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Golden rice: what role could it play in alleviation of vitamin A deficiency?

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Abstract

Golden rice (GR) is a new rice variety that has been genetically modified to contain beta-carotene, a source of vA. This modification was undertaken as a strategy to address VAD, which is widespread in less developed countries of Asia. Children's food intake data from a poor rural region of the Philippines are used to simulate the potential impact of GR on vA intake. The potential impact, coverage of deficient subpopulations, and costs of GR are compared to two other interventions, food fortification and supplementation. While investments in future development of GR compare favorably with other interventions in terms of costs and coverage, GR would deliver amounts of vA that are modest, and unlikely to fulfill requirements. Thus, it should be viewed as a complement to existing interventions. To have greatest impact at a cost comparable with wheat fortification, GR varieties should be suited for widespread adoption in Asia and should deliver as much beta-carotene as possible.

Keywords: Rice; Nutrition; Vitamin A deficiency; Household consumption

Introduction

Vitamin A deficiency (VAD) is an important nutritional problem in the developing world (World Bank, 1993).[1] Vitamin A's (vA) primary physiologic role is in vision

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[1] The World Bank estimated that VAD accounted for 11.8 million disability adjusted life years lost in the world in 1990; with an additional 39.1 million DALYs (Disability Adjusted Life Year) lost from associated diseases. This is roughly one-quarter of the total global burden of disease from malnutrition.

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and maintenance of the general health of the eye, with a myriad of secondary roles, such as maintenance of the immune system. Supplementation or increased consumption of carotenoids in deficient populations has been found to substantially reduce morbidity and mortality for children (Sommer, 1997). VAD is prevalent among the poor in Asia, because their diets are dependent on rice, which does not contain vA precursors (FAO and IRRI, 1993).

Golden Rice (GR) was developed to provide a new, alternative intervention to combat VAD by genetically engineering rice to contain beta-carotene (the vA precursor found in plants) in the endosperm of the grain (Toenniessen, 2001). GR's genetic engineering heritage has inspired conflicting opinions concerning its possible effectiveness and desirability. Critics have argued that the resources devoted to GR development could be better used to support traditional interventions (MASIPAG, 2001). Proponents have argued that GR represents an important complementary intervention that could succeed in reaching more of those at risk for VAD (Toenniessen, 2001).

This paper examines the potential benefits from GR in two ways. First, if GR can be developed into a viable field crop, can it deliver significant amounts of beta-carotene into the diets of high-VAD-risk children? We use children's food intake data from the Cebu region of the Philippines to simulate the potential benefits of GR consumption. Accurate food intake data for at-risk populations are relatively rare, and the publicly available Cebu Longitudinal Health and Nutrition Survey provides a valuable data set to simulate the potential benefits of GR. Secondly, how would GR compare to existing interventions in terms of monetary cost, effectiveness of delivery, and coverage of subpopulations at risk? We examine evidence from the Philippines to see how GR would compare to mandated food fortification that will begin in 2004. We also compare the cost of developing and delivering GR to several countries in Asia with the costs of food fortification and supplementation.

Vitamin A deficiency in Asia

Of the various macro- and micronutrient deficiencies afflicting poor populations, VAD is unique with its well defined and debilitating effects. VAD is caused by insufficient consumption of foods containing vA and beta-carotene (which is metabolized into vA). Preformed vA is found in animal products while beta-carotene resides in dark green, yellow, and orange plants as well as in some animal products.

Vitamin A (in the form of various retinol derivatives) is a fat soluble vitamin stored primarily in the liver with various roles, the primary being sight and general eye health. When a person does not eat enough vA and beta-carotene for long periods of time, the most obvious results are nightblindness, Bitot's spot (foamy patches on the surface of the eye), xeropthalmia, and in extreme cases, blindness (National Academy of Sciences, 2001). VAD in children has also been associated with poor growth, increased mortality, and vulnerability to infection, particularly measles and diarrhea (Sommer, 1997). The increased morbidity and mortality are apparent even before the appearance of xerophthalmia, and supplementation has had a dramatic effect in reducing mortality among children aged from 6 months to 6 years in Nepal, Indonesia, India, and Ghana (Sommer, 1997).

VAD is assessed through looking for the clinical signs or by monitoring blood serum levels (<10 μg retinol/dl considered deficient; <20 μg/dl considered low). However, due to the liver's storage capacity, bloodstream levels are depressed only when liver stores are virtually gone. Thus, a deficiency detectable in this way is indicative of a chronic problem. Lastly, VAD is detected by dietary analysis. This method is not as definitive as the other two, but is the primary method of identifying broad populations at risk.

VA requirements, as estimated by the National Academy of Sciences (2001) are summarized in Table A1 (see appendix). There are two different numbers reported for requirements: the estimated average requirement (EAR) and the recommended daily allowance (RDA). The EAR measures the average requirement over all persons in the category. The RDA is set so as to provide 97–98% of individuals with a sufficient intake and is thus 40% higher than the EAR in the case of vA. For children under 13 years of age, the RDA is in the range 300–600 retinol activity equivalents (RAE) per person per day, depending upon age and gender.

