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Food Policy 29 (2004) 147–168

FOOD POLICY

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Potential health benefits of Golden Rice: a Philippine case study

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Abstract

Golden Rice has been genetically modified to produce beta-carotene in the endosperm of grain. It could improve the vitamin A status of deficient food consumers, especially women and children in developing countries. This paper analyses potential impacts in a Philippine context. Since the technology is still at the stage of R&D, benefits are simulated with a scenario approach. Health effects are quantified using the methodology of disability-adjusted life years (DALYs). Golden Rice will not completely eliminate the problems of vitamin A deficiency, such as blindness or increased mortality. Therefore, it should be seen as a complement rather than a substitute for alternative micronutrient interventions. Yet the technology could bring about significant benefits. Depending on the underlying assumptions, annual health improvements are worth between US$ 16 and 88 million, and rates of return on R&D investments range between 66% and 133%. Due to the uncertainty related to key parameters, these results should be treated as preliminary.

Keywords: Biotechnology; Vitamin A; Micronutrient malnutrition; Health impacts; DALYs

Introduction

Vitamin A deficiency (VAD) is a major problem in large parts of the developing world. An estimated 250,000–500,000 VA-deficient children go blind every year (West and Darnton-Hill, 2001). Apart from acute eye symptoms, VAD also weakens the immune system, thus increasing the incidence and severity of infectious

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0306-9192/$ - see front matter
doi:10.1016/j.foodpol.2004.03.001

diseases. For adults, the implications can be serious too, especially for pregnant and lactating women. Nearly 600,000 women die from childbirth-related causes each year, many of them from complications which could be reduced through better provision of vitamin A (Sommer and West, 1996). The most affected are the poor, whose diets are predominated by less nutritious staple foods on account of lacking purchasing power and limited awareness.

During the last decade, a lot of efforts have been made to reduce VAD in developing countries. Food fortification, supplementation and dietary education programmes have been undertaken. A complementary approach is to enrich major staple foods with beta-carotene through plant breeding. For some crop species, such as maize and sweet potato, cultivars with high beta-carotene contents have been identified, which can be used in traditional breeding programmes. However, beta-carotene does not occur naturally in the endosperm of rice—the major staple food in large parts of Asia. Hence, for rice, use of biotechnology is required (Bouis, 2000). Recently, so-called Golden Rice (GR) has been developed through genetic engineering at Swiss and German universities (Ye et al., 2000). Three gene constructs were inserted into the rice genome, which complete the biochemical pathway needed for beta-carotene production in the grain. Although GR is still at the stage of research and development (R&D), it is already surrounded by a lot of public controversy. Some optimists praise it as the solution to overcome malnutrition and VAD. Others denounce it as a mere child of the biotech lobby and consider it a useless and rather harmful innovation for the poor.

The aim of this study is to analyse the potential benefits of GR in the Philippines. VAD constitutes a serious problem there. Moreover, in 2001, GR technology was transferred to the Philippine-based International Rice Research Institute (IRRI), where adaptive research is now being carried out. Scientists are currently working on verifying and improving the gene constructs and incorporating them into popular indica varieties. After that, a testing phase will follow. GR could become commercially available in 2007.

Given that actual impacts are not observable at this stage, the study takes an ex ante perspective. Since the main effect will be an improvement in the health and nutrition status of rice consumers, the methodological challenge is to appropriately combine issues of agricultural, nutrition and health economics. At first, an analytical framework is developed to conceptualise the research and identify key issues that might influence the innovation's impact. Then, health problems associated with VAD in the Philippines are described and classified. Resulting costs are quantified using the methodology of disability-adjusted life years (DALYs). These costs are expressed in DALYs lost. In a further step, DALYs to be gained through GR are calculated, and a preliminary cost–benefit analysis is provided. This is among the first studies to quantify the health benefits from micronutrient-enriched crops.[1]

[1] Based on detailed food intake data from one region in the Philippines, Dawe et al. (2002) analysed the role that GR could play for the VA supply of children. However, they did not explicitly consider the health effects and economic benefits resulting from an improvement in VA status.

Many of the parameters needed for the analysis are not yet known in the ex ante framework. Therefore, the calculations build on scenarios and assumptions. To use the best information available at this stage, assumptions are based on interviews with local and international plant researchers, nutritionists and health experts. A sensitivity analysis suggests that the exact numerical results should be interpreted with some caution. Nonetheless, the study might help rationalise the controversy surrounding GR technology. More generally, it will contribute to a better understanding of the ramifications of food crops with enhanced nutritive values in developing countries. The breeding approach is increasingly seen as a powerful tool to fight micronutrient deficiencies (CIAT/IFPRI, 2002), but empirical evidence is still lacking.

Analytical framework

Conceptual issues

New crop technologies are usually evaluated by looking at productivity effects in agricultural production. Aggregate benefits can then be calculated by modelling a shift in the commodity supply curve. This approach, however, is only suitable when the technology involves improved agronomic traits. Technologies that enhance the quality of commodities are rather associated with benefits at the level of consumption. The primary goal of GR is to improve the health and nutrition status of rice consumers. Generally, quality improvements would increase the consumers' willingness to pay, entailing an upward shift in the demand curve. But this presupposes that consumers recognise and appreciate the quality improvement. Awareness of VAD is generally low among the poor. Moreover, due to limited purchasing power, nutritional needs are often not translated into effective market demand. Capturing the benefits of GR in a market model is therefore not appropriate. Instead, the technology's positive health effects have to be identified and measured.

As Fig. 1 illustrates, the impact will mainly depend on two factors: (i) the technology's efficacy and (ii) its coverage rate. The efficacy of GR is defined as the capacity to improve the health status of a VA-deficient individual. This is influenced inter alia by the beta-carotene content in the grain and its bioconversion to VA in the human body. Coverage, on the other hand, is defined as the fraction of the population actually eating GR. This is a function of technology accessibility and producer and consumer acceptance. To some extent, these factors can still be influenced through adaptive research. But there are also exogenous variables which are harder to control.

