly, the conventional approach is to resort to supplementation, fortification, dietary diversification and nutrition education. Further measures may include public health measures like control of parasites (e.g. deworming) and efforts to improve sanitation and personal hygiene. Depending on the context, these interventions may be effective in reducing the prevalence of the targeted deficiency.[5] However, to work properly all these interventions have different prerequisites and they also have their particular restrictions and weaknesses, which limit the overall progress in controlling micronutrient deficiencies (Hotz and Brown 2004; Allen 2003; Kennedy 2003; ACC/SCN 2000; Elder 2000; Underwood and Smitasiri 1999; Buyckx 1993). Nevertheless, micronutrient interventions in general are considered to be very cost-effective (World Bank 1993 and 1994; Horton 1999; WHO 2002; Behrman 2004).

In recent years a new, complementary approach to address micronutrient deficiencies has emerged: biofortification. Starting from the premise that micronutrient malnutrition is essentially a food-based problem (but that producing micronutrient-dense food crops (still) is of little relevance in agricultural production systems), the underlying idea is to enlarge the scope of agricultural research and breeding programmes to include the micronutrient content in food

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[5] This is particularly true for the iodisation of salt, through which the control of iodine deficiency has become very successful (e.g. Ramakrishnan 2002; ACC/SCN 2000).

crops as an explicit goal. In this case, plants could be bred to fortify themselves (Bouis et al. 2000). Moreover, focusing this approach on staple crops could increase the micronutrient intake of the poor, who are most at risk of suffering from vitamin and mineral deficiencies because they cannot afford a diet adequate in better sources of micronutrients like fruits, vegetables and livestock products. Hence, biofortification is expected to be self-targeting (Welch and Ross 2000; Bouis 2002a). Consumer acceptance of biofortified crops is not expected to be an issue, because – at least in the case of iron and zinc – micronutrient density is largely an unnoticeable trait. However, these traits have to be bred into agronomically superior varieties to ensure adoption among farmers. In this context, one welcome side effect is that biofortified crops may perform better on micronutrient-poor soils (Welch 2002). Apart from these more technical arguments, the major reason that is put forward in support of biofortification is an economic one: because a largely one-time investment into the development of a biofortified crop may benefit various countries around the world, and farmers everywhere can grow and reproduce the crops year on year, the result could be a continuous stream of widespread benefits. With the benefits thus accumulating over time and space, the investment in research and development (R&D) of biofortified crops has the potential to reap huge returns in terms of improved public health, overall welfare and economic growth. Given the annually recurring costs of the major current alternatives (fortification and supplementation), biofortification holds the promise to be a more cost-effective intervention (Bouis 2002b).

To promote the development and dissemination of biofortified food crops, the International Food Policy Research Institute (IFPRI) and the International Maize and Wheat Improvement Centre (CIMMYT) of the Consultative Group on International Agricultural Research (CGIAR) have initiated the HarvestPlus programme (Bouis et al. 2000; HarvestPlus 2006); the more narrow aim of promoting beta-carotene-rich “Golden Rice” is pursued by the Golden Rice Humanitarian Board, which is formed by members of the University of Freiburg, the Swiss Federal Institute of Technology, the Swiss Agency for Development and Cooperation, the Rockefeller Foundation, the US Agency for International Development (USAID), Syngenta, the International Rice Research Institute (IRRI) and Tufts University (Golden Rice 2005).

Biofortified crops are still at an – albeit advanced – stage of R&D. Their actual effectiveness in terms of agronomic and health outcomes remains unknown. However, to compare this new approach with existing interventions, information on the cost-effectiveness of biofortification is sorely needed, whether it is carried out through conventional breeding or genetic engineering. Filling this knowledge gap regarding the possible impact of biofortification is both vital and urgent: neglecting a potentially effective intervention and any delays in its implementation may literally cost lives.

