The Poor, Malnutrition, Biofortification, and Biotechnology[*]

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Abstract: While less apparent than outright hunger or obesity, the lack of essential vitamins and minerals in people's diets is one of the leading contributors to the global burden of disease. Current interventions, such as supplementation or fortification, are being implemented with varying success, but—while important—overall progress in the fight against micronutrient malnutrition has been limited. Biofortification, the breeding of crops for higher contents of vitamins and minerals, is a new approach to complement existing interventions. This chapter gives an overview of the problem of micronutrient malnutrition and how it is measured; it briefly discusses current micronutrient interventions, and then presents the reasoning behind biofortification before it examines the feasibility of biofortifying crops and summarizes studies on their potential impact and economic justification. After listing current biofortification programs, the chapter looks into the political controversy surrounding genetic engineering in agriculture and how it relates to biofortification; it then concludes with an assessment of the current status of biofortification and its potential.

Keywords: hunger, malnutrition, vitamin A deficiency, iron deficiency, zinc deficiency, public health, biofortification, plant breeding, genetically modified organisms, disability-adjusted life years

1 Introduction

This chapter deals with agricultural approaches that are aimed at improving the nutritional status—and ultimately the health—of the poor in developing countries. Conventionally, nutrition problems in poor countries are first and foremost equated with outright hunger, meaning an insufficient consumption of dietary energy (see FAO 2010). Correspondingly, the discussion about how to solve the world food problem primarily revolves around the question of whether hunger is a (technical) problem of food production or a (social) problem of food distribution. This is an especially important question because agricultural biotechnology is being used for crop improvement (Chrispeels 2000). However, while the fact that there are about one billion hungry people in the world is an issue of serious concern, there is another nutrition problem that often goes unnoticed; namely, micronutrient malnutrition, which is also aptly dubbed "hidden hunger" (Kristof 2009; Hidden Hunger 2011; Micronutrient Initiative 2011a).

While undernourishment due to insufficient energy intakes is directly felt by those suffering from hunger, and is also easily recognized by others because it causes wasting and stunting, a lack of micronutrients in people's diets has less directly perceptible but nevertheless potentially serious consequences for the health and well-being of the affected individuals. Micronutrient deficiencies can cause, inter alia, lack of stamina, impaired physical and cognitive development, morbidity, blindness and—via increased susceptibility to infectious diseases—premature death.

Even if insufficient dietary intakes are recognized as the main cause of micronutrient deficiencies—that is, even if "hidden hunger" is identified as being a food-based problem—micronutrient deficiencies are nevertheless often regarded primarily as health problems. Indicative of this view is that the World

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Health Organization has a dedicated section on micronutrient deficiencies on its website (WHO 2011f). In this context, the most common approaches to control vitamin and mineral deficiencies are fortification or supplementation (e.g., WHO 2011f, UNICEF 2011, Micronutrient Initiative 2011b, GAIN 2011). In addition to these interventions, and as micronutrient malnutrition persists, a complementary approach has emerged: breeding staple food crops for higher micronutrient content. Given that micronutrient deficiencies are essentially a food-based problem, the idea of adding to people's food what is lacking in their diets is not new; this is already being done through fortification. However, using plants to fortify themselves with micronutrients had not been pursued as a coherent strategy to tackle vitamin and mineral deficiencies on a broader front until the late 1990s, when, inter alia, the "Micronutrients Project" of the Consultative Group on International Agricultural Research was initiated (Bouis et al. 2000).[1] Only a little later the term "biofortification" was coined to describe micronutrient fortification of plants through breeding approaches (CGIAR 2002), and the concept was introduced in the literature (e.g., Bouis et al. 2000; Welch and Graham 2000; Bouis 2002). Moreover, given that one of the first biofortified crops—Golden Rice—reached the headlines because it was genetically engineered (see Nash 2000), and given the political and social controversies surrounding this technology, it is pertinent to have a more detailed look at biofortification and how and where this concept overlaps with genetically modified crops.

2 Micronutrient Malnutrition

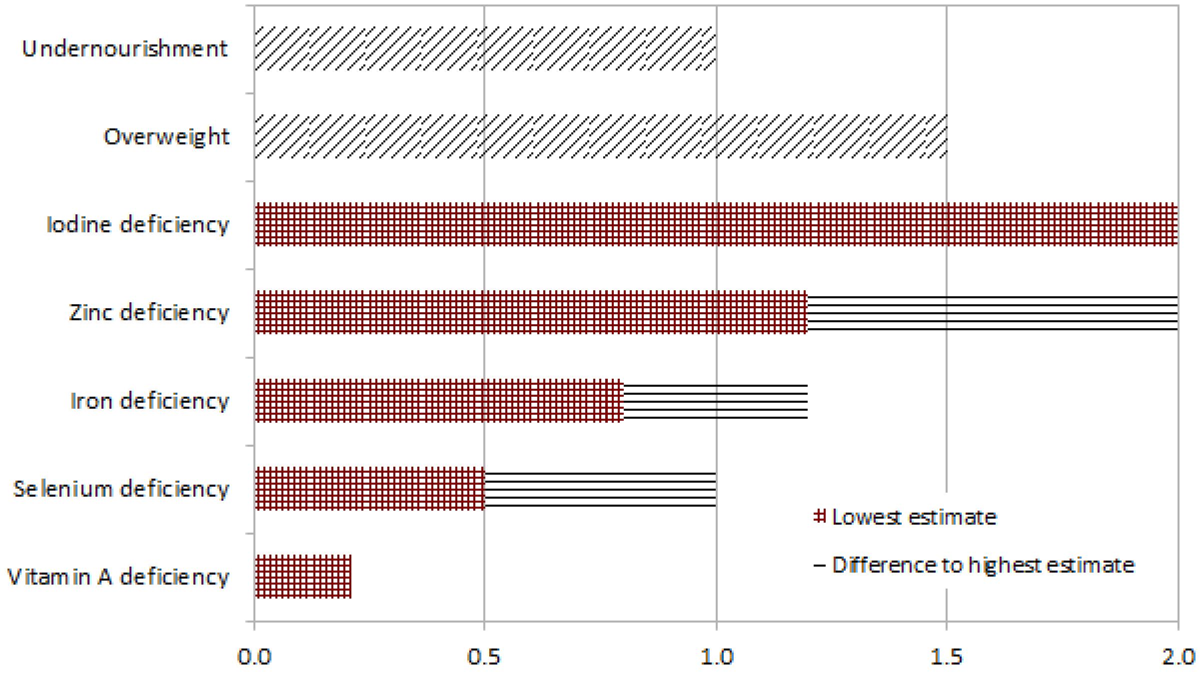
Each year the Food and Agriculture Organization of the United Nations publishes its estimates of the number of undernourished people in the world, which over the last forty years oscillated around 900 million people (FAO 2010). Over the same period the world population was continuously increasing, which means that the share of hungry people has fallen over the last four decades. Even so, about one in seven people still suffer from a lack of food, so that fighting hunger continues to be a challenge for humanity. On the other hand, the World Health Organization estimates that, worldwide, 1.5 billion people are overweight (WHO 2011g). Increasingly, these two forms of malnutrition, underweight and overweight, are occurring simultaneously within the same societies or even within the same households (Gillespie and Haddad 2003; FAO 2006).