There are several ways to measure quantities of vA and beta-carotene; all are expressed in micrograms (μg). An international unit (IU) of retinol is 0.3 μg and an IU of beta-carotene is 0.6 μg. Retinol equivalents (REs) were devised to normalize by biological activity since carotenoids have less of an effect than retinol for the same mass. Thus, 1 REs is 1 μg retinol, 6 μg beta-carotene or 12 μg other carotenoids. However, more recent evidence has led nutritionists to believe that beta-carotene is even less effective than previously thought (National Academy of Sciences, 2001). Thus, the National Academy of Sciences report introduces the idea of RAE to distinguish from the earlier REs. So, 1 RAE is 1 μg retinol, 12 μg beta-carotene, or 24 μg of other carotenoids. One implication of the recent thinking regarding RAE is that plant-based diets may be even more deficient than previously thought, and hence more people who consume such diets may be at risk for VAD (UN ACC/SCN, 2000).

Drawing on a variety of sources, the *Fourth Report on the World Nutrition Situation* reports varying estimates of 2.8 or 3.3 million preschool children with clinical VAD, and an additional 251 or 75–140 million are subclinical (sources are WHO/UNICEF and the Micronutrient Initiative/UNICEF/Tulane, respectively). It is noted that, "[d]espite the discrepancies in these estimates, which ultimately reflect the paucity of real data, it is clear that vitamin A deficiency remains a major public health problem of immense proportions." (UN ACC/SCN, 2000, p. 30).

A lack of diversity in diets of the poor is the determining factor in VAD. In particular, poor people whose diets are based on rice are at greater risk for VAD, since rice contains no beta-carotene. Table 1 shows data on the importance of rice in Asian diets and the estimated per capita intake of vA from the mid-1980s. Most of the less developed Asian countries have estimated average intakes of less than 120 REs/day, which is well below the EAR or the RDA for most of the population. In these poor Asian countries, rice accounts for a large percentage of calories and of food expenditures. More recent data confirm that in Bangladesh, Myanmar, and Vietnam, rice continues to account for at least two-thirds of caloric intake for the average citizen (FAOSTAT, 2001) with the share being even higher for many of the

Table 1
Rice consumption, energy availability, and vA intake in selected Asian countries

Country	Calories (kcal/caput/day)	Rice consumption (kg/caput/year)	Rice as percentage of calories	vA (μg REs/caput/day)
Bangladesh	2201	168	76	40
Cambodia	2000	165	76	60
India	2417	74	30	70
Indonesia	2931	154	52	50
Japan	2782	60	23	480
Korea DPR	2100	75	35	80
Korea, Rep	3073	94	33	160
Malaysia	2946	88	29	140
Myanmar	2803	211	73	60
Nepal	2264	93	38	120
Philippines	2357	100	41	90
Sri Lanka	2411	99	40	50
Thailand	2411	101	42	280
Vietnam	2564	170	65	70

Source: columns two to four are from FAO (1999). Rice amounts are milled, uncooked. Last column is from FAO and IRRI (1993). Unfortunately these data in the last column refer to the mid-1980s; we could not find later data for vA intake on a country basis.

poor. Dark green leafy vegetables are the most affordable dietary source of vA, but may not be consumed in sufficient quantities due to dietary preferences or seasonal availability. Animal products contain vA in a more directly available form, but these are much more expensive and thus less accessible for the poor (Helen Keller International, 1999). Asian countries with low income and rice-based diets are also those classified as having a significant public health problem with xerophthalmia in a study by West and Somer (1987), including India, Bangladesh, Nepal, Indonesia, the Philippines, Vietnam, Cambodia, and Laos. More recent surveys confirm that VAD is a continuing public health problem in these countries (Helen Keller International, 1999; FAO, 1999).

This study uses data from the island of Cebu in the Philippines, where there are still large numbers of at-risk groups with deficient or low levels of plasma vA. The 1998 Fifth National Nutrition Survey in the Philippines (National Nutrition Council, 2001) found that moderate VAD (serum retinol <20 μg/dl based on blood assays) affected 38% of children aged 1–5 years, 22% of pregnant women, and 17% of lactating women. (Severe deficiency, measured by serum retinol <10 μg/dl, affected 8.2% of children, 7.1% of pregnant mothers, and 3.9% of lactating mothers.) These fractions are a bit higher than those of the Fourth National Nutrition Survey of 1993 when they were 35, 16, and 16% (Kuizon et al., 1995), possibly because of the effects of the currency crisis that began in the second half of 1997 and the impact of the severe El Niño that hit the region at around the same time. Both surveys indicate that VAD is a continuing problem in the Philippines. The persistence of this public health issue was behind the development of GR as a potential source of vA in the diets of the Asian poor. Next we examine what role GR could play in the diets of a particular region of the Philippines.

Case study of potential GR impacts in Cebu, the Philippines

Cebu is a relatively poor region of the Philippines and has historically been found to have high incidences of VAD (Solon et al., 1978). In the National Nutrition Survey of 1998, Cebu had higher than the national average incidence of severe deficiency and low (but not deficient) vA blood serum levels were found among 52% of children under 5 years (National Nutrition Council, 2001).