One contribution of my work is to narrow this knowledge gap, i.e. I determine the effectiveness of biofortification for five biofortified crops (iron-rich rice, iron-rich wheat, zinc-rich rice, zinc-rich wheat and Golden Rice)[6] that address three different micronutrient deficiencies (iron deficiency, zinc deficiency and vitamin A deficiency). Yet, to assess such health interventions, determining their effectiveness is necessary but not sufficient: in a world of scarcity (relative) costs matter. Indeed, as the World Bank (1993, p. 61) puts it: “Because interventions can dif-

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[6] While research is also being carried out to increase the levels of bioavailable micronutrients in various staple crops through transgenic approaches (Goto et al. 1999; Holm et al. 2002; Lucca et al. 2001 and 2002; Murray-Kolb et al. 2002; Vasconcelos et al. 2003; Shivaprakash 2004; Lakshmikumaran 2004; Ducreux et al. 2005; Drakakaki et al. 2005), my analyses of mineral-rich cereals are based on ongoing R&D efforts to increase the iron and zinc content through conventional breeding. In my analysis Golden Rice is the only transgenic crop.

fer so much in cost-effectiveness, making allocative decisions badly in either the public or the private sector costs lives. [...] Insisting on value for money is not only fully consistent with compassion for the victims of disease, it is the only way to avert needless suffering." And in a more recent assessment of strategies to achieve the millennium development goals, the World Health Organization's CHOICE Team (Evans et al. 2005a, p. 1133) finds that "making best use of resources is vital in developing countries that are struggling to improve public health with limited funds." Hence, a further contribution of my work is the establishment of the cost-effectiveness of biofortification with regard to potential alternatives (and other suitable benchmarks).

Prior to analysing the effectiveness of an intervention it is necessary to quantify the underlying problem, though. While the *cause* of micronutrient deficiencies is essentially poor nutrition, the *outcome* is poor health. Therefore, the methodological challenge when analysing and comparing these deficiencies is to measure "health" in a consistent manner. Once the different health outcomes of micronutrient deficiencies are combined in a single index, they can be aggregated to determine the underlying "burden" of each deficiency. One method that avoids the rather inegalitarian results of cost-of-illness or willingness-to-pay (WTP) approaches are "disability-adjusted life years" (DALYs). DALYs weight different health states according to their respective severity before adding up their durations to obtain the burden of a disease expressed in "healthy life years" that are lost. This method was introduced by the World Bank (1993) and subsequently popularised by Murray and Lopez (1996a). The method has become widely adopted and accepted (for a literature review see Fox-Rushby 2002). It has been used by other international organisations (WHO 2001a and 2002; UN-SCN 2004; FAO 2004a) and for analyses in the context of developing countries (Gwatkin 1999); it is now used to quantify health-related costs in such diverging areas as the global incidence of civil war (Collier and Hoeffler 2004), poor water and sanitation infrastructures (Rijsberman 2004) or communicable diseases (Mills and Shillcutt 2004). Hence, DALYs are not only methodologically adequate to measure the health burden of micronutrient malnutrition, results expressed in DALYs are also widely comparable.

More recently, DALYs have been used to carry out a cost-benefit analysis (CBA) for a single biofortified crop (Zimmermann and Qaim 2004). In other economic analyses of biofortified crops, assessments have been based on potential improvements in micronutrient intake or on expected reductions in the prevalence rates of the respective deficiency (Bouis 2002a; Dawe et al. 2002; Albrecht 2002), i.e. the actual adverse functional outcomes of the underlying micronutrient deficiencies were ignored. And all these studies either rely on limited, regional food intake data from small-scale surveys, on highly aggregated national food consumption data or on assumptions on the food intake of a representative adult only.

In this study I discuss and refine the DALYs methodology to analyse iron deficiency anaemia (IDA), zinc deficiency (ZnD) and vitamin A deficiency (VAD) within a single, systematic and consistent framework. To do so, I model the individual health outcomes of these micronutrient deficiencies more explicitly and consider more nutritional and epidemiological details than previous studies. I then use this improved framework to compare and assess the potential impact of the five different biofortified crops mentioned above on the burden of IDA, ZnD and VAD, respectively. (So far burdens of ZnD had not been calculated explicitly.) Because all these crops are still at the R&D stage I resort to an ex ante analysis and simulate their consumption for different scenarios. In an improvement over previous work, these simulations are based on detailed food consumption data from a nationally representative household survey, which – although more demanding in terms of data, computing power, programming and time – adds further accuracy and robustness to the result of the analysis. The shift in the whole intake distribution of the different micronutrients, which occurs when biofortified crops are consumed, is then explicitly translated into a reduction of the incidence of the different health outcomes of each of the three micronutrient deficiencies. (In this context I develop a new approach to link iron intakes to the incidence of health outcomes of IDA.) Hence, my results represent a more precise and more detailed estimation of the burden of the micronutrient deficiencies and of the potential impact of biofortification on public health.

