

Genetically modified rice with health benefits as a means to reduce micronutrient malnutrition: Global status, consumer preferences and potential health impacts of rice biofortification

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Summary

Micronutrient malnutrition, characterized by insufficient intake levels of vitamins and minerals, is a major public health problem that affects about 2 billion people worldwide. In order to reduce the burden of this ‘hidden hunger’, biofortification is more and more advocated as an alternative to the current micronutrient interventions. Through the enhancement of the micronutrient level of staple crops, it could address micronutrient malnutrition where the need is highest. Because staple crops are characterized by low micronutrient concentrations, genetic breeding techniques are often applied to increase specific vitamin levels, such as folate and pro-vitamin A. This study sheds a light on the global status of micronutrient malnutrition, biofortification and GM biofortified rice as both a GM food product with health benefits and a micronutrient intervention. Thereby, key consumer preference studies and cost-effectiveness analyses on Folate Biofortified Rice and Golden Rice are presented. Support is found for GM biofortified rice as a well-accepted GM food crop and a highly cost-effective health intervention.

Key words: burden of disease; cost-effectiveness; rice biofortification; Folate Biofortified Rice; GM rice with health benefits; Golden Rice; micronutrient malnutrition; willingness-to-pay.

Abbreviations: DALY, disability-adjusted life year; GBD, Global Burden of Disease; GM, genetically modified.

I. Introduction

Within the scope of crop improvement, biofortification of rice is more and more advocated as a tool to improve human nutrition. By enhancing the micronutrient level of the worlds' most consumed staple crop, micronutrient malnutrition could be addressed where the need is highest. As rice varieties are mainly characterized by a low vitamin and mineral content, agricultural biotechnology is applied to increase specific micronutrient levels in rice, such as folate and pro-vitamin A (beta-carotene). This chapter describes the history and trends in biofortification and GM rice with health benefits in particular. In spite of the potential consumer benefits of this new generation of GM crops, the use of biotechnology in food products remains controversial. As none of these crops are available at the marketplace, they were subject of various ex-ante evaluation studies in order to examine the consumer demand, the potential health benefits and the cost-effectiveness of their introduction. By reviewing the current state-of-the-art, this study sheds a light on the potential of GM biofortified rice as both a GM food product with health benefits and an alternative policy intervention to tackle micronutrient deficiencies.

As a starting point, the global burden of micronutrient malnutrition and the main micronutrient deficiencies is described (section II). In the following two sections, (GM) biofortification is described within the framework of health interventions to address micronutrient malnutrition (section III) and within the scope of agricultural crop improvement (section IV). Next, the global status of the development and commercialization of (GM) biofortified crops and GM rice (section V) as well as GM biofortified rice (section VI) is presented. While the section IV looks at the amount of published research on GM food, GM rice, biofortification and Golden Rice, section VIII and IX summarize the key research findings on the consumer preferences for, and the potential cost-effectiveness of GM

biofortified rice. These two research topics are crucial to ex-ante evaluate micronutrient interventions and GM foods. Finally, some key challenges (section X) and conclusions are formulated (section XI).

II. What is at stake? The global burden of micronutrient malnutrition

Micronutrient malnutrition^{a1} is defined by a chronic lack of micronutrients, i.e. essential vitamins and minerals that are needed in small quantities, and has a large impact on global health and (indirectly) hinders social and economic prosperity, e.g. through productivity losses, cognitive impairment and soaring health care costs^{2,3}. Malnutrition is considered one of the principal causes of morbidity and mortality among the poor⁴.

Most people are not aware of their lack of micronutrients, due to the subclinical character of such deficiencies, and because the underlying causes and health functions of different micronutrients are neglected, poorly addressed, or still undiscovered. Therefore, this form of malnutrition is often referred to as the ‘hidden hunger’. Insufficient intake of micronutrients reflects a lack of dietary quality and especially strikes poor people living in rural, less developed areas, because these populations are largely dependent on staple crops (e.g. rice, maize and wheat), which are known to contain little micronutrients²⁻⁵. As a consequence, multiple micronutrient deficiency is the rule rather than the exception. Half of malnourished children, for instance, are deficient on several vital micronutrients⁵.

^aThere is a clear difference between under- and malnutrition in that the former is a specific type of the latter. Whereas undernutrition refers to an inadequate intake of specific nutrients, malnutrition covers both under and over-nutrition, such as obesity but also micronutrient deficiency. In the scope of micronutrient malnutrition, “malnutrition” generally refers to undernutrition and, thus, micronutrient deficiencies. Therefore, this paper will use the term ‘micronutrient malnutrition’ to define all vitamin and mineral deficiencies.

Despite an increasing number of local and global programs to control micronutrient malnutrition, especially the main micronutrient deficiencies (Vitamin A, iodine, zinc and iron)⁶, it remains a major public health problem, in particular for children and (pregnant) women. According to global estimates of micronutrient malnutrition, nearly two billion people fail to achieve the recommended nutrient intake levels, mainly populations from low-income countries². As a consequence, an annual number of 10.3 billion US\$ is still required to successfully fight the global burden of malnutrition, of which at least 1.5 billion US\$ is needed to adequately combat micronutrient deficiencies⁷. Its magnitude differs when looking at specific micronutrient deficiencies and different data sources. The number of people with insufficient vitamin A intake, for example, varies between 140⁸, 190⁹ and 254 million^{8, 10}. Iodine and zinc deficiency figures show that a total estimate of nearly 2 billion people is at risk^{3, 11, 12}. Iron deficiency is another widespread type of micronutrient malnutrition, with 1.7 billion people below the recommended intake levels^{3, 11}. However, the public health significance of a micronutrient deficiency must be evaluated by looking beyond its prevalence, i.e. by estimating its health impacts.

Table 1 lists some key figures regarding the devastating health and socio-economic impact of global micronutrient malnutrition. Its large importance is underpinned by its share in the global burden of disease (GBD). Together, vitamin A, iron, zinc and iodine deficiencies account for 4 % of the GBD in 2004. Regarding regional malnutrition, Southeast Asia is found to be the most problematic region, followed by Africa¹³. However, not all micronutrient deficiencies are included in the current burden analyses of the World Health Organization (WHO), among which folate deficiency. Rough estimations of the global burden of this type of vitamin deficiency, i.e. 4.8 million DALYs per year¹⁴, show that the contribution of

micronutrient malnutrition to the GBD is underestimated. According to the Micronutrient Initiative¹⁵, the total share in the GBD is expected to be around 10 %.