Data and Methods[2]

The data used are from the 1994 Cebu Longitudinal Health and Nutrition Survey. This survey identified and is following about 2000 families who had a child between May 1983 and April 1984. The mothers were selected while still pregnant. In addition to being interviewed at that time, the families were surveyed immediately after the birth of the child and every two months for the first 2 years. Follow-up surveys were conducted in 1991–1992, 1994–1995, and 1998–1999, expanding the range of information collected. We use the 1994 data for this paper as they include detailed food intake data for 1839 children aged 10–12 years. The consumption data record how much of which foods were eaten by the child throughout the course of one full day.

These data were selected for our analysis because they provide recent, accurate food intake information for a population known to be at risk for VAD. These data are publicly available through the University of North Carolina (see web site at http://www.cpc.unc.edu/cebu/). An important drawback to use these data is that Cebu is one of the places in Asia where rice is not the only staple.[3] White flint maize (mainly in the form of grits) is of almost equal importance to rice in Cebuano diets (very little rice is grown and is thus imported from other Philippine regions), which will limit the potential impact of GR. On the other hand, adoption of GR will be a matter of consumer preference only and will not depend upon whether or not GR can be successfully produced for home consumption.

The consumption of rice, maize, vegetables, and animal products is determined (as averages) for the original children in the survey who range from 10 to 12 years of age in 1994. These measurements are further broken down by asset quintile as measured by total reported value of houses and lands owned by the household. Total

[2] Details of the methods used for dietary analysis are available in Appendix A to this paper, which is posted at this website: http://web.aces.uiuc.edu/wf/workingpapers/wrkngpapersindex.htm.

[3] Other regions where rice is the preferred but not the only major staple include part or all of the following areas: central and east Java in Indonesia, eastern Indonesia, Mindanao in the Philippines, and central India.

household assets provide a measure of permanent income and are more easily obtained from these data than annual income.

We use the consumption patterns of rice and white maize grits to estimate the effects of substituting GR and yellow maize grits. The amount of beta-carotene provided by GR is that reported by Ye et al. (2000); the vA content of yellow maize grits is from the USDA (2001) food composition tables. In both cases, RAE are derived according to the conversion suggested by the National Academy of Sciences report (2001). For GR, we use two possible values, one reflecting the actual beta-carotene in the original variety created in Europe and another higher value reflecting the potentially achievable level in the future (Ye et al., 2000). These increases in vA from hypothetical substitutions are considered as fractions of the EAR and RDA, as well as compared to estimates of current vA intake and potential vA intake from wheat fortification.

Results

Food consumption relates to asset level as expected: rice increases, maize decreases, vegetables decrease slightly, fish intake remains roughly constant, and animal products increase (Table 2). These preferences are typical of rural Southeast Asia where maize and rice are both staples (e.g. see Foster and Leathers, 1999, chapter 8, for similar data from East Java).

The current vA intake for these children is presented in Table 3; average vA intake for all children is only 186 RAE. While vA intake is higher for those children in the top asset quintile, at 225 RAE it is still substantially lower than the EAR of about 430 RAE. Retinol is obtained only from animal product consumption and beta-carotene is primarily from plant sources. As would be expected, the importance of retinol as a source of RAE rises with income. The low level of vA intake relative to requirements for children in all rural households illustrates the need for supplementing this intake in some way.

We examine two possible scenarios for substitution of cereal staples with beta-carotene containing alternatives (Table 4). The high substitution scenario assumes that all rice and maize consumed contain beta-carotene, and assumes that the beta-carotene content of GR would be 2.0 μg/g uncooked milled rice. In a low substitution scenario, only one-third of rice and one-third of the maize grits are assumed to contain beta-carotene; GR beta-carotene content is assumed to be the one in the best existing strains (1.6 μg/g). For comparison, the beta-carotene content of the existing GR converts to 4.67 RAE/100 g of cooked rice, and yellow cooked grits have 3 RAE/100 g. Switching to GR delivers more RAE per unit consumed, but the impact of the two hypothetical substitutions will depend on the relative importance of rice and maize in these children's diets.

For the top and bottom quintiles, in the low substitution scenario the total increases from both maize and rice are 8.3 and 7.5 RAE, respectively (Table 4). This corresponds to only 2.1 and 1.9% of the EAR, or 1.4 and 1.2% of the RDA. This amount is a very modest, and possibly insignificant, increase in intake. In the high substitution scenario, the total vA intake increase from both staples is 30.1 and 25.2 RAE

Table 2
CLHNS index children's consumption of foods by household asset level (g)

Asset distribution/food	Bottom quintile (n = 518)	Near bottom (n = 432)	Middle quintile (n = 442)	Near top (n = 357)	Top quintile (n = 417)	All children (n = 2166)	Boys (n = 1130)	Girls (n = 1036)
Rice	191	243	303	367	362	286	301	270
Maize	264	205	137	89	87	163	171	154
Wheat	46	50	54	62	70	56	58	53
Vegetables	14.9	12.7	12.6	10.9	9.7	12.3	12.1	12.6
Fruit	28	26	44	31	29	32	31	32
All animal products, of which:	52	59	78	90	114	77	83	70
Dairy	2.2	1.7	2.7	5.0	10.6	4.3	4.6	4.0
Eggs	4.5	4.1	7.5	7.5	6.9	6.0	6.6	5.3
Fish	24	28	27	27	28	28	28	26
Meat	21	25	40	50	68	40	44	35

Source: 1994 CLHNS survey; all units are grams cooked. One unit of cooked rice equals 0.34 units of raw rice.