Based on the estimated health benefits, I proceed to carry out a cost-effectiveness analysis (CEA) of biofortification. Given that DALYs are a standardised unit of "health", the potential health benefits of the biofortified crops – which are expressed in the number of DALYs that may be saved – are comparable across different interventions. Juxtaposing these health benefits and the costs of biofortification (for R&D, dissemination, social marketing, extension and maintenance) over a suitable period of time yields a cost-effectiveness indicator in the form of the "cost per DALY saved". These relative costs of the different biofortified crops are ranked and compared with other micronutrient interventions and benchmarks set by international organisations. Yet, focusing on DALYs has its limits because not all scientists and policy-makers are familiar with this concept and not all interventions can or will be assessed using this method. Therefore, in an additional step, a monetary value is attached to DALYs to transform the health benefits into monetary benefits. (In this context, where previous work has resorted to more ad hoc valuations, I discuss in more depths the different approaches that are possible to value one DALY.) Having expressed both costs and benefits in monetary terms, a CBA is carried out and economic indicators like the internal rate of return and benefit-cost ratios are produced for the different biofortified crops. These results are then compared with average returns of agricultural R&D projects and recommended cut-off levels for health programmes, which allows for assessing the relative profitability of biofortification. The conversion of DALYs into monetary terms is also used to estimate the impact of micronutrient malnutrition on overall economic growth in India, which has not been done this way before. In an extension to the main discussion of the results, I enter the controversy about plant biotechnology and Golden Rice, challenge the validity of often quoted arguments of critics of Golden Rice and discuss the corresponding background as well as the implications of my findings in greater detail.

The regional focus of this economic analysis of biofortification is India. In a nutrition index of 106 countries, India ranked 77th and its nutrition situation was defined as "bad" (Wiesmann 2004). In India about half of the women and three quarters of the children are anaemic (NFHS 2000),[7] the risk of ZnD is estimated to be high (Hotz and Brown 2004) and almost one-third of all preschool children are vitamin A (VA) deficient (UN-SCN 2004). Moreover, the efficacy and coverage levels of India's existing iron and VA supplementation programmes are low (Kapil 2003; GoI 2002) and for zinc there are no significant interventions at all (MI 2005).[8] At the same time rice and wheat are consumed widely – for example, in rural India the average

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[7] IDA is only a subgroup of anaemia, but because it is the most important one it is often used as proxy for IDA. Yet, individuals can also suffer from ID without being anaemic (Nestel and Davidsson 2002).

[8] While ZnD in humans is known since over 40 years (Prasad 2003), the extent and severity of this deficiency has only become apparent more recently (Hotz and Brown 2004; UN-SCN 2004), largely because of the difficulty in measuring zinc status.

monthly per capita consumption of rice is 6.8 kg and of wheat 4.6 kg (NSSO 2001).[9] And for India data is available of a nationally representative survey of 120,000 households. The survey was carried out by the National Sample Survey Organisation (NSSO 2000) and comprises the households' consumption of over 140 different foodstuffs. This background makes India an ideal test case for the purpose of my analyses.

Apart from this introduction, the study comprises five more chapters. The next chapter provides some background information to put this study into its wider context. This includes an overview of the problem of micronutrient malnutrition, of possible interventions in general and of biofortification in particular; biofortification and genetic engineering are put in perspective to the technological developments in agriculture and society; and economic as well as legal reasons for addressing micronutrient deficiencies are offered. In chapter 3 the actual analysis begins with an explanation and justification of the DALYs method, which is used for quantifying the amount of ill health that is caused by IDA, ZnD and VAD in India. In this chapter the data that is used in the analyses is presented, too, and the concepts that are used for linking micronutrient intakes to health outcomes are described and developed. In the last section of chapter 3 the different approaches that are used in the economic analyses are clarified. In chapter 4 the results of the analyses of the three case studies of (i) iron-rich rice and wheat, (ii) zinc-rich rice and wheat and (iii) Golden Rice are reported, before they are condensed, compared and discussed in chapter 5. In a separate section of chapter 5 popular criticisms of Golden Rice are examined. Finally, in the last chapter, conclusions are drawn and policy implications of the findings are pointed out.