Methodology

We quantify health costs of VAD and benefits of GR using the methodology of DALYs. This approach was developed by Murray and Lopez (1996), and is promulgated by the World Health Organisation (WHO) and the World Bank as a means of combining information about mortality and morbidity within a single

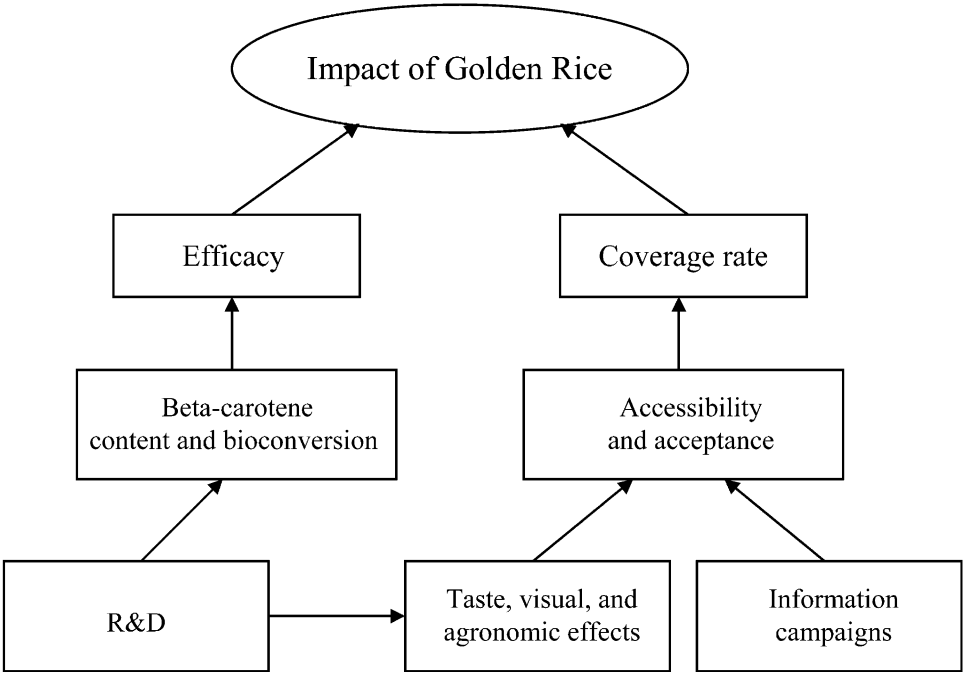

Fig. 1. Factors influencing the impact of Golden Rice.

index (WHO, 2002; World Bank, 1993). To our knowledge, it has not been used previously for the evaluation of agricultural technologies.

The general formula suggested by Murray and Lopez (1996) was adapted to our context, so that the total number of DALYs lost through VAD is defined as

$$\mathrm{DALYs_{Lost}} = \mathrm{YLL} + \mathrm{YLD_{temp}} + \mathrm{YLD_{perm}} \qquad (1)$$

where YLL is the number of life years lost due to mortality, and $\mathrm{YLD_{temp}}$ and $\mathrm{YLD_{perm}}$ are years of life with temporary and permanent disability, respectively. We concentrate on three target groups—children under the age of seven, pregnant women and lactating women. Furthermore, different disease levels resulting from VAD are taken into account. DALYs lost are calculated on an annual basis. Only deaths and new cases of disease occurring in the reference period are considered, whereby health costs are accumulated over the duration of particular conditions.

Thus, we can write

$$\mathrm{DALYs_{Lost}} = \sum_j T_j M_j \left(\frac{1 - \mathrm{e}^{-rL_j}}{r}\right) + \sum_i \sum_j T_j I_{ij} D_{ij} \left(\frac{1 - \mathrm{e}^{-rd_{ij}}}{r}\right) + \sum_k \sum_j T_j I_{kj} D_{kj} \left(\frac{1 - \mathrm{e}^{-rL_j}}{r}\right) \qquad (2)$$

where T_j is the total number of people in target group j, M_j is the mortality rate associated with VAD, and L_j is the average remaining life expectancy. I_{ij} is the incidence rate of temporary disease i, D_{ij} is the corresponding disability weight, and d_{ij} is the duration of the disease. I_{kj} is the incidence rate of permanent disease k, while r is the rate at which future costs are discounted. As is standard in DALY calculations (World Bank, 1993), we use a discount rate of 3%. Unlike Murray and Lopez (1996), we do not include an age-weighting function, because children are among the most affected by VAD. Age-weighting is controversial on equity grounds (Anand and Hanson, 1998), and Mathers et al. (1999) showed that it does not significantly change the results in many cases.

The number of DALYs lost through VAD is calculated with and without GR, and the difference is interpreted as the technology's impact. Without GR is the situation in the Philippines today, so we use existing epidemiological data. Health problems will be reduced if people start eating GR on a regular basis. To derive the expected reduction in incidence rates, we build on a model adapted from Brenzel (1993):

$$I_{ij}^{\text{new}} = \left[1 - (E_j C)\right] I_{ij}. \tag{3}$$

The new incidence rate of disease i in group j (I_{ij}^{new}) is a function of the group-specific efficacy rate of GR (E_j), and the technology's coverage rate (C). Changes in the incidence of permanent diseases and mortality rates are calculated accordingly. Efficacy and coverage were already introduced conceptually in Fig. 1. These two variables will be further discussed and specified in later sections.

DALYs are expressed in years of "healthy" life lost, which is a handy measure for the comparison of diseases or health interventions. For a cost–benefit analysis, however, a monetary value is needed, so that a dollar amount can be attributed to each DALY lost. The value should be adjusted to the living standard in a particular context. One possibility is to take the per capita income, albeit in developed countries much higher values are often imputed (Tolley et al., 1994). For the Philippines, we use the annual per capita income of US$1030 (NSCB, 2000). This is just a convenient device for economic analysis, not an attempt to quantify the intrinsic value of life. The latter would certainly entail serious ethical concerns.