Adding to this, estimates indicate that 2 billion people worldwide are anemic, many due to iron deficiency (WHO 2011c). A further 2 billion people likely have insufficient iodine intakes (de Benoist et al. 2008), and a similar number (1.2 to 2 billion people) are affected by zinc deficiency (Hotz and Brown 2004; WHO 2002). Moreover, at least half a billion people are estimated to suffer from selenium deficiency (Combs 2001), and an estimated 250 million preschool children alone are vitamin A deficient, with a substantial proportion of pregnant women in at-risk areas equally being suspected of suffering from vitamin A deficiency (WHO 2011d). For calcium, vitamin D, the B vitamins, and folate, low intakes can also be common (Allen et al. 2006). However, for many micronutrients, reliable prevalence data are not available, which makes substantiating the occurrence of vitamin and mineral deficiencies difficult (Borwankar et al. 2007).

Summing up these figures gives a total of at least 7 billion cases of people suffering from one form of malnutrition or another (Figure 1); in at least 5 billion cases this includes a micronutrient deficiency. Therefore, because not all of the entire human population is affected by malnutrition, many individuals must suffer from multiple nutrition problems. What these headcount figures do not show, though, is how severe the suffering is in each case—for instance, being iodine deficient is not necessarily comparable to being vitamin A deficient.

To address the issue of how different health outcomes can be quantified and compared, in the 1990s the World Bank and the World Health Organization introduced a summary measure for population health called "disability-adjusted life years," or DALYs (World Bank 1993; Murray and Lopez 1996). One DALY can be thought of as one "healthy" year of life that is lost due to mortality or morbidity. Each year of life lost due to premature death is counted as one DALY, and each year lived with a disease or injury is counted as a fraction of one DALY, depending on the severity of the condition.[2] The sum of DALYs across all health outcomes and across the entire population can be thought of as a measure of the overall gap between current health status and an ideal situation where everybody lives to an advanced age, free of disease and disability. This gap is also called the "burden of disease" (WHO 2011b).

Figure 1: Billion people suffering from malnutrition worldwide

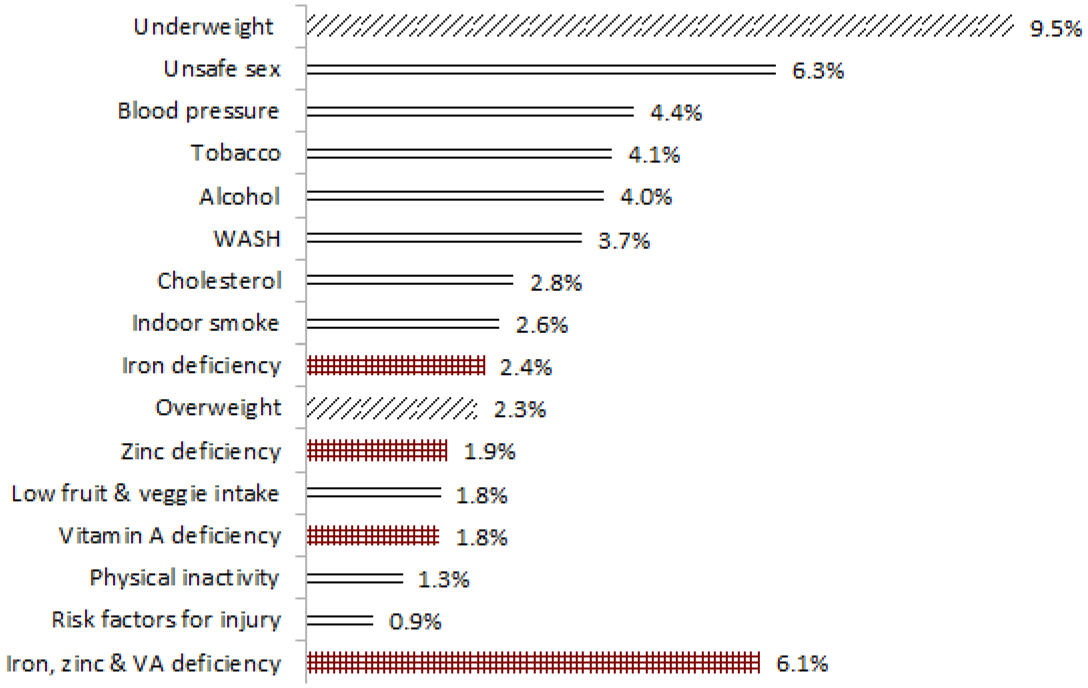


Sources: See text.

Based on this concept, the WHO calculated the "global" burden of disease and attributed it to leading risk factors (WHO 2002). As can be seen from Figure 2, the biggest single risk factor contributing to the global burden of disease is underweight—almost one-tenth of the global potential for good health is lost due to this cause. However, adding up the three major micronutrient deficiencies represents the third most important risk factor. On the one hand, this shows that vitamin and mineral deficiencies are indeed a serious problem for public health, while on the other hand, it shows that not all forms of malnutrition are equally severe. For instance, many more people suffer from iodine deficiency than are undernourished, but the aggregated health consequences are more severe for underweight.

Apart from this quantification of the amount of ill health caused by micronutrient deficiencies, the economic loss these deficiencies impose on society has been estimated. In 1994 the World Bank suggested that iron, iodine, and vitamin A deficiencies could reduce the gross domestic product (GDP) in developing countries by as much as 5 percent. Subsequent estimates also placed the possible losses of GDP due to micronutrient deficiencies in different developing countries into the range of 2–4 percent (Horton and Ross 2003; Micronutrient Initiative 2004; Stein and Qaim 2007), with lower estimates still amounting to an annual loss of at least US$5 billion in China and India alone (Micronutrient Initiative 2009). On the other hand, in the long run, better nutrition can have a much larger impact; for instance, a historic analysis by Fogel (2004) shows that 30 percent of the growth of British per-capita income over the last 200 years can be attributed to improved nutrition.