Table 3
Estimates of current daily intake of beta-carotene, retinol, and vA (RAE) for CLHNS index children

	Beta-carotene	Retinol	Total RAE	Fat (g)
Bottom quintile	655	121	176	16.6
Near bottom quintile	564	122	169	19.9
Middle quintile	484	129	169	26.7
Near top quintile	444	162	199	30.0
Top quintile	428	189	225	38.9
All children	524	143	186	25.8
Boys	535	155	199	27.3
Girls	511	129	172	24.2

Table 4
Impact of hypothetical staple substitutions on vA intake for CLHNS index children and for top and bottom quintiles of household asset distribution

	RAE increase	% EAR	% RDA	Percentage of current vA intake
Bottom quintile high substitution				
Rice	13.9	3.5	2.3	7.9
Maize	11.3	2.8	1.9	6.4
Total	25.2	6.3	4.2	14.3
Bottom quintile low substitution				
Rice	3.7	0.9	0.6	2.1
Maize	3.8	0.9	0.6	2.1
Total	7.5	1.9	1.2	4.2
All children high substitution				
Rice	20.9	5.2	3.5	11.2
Maize	7.0	1.8	1.2	3.8
Total	27.9	7.0	4.6	15.0
All children low substitution				
Rice	5.6	1.4	0.9	3.0
Maize	2.3	0.6	0.4	1.3
Total	7.9	2.0	1.3	4.2
Top quintile high substitution				
Rice	26.4	6.6	4.4	11.8
Maize	3.7	0.9	0.6	1.7
Total	30.1	7.5	5.0	13.4
Top quintile low substitution				
Rice	7.0	1.8	1.2	3.1
Maize	1.2	0.3	0.2	0.6
Total	8.3	2.1	1.4	3.7

Notes: High substitution replaces all rice with GR and all maize with yellow maize. GR assumed to have future potential level of beta-carotene. Low substitution replaces one-third of rice with GR and one-third of maize with yellow maize. GR is assumed to have beta-carotene of current best strain. EAR and RDA are midpoint of those for girls and boys 9–13 years in Table A1 (see appendix).

for the top and bottom quintiles, which are 7.5 and 6.3% of the EAR. From GR alone, the increases are 26.4 and 13.9 RAE, respectively. This complete substitution results in more noticeable increases in intake. As a percent of current intake, GR alone would boost vA intake by 7.9% for the bottom quintile in the high substitution scenario, while GR and maize would boost intake by 14.3% (Table 4).

There are two qualifications about increased beta-carotene from cereal staples. First, bioavailability is enhanced if the cereals are consumed along with some fat. One study suggests that 10 g per day is adequate to ensure vA availability (Roodenburg et al., 2000); at least 5 g of fat at the same meal is desirable (Erdman, 2002). Average fat intake for these children varies from 16 to 39 g per day across asset quintiles (Table 3). Furthermore, at least 90% of all meals where rice was consumed contained some form of fat. Therefore, fat intake should be adequate in most cases to ensure bioavailability, although the low fat intake for the bottom quintile indicates that this may be a concern for future study.

The second qualification regarding bioavailability is that the beta-carotene from GR is likely to be more available than that from some other plant sources, and hence the RAE available may be more than assumed in Table 4. Underwood (2000) proposes a hierarchy of bioavailability among plant sources, although without specific conversion factors. Starchy sources such as sweet potatoes have greater bioavailability of vA from beta-carotene than fibrous sources such as dark green leafy vegetables. It has been speculated that beta-carotene in GR will be converted to RAE at a ratio of 6:1 instead of the 12:1 conversion factor for other plant-based sources (Beyer et al., 2002), although no specific tests or studies have been carried out yet. If so, then the RAE amounts from GR in Table 4 would be twice as large, and GR might deliver a 16% increase over current vA intake to the poorest Cebuano children.

As fortification of wheat flour, cooking oil and sugar with vA will become mandatory in the Philippines in 2004, its potential impact in these Cebuano children's diets is examined. Levels of fortificant are assumed to be the minimum amounts required by law (300 RAE per 100 g of wheat flour, 500 RAE per 100 g of sugar, and 1200 RAE per 100 ml of cooking oil). Children in the top and bottom quintiles consume 70 and 46 g of wheat products, respectively, and would gain 210 and 139 RAE from wheat fortification alone (Table 5). This amounts to 52 and 33%, respectively, of the EAR. Including sugar and cooking oil raises the percentages to 72 and 52%. Because these foods can be fortified with very high levels of vA, these expected increases in intake are much larger than those estimated for GR, which has more modest levels of vA, and is not the sole staple in this region. It should be noted that a study in the Philippines showed that as much as 63% of the vA in fortified wheat is lost in storage, milling, and baking (Solon et al., 2000a). Therefore, our estimates provide an upper bound of the expected impact of fortification.