Vitamin A deficiency and related diseases

In order to assess the costs of VAD and the potential impact of GR, it is essential to understand the linkages between nutrition, VA status and health. VA is a fat-soluble vitamin. It occurs in two forms, the active (preformed) and the precursor form. The most frequent active form is retinol, which can only be synthesised in animals and humans. Precursor forms, also known as carotenoids, are common in many fruits and vegetables. The most well-known carotenoid is beta-carotene, which the human body can convert to retinol. When VA supply is lower than the recommended dietary allowance (RDA), the individual will suffer acute and chronic health impairments.[2]

VAD is subdivided into two categories: sub-clinical and clinical VAD. Sub-clinical VAD is usually not associated with immediate symptoms. But—as VA plays an important role in maintaining immune competence—it can cause high morbidity and mortality, especially among children. Occurrence of measles, diarrhea and other infectious diseases, as well as case fatalities from these conditions, are significantly higher in VA-deficient groups than in populations with normal VA status (Underwood, 1998). A link has also been established between VAD and maternal survival up to two years following delivery (WHO, 2002; West and Darnton-Hill, 2001). Clinical VAD involves the characteristic ocular manifestations, usually referred to as "xerophthalmia". Xerophthalmia can be subdivided into the following levels according to degree of VAD and medical severity (WHO, 1982): (i) night blindness (XN), (ii) Bitot's spot (X1B), (iii) corneal ulceration (X2, X3A, X3B), and (iv) corneal scars (XS).

Night blindness is the earliest clinical manifestation and is associated with the inability to see in dim light. *Bitot's spots* are irregular shaped foam-plaques on the underside of the eyelid. Often, they are associated with a dryness of the white of the eye. Night blindness and Bitot's spot can develop into more severe manifestations when not medicated. When treated with high-potency VA, however, the eye usually fully recovers within a matter of weeks. *Corneal ulceration* and *corneal scars* indicate destruction of a part or all of the cornea, the outermost layer of the eye. While with immediate VA treatment, corneal xerophthalmia can heal with only minimal structural damage, it can rapidly lead to irreversible blindness when not treated on time (Sommer and West, 1996).

These four levels of xerophthalmia are included as temporary diseases in this study, whereas blindness is the only permanent disease. VAD-related mortality is considered independent of eye symptoms, because it can already occur at sub-clinical deficiency levels. Temporal disabilities associated with infectious diseases from which individuals recover later on are neglected. This leads to an underestimation of total health costs. But, as non-fatal infectious diseases are usually of short duration, the resulting inaccuracy will be rather small.

Vitamin A deficiency in the Philippines

Nutrition situation

In the Philippines, the Food and Nutrition Research Institute (FNRI) carries out nutrition and health surveys every five years. Nutrition data are based on actual

[2] The RDA is the average daily dietary intake level that is sufficient to meet the nutrient requirements of healthy individuals in a particular life stage and gender group (IOM, 2002). It has been established to give approximately three months of body stores, so that temporary undersupply can be compensated. However, insufficient VA intake over an extended period of time will lead to a depletion of body stores. When determining the average age of onset of health impairments, we take into account such delays.

food intake. The typical Filipino diet is rice, boiled fish or meat and relatively little vegetables. On average, this diet only meets 88% of the RDA for energy, and even less for other nutrients. Vulnerable groups, such as pre-school children and pregnant and lactating women, usually achieve less than 70% of their energy requirements (FNRI, 1993, 1998).

Micronutrient deficiencies are widespread too. In addition to iron and iodine deficiencies, VAD is considered a major health problem, with prevalence rates exceeding the WHO cut-off points. Since the early 1990s, the government has been implementing and encouraging different public interventions. Initiatives include the distribution of VA capsules and the fortification of margarine and other processed food items. Such interventions are successful in improving the VA status of the population, but coverage rates are incomplete (Fiedler et al., 2000).

DALYs lost

Using the methodology described above, the annual costs of VAD in the Philippines are calculated in the following. We take the late 1990s as the reference period. Prevalence rates for different levels of VAD and associated diseases were taken from FNRI survey data. Unfortunately, the most recent survey of 1998 only looked into sub-clinical levels of VAD, so we use 1993 data for the prevalence of clinical manifestations. Based on sub-clinical VAD alone, prevalence rates were slightly higher in 1998 than in 1993 for all three target groups, but otherwise quite similar. Hence, a combination of data from both surveys should be in order. The prevalence rates used in this study are shown in Table 1. Missing values were replaced by estimates of local epidemiologists.

Eq. (2) above indicated that the DALY calculations should be based on incidence rather than prevalence rates. However, incidence rates of particular diseases are rarely available in health statistics. Different authors suggested that, when using prevalence instead of incidence rates, the duration of diseases should be taken as one year, in order to avoid inflation of annual health costs (e.g., Brenzel, 1993; Murray and Lopez, 1996). We follow this approach for temporary diseases. For blindness, neither prevalence nor incidence rates are available in Philippine statistics. Yet VAD-related blindness is always preceded by corneal xerophthalmia. Approximately, half of all corneal cases lead to blindness within a short period of time (West and Darnton-Hill, 2001). Therefore, the incidence rate of blindness is around 50% of the combined prevalence rates of corneal ulceration and corneal scars.

Especially breast-fed infants have body stores of VA, which have to be depleted before eye symptoms emerge (Newman, 1993). The incidence of corneal xerophthalmia usually peaks at two to three years of age (West and Darnton-Hill, 2001). Hence, we assume that the average age of onset of blindness among children is 2.5. For pregnant and lactating women, the average age of onset is assumed to be 30. This is beyond the midpoint of their reproductive life, which is plausible considering a gradual exhaustion of body stores with repeated pregnancies. Disability weights for temporary and permanent diseases were specified together with health

Table 1
Prevalence rates and number of people affected by VAD

	Children (<7 years)		Pregnant women		Lactating women	
	Prevalence rate (%)	Number of affected[a] (thousand)	Prevalence rate (%)	Number of affected[a] (thousand)	Prevalence rate (%)	Number of affected[a] (thousand)
Sub-clinical VAD	38.00[b]	5082.81	22.20[b]	359.23	16.50[b]	260.36
Night blindness	0.40[c]	53.50	0.60[c]	9.71	0.90[c]	14.20
Bitot's spot	0.10[c]	13.38	0.40[d]	6.47	0.70[d]	11.05
Corneal ulceration	0.05[d]	6.69	0.30[d]	4.85	0.50[d]	7.89
Corneal scars	0.00[c]	0.00	0.15[d]	2.43	0.30[c]	4.73
Blindness	0.03[e]	3.34	0.23[e]	3.64	0.40[e]	6.31

[a] Derived by multiplying prevalence rates with the total number of people in each group (NSCB, 2000).
[b] Based on FNRI (1998).
[c] Based on FNRI (1993).
[d] Based on expert estimates.
[e] These are incidence rates, derived as 50% of the combined prevalence rates of corneal xerophthalmia.

experts in the Philippines. For night blindness, the disability weight is 0.15, for Bitot's spot, it is 0.25, and for corneal ulceration, corneal scars and blindness, it is 0.5—equal across the three target groups.[3] These weights are consistent with values that were used in other studies in a similar context (e.g., World Bank, 1994).