Currently, public health programs are primarily targeted towards vitamin A, iodine, zinc and iron deficiency^{7, 16, 17}, which are perceived as the four most important types of micronutrient malnutrition. Because children below 5 years mainly suffer from such deficiencies, it is not surprising that the nutritional targets of the Millennium Development Goals (MDG)¹⁸ and the nutritional challenge of the 2008 Copenhagen Consensus¹⁹ focus on this age group. In the framework of MDG 1 (eradicate extreme poverty and hunger), for instance, the United Nations strives to halve the prevalence of underweight children, i.e. one of the proxy indicators of poor nutrition, between 1990 and 2015^{20, 21}. Furthermore, malnutrition also needs to be addressed in order to reduce child mortality (MDG 4), maternal health (MDG 5) and, indirectly, other major diseases (MDG 6), and to help achieve the goals on education (MDG 2) and gender equality (MDG 3)¹¹.

[Insert Table 1 here]

III. GM biofortification as a novel micronutrient intervention

There are currently four main strategies or (potential) policy interventions to address micronutrient malnutrition or particular vitamin or mineral deficiencies: pharmaceutical supplementation, food fortification, dietary diversification and biofortification (see Table 2). Pharmaceutical supplementation refers to micronutrient programs that distribute (multi-) micronutrient supplements for free or which promote the use of supplements. Key supplementation programs are based upon iron, zinc, vitamin A and/or folic acid

supplementation. The latter aims to reduce folate deficiency through increased consumption of folic acid, i.e. the synthetic form of folate. Industrial fortification refers to the insertion of micronutrients in staple crops, like rice and wheat, which takes place during flour milling. Dietary diversification is considered the most sustainable intervention and is targeted towards an increased intake of micronutrient-rich foods through nutrition education, promotion of diverse diets, improved access to locally produced foods rich in vital micronutrients. Although one could opt to address a particular micronutrient intervention through diversifying food habits, such as the promotion of green vegetables and citrus fruits to elevate folate intake levels, the ultimate goal of diversification strategies is usually to improve the dietary habits as whole, which encompasses a multi-micronutrient approach.

Biofortification is considered a novel strategy to combat the ‘hidden hunger’, by which the nutritional content of staple crops is enhanced. By sharing the advantages of fortification (e.g. wide coverage) and addressing the limitations of supplementation (e.g. short term strategy, limited coverage, compliance of taking pills), it is intended to be a pro-rural and pro-poor health intervention (see Table 2). According to Welch³⁵, agricultural approaches are a prerequisite to sustainably control micronutrient malnutrition. Biofortification is considered an agriculture/food based approach as it uses the regular food chain and goes beyond fortification, because the crops are fortifying themselves^{36, 37}. This general definition of biofortification does not include agronomic biofortification, by which mineral contents are enhanced through the application of fertilizers³⁸. Other biofortification strategies focus on the factors that increase the bioavailability of micronutrients rather than enhancing the production of micronutrients³⁹. It is also important to note that also non-staple crops could be biofortified. A more exhaustive overview of biofortified staple and non-staple products, including

strawberries (vitamin C), maize and canola (vitamin E), potatoes and mustard (beta-carotene), carrots (calcium), lettuce (iron) is available in Hirschi⁴⁰ and Johns and Eyzaguirre³⁷.

Contrary to dietary diversification and supplementation, biofortification uses staple crops as its food vehicle, by which behavioral changes are unlikely to be required. As a consequence, biofortification is self-targeting: as poor malnourished people mainly rely on staple crops, the groups at risk that need to benefit the most from the biofortified crops are addressed⁴¹. In that way, biofortification can be a complementary policy intervention by fighting micronutrient malnutrition where other interventions fail to do so. First of all, unlike food fortification or pharmaceutical supplementation, biofortification does not rely on an (centralized) industrial food processing sector or accessible public health infrastructures. Although food fortification is often promoted as the primary option to reduce micronutrient malnutrition⁴², the key target group of micronutrient interventions (i.e. poor, rural populations) rarely consumes processed foods suitable for fortification⁴³. In addition, supplementation programs are often less successful on the long term^{44, 45}. For example, folic acid supplementation programs in China⁴⁶, Europe⁴⁷⁻⁴⁹ and the United States⁵⁰ were not sustainable once the program finished, partly due to poor compliance and obedience to take folic acid supplements (correctly)⁵¹. Second, given the technical and practical difficulties it will be hard to successfully implement fortified rice, like folic acid fortified rice⁵², in developing malnourished regions. Third, biofortification uses staple crops as its food vehicle and, therefore, can easily target the micronutrient deficient subgroups, without the need to administer pills or to promote the consumption of, generally more expensive, micronutrient-rich foods. Furthermore, industrial fortified foods and supplements are often only available in cities and hence cannot reach the poor rural populations. Fourth, possible negative side effects of food fortification, such as the

relation between folic acid fortification and masking Vitamin B₁₂ deficiency or an increased risk of colorectal cancer, are less likely to occur with biofortification⁵³.

Due to the relatively low costs of biofortified crops, e.g. a one-time investment in R&D and the ability of farmers to reproduce their biofortified crop seeds, the cost-effectiveness of biofortified crops is often argued as one of the main arguments in favor of this strategy^{36, 41, 54}.

Whereas supplementation and fortification were the two key strategies to control micronutrient malnutrition in the past, biofortification receives more and more attention².

During the 2008 Copenhagen Consensus, where a panel of economists evaluated the top priorities to counter the world biggest challenges, biofortification was placed fifth⁵⁵.

Notwithstanding the large potential of single biofortified crops, one could argue that the large prevalence of multiple micronutrient deficiencies and the generally low micronutrient contents of rice and other staple crops require a combined biofortification strategy. In other words, there is a need to increase the intake of different micronutrients simultaneously through nutritionally complete crops. This is where multi-biofortification enters the public health debate. By enhancing different vitamins and minerals, through conventional or transgenic technologies, multi-biofortification could address micronutrient malnutrition more adequately and efficiently.

In spite of several ongoing initiatives that attempt to develop multi-biofortified crops, especially those that were or are supported by the Bill & Melinda Gates Foundation under the Grand Challenges in Global Health Initiative, such as rice, sorghum, cassava and banana^{56, 57}, evidence of a developed staple crop which stacks different nutrient traits is scarce. Recently, Naqvi et al.⁵⁸ published the development of the first transgenic multi-biofortified crop, i.e. maize enriched with vitamin A, vitamin C and folate. Such gene stacking applications are already successfully applied and commercialized in the field of 1st generation GM crops,

mainly crops that combine herbicide-tolerance and insect-resistance traits⁵⁹. However, these technologies are still in the research pipeline, and little is known about their potential from a public health, an agricultural and an economics perspective.

Targeting different micronutrient deficiencies at once is a strategy which is also found in other policy interventions, such as pharmaceutical multi-vitamin supplementation, e.g. iron-folic acid multivitamin pills in India⁶⁰ and other Asian countries⁶¹, multi-micronutrient food fortification, e.g. fortifying grain with folic acid, Vitamin B₁₂ and several minerals⁶², and dietary diversification.