Implications for the hypothetical benefits from golden rice

The estimates presented in this paper indicate that the potential impact of GR on vA intake will vary with dietary patterns. It would clearly be more important where

Table 5
Potential impact of wheat, sugar and oil fortification on vA intake of CLHNS index children

	RAE increase	% EAR	% RDA	Percentage of current vA intake
Wheat, sugar and oil				
Bottom quintile	208	52.0	34.7	118.2
Near bottom	229	57.2	38.1	135.8
Middle quintile	249	62.1	41.4	147.0
Near top quintile	278	69.4	46.3	139.7
Top quintile	309	77.1	51.4	137.4
All children	252	62.9	41.9	135.0
Wheat alone				
Bottom quintile	139	34.7	23.2	79.0
Near bottom	150	37.5	25.1	89.2
Middle quintile	162	40.4	26.9	95.6
Near top quintile	186	46.5	31.0	93.6
Top quintile	210	52.4	35.0	93.4
All children	167	41.8	27.9	89.8

rice is the main staple and if its beta-carotene content were enhanced. In this particular region, its impact is modest due to the fact that rice is not the main staple, and is less important in the diets of the poor, although the sum of the substitution effects for rice and maize in Cebu is likely to be a close approximation to the effects of rice substitution alone in other parts of Asia. Only full substitution results in significant contributions to vA intake.

When compared to the current intake of vA and beta-carotene, it is clear that it could provide a significant relative boost to current total intake. As Sommer and West (1996, p. 301) state, “It is now clear that children suffer consequences of inadequate vA nutriture long before they ever become xerophthalmic: increased rates of severe infection, anemia, mortality, and quite possibly growth retardation… However, the point at which they first begin to be affected and the quantitative nature of the relationship between their severity and vitamin A status, have not been established.” Thus any increase in vA intake over and above current low levels should have positive benefits for health in the general population by shifting the distribution of vA intake rightward, but these benefits are difficult to measure ex-ante.

GR’s importance in comparison to other interventions depends on existing dietary patterns. In Cebu, GR would probably have a larger effect than a change from white to yellow maize grits, mainly because it delivers more RAE per unit consumed. Given the amounts of wheat and cooking oil consumed by this population and the high levels of vA delivered by fortification, fortification would have a much larger impact on vA intake. But current vA intake is less than half of the EAR, and for the bottom quintile, fortification plus staple substitution would still leave intake at 95% of the EAR (and 68% of the RDA), assuming no loss of vA in cooking or storage. Therefore, *both* fortification and GR would help to improve the health status of the poor, and GR may have a role to play as a complement to other food-based interventions.[4]

An important insight from this analysis is the importance of both wheat and animal products in assessing vA intake and the potential benefits from fortification. Animal product consumption is rising rapidly throughout Asia (Delgado et al., 1999), and this will influence vA intake and the incidence of VAD. This is particularly true in light of the revised understanding of how much vA is delivered from plant sources. Wheat consumption is also rising throughout Asia, and this will make fortification more effective. However, the very poorest households will be much slower in following these consumption trends, and GR may have an important role for low income consumers.

The importance of targeting foods eaten by the poor can be seen in household consumption survey data from Indonesia and Bangladesh (Table 6). Although these

Table 6
Potential additions to vA intake from GR and wheat fortification in Indonesia and Bangladesh compared to Cebu, Philippines

	Income group				
	1	2	3	4	5
Indonesia					
Rice consumption per caput (kg daily)	0.255	0.297	0.319	0.325	0.306
Wheat consumption per caput (kg daily)	0.006	0.010	0.015	0.023	0.034
GR (daily RAE)	42	49	53	54	51
Fortified wheat (daily RAE)	17	29	45	68	103
Ratio wheat RAE to GR RAE	0.4	0.6	0.9	1.3	2.0
Bangladesh					
Rice consumption per caput (kg daily)	0.393	0.456	0.485	0.508	0.498
Wheat consumption per caput (kg daily)	0.035	0.033	0.035	0.026	0.040
GR (daily RAE)	65	76	81	85	83
Fortified wheat (daily RAE)	105	99	106	79	120
Ratio wheat RAE to GR RAE	1.6	1.3	1.3	0.9	1.4
CEBU, Philippines					
GR+yellow maize RAE	26	28	29	32	33
Fortified wheat RAE	132	150	153	159	203
Ratio wheat RAE to GR RAE	5.0	5.4	5.3	4.9	6.2

Sources of raw data on consumption of rice and wheat: Bangladesh Bureau of Statistics (1998) and Indonesia Central Bureau of Statistics (2000).

[4] In comparison with GR, fortification has the advantage that it does not rely on any change in consumer preferences, but past experience has shown that it may be difficult to enforce full compliance on the part of industry (Solon et al., 2000b).

are less precise than the individual food intake data from Cebu, they provide a useful comparison. GR would deliver 2–3 times as much vA to the poor in Indonesia and Bangladesh compared with GR and yellow maize in Cebu. The poorest consumers in Indonesia would obtain three times as many RAE from GR as from wheat fortification; and in Bangladesh RAE from GR would provide half as many as those from wheat. This is in contrast to Cebu, where wheat fortification provides five times as much as GR. While well-implemented fortification of wheat flour and cooking oil would each provide the poor with higher absolute levels of vA in Cebu, this would not be the case for the poor in other Asian countries. Thus, GR is better targeted towards the poor than wheat fortification.