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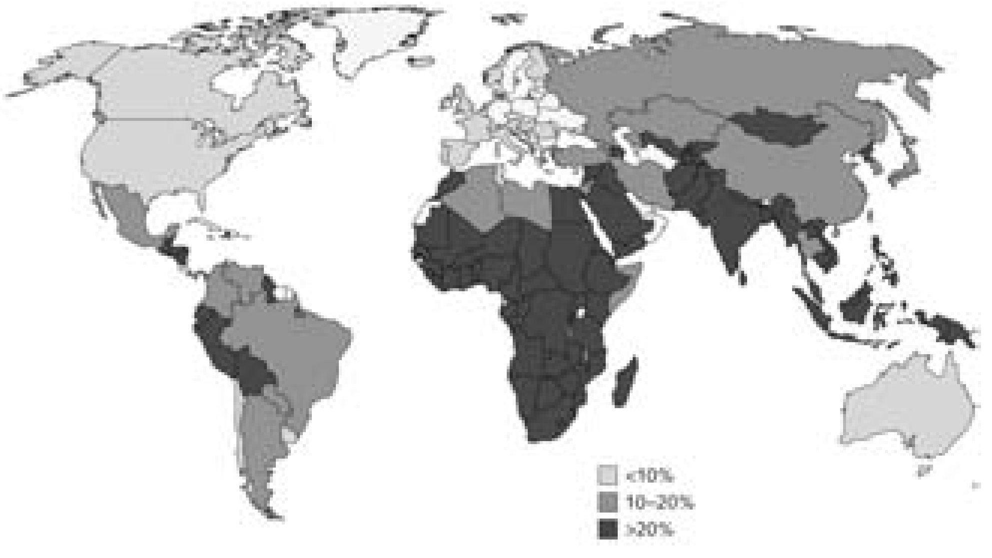
[9] Of course such aggregate figures mask regional and socioeconomic differences: while in the south of India rice is the predominant staple crop, in the north wheat is more important. Moreover, there are also inter-household differences. In my analysis this is taken care of through the use of household data.

2 Background

2.1 Micronutrient malnutrition worldwide

As already described in the introduction, billions of people are deficient in iron, iodine, zinc and/or VA (Figure 1). Yet, while micronutrient deficiencies, in particular iron deficiency, may also be a health problem for sub-groups within the societies in industrialised countries – like low income populations (Ramakrishnan and Yip 2002), children (Marx 1997; Moy and Early 1999; Ramakrishnan 2002; Ganji et al. 2003), women (Marx 1997; Ramakrishnan 2002; Biesalski et al. 2003; Cogswell et al. 2003), the elderly (Marx 1997; Wakimoto and Block 2001; Mukhopadhyay and Mohanaruban 2002; Biesalski et al. 2003), migrants and minorities (Marx 1997; Looker et al. 2002; Ramakrishnan and Yip 2002; Ganji et al. 2003), blood donors (Marx 1997), vegetarians, some groups of athletes (Marx 1997; Biesalski et al. 2003), indigenous populations (Ramakrishnan and Yip 2002), people on a weight reduction diet, hospitalised and institutionalised people, subjects with a chronic inflammatory disorder, subjects with chronic administration of certain drugs and clinically defined groups of patients (Biesalski et al. 2003) –, micronutrient deficiencies as public health problem are largely under control in industrialised countries since the first half of the 20th century. Although, poor eating habits around the world contribute to increasing consumption of processed, energy-dense but micronutrient-poor foods (DellaPenna 1999; WHO 2003b). Where micronutrient deficiencies are controlled, this is generally attributed to successful food fortification efforts (Mannar 2001; Clugston and Smith 2002; Beinner and Lamounier 2003), even if the respective policies may differ between industrialised countries (Nugent and McKevith 2004).