Figure 2: Global distribution of burden of disease of 15 leading risk factors



Source: WHO (2002). *Notes*: WASH stands for "Unsafe water, sanitation & hygiene." Apart from the risk factors explicitly linked to malnutrition, "Cholesterol" and "Low fruit & vegetable intake" are related to poor nutrition.

3 Conventional Micronutrient Interventions

As explained in the previous section, micronutrient malnutrition is a serious nutrition problem with negative consequences for public health and overall economic growth. Consequently, different approaches have been pursued to control vitamin and mineral deficiencies. Apart from fortification or supplementation, this also includes dietary diversification and nutrition education. These are often considered preferable strategies to improve the micronutrient status of populations (Scrimshaw 2000; Müller and Krawinkel 2005; Thompson and Amoroso 2010).

Of these interventions, iodization of salt is considered to be a particular success, since the number of iodine-deficient countries has been reduced by almost half since 2000 (Micronutrient Initiative 2009; WHO 2011e; Speeckaert et al. 2011). In addition vitamin A supplementation has seen progress since the early 2000s (UNICEF 2007; Micronutrient Initiative 2009; Hellen Keller International 2011). Other major interventions are iron fortification and iron supplementation programs, and more recently the use of zinc supplements as part of diarrhea management (ILSI 1998; WHO 2001; Micronutrient Initiative 2009). Yet, not least because of poor health infrastructure, dispersed processing of foodstuffs that could otherwise be used for fortification, and limited financial resources, these strategies do not necessarily reach vulnerable populations to a sufficient extent (e.g. Hagenimana and Low 2000; Müller and Krawinkel 2005; Horton et al. 2011). Even for vitamin A supplementation, experience has shown that too many barriers exist to make this intervention the primary approach for achieving high coverage (Micronutrient Initiative 2009). On the other hand, dietary diversification efforts are deemed relatively expensive and difficult to sustain on a large scale (e.g. Unnevehr et al. 2007).

In other words, these measures are implemented with varying success and face hurdles such as low consumption of processed foodstuffs; difficulties with the supply, distribution, or acceptance of supplements; the need for behavior change; hidden opportunity costs for the beneficiaries; and a limited reach of projects. Moreover, most projects cause recurrent annual costs that are difficult to meet regularly for developing countries. Micronutrient interventions are nevertheless considered to be very cost-effective measures compared to other public health interventions, with supplementation and fortification costing around US$10–$100 per DALY saved (Fiedler et al. 2008; Micronutrient Initiative 2009; Meenakshi et al. 2010; Copenhagen Consensus 2011).

4 Rationale for Biofortifying Crops

Over the last years, biofortification has been added as a micronutrient intervention that should be considered by decision makers. While initially only referring to breeding for higher micronutrient concentrations, the term “biofortification” has been extended to encompass mineral fertilization of crops to increase their micronutrient content (e.g., White and Broadley 2009). In this case the crops are not bred to accumulate more micronutrients, but rather mineral fertilizer is applied to mineral-deficient soils to increase the availability of essential minerals to the crops. Other approaches that are sometimes also subsumed under “biofortification” include the improvement of the nutrient profiles of crops in general, such as quality-protein maize, crops with higher levels of omega-3 fatty acids, or a modified composition of starch or dietary fibers (Pray et al. 2007; de Groote et al. 2010; Nuss and Tanumihardjo 2011; Zhao and Shewry 2011).

Therefore, “biofortification” could be more widely understood as “the process of adding nutritional value to a crop” (Montagnac et al. 2009); this is in contrast to “fortification,” where nutritional value is added to a processed food product. To differentiate the breeding approaches from the fertilizer approach, sometimes these concepts are referred to as *genetic* and *agronomic* biofortification, respectively (e.g. Cakmak 2008). In this chapter the main focus is on biofortification through plant breeding, which can be further differentiated into conventional breeding and the use of genetic engineering. While the rationale to do biofortification is the same in both cases, regulatory requirements and acceptance can be different for these two approaches, which will be discussed in more detail throughout this chapter.

Biofortification builds on the regular consumption of important amounts of a crop by all members of the respective target groups. For this reason biofortification is usually done with staple crops. Given that the poor often consume large quantities of these crops (but little else), and that it is primarily the poor who are malnourished, biofortification is also self-targeting. Moreover, in contrast to the other micronutrient interventions that are linked to (centralized) food processing facilities, health centers, or extension services, biofortification can take place on the farmers’ fields; that is, biofortification can help reach the malnourished in remote rural areas. As these people usually have less access to other programs, biofortification complements these approaches (Nestel et al. 2006; Tanumihardjo et al. 2008; Mayer et al. 2008; Meenakshi et al. 2010; Bouis et al. 2011). Biofortification efforts are explicitly targeted at regions where at-risk populations live, also taking into account the major crops already grown and consumed in these areas. To this end, methods are developed to help set the regional focus of biofortification interventions by using spatial data on the risk of nutrient deficiency and on crop production, as well as socioeconomic and food consumption data (Zapata-Caldas et al. 2009; Rose et al. 2009).

Apart from this complementary focus of biofortification, another argument in favor of this approach is its expected sustainability. Other micronutrient programs impose recurrent costs at the individual or national level. With commercial fortification, consumers may decide to buy cheaper unfortified products when they come under economic hardship; in the case of mandatory fortification, food producers have an incentive to reduce the fortificant in their products; and supplementation programs are vulnerable to changing funding priorities of governments or donors. Once developed and disseminated, biofortified crops are not subject to such vagaries; rather, they can be grown and consumed year after year and provide a continuous benefit stream (Nestel et al. 2006; Pinstrup-Andersen 2006; Mayer et al. 2008; Bouis et al. 2011). Moreover, the germplasm of biofortified crops can be shared between countries to incorporate it into locally adapted varieties. Thus, after a largely one-time investment in the development of biofortified crops, their benefits can not only spread across time, they can also extend over space. The exploitation of such economies of scale can make genetic biofortification a very cost-effective intervention (Nestel et al. 2006; Tanumihardjo et al. 2008; Qaim 2009; Bouis et al. 2011). Biofortification can also be more economic for very practical reasons. For instance, breeding micronutrients into rice is less expensive than fortifying rice grains industrially (Horton 2006). A reason advanced for agronomic biofortification is the shorter time span needed to implement fertilizer programs (Broadley et al. 2006, Cakmak 2009).