Table 2 presents an overview of the key characteristics of the different micronutrient interventions. The common objective of these interventions is primary prevention, i.e. tackling micronutrient deficiencies as a risk factor of various diseases. While the two ‘industry’ based interventions, supplementation and food fortification, aim to reduce micronutrient malnutrition through the enhancement of micronutrient levels in, respectively, supplements (pharmaceutical industry) and staple crops (milling sector), the objective of dietary diversification and biofortification is to increase the natural micronutrient levels.

[Insert Table 2 here]

IV. GM biofortification as a novel approach of crop improvement

Before biofortification, efforts to improve crop content were mainly focusing on agronomic traits, such as increasing yield potential and productivity, drought resistance and pest resistance, which primarily benefit the farmer. Table 3 gives an overview of the main stages of crop improvement. As these developments in agriculture were based on two different

techniques, conventional versus transgenic technology, they marked the Green and Gene Revolution, respectively^{36, 39, 63, 64}. The Green Revolution refers to a broad public sector led transformation of agricultural sectors in developing countries, mainly between the 1960s and 1980s, which focused on developing high yielding staple crop varieties (wheat, rice), promoting the utilization of hybridized seeds, pesticides (insecticides) and fertilizers, and providing agricultural extension in order to reduce food shortages and hunger and stimulate overall development⁶⁵. Nobel Peace Prize winner Norman Borlaug is seen as the founding father of this breakthrough in crop development. In the last decennium of the 20th century, a novel private led agricultural revolution took place, the Gene (biotech) Revolution, which built upon the previous revolution by implementing GM technology in agriculture to improve productivity and, thereby, reduce hunger.

The history of biofortification followed a similar approach, starting with the introduction of conventionally bred nutritionally enriched products in the 2000s (conventional biofortification), and now making progress to commercialize the ‘gene revolution’ in biofortification through private-public partnerships (GM biofortification). What the Green and Gene revolutions meant for agricultural productivity and hunger (food quantity), these biofortification trend hopes to achieve in the field of malnutrition and the ‘hidden hunger’ (food quality). In this respect, one can refer to a shift from producer, input or quantity traits to consumer, output or quality traits⁶⁶. Although an increased micronutrient content is certainly one of the most advanced improved quality trait in crops, also other quality traits can be addressed, like the elimination of allergens, improved taste, texture or other sensory characteristics, and the prolongation of shelf life. Nevertheless, ‘GM biofortified crops’ and ‘GM crops with health benefits’ are treated as synonyms in this study.

Within the scope of crop improvement through GM technology, broadly two product categories can be distinguished: 1st versus 2nd generation GM products. GM biofortified crops belong to the 2nd generation of GM crops, which are primarily designed to benefit the consumer by improving quality traits, among which nutritional properties. The application of GM technology to develop nutrient-dense crops is sometimes referred to as ‘nutritional genomics’⁶⁷. These developments followed the Gene Revolution and its 1st generation of GM products, which dealt with enhanced agronomic traits, such as insect resistance and herbicide tolerance. In other words, the evolution from first to second generation involves a shift from producer-friendly to consumer-friendly genetic modification⁶⁸. An overview of the consumer and farmer benefits of first and second generation GM food products is described in Toenniessen et al.⁶⁹ and Lönnerdal⁷⁰, respectively.

Despite these ‘generation’ differences, future GM crops are more likely to combine improved traits from both the 1st and 2nd generation. In order to make GM biofortified crops attractive to consumers as well as producers, both the health and agronomic benefits have to be addressed. While farmers will be more in favor of adopting biofortified crops when the yield characteristics are beneficial^{12, 71}, multi-biofortification will be more likely accepted and consumed by consumers. In this way, stacking refers to the improvement of different output and input traits.

Next to this tendency, some people argue the need for an ‘evergreen’ revolution, which combines the economic viability of the Green and/or Gene revolution with a need for ecological sustainability, while improving awareness and knowledge⁷². There is also a third generation of GM crops, where products are developed for industrial or pharmaceutical use. Among the examples are vaccines or biodegradable plastics⁷³.

[Insert Table 3 here]

V. The global status of (GM) biofortification and GM rice

Biofortification research was accelerated when the international, multidisciplinary HarvestPlus (Biofortification Challenge) program was launched in 2004 by the Consultative Group on International Agricultural Research (CGIAR) and the International Food Policy Research Institute (IFPRI)^{65, 74}. It became the key project in development and dissemination of biofortified crops, with an emphasis on iron, zinc and vitamin A deficiencies in Africa and Asia. Initially, only conventional biofortified crops were explored, until the development of Golden Rice as the first biofortified staple crop that was genetically engineered to tackle Vitamin A deficiency in 1999^{75, 76}. This was the starting point of the humanitarian HarvestPlus supported Golden Rice project⁷⁷.

While Africa and Asia fall within the scope of HarvestPlus, AgroSalud coordinates the biofortification efforts in Latin America and the Caribbean (LAC), and aims to increase the iron and zinc content of beans, rice, maize, and sweet potatoes, and develops yellow maize and orange-fleshed sweet potato with higher beta-carotene contents^{78, 79}. Between 2007 and 2010, AgroSalud introduced 42 biofortified cultivars in 13 LAC countries⁸⁰. Depending on each country's policy, the seeds are sold at full or subsidized price, or given for free to farmers.

The global status of biofortified staple crops, developed and/or released by HarvestPlus or AgroSalud, is shown in Table 4. To date, only conventionally bred biofortified staple crops, such as vitamin A enriched sweet potatoes, iron biofortified beans and rice, and maize with a higher vitamin B3 content, are released. Also the future releases will be mainly dominated by

conventional breeding techniques, such as vitamin A biofortified cassava and maize, and wheat, rice and beans with higher zinc and iron levels. However, the progress of Golden Rice or vitamin A biofortified rice shows that transgenic biofortified staple crops are in the pipeline of approval. Also other crops, like banana, barley, cowpeas, groundnuts, lentils, pigeon peas, potatoes and sorghum, are expected to become the subject of biofortification³⁶. It is important to note that not all R&D efforts in the field of biofortification are presented. In China, for example, a conventional biofortified zinc enriched wheat crop (“Jingdong 8”) is commercialized, but at a very small-scale. Nevertheless, about 16 Chinese crop varieties/lines are developed, of which 4 have been approved for advanced testing (2011 figures).

[Insert Table 4 here]

The current status and future pipeline of GM biofortified rice, i.e. GM rice with health benefits, is described in Table 5 and Table 6, respectively. When looking at the approval of GM rice events, it is clear that only first generation GM rice crops, such as herbicide tolerant and insect resistant rice, are currently approved for food, feed and cultivation. There are eight different GM rice events listed. The insect resistant GM rice in Iran is the only event that has been commercially cultivated in the past, but is currently not authorized⁸⁴. The targeted GM rice traits are insect resistance, herbicide tolerance and antibiotic resistance. Apart from the Liberty Link rice crops, developed by Bayer Crop Science, all events are approved in only one country (Japan, China and Iran). GM Shanyou 63, as well as LLrice601, LLrice62 and the Iranian event are approved for food, feed as well as cultivation. None of these events are grown or commercialized for food or feed. In other words, GM rice is yet to be commercialized in the world.