Comparing the costs of alternative interventions to address VAD

The major interventions to address VAD include supplementation through administration of mega-doses of vA, fortification of widely consumed foods, nutrition education programs, and promotion of home gardens. We focus on the first two interventions as those with widest impact, and most comparable to GR. Supplementation with vA capsules is now widely practiced in many countries, and USAID has supported supplementation programs in Nepal, Indonesia, and the Philippines (USAID, 2002b). Once the retinol in the capsules is stored in the liver, it is excreted slowly and can sustain vA requirements for 4–6 months (De la Cuadra, 2000). Thus, semiannual distribution is feasible and is the preferred method because it reduces the labor costs associated with distribution.

From 1993 to 1996, the Philippines delivered vA supplements to a large percentage (88–93%) of children between the ages of 12–59 months (Fiedler et al., 2000). However, coverage declined to 78% in 1997. Distribution of the vA capsules was initially integrated with widespread polio immunizations, which are now being administered more selectively. This will make it more difficult to continue with universal supplementation of vA. Furthermore, supplementation does not reach sizable number of individuals at risk outside the primary target group. Despite the supplementation program from 1993 to 1997, the National Nutrition Survey of 1998 found widespread problems with VAD.

Fiedler et al. (2000) estimated the cost of achieving one person-year of adequate vA intake through supplementation at US$ 7.50–9.00, depending on the coverage rate assumed (based on the exchange rate at that time of about 40 pesos to US$). About 80% of these costs were personnel costs; capsules were only 2% of total costs. This estimated cost for the Philippines is somewhat higher than others reported in the literature and summarized by Fiedler et al. (2000) in Table 1 (these vary from US$ 0.50–0.81 per person per year cited by Levin et al., 1993 to over US$ 2.00 cited in Phillips et al., 1996), but it is not clear how other studies allocated the fixed costs of distribution. Furthermore, distribution costs will be a function of wage rates, and wages in the Philippines are higher than in many other developing countries. Thus, while supplementation capsules may be inexpensive, distribution programs have substantial costs, and may have difficulty sustaining government financial support.

Fortification is another strategy for reducing VAD. Fortification requires a food vehicle with widespread consumption, no downside risks to any segments of the population, and a regulatory system that can enforce adherence to requirements for processing and labeling. If production of the commodity is relatively centralized, this substantially reduces the burden on the regulatory authorities. In Asia, vA fortification is most common in margarine (India, Indonesia, Philippines, Malaysia) and in condensed and filled milk (Malaysia, Thailand, Philippines). Some wheat flour and cooking oil in the Philippines are also fortified, and as mentioned above, this will become mandatory in 2004. In other parts of the world, margarine is also an important vehicle for vA fortification, but other foods are used as well, the most common being maize meal in parts of Africa and sugar in Central America (Mora et al., 2000).

Fiedler et al. (2000) found that fortification of wheat flour was more cost-effective than supplementation in the Philippines. They estimated that fortification of wheat flour with 490 REs per 100 g flour would leave 28% of all children of 12–59 months old with vA intake below 350–375 REs. This percentage was 40% in rural areas, where consumption of wheat products is lower. Estimated fortification costs for this level of REs are US$ 3–5 per person-year of adequate vA intake achieved, with most of that amount due to the fortificant costs. These estimates are higher than the US$ 0.14 per capita for sugar fortification in Guatemala cited by Levin et al. (1993), but those cost figures are on a per capita basis. Fiedler et al. (2000) implicitly assume that fortified wheat flour that reaches individuals with adequate vA intake is wasted, so that the cost per person-year of adequate intake achieved is greater than the annual cost per person consuming the flour. Although fortification seems to be substantially lower cost than supplementation in the Philippines, this comes with a disadvantage of less targeting, however, because wheat flour is primarily consumed by the non-poor.

Rice would seem to be an obvious candidate for a fortification vehicle in Asia, but it is not technically feasible to fortify rice with vA (Dexter, 1998).[5] Thus, GR was developed to accomplish fortification through genetic modification. GR could be a relatively cost-effective intervention because, unlike supplementation and fortification, there are only minor recurring costs (Bouis, 2001). Next, we compare the cost of delivering RAE in developing Asia through wheat fortification, supplementation or GR.[6]

The total RAE delivered and associated costs are estimated for Bangladesh, Bhutan, Cambodia, India, Indonesia, Laos, Myanmar, Nepal, the Philippines, Sri Lanka, Thailand, and Vietnam for the period 2007–2016.[7] Rice and wheat consumption

[5] One technology that has been tested in Indonesia and Brazil fortifies rice flour with vA and then extrudes the flour into rice kernel shapes, which are blended with regular rice (Dexter, 1998). This would seem to be an expensive and cumbersome method to implement on a nation-wide basis.

[6] Details of the methods used for cost analysis are available in Appendix B to this paper, which is posted at this website: http://web.aces.uiuc.edu/wf/workingpapers/wrkngpapersindex.htm.

[7] Among rice eating countries, China and Malaysia are notably excluded from this list. According to the FAO (1999) Nutrition Country Profile for China, “VAD does not represent a public health problem and clinical cases have only been reported sporadically,” so we assume GR is not adopted there. For

projections are from the IFPRI IMPACT model (Rosegrant et al., 2001). Costs are estimated and discounted to the present using a rate of 10%. These costs are then divided by the RAE delivered through each intervention to obtain the net present cost of one million RAE per year for the duration of the period 2007–2016 (Table 7).