While biofortified crops are developed to provide nutrition benefits for the poor, they may also offer agronomic benefits, since minerals help plants resist diseases and other stress factors. Consequently, at least on mineral-deficient soils, biofortified crops can even contribute to higher yields (Nestel et al. 2006; Pfeiffer and McClafferty 2007; Khoshgoftarmanesh et al. 2010). This is a crucial point because yields—and agronomic traits in general, such as drought tolerance, pest resistance, or ease of propagation—are important for the adoption of biofortified crops through farmers. Their preferences are specifically taken into account when farmers are, for example, given the possibility to test and select biofortified varieties during crop trials (Tanumihardjo 2010). Other factors that influence the adoption of biofortified crops by the farmers are seed prices, availability of appropriate varieties, and their marketability.[3]

Marketability requires the existence of markets as well as acceptance of the crops by consumers (whereby farmers themselves are also consumers). Mineral biofortification through conventional breeding represents an “invisible” trait that neither requires consumers to change their behavior nor induces sensory changes, so it is unlikely to cause acceptance problems. However, biofortification with carotenes may result in changes in crop color, taste, or dry matter content. In these cases, consumer acceptance hinges on consumers’ awareness of the nutritional properties of the crops and on the degree to which they are affected by micronutrient deficiencies; that is, it depends on consumers’ awareness of the benefits the crops have for themselves and their families.[4]

5 Feasibility of Biofortifying Crops

Targeting, economic feasibility, adoption by farmers, and consumer acceptance are all necessary conditions for the success of biofortification. However, the idea of putting more micronutrients into crops and improving the nutrition status of the beneficiaries also needs to work in reality (Bouis and Welch 2010; Bouis et al. 2011). For different micronutrients and various crops, studies have confirmed that biofortification is possible in principle: micronutrient-dense varieties can be bred, the micronutrient density remains stable across several plant generations and in different environments, fertilization can increase mineral accumulation in the crops, and increasing the micronutrient content in plants does not reduce yields.[5]

In the case of genetic biofortification, relying exclusively on conventional breeding is not always expedient. Some traits—like the accumulation of provitamin A in the endosperm of rice—cannot be achieved through conventional breeding; if desired traits are not present in any variety of the crop, cross-breeding is out of the question. Hence, in many cases, biofortification requires the use of genetic engineering. Using more advanced breeding technologies also facilitates the stacking of different traits in one plant, and it can speed up the overall development process.

For plant breeders and crop scientists, using the full array of breeding approaches is a matter of course, but genetically modified organisms have generated much discussion in the field of politics and society (e.g., Herring 2008). This debate will be covered in a subsequent section, but addressing micronutrient malnutrition is one of the fields where potential benefits of genetically engineered crops can unfold.[6]

The main crops and micronutrients that are targeted in biofortification research have been identified in a review of the literature on biofortification by Stein and Qaim (2009). They found that by far the most frequently named crop is rice, followed by maize and wheat, and then pulses, vegetables and fruits, cassava, sweet potato, sorghum, and model plants. Among the micronutrients, it is iron, vitamin A (including carotenes), and zinc that are referred to most often, followed by selenium, folic acid, calcium, iodine, magnesium, and copper.

For many of these crop-micronutrient combinations, promising results regarding their potential impact on people's nutrition status are reported, based on models, animal trials, or even studies with human subjects.[7] Moreover, first sensory analyses have shown that biofortification is possible without introducing a detectable difference in flavor or consistency (Park et al. 2009).

6 Impact and Cost-Effectiveness of Biofortification

So far the only biofortified crops that have been introduced on a larger scale are orange-fleshed sweet potatoes (OFSP) in sub-Saharan Africa (Low et al. 2007a, 2007b). However, for a number of other crops, ex ante impact assessments and cost-effectiveness analyses have been carried out.[8] These studies have shown that in many cases genetic biofortification promises to be a very cost-effective public health intervention, thus representing a sensible investment of the limited resources that are available for research into agriculture, nutrition, and public health in developing countries. To the author's best knowledge, no such studies have been done yet for biofortification through fertilization.

Most of these studies build on the DALY framework previously described, and more specifically on Stein et al. (2005), who adapted the methodology for the evaluation of iron, zinc, and vitamin A deficiencies. In short, the procedure is the following: First the burden of a deficiency in a given regions is quantified and expressed in the number of DALYs lost, then the consumption of a biofortified crop is simulated (which leads to higher micronutrient intakes). Based on the new (higher) micronutrient intakes, the new (lower) prevalence of the deficiency is derived and used to calculate its new (lower) burden. The difference between the old and new burden, which is expressed in the number of DALYs that can be saved, represents the potential impact of the biofortified crop.

This step of the analyses demonstrates the potential effectiveness of the biofortified crops, which is a necessary condition for a positive evaluation. However, in a world of scarcity, costs also matter, so that superior cost-effectiveness is a sufficient condition. As the World Bank (1993, 61) explains, "Because interventions can differ 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." Similarly, the World

Health Organization confirms that “making best use of resources is vital in developing countries that are struggling to improve public health with limited funds” (Evans et al. 2005, 1133).

To determine the cost-effectiveness of a biofortified crop, its potential impact (measured in DALYs) is divided by the costs that need to be incurred for its development, dissemination, and use. Where appropriate, these costs are shared among several beneficiary regions. The metric that is thus generated is “Dollars per DALY”, which indicates how much it would cost to save one “healthy” life year (DALY) if the given biofortified crop was consumed by the target population. Obviously, the less it costs to save one DALY, the more cost-effective the intervention, and with a given budget more DALYs can be saved. Moreover, because DALYs are not only used for the evaluation of micronutrient malnutrition but for a wide range of negative health outcomes (Figure 2), the results for biofortification can be compared with those for other interventions—to rank and prioritize different programs, for example.

An overview of the biofortification results from the different evaluations is given in Table 1. What can be seen is that results can vary by an order of magnitude between studies; across crops, micronutrients, and countries; and even between different scenarios within a study. One explanation is that these studies are ex ante analyses that rely on different data and assumptions (Figure 3) and are carried out at different levels of aggregation. In particular, the prevalence of the micronutrient deficiency, the size of the target population, the importance of the crop in their diet, the success of biofortification in terms of additional micronutrient content that can be bred into a crop, the expected coverage of the crop, and the current intake gap of the micronutrient all determine the ultimate success of biofortification. Consequently, the less that is known about these parameters, the wider the range of possible results. Filling such knowledge gaps and refining the parameters is part of the ongoing scientific and policy process. Moreover, such diverging results are not limited to analyses of biofortification. In a review of the literature on general micronutrient interventions, Fiedler et al. (2008, 373) found “enormous variation in the estimated costs of these programs due to differences in program structure, delivery systems and a host of country-specific factors, differences in the studies’ objectives, designs and costing methodologies.”