Second generation GM rice crops, and GM biofortified rice in particular, are only present in the R&D pipeline. According to the study of Stein and Rodriguez⁸⁴, it is expected that by 2015 more or less than 15 GM events will be cultivated, among which also stacked traits. Especially the Chinese traits are expected to be commercialized in the near future, in line with the recent approval of Bt rice⁸⁵. In the field of GM biofortification, only the vitamin A enriched Golden Rice (1st and 2nd variant) is currently in an advanced development stage.

Since most of the GM rice product in the R&D pipeline are developed by Asian providers for direct use at the domestic market, the number of GM rice events that will be approved and commercialized in the future, are expected to be low. Today, only LLrice62 is submitted for approval in the European Union. Despite the positive evaluation of the European Food Safety Authority, this application is currently not moving forward to a decision in the European Commission, leading to a delay of the potential authorization (EFSA received the application dossier in August 2004). If this and other GM rice events would be approved and introduced only at the Asian marketplace, global trade problems are expected to occur due to the Low Level Presence thresholds for rice imports in the EU.

[Insert Table 5 here]

[Insert Table 6 here]

VI. GM rice crop with health benefits: the case of rice biofortification

In order to successfully tackle micronutrient malnutrition through GM biofortification, one should carefully select the food vehicle for biofortification. In principle, a staple crop like rice, wheat, corn or potato should be selected in order to reach the rural, poor populations who

need to increase their micronutrient intake levels the most. There are several reasons which underpin the focus on rice to reduce micronutrient malnutrition. Rice is not only the most consumed and produced product in the world. It is also known to have low micronutrient contents, such as folate and provitamin A. Furthermore, the selection of rice as the food vehicle for biofortification is in line with the technical considerations of fortification, i.e. using an inexpensive, country-wide staple crop, as postulated by the Asian Development Bank^{17, 87}.

In some cases, it is feasible to increase micronutrient concentrations in rice through conventional breeding techniques, similar to biofortified maize, wheat, beans, cassava⁴¹. This is, for example, true for zinc and iron levels in rice⁸⁸. In other cases, however, the application of conventional plant breeding techniques to enhance the micronutrient content of rice is less (e.g. folate) or not possible (e.g. provitamin A). Even though there is a clear potential for conventional bred folate enriched rice, achieving similar folate improvements as in transgenic techniques will be difficult, because of the low folate levels in natural rice^{89, 90}. Therefore, folate enriched rice in this study is seen as a transgenic biofortified staple crop or 2nd generation GM crop.

Below, the focus will be mainly on two GM biofortified rice crops, namely Folate Biofortified Rice and provitamin A enriched 'Golden Rice'. Three reasons can be cited for this choice. First of all, there are several studies in international peer-reviewed journals which report the reconstitution of the folate^{79, 86, 88} and carotenoid biosynthetic pathway^{75, 91, 92}. Second, while rice with a higher folate content, developed by metabolic engineering, is currently the most advanced folate enriched staple crop^{89, 93}, Golden Rice is the most advanced GM biofortified crop and will be most likely the first to be commercialized (An overview of the typical steps in the development process of transgenic biofortified crops, e.g. efficacy testing, elite event selection and trait integration, is available in Dubock⁹⁴). We further refer to several biotech

studies for a detailed discussion on the technological issues regarding folate biofortification of food plants^{89,95}, including rice⁸¹, wheat⁹⁶ and tomatoes⁹⁷). Third, both GM crops were subject of various consumer studies on acceptance and willingness-to-pay, health impact analyses and cost-effectiveness studies. In addition, the link will be made with multi-biofortification. Here, multi-biofortification of rice is understood as rice enriched with folate, beta-carotene (provitamin A), zinc and iron, in line with De Steur et al.²⁶. Although iron^{98,99} and/or zinc^{100,101} may also be increased through transgenic approaches, and about 43 genes of five protein families are expected to be involved in rice¹⁰², they are not included in this study due to the lack of socio-economic studies on these GM biofortified rice crops.

Table 7 describes the key characteristics of Folate Biofortified Rice and Golden Rice. Taking into account the biotechnology characteristics, such as the elevated levels of folate and provitamin A in rice, the post-harvest losses (e.g. cooking) and the bioavailability, i.e. of the absorption of folate or provitamin A - converted into vitamin A - in the human body, vitamin concentrations after GM biofortification of rice vary between 1.5 µg – 3.0 µg folate per g rice, and 1.0 µg – 6.5 µg provitamin A per g rice, depending on the impact scenario. These micronutrient levels are substantially higher than in regular rice varieties. In the case of Folate Biofortified Rice, the total folate intake level after biofortification is 40 times larger than without biofortification. The amount of GM biofortified rice needed in order to recover from folate and vitamin A deficiency depends on the current rice consumption patterns, and whether these patterns are still maintained when (partially) switching to GM biofortified rice, and on the current (dietary) vitamin intake. The table below demonstrates how much GM biofortified rice a consumer needs to consume in order to achieve the daily recommended nutrient intake level (RNI) of the target group. This refers to a theoretical scenario where a consumer does not consume any vitamins through its diet. In other words, these figures

represent the (GM biofortified) rice consumption threshold to avoid being micronutrient deficient in a situation where only rice could be consumed. In the current situation, i.e. without folate biofortification, a consumer should eat about 5 kg of rice per day in order to reach the RNI for folate, if he/she only depends on rice. When the same consumer eats Folate Biofortified Rice instead, he/she only needs 281 g (pessimistic) to 137 g rice (optimistic) to achieve adequate folate levels. In the case of Golden Rice, it is even not possible to consume vitamin A through a regular rice diet. The two biofortification scenarios demonstrate that between 500 g and 77 g (children under 5 years) and 800 g - 122 g golden rice (pregnant women) is daily needed to exceed the RNI for vitamin A. And even if the biofortified rice consumption should be below these theoretical thresholds, it should lead to positive health impacts, - although a full protection from the health outcomes of these micronutrient deficiencies is then impossible. Nevertheless, one could also argue that transgenic lines with a higher micronutrient content could be developed in order to tackle micronutrient deficiencies in regions with medium or low rice consumption. Storozhenko⁸¹, for example, reported transgenic rice lines with elevated folate levels up to 17 µg per g rice, as compared to an average of 12 µg folate per g rice.

[Insert Table 7 here]

The aforementioned GM biofortified crops are presented as examples of ‘single trait’ biofortification. However, a multi-biofortification approach might be more likely to occur in the future. Such biofortified crops with enhanced micronutrient concentrations can be developed in two ways. In the so-called ‘single insertion’ approach, the targeted micronutrient traits are stacked as one gene construct. A ‘backcrossing’ approach, where all traits are separately developed and combined through backcrossing^{81,93}, is expected to be more costly,

due to high regulatory and financial costs to approve all new events as single traits, as well as the time and financial costs required for the testing and approval of each event¹¹¹. Moreover, micronutrient traits are mainly developed by different research institutes, which makes a single insertion approach the most realistic scenario.