We calculate the total costs of GR development both with and without the costs of developing GR in Europe. When these costs are excluded, we are treating them as sunk costs, and the analysis thus asks whether it is cost-effective to pursue GR further. We also incorporate those sunk costs into an alternative estimate, because this may give an idea of whether it is worth pursuing other similar interventions in the future, which assumes that the development costs of other biofortified foods

Table 7
Cost-effectiveness comparison of GR, fortified wheat flour, and supplementation in developing Asia. The numbers in the table represent the cost of delivering one million RAE per year in each year from 2007 to 2016 (in year 2002 in US dollars)

Intervention	Base case	Sensitivity analysis: discount rate	Sensitivity analysis: no storage losses	Sensitivity analysis: increase in costs	Sensitivity analysis: greater GR impact
GR with sunk costs	7.45	7.24	2.73	9.14	2.98 3.73
GR without sunk costs	4.24	5.08	1.55	5.93	1.70 2.12
Wheat fortification	6.93	12.63	2.54	8.32	–
Supplementation scaled by target population	73.29	131.96	–	–	–
Supplementation from cost per child	29.53	53.18	–	–	–

Notes: cost per million RAE per year is the NPV (year 2002, US dollars) of the cost of delivering one million RAE per year in each year from 2007 to 2016 in Bangladesh, Bhutan, Cambodia, India, Indonesia, Laos, Myanmar, Nepal, the Philippines, Sri Lanka, Thailand, and Vietnam. GR with sunk costs includes costs already incurred in its development; GR without sunk costs considers only future costs of development (year 2002 forward). Supplementation scaled by target population uses distribution costs from the Philippines as reported by Fiedler et al. (2000) and scales by size of target population and wage rates for each country relative to the Philippines. Supplementation from cost per child uses an estimate of US$ 0.74 per child from Nepal (USAID, 2002a) and multiplies times target population in all countries.Sensitivity analysis reports these alternative assumptions: third column shows discount rate of 3%. Fourth column shows no storage or cooking losses of vA for either GR or wheat flour. Fifth column shows an increase in future GR development costs of 50% and 20% increase in price of fortificant for wheat. The last column shows impact of 25% adoption of GR in top cell and double the amount of bioavailability in bottom cell. Dashes (–) indicate no change from base case.

Malaysia, we have no good information on VAD, but because of the relatively high level of per capita income, we assume for the purposes of this analysis that VAD is not a serious problem.

would be similar. For the costs of development in Europe, we use a figure of US$ 2 million (MacPherson, 2002), and pro-rate this over 10 years.

Future GR costs include development at IRRI; bioavailability and biosafety testing; and promotion campaigns to educate consumers. Development costs of US$ 600,000 annually (Datta, 2001) cover staff salaries and operating costs for development and field testing of GR. This process aims to incorporate the necessary genes into several popular varieties of rice currently being grown in the Philippines, Indonesia, Vietnam, and Bangladesh. Little additional expenditure will be necessary at national research stations, so we ignore those costs. Future maintenance breeding costs for GR are also ignored, because maintenance breeding must continue in any event for the many rice varieties already being used, and the marginal costs of maintaining traits such as insect and disease resistance in GR are likely to be small. Testing costs for bioavailability and safety in humans are difficult to ascertain, and we assume these costs to be US$ 1 million per year for three years starting from 2003 (Datta, 2001). The cost of a promotion campaign is estimated to be US$ 1.8 million for 1 year after the introduction of GR. This cost is extrapolated from the costs of the wheat fortification campaign in the Philippines (Fiedler et al., 2000); these are the costs of developing and distributing posters to all rice retailers in these Asian countries. The investment in GR delivers RAE through rice consumption in these Asian countries; 10% of projected rice consumption is assumed to be GR. Conversion of beta-carotene to RAE is assumed to occur at a ratio of 12:1 in the base case. Cooking and storage losses of vA from GR are unknown, but we assumed them to be equal to those for wheat flour (see subsequently).

The costs of fortifying wheat flour are based on the cost of retinol palmitate 250 SD, which has an imported cost in the Philippines of US$ 46 per kg. Projected wheat consumption in the developing Asian countries is used to obtain the total cost of RAE and the total RAE that could be delivered through this vehicle. Cooking and storage losses of vA are assumed to be 63%, based on Philippine data presented by Solon et al. (2000a).

The cost of supplementation is estimated in two ways. In the first method, the Philippine costs ascertained from Fiedler et al. (2000) are scaled by the size of the target population (children under 5 years), and the personnel costs are scaled by wage rates in each Asian country relative to the Philippines. The second method uses fixed costs of US$ 0.74 per child under 5 years, as reported for a current program in Nepal (USAID, 2002a). Total RAE delivered are a function of the supplementation amount and the size of the projected target subpopulation.