Although sensitivity analyses in many of the biofortification case studies show that results are fairly robust to smaller variations of key parameters, what affects the success of biofortification most is the reach of the biofortified crops. This is probably intuitive: biofortification can have the biggest impact when the crops are consumed in greater quantities by deficient populations in many countries (or in countries with big populations like India or Brazil). In such cases, economies of scale can be exploited, making biofortification a cost-effective intervention. This is not to say that biofortified crops cannot also benefit smaller groups of beneficiaries who suffer from micronutrient malnutrition, but to offset the breeding and dissemination costs—and thus to make biofortification an economically viable intervention—achieving maximum coverage is paramount.

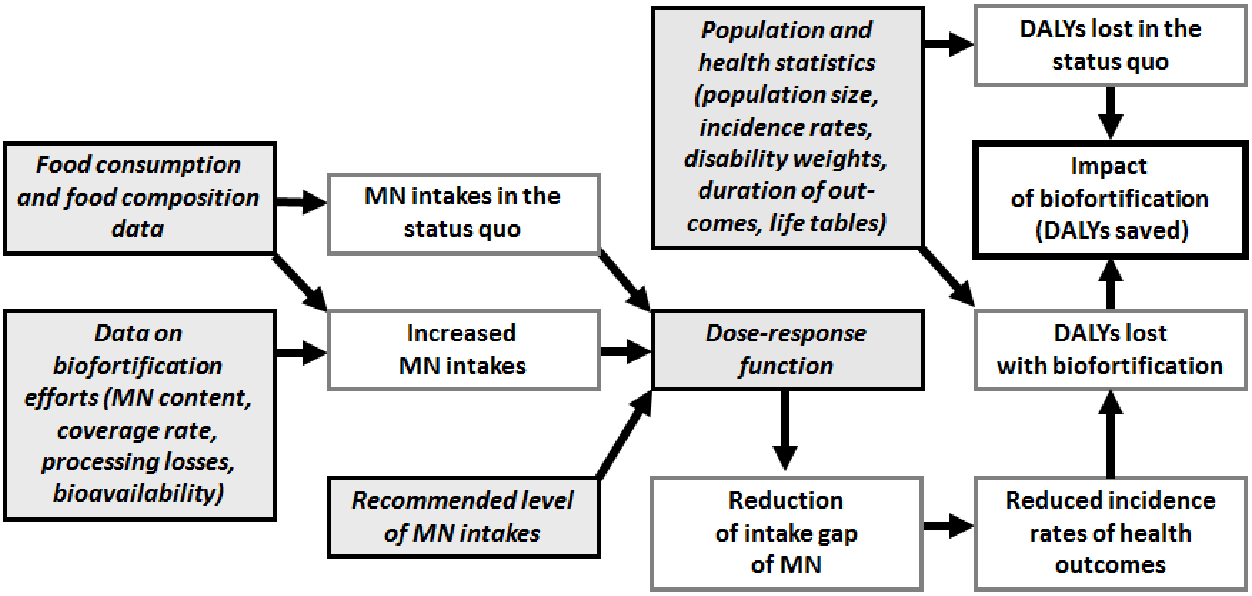
This points to several implications. First, only biofortification of crops that are eaten by a large number of deficient people is likely to be cost-effective, so that knowing the dietary patterns of the malnourished in target regions is important before biofortification efforts are started. Second, once elite lines with micronutrient-rich traits are developed, the germplasm should be disseminated widely across countries to facilitate further development and adaptive breeding into popular existing and promising new varieties. Finally, once biofortified varieties are adapted and introduced, their large-scale dissemination at national levels should be a top priority.

Table 1. Impact and cost-effectiveness of biofortified crops

	Reduction of burden of disease		Cost per DALY saved	
	Optimistic	*Pessimistic*	*Optimistic*	*Pessimistic*
Iron biofortification				
Wheat				
India [a]	39%	7%	$1	$10
India [b]	26%	7%	<$1	$9
Pakistan [a]	28%	6%	$3	$13
Rice				
India [a]	15%	5%	$3	$17
India [b]	38%	12%	<$1	$4
Bangladesh [a]	21%	8%	$5	$18
Philippines [a]	11%	4%	$55	$234
Northeast Brazil [e]	76%	39%	$2	$10
Beans				
Northeast Brazil [a]	36%	9%	$20	$134
Northeast Brazil [e]	99%	93%	$2	$3
Honduras [a]	22%	4%	$66	$402
Nicaragua [a]	16%	3%	$65	$439
Zinc biofortification				
Wheat				
India [a]	48%	9%	$1	$11
India [c]	12%	2%	$2	$39
Pakistan [a]	33%	5%	$2	$18
Rice				
India [a]	56%	20%	$1	$6
India [c]	41%	18%	<$1	$4
Bangladesh [a]	33%	17%	$2	$7
Philippines [a]	43%	13%	$12	$55
Honduras [e]	19%	10%	$35	$165
Nicaragua [e]	20%	10%	$73	$337
Beans				
Northeast Brazil [a]	20%	5%	$153	$1900
Honduras [a]	15%	3%	$160	$1494
Honduras [e]	17%	13%	$46	$81
Nicaragua [a]	11%	2%	$576	$5940
Nicaragua [e]	14%	11%	$116	$225
Maize				
Honduras [e]	17%	2%	$32	$835
Nicaragua [e]	22%	6%	$55	$604
Provitamin A biofortification				
Rice				
India [d]	59%	9%	$3	$19
Philippines [f]	32%	6%	$18	$102
Bangladesh [g]		30%		$25
Sweet potato				
Uganda [a]	64%	38%	$9	$30
Uganda [g]		38%		$2
Cassava				
DR Congo [a]	32%	3%	$8	$124
Nigeria [a]	28%	3%	$8	$137
Northeast Brazil [a]	19%	4%	$127	$1006
Haiti [e]	33%	8%	$10	$87
Maize				
Kenya [a]	32%	8%	$18	$113
Ethiopia [a]	17%	1%	$11	$289
Mexico [e]	81%	<1%	$18	$1408

Sources: [a] Meenakshi et al. (2010), [b] Stein, Meenakshi, et al. (2008), [c] Stein et al. (2007), [d] Stein, Sachdev, and Qaim (2008), [e] Stein (2010), [f] Zimmermann and Qaim (2004), [g] Sandler (2005).
Notes: DR = Democratic Republic.