VII. Published research coverage on GM food, GM rice, biofortification and Golden Rice

This section gives a brief overview of the number of publications (2000-2011) in four relevant research domains: GM food, GM rice, biofortification, and Golden Rice. Whereas GM food and (GM or conventional) biofortification are broad food research topics, the topics GM rice and particularly Golden Rice deal with research applied on a specific staple crop. In this way, this exercise aims to summarize the evolution of international peer-reviewed journal publications in these different, but closely related research fields and particularly in the domain of GM rice crops with health benefits. Golden Rice was selected as it is the GM biofortified crop that received most attention, both at research and policy level.

This rudimentary, targeted trend analysis is based on a literature search in the electronic literature database Web of Knowledge. The database search used the following keywords in the topic field: GM food; GM rice; biofortification and Golden Rice. It is important to notice that the selection of publications is based on studies from various research disciplines, like biotechnology and genetic engineering (e.g. R&D), agriculture (e.g. impact analyses), politics (e.g. policy level analysis), marketing (e.g. consumer studies), economics (e.g. cost-effectiveness assessment), and so on. Furthermore, some of the selected studies, for example, did not focus on Golden Rice alone but included it as a case-study, a benchmark exercise or

referred to, or built upon this application as a part of the study. Therefore, the extent to which these studies actually explore GM food or another topic (keyword) varies substantially, by which the total numbers should be interpreted with caution. Nevertheless, as this potential selection bias occurs in each database search, it is possible to benchmark the importance of these GM related fields in scientific literature. Stated differently, one should evaluate the trends, rather than the absolute figures.

The results in Figure 1 show that the number of publications in all four research domains increased in the last decade. The total research coverage between 2000 and 2011 amounts, from small to large, Golden Rice (142), GM rice (362), biofortification (459) and GM food (1631). GM food research publications almost doubled since 2000. The other topics were still marginal in the beginning of this century. The publications on Golden Rice, i.e. vitamin A enriched GM rice, follows a similar trend as GM rice in general. Both research topics steadily increased since 2004. But what is more striking is the progression in biofortification research. While this topic was hardly addressed at the start of the targeted period, with only 3 publications between 2000 and 2002, the number of publications progressively increased since 2004, rising to about 251 publications in 2009-2011. Together with the figures of biofortification and GM rice, this demonstrates the growing importance of GM crops with health benefits and GM biofortified rice in particular.

[Insert Figure 1 here]

VIII. Consumer preferences for GM biofortified rice

As none of the GM biofortified crops are currently approved for cultivation and consumption, it is crucial to determine ex-ante the potential demand for such novel crops. Within the large body of literature on biofortification and GM food/rice, there are several studies that aimed to determine consumers' willingness-to-pay for GM biofortified rice. Given the direct health benefits associated with GM biofortification, due to the enhanced micronutrient content, these studies mainly aimed to assess the amount consumers are willing to pay more for nutritionally enriched rice. In Table 8, seven economic valuation studies on GM biofortified rice crops are presented. While the study of Li et al.¹¹² focuses on GM biofortified rice in general, without making reference to a specific micronutrient trait, the other consumer studies examine either folate or provitamin A enriched 'Golden' Rice. Depending on the applied methodology, Chinese consumers are willing to pay a premium between 34 % (hypothetical method, i.e. contingent valuation)¹¹³ and 72 % (non-hypothetical method, i.e. experimental auctions) for Folate Biofortified Rice¹¹⁴. With respect to Golden Rice, willingness-to-pay values vary between 19.5 %¹¹⁵ (India) and 40.0 %¹¹⁶ (Philippines) in Asia. In the United States, premiums for Golden Rice are substantially lower, i.e. 16.0 % on average¹¹⁷. Besides the GM biofortified rice studies, other studies obtained economic valuations for conventional biofortified crops. The high consumer preferences for vitamin A enriched cassava in North-East Brazil (60%-70%)¹¹⁸, for example, are partly due to the high prevalence rate of vitamin A deficiency in this region. Also De Groote et al.¹¹⁹ elicited valuations for a crop with a higher vitamin content, namely willingness-to-pay for biofortified corn. Their results showed that consumers in Kenya are prepared to pay 24 % more for corn if it would be enriched with provitamin A. Although these findings provide insight in the consumer preferences for GM biofortified rice, caution is needed when benchmarking these premiums, due to the study specific characteristics (e.g. the valuation method, the sample selection, the targeted product

and the selected trait). Nevertheless, when looking at the high premiums, these positive reactions support the high potential demand for GM biofortified crops.

[Insert Table 8 here]

IX. Potential cost-effectiveness of GM biofortified rice

As GM biofortified rice is not only an innovative food crop, which is based on agricultural biotechnology, but also a potential alternative policy intervention to reduce the burden of micronutrient malnutrition, health impact and cost-effectiveness analyses are also considered a crucial aspect to adequately evaluate its socio-economic potential¹²⁰. In Table 9 five key health impact studies are described, of which four also assessed the potential health impact. The Chinese regional health impact analysis of De Steur et al.²⁷ is not included, as the study on multi-biofortification further builds upon their results by including a cost-effectiveness study on folate and three other micronutrient traits in rice (provitamin A, zinc and iron). For an overview of cost-effectiveness studies on other biofortified crops, see Meenakshi et al.¹²¹. The potential health benefits of folate, provitamin A and multi-biofortified rice are measured by their potential contribution to lower the current burden of micronutrient deficiencies. The results vary between 6 % and 20 % in the pessimistic scenario and 32 % and 60 % in the optimistic scenario. The cost-effectiveness is expressed by the cost (US\$) to save a Disability-Adjusted Life Year (DALY) that is initially lost due to the targeted micronutrient deficiency. When looking at the World Bank cost-effectiveness cut-off level for highly cost-effective health interventions¹²², i.e. 258 US\$ per DALY saved in 2011¹²³, all GM biofortified rice crops fall below this threshold. Due to the combined health impacts multi-biofortified rice,

and the associated cost reductions, the cost-effectiveness of this GM rice crop is substantially lower than the so-called single GM biofortified rice crops.

Although these studies differ in its targeted trait and country, but also in the data assumptions, this table is not intended for comparison of different figures. Instead, one should interpret the evaluation of the introduction of the different GM biofortified rice crops as a whole. Taken together the health impact and cost-effectiveness figures, GM biofortified rice, regardless of the targeted trait or region, is considered a highly cost-effective intervention to combat micronutrient malnutrition.