Sub-clinical levels of VAD have a disability weight of zero, because there are no immediate symptoms. However, health costs of related infectious diseases are captured in the form of increased mortality rates. In countries where micronutrient malnutrition presents a moderate risk for the population, at least 3% of all infant deaths, and 10% of all deaths among pre-school children, are attributable to VAD (World Bank, 1993). Although in high-risk countries, the proportions can be much higher (Sommer and West, 1996), we use these figures for the Philippines as cautious assumptions. According to our interviews with local experts, about 6% of all maternal deaths during pregnancy and delivery, and 4% of all deaths during lactation, could be prevented through a better provision of VA.

The results of the DALY calculations without GR are shown in Table 2. In total, VAD causes an annual loss of about 270,000 years of "healthy" life in the Philippines. The highest cost occurs among children. Losses due to mortality are much higher in this group than in the other two groups, which underlines that blindness and visual problems constitute only part of the overall burden. Also, the total number of children affected by xerophthalmia is higher than the number of

[3] Blindness can be monocular, for which the disability weight might be lower, or binocular, for which the weight might be higher. Since available statistics do not differentiate, we assume an average value.

Table 2
DALYs lost due to VAD without Golden Rice

	Children	Pregnant women	Lactating women	Total
Loss due to mortality	80,040	2235	1424	83,700
Loss due to disability	59,478	46,590	80,335	186,403
Total loss	139,518	48,826	81,760	270,103
In monetary terms (million US$)	143.7	50.3	84.2	278.2

affected pregnant and lactating women. Nonetheless, disability costs for lactating women exceed those for children because of higher prevalence rates for corneal ulceration and corneal scars. In fact, the incidence of blindness among Filipino children is lower than in other countries of South and Southeast Asia, which might partly be due to the country's VA supplementation programme. Converting the total DALYs in Table 2 into monetary terms, we result in a loss of about $278 million per year. This is equivalent to 0.3% of the Philippine gross national product (GNP).

Efficacy of Golden Rice

The main effect of GR will be to reduce the prevalence of VAD. Eq. (3) showed that this is a function of the technology's efficacy and coverage. This section explains the factors influencing efficacy, while the next discusses issues of coverage. Because exact parameter values are unknown, we use two scenarios for calculating the potential impact of GR: one more pessimistic scenario and another which is rather optimistic. Parameter variations beyond these assumptions are tested later on in a sensitivity analysis.

Amount of beta-carotene

The current amount of beta-carotene that researchers managed to get into GR is 1.6 μg/g. Ye et al. (2000) argued that the same technology could yield 2.0 μg, if a homogenous line with uniformly coloured grains were produced. With slight modifications in the gene constructs, such as using more efficient promoters, the amount could be further increased. According to Datta (2001), it could be possible to achieve 3.0 μg within the adaptive research phase. Even higher amounts are theoretically possible, but they could potentially have undesirable effects on agricultural yields or taste. In the pessimistic scenario, we assume a beta-carotene content of 1.6 μg/g, whereas in the optimistic scenario, we assume 3.0 μg/g.

Post-harvest treatment, storage and processing of GR might also influence its beta-carotene content at the time of consumption. For leafy vegetables, it has been reported that exposure to sunlight after harvesting can result in a considerable loss of beta-carotene (Boileau et al., 1998). The same study found that losses are negligible for carrots, which is probably due to their more compact structure and smaller surface area. Given these results, it is likely that post-harvest losses of beta-carotene in GR can be kept relatively low. Still, some losses might occur with improper storage. In terms of processing, prolonged exposure to extreme heat often reduces the bioavailable portion of beta-carotene, while cooking at temperatures up to 100 °C can even increase the extractable amount of carotenoids (Dietz et al., 1988). In the Philippines, rice is usually steamed at temperatures below the boiling point, so that processing might not lead to significant additional losses. It is assumed that total post-harvest losses are 25% in the pessimistic, while they are zero in the optimistic scenario.

Bioconversion

Bioconversion is defined as the process of beta-carotene absorption by the human body and its transformation to retinol. After absorption, transformation takes place with a factor of approximately 2:1. However, variation in terms of absorbability occurs between different types of food. Absorption is most efficient when physiological amounts of beta-carotene are dissolved in oil. For spinach, an absorption efficiency of only 7% has been reported (Castenmiller et al., 1999). Other authors reported values of 11–12% for broccoli, and of 18–26% for carrots (Micozzi et al., 1992; Törrönen et al., 1996). In a study with school children in Indonesia, de Pee et al. (1998) found that the VA activity of beta-carotene in fruits and yellow tubers was more than double the activity of the same carotenoid in dark-green leafy vegetables. Generally, absorbability depends on the state of beta-carotene and its association with plant matrix materials in the food source. Also, it is correlated with the intake of complimentary ingredients in the diet. Low fat consumption reduces the absorption of beta-carotene significantly.

Using these recent findings, IOM (2002) estimated the retinol equivalency ratio for beta-carotene from food in a mixed diet, which includes fruits and vegetables, to be 12:1.[4] For GR, feeding tests will only be carried out over the next few years, so that specific data and information are not available. We take the 12:1 bioconversion rate as our pessimistic assumption. However, since rice has a simple food matrix with totally digestible carbohydrates, beta-carotene absorption might be higher than when obtained from fruits and vegetables (cf. Underwood, 2000). As part of a balanced diet, the retinol equivalency ratio could even be as high as for beta-carotene dissolved in oil, that is, 2:1 (Russell, 2002). Yet this is the absolute upper bound, which might not be reached under normal conditions in the Philippines. Especially among the poor, the low fat content in the diet could constrain beta-carotene absorption. Therefore, we use a more cautious bioconversion rate of 6:1 in the optimistic scenario.