Figure 3: Parameters entering the DALY calculation for micronutrient deficiencies



Source: Stein (2006) and Meenakshi et al. (2010). *Notes*: Grey shaded boxes with text in italics indicate where (potentially different) data or assumptions enter the DALYs calculation; MN = micronutrient.

Where there are potential acceptance issues (e.g., because of a more intensive color of the crops due to a higher carotene content, or because the crops were developed through genetic engineering), dissemination efforts may require additional campaigns to increase consumer awareness and trust. For instance, in the projection of the cost-effectiveness of Golden Rice in India, in the high-impact scenario the costs for dissemination activities were assumed to be twice as high as those in the low-impact scenario. This reflected more costly dissemination efforts that were assumed to lead to higher coverage rates and ultimately to a much larger impact, thereby easily compensating the additional costs (Stein, Sachdev, and Qaim 2008). In this context it also becomes clear that political backing and the support of opinion leaders is crucial for the success of such crops. Especially when biofortification is done through genetic engineering, this may require supportive communication activities (see below).

In summary, what all studies show is that appropriately chosen target crops that reach a sufficient number of beneficiaries can have a substantial positive impact on micronutrient deficiencies and considerably reduce their burden of disease in the target countries. In general, biofortification promises to be a very cost-effective micronutrient intervention that in most cases is more efficient than other measures; in the other cases its cost-effectiveness is in about the same range as alternative interventions. What the studies discussed here have not considered, though, is the current impact of alternative interventions. Calculating the impact of biofortified crops in the presence of other micronutrient interventions may indicate only limited benefits, whereas the introduction of biofortified crops may in fact allow scaling back more costly programs.

Another approach to quantifying the potential impact of biofortification was taken by Anderson and colleagues) and (see Anderson 2010; Anderson and Jackson 2005; Anderson, Jackson, and Nielsen 2005), who used a global economic model to simulate the benefits of Golden Rice at a more aggregated level by assuming a productivity increase of unskilled labor of 0.5 percent. According to their calculations, Golden Rice could add the equivalent of over US$3 billion per year to the welfare of developing countries. Assuming the consumption of biofortified rice and wheat in sub-Saharan Africa and a related increase in the productivity of unskilled labor of 2 percent, they even project annual welfare gains of over US$3.5 billion.

7 Biofortification Programs

As noted above, so far the only biofortified crops that have been introduced on a larger scale are OFSP in sub-Saharan Africa, with cassava and maize rich in carotenes as well as high-iron pearl millet beans being set for release in 2012 in Nigeria, Zambia, India ,and Rwanda (HarvestPlus 2011b, 2011c). All crops were developed in the context of the HarvestPlus Challenge Program of the Consultative Group for International Agricultural Research (HarvestPlus 2011a, 2011b). HarvestPlus has identified seven crops that are consumed by the poor and malnourished in Asia and Africa, namely beans, cassava, maize, pearl millet, rice, sweet potato, and wheat. These crops are bred for higher levels of iron, zinc, and provitamin A. In its biofortification efforts, HarvestPlus relies, for most of the work, on traditional plant breeding, mainly for reasons of consumer acceptance and to avoid regulatory problems (see next section); the work in Latin America is carried out in collaboration with AgroSalud (2011).

Another group of projects is funded by the Grand Challenges in Global Health program of the Bill & Melinda Gates Foundation. These projects rely on genetic engineering, not least because for some crop-micronutrient combinations, biofortification is not possible otherwise (see Bill & Melinda Gates Foundation 2011a, 2011b). The crops targeted in these projects are rice, cassava, sorghum, and bananas, which are bred for higher contents of iron, zinc, provitamin A, and vitamin E, but also protein. These projects are the Golden Rice Project (Golden Rice Project 2011, IRRI 2011a), the BioCassava Plus Project (Sayre et al. 2011, BioCassava 2011), the Africa Biofortified Sorghum Project (ABS 2010) and the Better Bananas for Africa Project (QUT 2011). It is foreseen that Golden Rice will be released to farmers for the first time in 2013 in the Philippines (IRRI 2011a). The BioCassava Plus Project received funding for its second Phase in April 2011 and will not be available to farmers before 2016 (BioCassava 2011); the other Grand Challenges crops are further away from dissemination.

In addition to these bigger projects there is also the INSTAPA (2011) project, which focuses, inter alia, on the potential of biofortified millet, sorghum, maize, and cassava in complementary food for young children in sub-Saharan Africa to prevent deficiencies of iron, zinc, and vitamin A. There are also two smaller projects on biofortification of cereals through fertilization (with zinc, selenium, and calcium) at the University of Nottingham and Sabanci University in Istanbul (Bagels 2008, HarvestZinc 2011).

8 Political Controversies

So far in this chapter, biofortified crops were differentiated into conventionally bred and genetically engineered ones. This was for a reason: While plant breeders tend to view genetic engineering and other approaches of modern biotechnology simply as one tool in their toolbox, and while the scientific consensus is that genetic engineering per se is not more risky than conventional breeding, in parts of society genetic engineering is much more of a controversial issue (e.g., *Economist* 2011, *New York Times* 2011, *Guardian* 2011).[9]

To what extent genetically modified (GM) crops are indeed a matter of concern for the greater public is not fully established, since consumer surveys are relatively scarce, and because they are methodologically so diverse as to preclude generalizations (Smale et al. 2009). In developed countries, consumer acceptance studies indicate that consumers have a greater willingness to pay for food products that are free of GM crops, but results vary between countries, consumers, their knowledge about genetic engineering, and the type of food or the GM crop (Qaim 2009). Yet, even in Europe, where acceptance of GM crops is usually considered to be low, only 8 percent of the respondents in the European Commission's "Eurobarometer" survey stated that they would be concerned about GM foods when asked an open question about food-related risks (European Commission 2010). Probing the real-life behavior of UK tourists to North America (where "GM food" is ubiquitous) showed that only 15 percent of respondents made attempts to avoid GM food (Moses 2008).