[Insert Table 9 here]

X. Key challenges of the commercialization of GM biofortified rice

Despite its large potential, GM biofortification has not been the magic bullet in the fight against micronutrient deficiencies. According to Hotz and McClaferty¹²⁴ there are numerous, technical, practical, market oriented or other concerns that need be addressed to successfully achieve the goal of biofortifying staple crops. For instance, although some target micronutrients need to undergo bioconversion before the body can utilize them, a process that is not 100% effective e.g. pro-vitamin A (beta-carotene) needs to be converted to vitamin A. Furthermore, although differences in appearance could be used to adequately position biofortified products in the market place⁴¹, several studies show that acceptance of GM crops will be compromised if they do not resemble the conventional products¹²⁵⁻¹²⁷. Rice fortification, for instance, may lead to an intensification of color, which negatively affected its acceptability in Thailand and Bangladesh¹²⁸. With respect to Golden Rice, the visible differences between this GM biofortified rice crop and its regular counterpart could be a

constraint to consumer acceptance, because its yellow color may be linked with a longer shelf life and, thus, lower quality. Similarly, orange, pro-vitamin A biofortified maize is less preferred than unfortified white maize^{129, 130}.

Although scientific evidence is lacking, GM biofortification may also change sensory attributes, which could reduce consumers' willingness to consume such micronutrient enriched crops. The aroma and taste of (conventional) pro-vitamin A enriched maize, for example, was negatively evaluated in Mozambique¹³⁰. Other negative product attribute changes that might be associated with GM biofortification of rice, such as shelf life, duration and sensory quality of cooking, could also play a role and need to be further investigated¹²⁹.

For a discussion on key issues and challenges to advance towards a successful implementation of Folate Biofortified Rice and Golden Rice, we refer to De Steur et al.¹²⁰ and the Bertebos foundation report¹³¹, respectively.

XI. Conclusions

GM biofortified rice as a specific GM crop with health benefits is more and more examined as an alternative policy intervention to combat micronutrient malnutrition. At the turn of the century, the first publications on biofortification and Golden Rice as the first GM biofortified crop appeared. From 2004 onwards, the amount of research in the field of GM food, GM rice and particularly biofortification drastically increased. When looking at consumer studies on GM biofortified rice, the findings show that consumers in target countries are willing to pay for improved micronutrient contents in rice. The high premiums for both Folate Biofortified Rice and Golden Rice, indicate that there is a consumer market for GM rice crops with health benefits. The high cost-effectiveness of single (folate, provitamin A) and multi-biofortified

rice (folate, provitamin A, zinc and iron) further support the potential of GM biofortification to tackle a major public health problem like vitamin A and folate deficiency.

GM biofortification of rice comes at a time when the debate is rife on the adoption of GM food in many countries in the developing world. Despite its additional health benefits, future research is needed to adequately and sustainably introduce GM biofortified rice at the market place. Even though pro-vitamin A enriched rice is on the verge of being released, it is evident that it will only serve regions where rice is a staple. Moreover, although GM biofortification (of rice) is technically “cost effective”, scientifically underpinned communication and promotion actions are needed to further convince governments and public health agencies of its potential in the developing world.

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Tables

Table 1. Key figures of the estimated global impact of micronutrient malnutrition, estimated burden of disease in million DALYs lost and as a percentage of the Global Burden of Disease, per main micronutrient deficiency

| Type of micronutrient deficiency | Estimated burden of disease ^f | | | |
|---|--|------------------------|-------------------------|------------------------|
| | 2000 ^g | | 2004 | |
| | mi. DALYs lost | % of GBD | mi. DALYs lost | % of GBD |
| Micronutrient malnutrition (MM) 2 million children may die each year due to MM ^a MM is the world's leading cause of mental impairment ^b MM is responsible for productivity losses of up to 2% of GDP ^b | 93.2 | 6.3 | 60.9 | 4.0 |
| Vitamin A deficiency (VAD) VAD-related night-blindness and blindness are affecting 5 million and 350.000 children, respectively ^c VAD is responsible for 0.5 to 1 million child deaths each year ^{b,c} | 26.6^h | 1.8^h | 22.1^l | 1.5^l |
| Iron deficiency (ID) ID affects the health and energy of 40% (women) ^a and the mental development of 40-60 % (children) ^{b,d} in developing countries. ID is estimated to result in the annual death of 841.000 persons ^g , of which 50.000 young women in pregnancy and child birth ^b | 35.1^d | 2.4^d | 19.7^l | 1.3^l |
| Zinc deficiency (ZD) About 800 000 child deaths per year are related to ZD ^e ZD is associated with approximately 176.000 diarrhea deaths, 406.000 pneumonia deaths and 207. 000 malaria deaths each year ^e | 28.0^e | 1.9^e | 15.6^l | 1.0^l |
| Iodine deficiency (IOD) Each year, IOD leads to an estimated number of 18-20 million mentally impaired babies are born ^{a,b} IOD is estimated to lower the intellectual capacity of developing countries by 10 to 15 percentage points ^b | 3.5ⁱ | 0.2ⁱ | 3.5^l | 0.2^l |
| Folate deficiency (FD) FD is estimated to result in approximately 200.000 severe birth defects every year ^b About 1 in 10 adult deaths from heart diseases are attributed to FD ^b . | ND^j | | ND^j | |

DALY, Disability-Adjusted Life Year; FD, folate deficiency; GBD, Global Burden of Disease; ID, iron deficiency; IOD, iodine deficiency; MM, micronutrient malnutrition; ND, no data available; VAD, vitamin A deficiency; ZD, zinc deficiency

Note: Figures on the global burden of all malnutrition are not presented. According to the FAO report on the state of food insecurity in the world³, malnutrition in the developing world leads to a total loss of 220 million (childhood and maternal undernutrition) to 430 million (including nutrition-related risk factors) DALYs.

^a Micronutrient Initiative¹⁵; ^b UNICEF^{5,22}; ^c Micronutrient Initiative report²; ^d Stoltzfus et al.²³; ^e Caulfield and Black²⁴; ^f More information on the application of DALYs and the DALY-approach, see De Steur et al.²⁵⁻²⁷; ^g The burden of different micronutrient deficiencies in 2000 are based on the Comparative Risk Factor Assessment (CRA) of the WHO¹³. The data are available at the WHO website²⁸; ^h Rice et al.¹⁰; ⁱ WHO World Health Report ²⁹; ^j The global folate deficiency prevalence is not established, as Kennedy et al.³⁰ demonstrate, but is expected not to be a marginal phenomenon ³¹. Based on the most important outcome of FD, i.e. Neural-Tube Defects, calculations of De Steur et al.¹⁴ reveal a global burden of FD of at least 4.8 million DALYs, which is significantly more than the rough 2.3 million estimation of Blencowe et al.³². However, this is still an underestimation, as other functional outcomes are not included; ^l WHO report on Global Health Risks³³. The statistics from the report are available at the WHO website³⁴.