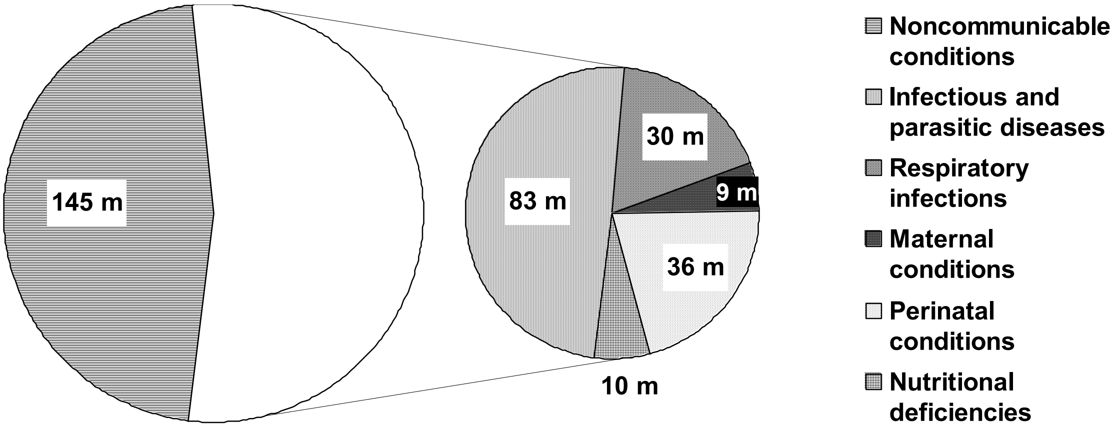
Figure 2. Estimated prevalence of stunting among children under 5 years of age[a]



Notes: [a]The prevalence of stunting is a proxy measure for malnutrition in general and for ZnD in particular.
Source: Hotz and Brown (2004).

However, it was probably a broader range of factors that contributed to the present situation, namely a combination of scientific advances, economic development, supplementation, fortification, commercialisation of food processing and improved infant formula (Ramakrishnan and Yip 2002). A relatively educated public that understood the concept of fortification and created a stable market for fortified products may also have helped, as may the consumption of over-the-counter supplements (Underwood and Smitasiri 1999). But the principal problem persists, namely that people do not necessarily relate ill health to the impact of micronutrient deficiencies and are frequently unable to reconcile their food preferences with nutritional requirements, i.e. they may change their consumption choices only partially (Behrman 1995; Smith 2002). Hence, some control mechanisms for micronutrient deficiencies are necessary both in industrialised and in developing countries.[10] Because in the developing world the income level is low *and* fortification and supplementation have only limited success (c.f. section 2.2), the biggest burden of micronutrient malnutrition is carried by Africa, large parts of Asia and some regions in Latin America (for example see Figure 2). Looking more particularly at Asia, Figure 3 gives an overview of the relative importance of micronutrient deficiencies in a region where, in total, more than 300 million DALYs are lost due to diseases and injuries.

Figure 3. The WHO's burden of disease in the SEAR-D-region in 2000 (DALYs lost)



Notes: "Nutritional deficiencies" include protein-energy malnutrition, iodine deficiency, IDA and VA-related visual problems; for more details c.f. section 5.1. "SEAR-D" corresponds to South Asia (c.f. list of acronyms).
Source: WHO (2002).

2.2 Micronutrient interventions

2.2.1 Current micronutrient interventions

There are three broad concepts of interventions to control micronutrient deficiencies. First, efforts that are aimed at increasing the micronutrient content in the food that people *usually* eat are called fortification. This can be (i) "industrial fortification", i.e. the addition of (synthetic) vitamin or mineral compounds during the processing of foodstuffs, whether commercially motivated, as part of public-private partnerships or required by law, (ii) "home fortification", e.g. the voluntary application of sprinkles, or (iii) fortification by distributors somewhere along the food chain, e.g. the blending of grains or flour with micronutrient premixes.