Still, even if large parts of society are probably indifferent about GM crops, there are vociferous opponents whose opinions are often given a disproportionate reception in the general media (e.g., Sample 2011, BBC 2011, Reville 2011). Generally, opposition to genetic engineering can be traced back to three broad groups of reasons: "risks," "social aspects," and "metaphysics" (Dürnberger 2011). Potential risks of new GM crops for human health or the environment are routinely assessed in the authorization process before the crops are commercialized. Hence using such alleged risks as justification for opposing safety-assessed and approved GM crops is more likely a sign of a deeper distrust of science or of government institutions and regulatory and political processes in general.

Often opposition to GM crops is also based on socioeconomic arguments regarding the alleged market power of agri-biotech companies, the patenting of GM crops, a feared control of the food chain through private corporations, or an expected structural change in rural areas due to technological change. Hence these arguments rather reflect political attitudes critical of market systems, "globalization," or technical progress, and GM crops are simply targeted as a convenient proxy. This view may also explain the inconsistencies in some arguments. For instance, conventional crops can also be patented, the market power of agri-biotech companies is probably much more limited than that of other players in the food chain (e.g., GM potatoes were taken off the market in the United States due to pressure from the downstream food industry), and GM crops are not exclusive to the private sector and industrial agriculture, since they can—and indeed are—also developed by public or humanitarian entities for use by small-scale farmers.

Finally, GM crops are also opposed because of metaphysical considerations, including respect for "nature." If these considerations take the form of categorical arguments, they generally preclude any compromise on the issue. For instance, if genetic engineering is seen as a violation of the sacredness of nature, potential benefits of GM crops can hardly compensate for what is perceived to be a fundamental mistake. Nevertheless, to be accepted as sensible arguments, these reasons need to be validated for consistency and rationality. This can be done by analyzing whether the arguments are also used to oppose biotechnology if used for other purposes, or if other technologies are opposed if used for the same purposes (Dürnberger 2011). In the case of GM crops, for instance, such metaphysical arguments are rarely used to oppose the application of modern biotechnology in the field of pharmaceutics and diagnostics, and neither are other breeding technologies opposed that are used to develop crops with novel traits. Hence, given this inconsistency, it is questionable whether such arguments are used out of genuine opposition to GM crops, or, again, whether they simply exploit GM crops to score points in a larger debate.

In this context biofortification has also come under fire, irrespective of any potential benefits it may bring, simply because—via Golden Rice—it can be linked to genetic engineering.[10] Most commonly Golden Rice is simply disparaged as a "Trojan horse" of the biotech lobby (Potrykus 2001), suggesting that the latter wants to use the social appeal of this project to make GM crops in general more acceptable. This ignores the fact that Golden Rice was conceived by public scientists and funded as a humanitarian project (Toenniessen 2009).

To further rationalize a rejection of Golden Rice, its effectiveness is often challenged by alleging that an impossible amount of rice would have to be consumed to prevent vitamin A deficiency. (Or the reverse, that too much vitamin A could be consumed and have a toxic effect.) Indeed, the first line of Golden Rice contained only limited amounts of carotene (provitamin A), but it merely represented a proof-of-concept study that showed that rice can be engineered to express carotenes in the endosperm (Enserink 2008). And while using data from such early R&D stages to discard a technology may be disingenuous in the first place, since peer-reviewed studies showed early on that even small amounts of carotene could have a beneficial effect and make Golden Rice an economic intervention (Zimmermann and Qaim 2004). Stein (2006) showed more explicitly that the activists' calculations were biased and unfounded. Moreover, subsequent research succeeded in increasing the levels of carotene in Golden Rice (Paine et al. 2005), and new, more detailed calculations confirmed the potential impact and cost-effectiveness of Golden Rice (Stein, Sachdev, and Qaim 2006). Over time new research also answered other questions, including those regarding the bioavailability of the carotenes in Golden Rice (Tang et al. 2009).

Further, detractors also claim that farmers will have to pay royalties on the seeds or cannot save them for resowing. Yet, also in this case, the issue had been solved early on, paving the way for the humanitarian use of Golden Rice and its dissemination to farmers in developing countries free of added charges (Potrykus 2001). Finally, the need for a new micronutrient intervention is often questioned by maintaining that current interventions can address micronutrient deficiencies. As discussed above, biofortification had been developed exactly to counter the shortcomings and weaknesses of existing interventions in eradicating micronutrient malnutrition.

As in the wider discussion of GM crops, in the case of Golden Rice it also seems that many opponents are not concerned with factual information or the validity and consistency of their arguments but, in opposing Golden Rice, rather follow another, wider agenda (Potrykus 2001). This is not to say that all conditions for the distribution of Golden Rice to farmers have already been fulfilled—not least, the food safety and biosafety of Golden Rice still need to be formally established, which is fully acknowledged by the developers (IRRI 2011b). Steps like the final safety assessment of a new product prior to its commercialization form part of any product development. Criticizing the lack of such an assessment while the rice is still in the R&D phase is not sincere.

Another facet of the controversy surrounding GM crops is that current regulations for their approval have become so demanding that only the biggest companies have the know-how and the financial standing to carry out the safety tests and compile the required dossiers—and that even for them doing so only pays off for major commercial crops. This clearly hampers the commercialization of humanitarian or other minor GM crops (Enserink 2008; Miller and Bradford 2010). Likewise, the time needed for these processes has led to delays in advancing the development of Golden Rice and other GM crops with product quality traits (Enserink 2008; Graff et al. 2009a; Potrykus 2010a, 2010b). This created a self-defeating situation: opponents of Golden Rice criticize that so far little has come out of the research, while, not least due to their opposition to GM crops, research on GM crops can only advance slowly.

In this context a main criticism of current regulation is the inconsistency with which GM crops are treated vis-à-vis crops produced through other breeding methods (Enserink 2008; Potrykus 2010a, 2010b; Fedoroff 2011). Whether this unequal treatment is likely to change any time soon is questionable, given that analyses of the underlying political economy indicate that "the sum of all interests involved ensures that subsistence farmers are systematically denied access to agricultural biotechnology" (Apel 2010, 635). For various reasons many stakeholders—whether the agri-biotech industry, agrochemical companies, the organic food industry, EU farmers, activist groups, Western consumers, or politicians in both developed and developing countries—have a self-interest in maintaining a strict regulatory framework even if the easier development of more and new GM crops would increase global welfare (Graff et al. 2009b).

9 Conclusions

Next to outright hunger and overweight, micronutrient deficiencies represent a third aspect of the global malnutrition problem. The lack of essential vitamins and minerals in people's diets may be less apparent at first sight, which is why it is also called "hidden hunger," but it is one of the leading contributors to the global burden of disease. While micronutrient malnutrition has been recognized as a public health problem, and interventions such as supplementation or fortification are being implemented with varying success in developing countries, progress has nevertheless been limited.