Table 2. Characteristics of the key interventions to reduce micronutrient deficiencies

| | Industry based interventions | | Natural micronutrient based interventions | |
|---------------------------|------------------------------|--|---|---|
| | Supplementation | Food fortification | Dietary diversification | (GM) Biofortification |
| Micronutrient dose | RNI dose | Micronutrient enriched staple crops | Micronutrient-rich foods | Micronutrient enriched staple crops |
| Potential coverage | People taking supplements | Consumers of processed staple crops | Consumers taking part in promotion/ education program | Consumers of (GM) staple crops |
| Target group | (Rural) risk regions | (Urban) populations | Rural risk regions | (Poor) populations |
| Behavioral changes | Taking pills (correctly) | None | Changing dietary habits | None, unless a product attribute is changed |
| Funding | Continuous | Continuous | Long-term | One-time R&D, continuous labeling & maintenance costs |
| Funding source | Public | Public or private | Public | Public |
| Development | Pharmaceutical industry | Food processing industry | Government | Research institutes |
| Distribution | Health workers/ system | Food supply chain (marketing channels) | Health, extension & education system | Seed distribution system |

Note: Own compilation, based on Stein et al.³⁶

GM, Genetically Modified; R&D, Research & Development; RNI, recommended nutrient intake

Table 3. The main stages of crop improvement

| | Crop improvement | | | |
|----------------------------|--|----------------------------|--|----------------------------|
| | Agronomic traits | | Quality traits | |
| | Green revolution | Gene revolution | Conventional biofortification | GM biofortification |
| Breeding technique | Conventional | GM technology | Conventional | GM technology |
| Timing | 60s-80s | 90s - ... | 00s - ... | NC - ... |
| Key beneficiary | Producer (input) | | Consumer (output) | |
| Key objective | Yield improvement | | Health improvement | |
| Long term objective | Hunger reduction | | Hidden hunger reduction | |
| GM crop generation | / | 1 st generation | / | 2 nd generation |
| Examples | herbicide tolerance, drought tolerance, pest resistance, and/or virus resistance | | enhanced vitamin and/or mineral contents | |

NC, not commercialized; GM, Genetic Modification

Table 4. A brief overview of the currently biofortified products in the world, developed by HarvestPlus or AgroSalud, according to the improved micronutrient, applied technology, target area of first release and (expected) release year.

| Micronutrient | Product | Applied technology | Target Area ^c | Release year (# cultivars released) | Expected release year |
|--|--------------|--------------------------------|--|-------------------------------------|-----------------------|
| Vitamin A (Beta-carotene) ^a | Cassava | CB | DR Congo and Nigeria | | 2011-2012 |
| | Maize | CB | Zambia | | 2012 |
| | Sweet Potato | CB | Uganda and Mozambique | 2007 | |
| | | | Brazil, Cuba, Dominican Republic, Haiti and Peru | 2009-2010 (8) | |
| Rice | TB | Philippines, Bangladesh, India | | 2012, 2013, 2014 ^e | |
| Iron | Pearl Millet | CB | India | | 2012 |
| | Rice | CB | Bolivia, Cuba and Panama | 2009-2010 (8) | |
| | | | Brazil, Colombia, Nicaragua and Dominican Republic | | 2011 |
| | Bean | CB | Bolivia, Brazil, Cuba and Guatemala | 2008-2010 (5) | |
| | | | Colombia, Costa Rica, El Salvador, Honduras and Nicaragua | | 2011 |
| Iron, Zinc | Wheat | CB | India and Pakistan | | 2013 |
| | Bean | CB | DR Congo and Rwanda | | 2011-2012 |
| | Rice | CB | India, Bangladesh | | 2013 |
| Vitamin B3 (Niacin) ^b | Maize | CB | Bolivia, Colombia, El Salvador, Guatemala, Haiti, Honduras, Mexico, Nicaragua and Panama | 2008-2010 (21) | ND |
| Folate | Rice | TB | China ^d | | ND ^d |

ND, No data

Source: Own compilation, based on Agrosalud⁸⁰ for Latin America and the Caribbean, and HarvestPlus⁷⁴ for Asia and Africa, except for Golden Rice⁷⁷ and Folate Biofortified Rice⁸¹.

^a The human body converts beta-carotene or provitamin A into vitamin A;

^b Niacin or Vitamin B₃ is an essential nutrient which is mainly lacking in maize consuming populations⁸². Niacin is available in different foods, but can also be made in the human body through tryptophan, i.e. an amino acid that is improved by biofortification;

^c These are the selected countries where the biofortified crops are released or expected to be tested and released. However, after the first release, these crops are intended to benefit also other countries characterized by similar micronutrient deficiencies;

^d Because these crops are still in a development phase, it is too early to select a target country and a release date. Here, China was selected due to its high folate deficiency prevalence rates, its recent approval of Bt rice and the potential high impact of the introduction of Folate Biofortified Rice¹⁴;

^e Although the transgenic Golden Rice was expected to be released in 2011⁸³, field tests and biosafety regulations are still ongoing in the Philippines. The GR trait was also bred into rice varieties in, for example, India, Vietnam, Bangladesh and Indonesia.

Table 5. Approved (non-commercialized) GM rice events.

| Event name | Developer (institute, country) | GM traits | Country | Type of approval (year) | | |
|------------------------------|---|------------------------------------|---|--|-------------------|--------------------------|
| | | | | Food ^b | Feed ^b | Cultivation ^c |
| 7Crp#10 | National Institute of Agrobiological Sciences (Japan) | Anti-allergy antibiotic resistance | Japan | 2007 | | 2007 ^d |
| 7Crp#242-95-7 | National Institute of Agrobiological Sciences (Japan) | Anti-allergy antibiotic resistance | Japan | | | 2007 ^d |
| BTShanyou 63 | Huazhong Agricultural University (China) | Insect resistance | China | 2009 | 2009 | 2009 |
| Huahui-1/TT51-1 | Huazhong Agricultural University (China) | Insect resistance | China | | | 2009 |
| LLRICE06^a | Bayer CropScience (Germany) | Herbicide tolerance | USA | 2000 | 2000 | 1999 |
| LLRICE601^a | Bayer CropScience (Germany) | Herbicide tolerance | Colombia USA | 2008 2008 | | 2006 |
| LLRICE62^a | Bayer CropScience (Germany) | Herbicide tolerance | Australia Canada Colombia Mexico New Zealand Russia South Africa USA | 2008 2006 2008 2007 2008 2007 2011 2011 2000 | 2006 | 1999 |
| Tarom molaii + cry1Ab | Agricultural Biotech Research Institute (Iran) | Insect resistance | Iran | 2004 | 2004 | 2004 |

Source: ISAAA GM approval database (www.isaaa.org/gmapprovaldatabase/)

^a Liberty Link rice

^b direct use or additive

^c domestic or non-domestic use

^d limited cultivation with proper isolation

Table 6. GM rice events in the pipeline.