Second, efforts that are aimed at supplying micronutrients in *addition* to the usual food (in the form of tablets or syrups) are called supplementation. This can be (i) "medical supplementation", e.g. VA mega doses that are administered by health personnel, (ii) "pharmaceutical supplementation", e.g. iron pills that are prescribed but taken at home, or (iii) dietary supplements of safe dosages that are taken voluntarily.

Third, dietary diversification refers to strategies that seek to (i) increase the production of micronutrient-rich foods (e.g. through appropriate agricultural policies or the promotion of

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[10] The reliance on fortification in richer countries has, for instance, become apparent during the "Humana baby food scandal" in Israel, where several infants were hospitalised and two have died – possibly because the fortified baby formula they were fed accidentally lacked vitamin B1 (Siegel-Itzkovich 2003; BBC 2003).

home gardens), (ii) directly increase the micronutrient content in people's diets through promoting the consumption of micronutrient-rich foods (which requires a *change* in people's usual diets) and (iii) improve the bioavailability of the micronutrients that are consumed in the everyday food (e.g. through the joint consumption of food rich in potential promoters or the promotion of new food preparation techniques); dietary diversification usually requires nutrition education and communication for behaviour change. Biofortification, the subject of this study, could be seen as a combination of fortification and dietary diversification.

These distinctions do not necessarily follow common definitions but are made here to structure the different approaches, because each of the interventions has several dimensions. For example, fortification and dietary diversification are preventive measures, while supplementation can also be used for treatment of micronutrient deficiencies; supplementation and dietary diversification programmes are usually funded by governments or by donors, while the costs of fortification may be handed down to the consumers; with legislated fortification consumers do not need to do anything, while they need to be more active for dietary diversification or in the case of supplementation (i.e. take the tablets). These approaches are well established and discussed in the literature to varying degrees and for different micronutrients (e.g. World Bank 1994; Underwood and Smitasiri 1999; ACC/SCN 2000; Kennedy et al. 2003; Allen 2003; Hotz and Brown 2004). Yet, while it is generally acknowledged that iodisation of salt is an effective solution that contributes successfully to the elimination of iodine deficiency, and while VA supplementation programmes are given some credit for reducing the prevalence of VAD, the overall success of micronutrient interventions in developing countries has been mixed (ACC/SCN 2000; Underwood 2000; Ramakrishnan 2002; Dalmiya and Schultink 2003; Allen 2003; Adamson 2004). An overview of successful programmes is given in Mason et al. (2004).

Supplementation

Supplementation may be an effective strategy to reach specific target groups that require larger doses of micronutrients in a short period of time (Hotz and Brown 2004; Allen 2003; Mora 2002; Underwood 2000). However, the success of supplementation efforts is often limited due to economic constraints and the intense requirements in terms of health personnel, which is also why it is considered to be unsustainable in the long run (Cook et al. 1994; Underwood and Smitasiri 1999; Underwood 2000; Beinner and Lamounier 2003; Hotz and Brown 2004). Another weakness is seen in bad delivery and poor health systems, ineffectively implemented programmes, inadequate supply of supplements and, hence, poor coverage (Cook et al. 1994; Gillespie 1998; Underwood and Smitasiri 1999; Dillon 2000; ACC/SCN 2000; Hotz and Brown 2004). On the side of the potential beneficiaries, poor compliance and adherence (because of side effects and forgetfulness, respectively) are often mentioned as factors limiting the success of supplementation programmes (Cook et al. 1994; Gillespie 1998; Underwood and Smitasiri 1999; ACC/SCN 2000; Dillon 2000; Allen 2003; Beinner and Lamounier 2003; Hotz and Brown 2004).[11] Pangaribuan et al. (2003) report for samples of rural and suburban households in Indonesia that limited knowledge of caretakers about the health benefits of VA reduces the likelihood of regular participation in VA supplementation

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[11] Evidence from the US and the UK indicates moreover that groups who could benefit most from supplements are often least likely to use them (Cogswell et al. 2003; Conner et al. 2003; Jasti et al. 2003). This is also reflected in the statement of Adamson (2004, p. 6) that "the children least likely to receive VA supplements are those most at risk from VAD."