Table 7 reports the results of the cost-effectiveness estimates, including some sensitivity analysis with respect to the discount rate, costs, and adoption/bioavailability of GR. In all cases, GR (without sunk costs) is more cost-effective than the alternative interventions. In the base case, the cost per million RAE delivered per year from 2007–2016 is US$ 4.24–7.45 for GR, depending upon whether the sunk costs are included, US$ 6.93 for wheat fortification, and US$ 29.53–73.29 for supplementation. Furthermore, GR is clearly more cost-effective under all of our alternative scenarios, and by a substantial margin, although with inclusion of already sunk costs GR is slightly less cost-effective than wheat flour fortification in certain scenarios. Lowering the discount rate makes GR less costly relative to the other interventions, because the future recurring costs of fortification and supplementation are discounted less heavily.[8] With an increase in costs of 50% for GR and 20% for wheat fortification, or alternatively no storage losses for either, GR (without sunk costs) remains the less costly alternative. If GR were more widely adopted or if bioavailability is greater, then its costs drop to only US$ 1.70–3.73 per million RAE per year, and it becomes much cheaper than wheat fortification, even with sunk costs included. In general, the analysis confirms that a plant breeding strategy does have cost advantages. If GR sunk costs are similar to the costs of future biofortified plant variety development, then the results also confirm that such varieties must have widespread adoption to justify investment.

As our cost figures are not known with certainty, it is worthwhile examining what set of assumptions would make GR inferior to other interventions in terms of cost. The annual cost of one million RAE from GR rises to US$ 7.86 without sunk costs and US$ 12.02 with sunk costs under the following combination of assumptions: (a) GR adoption is initially only 1%, growing to 5% after 5 years; (b) advertising costs are doubled; and (c) US$ 1 million is added to each of the last 3 years of development for additional costs of adaptation by national research systems. Thus, under certain assumptions, GR could cost about the same as wheat fortification.

There are several limitations of this analysis. One of the most important is that it does not directly measure how well each intervention performs in terms of targeting and coverage of those at risk for VAD. Supplementation is highly targeted, but does not cover all subpopulations at risk.[9] As we have discussed above, in comparison with wheat fortification, GR is better targeted to the poor in Asia, who are more likely to be at risk for VAD.[10]

Concluding comments

Although GR compares favorably with other interventions in terms of costs and coverage, there are still many other unresolved issues. First, a larger amount of vA delivered in the grain will increase the impact of GR, especially if consumers do not fully switch to GR due to dietary preferences. Efforts to increase beta-carotene

[8] As the costs of fortification and supplementation are recurring, and the GR costs are only incurred once at the beginning of the period, GR dominates more clearly in any scenario that includes an extended time period (more years of benefit) or a lower discount rate. Given the speculative nature of our estimated benefits and costs, we hesitated to extrapolate beyond 10 years in the future.

[9] Fiedler et al. (2000) found supplementation to be more expensive than wheat fortification in terms of cost per person-year of VAD alleviation within the target group in the Philippines. Its higher cost may be justified by the high levels delivered which may result in more measurable benefits, but a comparison of benefits with costs is beyond the scope of this analysis.

[10] An alternative cost-effectiveness analysis compares the cost of delivering the required amount of vA to the entire population through alternative methods. The results of that analysis also show that GR without sunk costs is cheaper than wheat fortification, reflecting its lower cost per RAE delivered. However, it is unrealistic to expect either source to deliver all vA requirements.

content are underway, and could result in levels triple those that have been achieved so far (Beyer et al., 2002). However, any attempts to increase the beta-carotene content of GR must be weighed against their potential impact on taste and consumer acceptance. This brings us to the second issue—consumer attitudes are clearly an important unknown. While there are speciality rice varieties consumed in small amounts in different Asian countries that have colored grains, such as red, black, and purple, the prospects for widespread acceptance of this very different looking commodity are uncertain. Thirdly, there are still questions of bioavailability, stability of beta-carotene during rice storage, and thermal stability during cooking. Finally, there is the issue of GR production cost, which will depend in part on whether it can be produced and marketed with costs similar to those of current MVs (Modern Variety). If GR has higher cost to consumers, this will reduce consumption and increase its cost as a vehicle for vA. Thus, there remain a large number of questions that must be answered before GR can be a viable intervention.

It appears that GR has the potential to be a low-cost, wide-coverage intervention. While it can deliver substantial amounts of vA under certain scenarios, it is unlikely to meet all requirements and thus would be an ineffective stand-alone strategy. GR is best viewed as a possible addition to the menu of options for combating VAD and a possible complement to existing interventions. Under certain cost assumptions GR is probably not worthwhile, but under other assumptions GR could have quite a significant impact. Furthermore, it points the direction for research priorities in the development of GR. To have greatest impact at a cost comparable with wheat fortification, GR varieties should be suited for widespread adoption in Asia and should deliver as much beta-carotene as possible. There are sufficiently high benefits under optimistic scenarios that it is worth the investment to explore what can be accomplished with this as yet unproven technology. Such exploration will provide lessons for other efforts to biofortify food staples for the poor.

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Appendix A

Table A1
Vitamin A requirements

Group	EAR (RAE)	RDA (RAE)
Infants 0–6 months	–	400
7–12 months	–	500
Children 1–3 years	210	300
Children 4–8 years	275	400
Boys 9–13 years	445	600
Girls 9–13 years	420	600
Boys 14–18 years	630	900
Girls 14–18 years	485	700
Men 18 and on	625	900
Women 18 and on	500	700
Pregnant 14–18	530	750
19 and on	550	770
Lactating 14–18	880	1200
19 and on	900	1300

Source: National Academy of Sciences (2001), dietary reference intakes for vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc.

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