Efficacy model

Once beta-carotene has been absorbed and converted to retinol, the human body can use it for physiological purposes. For the treatment of acute cases of xeroph-

[4] This is only half the value of 6:1, which was assumed for a long time in the nutrition community. The established assumption was mainly challenged through the work of de Pee et al. (1998) in Indonesia.

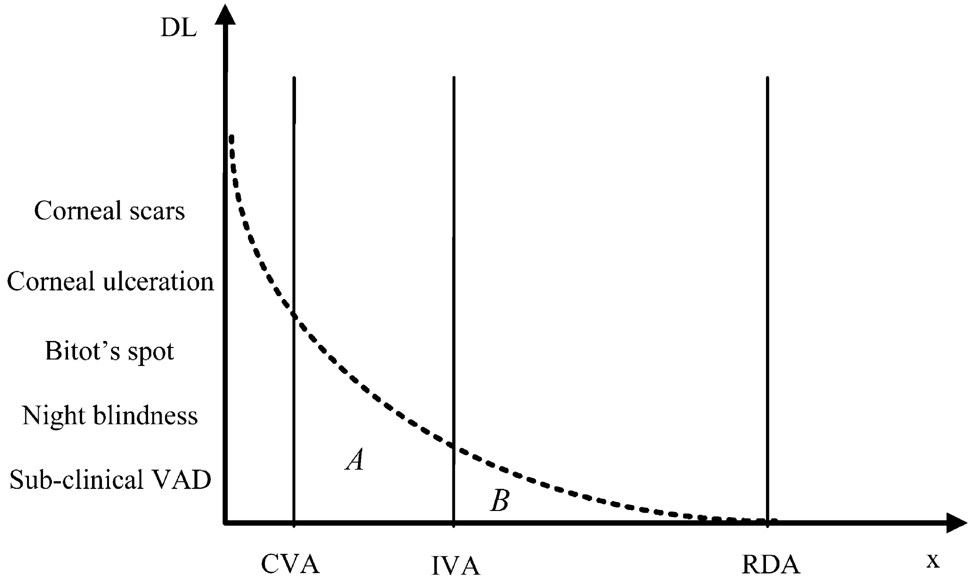

Fig. 2. Relationship between VA supply and disease levels.

thalmia, a minimum threshold intake is required, so that one or several doses of high-potency VA are administered (Sommer, 1995). However, GR is meant as a daily source of beta-carotene that helps prevent health problems and improve the overall VA status of the population. Therefore, therapeutic threshold models are inappropriate in this context.

Bauernfeind (1980), Olson (1994) and Underwood (1998) describe the relationship between regular VA supply and the occurrence of health problems as a continuous, logarithmic function. That is, incremental supply leads to a steady improvement in health status, whereby the response is more pronounced at higher levels of deficiency. This relationship is shown in Fig. 2. VA supply (x) is depicted on the horizontal axis, whereas disease levels (DL) are shown on the vertical axis. Current VA supply (CVA) is below the RDA, a situation which we actually observe for the target groups in the Philippines. Improved VA supply (IVA) represents current supply plus the increment from GR consumption. This level might still be lower than the RDA. However, the lower the initial supply, the higher is the technology's positive health effect. Beyond the point of RDA, no further improvement is possible.[5] Without having to specify units of measurement for DL, efficacy (E) can be calculated as the ratio of two areas, namely area A divided by

[5] Although excessive intake of preformed VA can be toxic, negative health effects are not known for over-supply of beta-carotene; unneeded amounts are excreted without conversion to retinol (Sommer and West, 1996).

area $A + B$. Thus, E can take any value between zero and one, whereby it is positively correlated with the convexity of the curve.

Although this general relationship is widely accepted in the literature, concrete evidence on the exact numerical association between VA supply and different disease levels is lacking (Underwood, 1998; Sommer and West, 1996). This makes parameterization of the function difficult. We use the following rectangular hyperbola, which has a moderate curvature and fulfils the condition of a zero point at $x = \mathrm{RDA}$:

$$\mathrm{DL}(x) = \frac{1}{x} - \frac{1}{\mathrm{RDA}}. \tag{4}$$

Other specifications are theoretically possible. We will return to this issue in the sensitivity analysis. Using Eq. (4), E can be calculated as:

$$E = \frac{\int_{\mathrm{CVA}}^{\mathrm{IVA}} \left(\frac{1}{x} - \frac{1}{\mathrm{RDA}}\right) \mathrm{d}x}{\int_{\mathrm{CVA}}^{\mathrm{RDA}} \left(\frac{1}{x} - \frac{1}{\mathrm{RDA}}\right) \mathrm{d}x} = \frac{\ln\left(\frac{\mathrm{IVA}}{\mathrm{CVA}}\right) - \left(\frac{\mathrm{IVA} - \mathrm{CVA}}{\mathrm{RDA}}\right)}{\ln\left(\frac{\mathrm{RDA}}{\mathrm{CVA}}\right) - \left(\frac{\mathrm{RDA} - \mathrm{CVA}}{\mathrm{RDA}}\right)}. \tag{5}$$

FNRI (1993) provides food intake data separately for the three target groups. This is the most recent nationally representative data available that takes into account intra-household distribution. Rice is the dominant staple, providing about half of the daily calorie consumption for children, and slightly more for pregnant and lactating women. While micronutrient deficiencies are more pronounced in poorer households, differences in rice intake are relatively small across income levels. For instance, average daily rice consumption for lactating women is 252 and 277 g in the poorest and richest households, respectively. Lactating women in medium-income households consume around 300 g. There are more pronounced geographical differences however. Rice intake is above average in the northern Philippines, whereas more corn is eaten in parts of Visayas and Mindanao. We use average national data for the three target groups, because the available epidemiological information does not allow disaggregation by income or region. Within the group of children, the average rice intake exaggerates the amount for infants below one year of age. But breast-fed infants benefit from the better VA supply of their mothers (Newman, 1993), and VAD-related health problems only peak at two to three years of age.