In this context a new approach has been developed that aims at complementing these existing interventions: staple crops are bred for higher contents of vitamins and minerals. This is called biofortification. The main advantage of this approach is its focus on rural areas, which are not as easily reached by conventional programs. Moreover, because these crops have to be developed only once, their widespread and continuous cultivation and consumption allows exploiting economies of scale in reaping the nutritional benefits. This makes biofortification potentially a very cost-effective intervention.

So far only very few biofortified crops have reached the stage of dissemination. Apart from orange-fleshed sweet potatoes (OFSP), their potential has not yet been confirmed in real-world settings. However, a substantial body of studies shows that increasing the micronutrient content in crops is possible, whether through breeding or agronomic approaches, and that the accumulated micronutrients have the potential to improve the micronutrient status of human subjects. Moreover, biofortifying crops does not affect relevant agronomic properties, which could reduce their acceptability to farmers. Perceptible changes to the crops, which may affect consumer acceptance, occur only when they are bred for higher carotene content, in which case the crops acquire a darker yellow or orange color. To ensure widespread acceptance of such crops, measures to raise awareness of micronutrient malnutrition and the related benefits of biofortification may be required.

Meanwhile, economic evaluations that simulated the consumption of biofortified crops have confirmed that if these crops can be targeted at large enough populations where vitamin and mineral deficiencies are prevalent, they can indeed represent very cost-effective public health interventions. However, in cases where biofortification is done through genetic engineering, the crops are bound to face resistance from activists that are opposed to the use of modern biotechnology in agriculture, even if it supports a humanitarian goal.

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Endnotes

[1] However, the idea as such, of making a plant produce an essential micronutrient, had been around at least since 1984, when the idea of developing provitamin A-rich “yellow endosperm” rice had been taken up by the Rockefeller Foundation (Toenniessen 2009), even if the actual proof of concept for such a genetically engineered “golden” rice, as it became known, could only be delivered in 2000 (Ye et al. 2000). And the idea of using plant breeding to improve the general nutrient content of staple crops has been around for decades, as evidenced by the first efforts to improve the protein content in maize in the latter part of the 19th century (Vasal 1999).

[2] For each condition, “disability weights” are defined that range from close to 1 for health outcomes that limit functioning severely to weights close to 0 for outcomes that affect overall health only marginally. Multiplying the time spent with a condition with its disability weight then yields the corresponding number of DALYs that are lost.

[3] For literature discussing the adoption of biofortified crops, see Hagenimana and Low (2000); Chong (2003); Mazuze (2007); Pray et al. (2007); Wolson (2007); Ortiz-Monasterio et al. (2007); and Muzhingi et al. (2008).

[4] For literature discussing consumer acceptance of biofortified crops, see Nestel et al. (2006); Hagenimana and Low (2000); Low et al. (2007a); Stevens and Winter-Nelson (2008); González et al. (2009); Chowdhury et al. (2009); and De Steur et al. (2010).

[5] For references to primary research supporting the possibility of biofortification, see Welch and Graham (2005); Welch et al. (2005); White and Broadley (2005); Lyons et al. (2005); Genc et al. (2005); Cichy et al. (2005); Broadley et al. (2006); Rébeillé et al. (2006); Dai et al. (2006); Ssemakula and Dixon (2007); White and Broadley (2007); Hawkesford und Zhao (2007); Shi et al. (2008); Harjes et al. (2008); Wissuwa (2008); Thavarajah et al. (2008); Cakmak (2008); Ríos et al. (2008); Jin (2008); White und Broadley (2009); Thavarajah et al. (2009); Salas et al. (2009); Cichy et al. (2009); Bóna et al. (2009); Šimić et al. (2009); Chen et al. (2009); Waters and Pedersen (2009); Khoshgoftarmanesh et al. (2009); Broadley et al. (2009a); Broadley et al. (2009b); Zhao et al. (2009); Phattarakul et al. (2009); Cakmak (2009); and Bai et al. (2011).

[6] For literature discussing the role of biotechnology in biofortification, see Ye et al. (2000); Scott et al. (2000); Paine et al. (2005); Storozhenko et al. (2005); Basset et al. (2005); Stupak et al. (2006); Sautter et al. (2006); Storozhenko et al. (2007); Zhu et al. (2007); Mayer et al. (2008); Connolly (2008); Aluru et al. (2008); Bekaert et al. (2008); Naqvi et al. (2009); Wirth et al. (2009); and Hirschi (2009).

[7] For references to primary research indicating an such impact, see Howe and Tanumihardjo (2006); Ariza-Nieto et al. (2006); Howe (2007); Nyhus et al. (2008); Tako et al. (2008); Denova-Gutiérrez et al. (2008); Mills et al. (2008); and Davis et al. (2008) for results from models and animal trials; see Haas et al. (2005); Low et al. (2007b); Tang et al. (2009); Rosado et al. (2009); and Wu et al. (2009) for studies with humans.

[8] For such analyses, see Dawe et al. (2002); Zimmermann and Qaim (2004); Sandler (2005); Anderson and Jackson 2005; Anderson, Jackson, and Nielsen 2005); Stein (2006); Stein et al. (2006); Javelosa et al. (2006); Stein et al. (2007); Qaim et al. (2007); Ma et al. (2007); Stein, Meenakshi et al. (2008); Stein, Sachdev, and Qaim (2008); Meenakshi (2008); Anderson (2010); Meenakshi et al. (2010); Stein (2010).

[9] Caveat: Given that this discussion is largely taking place outside the academic literature, this section is also more of a subjective presentation of the topic than a fully referenced review, thereby also drawing on the authors' personal experiences from years of work in the field of agricultural biotechnology. Factual information on genetic engineering can be obtained from various reviews and FAQs on GM crops or from scientific outreach websites (e.g. Lemaux 2008, 2009; WHO 2011a; Chassy and Tribe 2010; PRRI 2011; GMO Compass 2011); no links are provided to websites that disseminate nonfactual information to avoid implicit endorsement.

[10] For instance, this categorical rejection of Golden Rice by some opponents became clear when the—then new and untried—executive director of Greenpeace, Kumi Naidoo, stated in an interview that he would like to have another look at the organization's position on Golden Rice to ensure that it is not passing up any new, good developments (Von Traufetter 2009). Within a day Greenpeace published a retraction in which Naidoo provided “guidance” on the interpretation of his statement, concluding that Golden Rice can never be an answer.