| Event name (product name) | Developer (institute, country) | GM traits | Development stage |
|--|-----------------------------------|--|-----------------------------|
| LLRICE62(Liberty Link rice) | Bayer (Germany) | Insect resistance Herbicide tolerance | commercial pipeline |
| Bt63 (MH63) | China | Insect resistance | regulatory pipeline |
| Xa21 | China | Other | regulatory pipeline |
| KMD1 | China | Insect resistance | regulatory pipeline |
| B827 | Iran | Insect resistance | regulatory pipeline |
| GR1 (Golden Rice 1) | IRRI (Philippines) | Crop composition | advanced development |
| Bar68-1 | China | Insect resistance Herbicide tolerance | advanced development |
| GR2 (Golden Rice 2) | Bayer (Germany) | Herbicide tolerance | |
| Bt | IRRI (Philippines) | Crop composition | advanced development |
| CP iORF-IV | Indonesia | Insect resistance | advanced development |
| RTBV-ODs2 | India | Virus resistance | advanced development |
| chi11 tlp | India | Virus resistance | advanced development |
| Bt | Bayer (Germany) | Insect resistance | advanced development |
| cry1Ac | India | Disease resistance | advanced development |
| Glyoxalase I & II | Pakistan | Insect resistance | advanced development |
| Osmotin | India | Insect resistance | advanced development |
| cry1Ab, cry1C & bar | India | Abiotic stress tolerance | advanced development |
| | India | Abiotic stress tolerance | advanced development |
| | India | Insect resistance | advanced development |

Source: Own compilation, based on Stein and Rodriguez⁸⁶.

Note: GM biofortified crops in bold.

Table 7.Characteristics of GM biofortified rice, per product and impact scenario

| Indicator | Folate ^b (Folate Biofortified Rice) | | Provitamin A ^c (Golden Rice) | |
|---|---|---------------------|--|---------------------|
| | Pessimistic scenario | Optimistic scenario | Pessimistic scenario | Optimistic scenario |
| Rice characteristics | | | | |
| Initial micronutrient content ^a | <i>µg per g rice</i> | 0.08 | | 0 |
| GM rice characteristics | | | | |
| Improved micronutrient content | <i>µg per g rice</i> | 12 | 20 | 30 |
| Post-harvest losses (e.g. cooking) | % | 75 | 50 | 80 |
| Bioavailability | % | 50 ^d | 50 ^d | 4:1 ^e |
| Added micronutrient content | <i>µg per g rice</i> | 1.4 | 2.9 | 1.0 |
| Total micronutrient content | <i>µg per g rice</i> | 1.5 | 3.0 | 1.0 |
| RNI, per key beneficiary | | | | |
| Women of cba | <i>µg</i> | 400 ^f | | |
| Children < 5 years | <i>µg</i> | | | 500 ^g |
| Pregnant women | <i>µg</i> | | | 800 ^g |
| Required rice consumption to achieve the RNI | | | | |
| <i>If current micronutrient intake = 0</i> | | | | |
| Without biofortification | <i>g rice</i> | 5000.0 | | NA ^h |
| With biofortification | | | | |
| Women of cba | <i>g rice</i> | 281.7 | 137.0 | |
| Children < 5 years | <i>g rice</i> | | | 500 |
| Pregnant women | <i>g rice</i> | | | 800 |

cba, childbearing age; NA, not applicable; RNI, recommended nutrient intake

Source: unless noted otherwise, based on De Steur et al.²⁶

^a USDA¹⁰³

^b Storozhenko et al.⁸¹ and De Steur et al.²⁷

^c Zimmerman and Qaim¹⁰⁴, and Stein et al.¹⁰⁵, updated by Golden Rice Project experts

^d Bailey¹⁰⁶

^e Bioconversion factors refer to the bioavailability of provitamin A and the conversion to vitamin A. Based on Tang et al.¹⁰⁷, updated by Golden Rice Project experts

^f WHO¹⁰⁸. The target group of Folate Biofortified Rice consumption is women of childbearing age, as the health benefits refer to newborns.

^g IOM¹⁰⁹(children) and FAO/WHO¹¹⁰ (pregnant women)

^hAs the initial provitamin A content of rice is nonexistent, one could not consume provitamin A through regular rice consumption.

Table 8. Willingness-to-pay for GM biofortified rice, main characteristics per study

| Study | Trait | Publication year | Methodology | Country | % premium (WTP) |
|-------------------------------------|-----------------------|-------------------------|-------------------------|----------------|------------------------|
| Li et al. ¹¹² | Vitamins ^a | 2002 | DC contingent valuation | Urban China | 38.0 |
| De Steur et al. ¹¹³ | Folate | 2010 | OE contingent valuation | Rural China | 71.7 |
| De Steur et al. ¹¹⁴ | Folate | 2012 | Experimental auction | Rural China | 33.7 |
| Deodhar et al. ¹¹⁵ | Provitamin A | 2008 | DC contingent valuation | India | 19.5 |
| Depositario et al. ¹¹⁶ , | Provitamin A | 2009 | Experimental auction | Philippines | 40.0 |
| Lusk et al. ¹¹⁷ | Provitamin A | 2003 | DC contingent valuation | United States | 16.0 |

DC, dichotomous choice; ND, no data; OE, open-ended

Note: In golden rice, provitamin A or beta-carotene levels are elevated in order to increase vitamin A consumption.

^a Valuations refer to rice with enhanced vitamin levels in general (without specification of the particular vitamin trait)

Table 9. Potential health impacts and cost-effectiveness of GM biofortified rice, main characteristics per study

| Study | Trait | Country | Health impact | | Cost-effectiveness | |
|---------------------------------|-------------------------|------------------------------|---------------------------|------------|------------------------|------------|
| | | | Pessimistic | Optimistic | Pessimistic | Optimistic |
| | | | <i>% burden reduction</i> | | <i>US\$/DALY saved</i> | |
| De Steur et al. ²⁶ | Folate | Shanxi Province ^b | 20 | 60 | 120.3 | 40.1 |
| De Steur et al. ²⁵ | | China | 20 | 60 | 64.2 | 21.4 |
| De Steur et al. ²⁶ | Provitamin A | China | 17 | 60 | 18.1 | 5.0 |
| Stein et al. ¹⁰⁵ | | India | 9 | 59 | 23.2 | 3.7 |
| Zimmerman & Qaim ¹⁰⁴ | | Philippines | 6 | 32 | / | / |
| De Steur et al. ²⁶ | Multi (GM) ^a | China | 11 | 46 | 9.6 | 2.3 |

DALYs, Disability-Adjusted Life Years; GM, genetically modified; WB, World Bank

Note: All cost-effectiveness figures are expressed in 2011 dollars, based on BLS inflation calculator¹²³

^a Multi-biofortified rice contains higher folate, provitamin A, zinc and iron levels;

^b Rural province in Northern China

Figures

Figure 1. Number of articles on GM food, GM rice, biofortification and Golden Rice, as derived from the Web of Knowledge literature database (2000-2011)

Source: own compilation, based on Web of Knowledge (2011).

Note: Recent figures (2012) were not included as they were incomplete at the time of the study.