Details and results of the efficacy calculations are presented in Table 3. In the optimistic scenario, efficacy is much higher than in the pessimistic one. Given the higher assumptions on beta-carotene content and bioconversion, this should not surprise. Noteworthy, however, is that even in the optimistic scenario, efficacy is significantly lower than 100% for all target groups. This means that GR alone will not eliminate VAD and associated health problems.[6] Nonetheless, its potential to improve the VA and health status of the Philippine population is considerable.

[6] Although Dawe et al. (2002) use a different approach and do not derive a clinical efficacy of GR, their results on technology contribution to VA requirements are similar to ours.

Table 3
Vitamin A supply and efficacy of Golden Rice

	Pessimistic scenario			Optimistic scenario		
	Children	Pregnant women	Lactating women	Children	Pregnant women	Lactating women
Rice intake (g/day)[a]	121.00	245.00	274.00	121.00	245.00	274.00
Current VA supply from all food sources (μg/day)[a]	234.30	597.10	404.10	234.30	597.10	404.10
RDA for VA (μg/day)[b]	500.00	800.00	1250.00	500.00	800.00	1250.00
VA deficit (μg/day)	265.70	202.90	845.90	265.70	202.90	845.90
Beta-carotene intake through GR (μg/day)	145.20	294.00	328.80	363.00	735.00	822.00
VA from GR after bioconversion (μg)	12.10	24.50	27.40	60.50	122.50	137.00
Improved VA supply (μg/day)	246.40	621.60	431.50	294.80	719.60	541.10
Contribution of GR to reduce VA deficit (%)	4.55	12.07	3.24	22.77	60.37	16.20
Efficacy (%)	11.54	24.64	9.65	47.97	86.08	40.30

[a] These figures are based on FNRI (1993).
[b] These figures represent internationally used RDAs (IOM, 2002).

Coverage rate

Accessibility

Access to GR by consumers will primarily depend on the extent to which the new rice varieties will be used in agricultural production, and, hence, their availability on local food markets and for home consumption. The first precondition is that the technology will be commercially approved under the bio- and food safety regulations. Although the biotechnology debate in the Philippines has been controversial in the last few years, the National Committee on Biosafety recently approved commercial cultivation of genetically modified corn. We take this as an indication that biosafety procedures for GR will be handled efficiently by national authorities, once the technology enters the testing phase.

Currently, researchers are incorporating GR technology into high-yielding varieties that are already established in the market, are consumed by the poor and are easily crossable with other breeding lines. These modified varieties will be handed over to farmers free of charge.[7] They can be reproduced by the growers themselves, so that there could potentially be a speedy dissemination through a farmer-to-farmer exchange of seeds. Experience from the green revolution shows that acceptable germplasm can diffuse very rapidly in the country (Hayami and Kikuchi, 2000). Thus, also subsistence rice farmers and poor consumers in remote rural

[7] Private companies, holding patents over certain technology components, agreed to waive royalty payments when GR is used by resource-poor producers. Most of the rice in the Philippines is produced by small-scale, semi-subsistence farmers.

areas could be reached with GR. Such groups are more difficult to target with other VA intervention programmes.

Acceptance

Technology acceptance depends on attitudes towards biotechnology in general and features of GR in particular. Although biotechnology opposition in the Philippines was fairly strong in the past, there are indications that public attitudes are gradually becoming more positive. With respect to acceptability of GR itself, very little is known so far. Only its yellowish colour has often been named as a possible constraint. Most of the rice consumed in the Philippines is polished and white.

In order to get a better understanding of acceptance issues, we carried out focus group discussions with rice producers and consumers in two typical rice villages in Laguna and Nueva Ecija provinces. Although participants were not representative of the Philippine population, the discussions revealed some interesting perceptions. Consumers were generally interested in obtaining VA-enriched rice, and they did not express reservations about the yellow colour of the grain. Their responses revealed, however, that changes in taste and price would restrict widespread use of GR. Rice farmers, on the other hand, were concerned about the fertility of harvested seeds. Yields will also be an important adoption factor: given that poor consumers are not willing to pay more for VA-enriched rice, a technology-related productivity loss would not be compensated by a market price premium.

Although IRRI researchers do not expect changes in taste and agronomic characteristics, related tests have not been conducted yet. Hence, undesirable effects cannot be ruled out with certainty. Furthermore, experience in different countries with adoption of other value-enhanced crops, such as quality protein maize, shows that education and information can be crucial determinants (Lauderdale, 2000). The transgenic approach has the advantage that GR technology can also be incorporated into newly bred varieties with superior agronomic traits, to increase adoption incentives for farmers. Nonetheless, the yellow colour requires explanation, so that public information campaigns will be essential for widespread use. Based on the limited information available thus far, it is extremely difficult to assess the future coverage of GR. The variable is not completely random however; researchers and policymakers can influence its outcome. For the pessimistic scenario, we assume that 40% of the consumers would switch to GR, while in the optimistic scenario, the coverage rate is 60%. Initially, consumers are likely to test GR in smaller quantities, but it is supposed that the whole rice intake, as shown in Table 3, will be substituted eventually. Different assumptions of coverage rates will be tested in the sensitivity analysis.

Potential benefits of Golden Rice

Based on the discussion in previous sections, we now turn to the evaluation of potential benefits of GR for the pessimistic and optimistic scenarios. For easy reference, the underlying assumptions are summarised in the following.

- *Pessimistic scenario*. The amount of beta-carotene is 1.6 μg/g of GR. Post-harvest losses are 25%. The bioconversion rate to VA is 12:1, and the technology coverage rate is 40%.
- *Optimistic scenario*. The amount of beta-carotene is 3.0 μg/g of GR. There are no significant post-harvest losses. The bioconversion rate is 6:1, and the technology coverage rate is 60%.

DALYs gained

Using the assumed values for the technology's efficacy and coverage, new prevalence and mortality rates were derived, and the remaining number of DALYs lost with GR was calculated. The difference between these values and DALYs lost without GR is the projected annual benefit, expressed in years of "healthy" life gained. The results are shown in Table 4.

The total gain in the pessimistic scenario is about 15,000 DALYs, while in the optimistic scenario it is about 85,000 DALYs. Compared to the situation without GR (see Table 2), the health burden is reduced by 5.7% and 31.5%, respectively. Although the biggest overall benefits accrue for the group of children, the gains resulting from reduced disability are higher for pregnant and lactating women. This is due to the lower initial prevalence of corneal xerophthalmia among children in the Philippines. For them, the gains due to reduced mortality are more important. After depletion of body stores, even moderate levels of deficiency can have fatal consequences, so that an improvement in the VA status can lower the death toll significantly. While in the pessimistic scenario, GR can avert 136 child deaths per year, in the optimistic scenario, the number of averted cases is 798. Table 4 also shows DALYs gained in monetary terms. In spite of the comparatively low value of $1030 per DALY, the annual benefits are sizeable.

Table 4
Potential annual benefits of Golden Rice (DALYs gained)

	Children	Pregnant women	Lactating women	Total
Pessimistic scenario				
Gain due to reduced mortality	3929	234	58	4221
Gain due to reduced disability	2920	4872	3298	11,090
Total gain	6849	5106	3357	15,311
In monetary terms (million US$)	7.1	5.3	3.5	15.8
Optimistic scenario				
Gain due to reduced mortality	23,035	1155	344	24,534
Gain due to reduced disability	17,118	24,062	19,423	60,602
Total gain	40,153	25,217	19,767	85,137
In monetary terms (million US$)	41.4	26.0	20.4	87.7

Cost–benefit analysis

This sub-section puts the anticipated monetary benefits of GR in relation to R&D investments. The project was started in 1992, with the first phase at Swiss and German universities focusing on basic scientific principles. The concept was successfully proven in 1999 (Ye et al., 2000). Research expenditures during this phase in Europe were estimated at $3 million. These costs are not considered in our analysis in the Philippines, because the knowledge and technology generated are likely to produce much wider international benefits.

A breakdown of the estimated cost of R&D at IRRI and technology testing and dissemination in the Philippines is given in Table 5. The three-year adaptive research phase includes the verification and improvement of available gene constructs and their incorporation into popular varieties. After this, a three-year testing phase is foreseen for field trials, feeding experiments and bio- and food safety evaluation. The budget also includes outlays for variety registration and commercialisation. The total cost for the six years of R&D and testing is estimated at around $3.7 million. IRRI has an international mandate, and the GR varieties will also be transferred to a number of other countries. Nonetheless, we consider the full costs in the Philippine context. Furthermore, it is reckoned that expenditures of about $7 million will be necessary after the testing phase for a broad information and dissemination campaign, including the first delivery of seeds to farmers. This value is based on a detailed cost estimate of promotional activities for the VA supplementation programme (Fiedler et al., 2000).[8] After commercial release of GR varieties, a recurrent annual cost of $0.5 million is assumed for germplasm maintenance and monitoring.

Returns on project investments were calculated, assuming a benefit stream of 10 years after technology release. In the pessimistic scenario, the internal rate of return (IRR) is 66%, while it is 133% in the optimistic one. Notwithstanding the low monetary value imputed per DALY gained, these figures are relatively high when compared to R&D projects focusing on improvements of agronomic traits in agricultural crops. This preliminary cost–benefit analysis confirms that breeding for micronutrient-dense staple foods can be an investment with high social returns.

It would certainly be interesting to compare these results for GR with other alternatives to reduce VAD. Unfortunately, cost–benefit studies for VA interventions in the Philippines or other countries are not available. Fiedler et al. (2000) carried out a cost-effectiveness analysis for the Philippines's supplementation and fortification programmes. But, as is common in cost-effectiveness studies of nutrition interventions, their measure of effectiveness is the number of people being lifted from deficient to non-deficient levels. Thus, a comparison with our results is difficult. In a mere juxtaposition of recurrent costs, GR appears to be a sustainable

[8] The $7 million for promotional activities in the supplementation programme include expenditures for printing and distributing promotional leaflets, radio and TV broadcasts, and the cost of social mobilization campaigns in urban and rural areas. Personnel costs account for over 70% of the total (Fiedler et al., 2000).

Table 5
Estimated cost of R&D and dissemination campaigns

Phase	Cost (US$)
Adaptive research phase (3 years)	
Infrastructure and operating expenditures	1,000,000
Personnel	423,000
Testing phase (3 years)	
Infrastructure and operating expenditures	2,000,000
Personnel	300,000
Information and dissemination campaigns	7,000,000
Total cost up to first technology release	10,723,000
Recurrent annual cost for maintenance research and monitoring	500,000

low-cost intervention: the total cost of VA supplementation is around $21 million per year, while the annual cost of a hypothetical wheat flour fortification programme was estimated at $4–6 million (Fiedler et al., 2000). However, this comparison should not be over-interpreted, because it neglects the benefit side. Each intervention has its advantages and shortcomings. Supplementation has a high efficacy, but especially in rural areas it is very costly. Industrial fortification is cheaper but less favourable in terms of targeting the poor. GR could be complementary to both. Although the technology's efficacy might be limited at present beta-carotene contents, its coverage among the rural poor could potentially be high.

Sensitivity analysis

Although extensive efforts have been made to derive realistic data and assumptions, many variables are still associated with uncertainty. Therefore, the sensitivity of results is tested with respect to variations in key parameters. Individual values are changed *ceteris paribus*, taking the original assumptions in the pessimistic and optimistic scenarios as benchmarks. Table 6 shows the impacts on annual DALYs gained and IRRs.

Table 6
Impact of parameter variations on results

	Pessimistic scenario		Optimistic scenario	
	DALYs gained	IRR (%)	DALYs gained	IRR (%)
Original assumptions	15,311	66	85,137	133
Post-harvest losses: 50%	9801	51	49,423	110
Coverage rate: 25%	9569	50	35,474	97
Coverage rate: 100%	38,278	100	141,895	155
Amount of beta-carotene: 5 μg/g	49,720	110	115,773	146
Efficacy function: linear	6356	37	44,693	106
Prevalence rates: half of present values	9766	51	54,836	114
R&D and dissemination costs: 150%	15,311	52	85,137	116
Technology depreciation: 5% per year	15,311[a]	60	85,137[a]	130

[a] It is assumed that these values decrease by 5% annually over the 10 year benefit stream.

At first, effects of higher post-harvest losses of beta-carotene are analysed. For instance, if GR will be stored or processed improperly, actually consumed amounts of beta-carotene could be lower than initially assumed. Accordingly, the technology's efficacy and health benefits would shrink. Smaller benefits could also be due to lower coverage rates. Following researchers' expectations, our initial scenarios build on the assumption that GR technology would have little or no impact on agricultural productivity or taste. However, acceptance problems would arise if consumer characteristics turned out to be notably different, or if the transgenic varieties were agronomically inferior to conventional ones. This underlines the importance of incorporating the technology into locally adapted germplasm, including newly bred varieties with superior producer traits. Adoption levels might also remain limited without appropriate information campaigns during the early stages of diffusion. However, with suitable policies, it is also possible that longer-term coverage rates are higher than initially assumed. Besides, biotechnologists might manage to further increase the beta-carotene content in the grain. The advantage of the transgenic approach is that new genes might be identified, which are more efficient in micronutrient synthesis. The results in Table 6 demonstrate that such developments would bring about notably higher benefits.

A different source of uncertainty relates to the convexity of the efficacy function. As was argued above, little is known about the exact parameterization, so that in Eq. (4), a function with moderate curvature was specified. A lesser curvature would lead to smaller positive health effects and thus lower benefits. In the worst case, the efficacy function would be linear, implying that a 1% reduction in VA deficit would lead to an equivalent change in efficacy, regardless of the initial VA status. Under this extreme assumption, the health benefits would be less than half the initial gains in the pessimistic, and slightly more than half in the optimistic scenario.

Next, the influence of changing prevalence and mortality rates is analysed. In 2004, the Philippine wheat flour fortification programme, which was voluntary for millers up till now, will become mandatory on a countrywide basis. This is before GR will become available commercially. Given abovementioned targeting problems, not all deficient people will be reached through wheat flour fortification. Nonetheless, the programme is likely to reduce the prevalence of VAD up to a certain point. For illustrative purposes, we reduce the initial prevalence and mortality rates by an exaggerated 50% for all three target groups. In that case, the health costs without GR would only be half the previous value, and the technological benefits would be significantly smaller too. Unsurprisingly, higher initial prevalence rates or a bigger population, both of which are found in many other countries of South and Southeast Asia, would have the opposite effect (not shown). Because GR varieties can be reproduced by farmers, the cost of scaling up their use will be much smaller than for other micronutrient interventions.

Finally, the sensitivity is tested with respect to increases in project costs and a possible reduction of benefits over time. Cost increases could happen through unexpected complications during R&D, testing and technology dissemination, while reduced benefits could occur through technology depreciation.[9] Increasing each individual cost item by 50% does not change the benefit side, but the IRRs are lower than those that were calculated with the original cost estimates. The impact of an assumed 5% technology depreciation per year would be small, albeit it would certainly challenge the technology's sustainability. Overall, Table 6 re-emphasises that the exact numerical outcomes of the scenario calculations should be interpreted with caution. Nonetheless, even under fairly extreme parameter variations, the health benefits and IRRs remain sizeable. Many of the project details can still be influenced by researchers and policymakers. Priorities should be set towards maximizing the social returns.

Conclusions

VAD is a severe problem in developing countries, causing temporary and permanent eye impairments and increased mortality, especially among children and pregnant and lactating women. The analysis shows that the annual health costs in the Philippines are in a magnitude of 0.3% of the country's GNP. These costs could be reduced through GR. The scenario calculations demonstrate that GR will mitigate problems of blindness and premature deaths, with social benefits ranging between $16 and 88 million per year.

Although these are remarkable gains, it must be clearly stated that GR alone will not eliminate VAD and related health costs. Micronutrient deficiencies are caused by a complex set of economic, social and cultural factors, so that a technological approach cannot be considered a magic bullet. The purpose of developing GR is not to replace other interventions such as food fortification, supplementation or dietary education programmes. Rather, the technology should be seen as a complementary tool in the fight against VAD. GR is particularly promising for remote rural areas, because, after the initial R&D investment, the cost and institutional effort to reach the target population is much lower than for other interventions. The advantage is that GR can be reproduced and multiplied by farmers themselves. With appropriate information and dissemination campaigns during the early stages of adoption, diffusion could potentially be fast and widespread through an informal exchange of seeds.

A preliminary cost–benefit analysis shows that R&D expenditures for GR are a highly profitable public investment. In the scenario calculations, IRRs range between 66% and 133%. These returns are higher than for many crop breeding projects focusing on the improvement of agronomic traits. Of course, the benefits of agronomically improved crops and micronutrient-dense staple foods are different in nature. While the former show up in terms of increased real incomes for agricultural producers and consumers, the latter consist primarily in a reduced

[9] Technology depreciation could be the result of genetic dilution of the value-added trait. Although rice is mostly self-pollinating, some dilution might occur when seeds are reproduced repeatedly. Depreciation should be detained through regular supply of fresh material to informal seed markets.

burden of disease for society in general and affected population groups in particular. These benefits might be less visible, but our analysis demonstrates their high economic significance. The breeding approach appears to be a promising and efficient way of reducing micronutrient deficiencies among the poor.

However, it has to be emphasised that there is still a large degree of uncertainty related to the technology's efficacy and coverage, which are key variables for the scenario calculations. Although the sensitivity analysis confirms the robustness of the general statements, more research and better data are needed before far-reaching conclusions can be drawn. Also, it should be pointed out that our analysis is only a first attempt to quantify the health impacts of micronutrient-enriched food crops within an economic framework. There is ample scope for refining and extending the methodology employed. In particular, a further disaggregation of target groups by income and/or region could deliver interesting results for decision-making processes. With slight adjustments, the methodology could also prove useful for the evaluation of crops containing other health-improving compounds such as nutraceuticals or edible vaccines.

Acknowledgements

The financial support to this project by the Eiselen Foundation, Ulm, Germany, and the German Agency for Technical Cooperation (GTZ), is gratefully acknowledged. The authors would like to thank researchers at the International Rice Research Institute (IRRI), especially Mahabub Hossain, David Dawe, and Swapan Datta, for their support during data collection in the Philippines. Constructive comments on earlier drafts of this paper were received from Joachim von Braun, Howarth Bouis, Robert Russell, Claudia Stein, Tessa Tan-Torres, Carl Pray, Ingo Potrykus and two anonymous referees of this journal. Possible errors are the sole responsibility of the authors.

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