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Biofortification: Evidence and lessons learned linking agriculture and nutrition

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Abstract: Biofortification, the process of breeding nutrients into food crops, provides a comparatively cost-effective, sustainable, and long-term means of delivering more micronutrients. The biofortification strategy seeks to put the micronutrient-dense trait in those varieties that already have preferred agronomic and consumption traits, such as high yield and disease resistance. Marketed surpluses of these crops may make their way into retail outlets, reaching consumers first in rural and then urban areas. Progress to date in breeding and delivering biofortified crops is discussed.

The nutrition evidence on bioavailability and efficacy is growing. Completed nutrition studies for each crop are briefly discussed. Human studies have included a variety of technologies, including stable isotope methods, which are among the most powerful to measure bioavailability and efficacy. Efficacy and effectiveness studies are available for orange-fleshed sweetpotato (OFSP); full evidence is not yet available for biofortified maize, cassava, or golden rice, but initial bioavailability and efficacy results are promising. Efficacy trials have been completed for iron crops (beans and pearl millet) and evidence for zinc biofortification is still developing.

Food-based approaches to improve nutrition face challenges in providing rigorous evidence that they can deliver nutrition improvements in a cost-effective and timely manner. The experience of delivering OFSP is reviewed and discussed, including the challenges of marketing a visible trait and changing perceptions of OFSP as merely a food security crop. Whether implementing or integrating OFSP programs, strong and effective partnering practices are required; strategies for successful implementation of cross-sectoral nutrition sensitive programming are discussed.

Biofortification is yet to be fully scaled-up in a single country, but much evidence and experience has been assembled to support its eventual effectiveness. Policies to support cross-sectoral implementation at all levels, as well as increasing the evidence base, will contribute to making biofortification a cost-effective investment in a more nourishing future.

Key words: Benefit-cost ratio, bioavailability, biofortification, consumer acceptance, efficacy, farm extension, iron, low-income countries, micronutrient deficiency, nutrition, plant breeding, provitamin A, zinc

Rationale for Biofortification

Modern agriculture has been largely successful in meeting the energy needs of poor populations in developing countries. In the past 40 years, agricultural research has placed increased cereal production at its center. Recently, however, there has been a shift: agriculture must now not only produce more calories to reduce hunger, but also more nutrient-rich food to reduce hidden hunger.[2] One in three people in the world suffer from hidden hunger, caused by a lack of minerals and vitamins in their diets, which leads to negative health consequences (Kennedy et al. 2003).

Biofortification, the process of breeding nutrients into food crops, provides a comparatively cost-effective, sustainable, and long-term means of delivering more micronutrients. This approach not only will lower the number of severely malnourished people who require treatment by complementary interventions, but also will help them maintain improved nutritional status. Moreover, biofortification provides a feasible means of reaching malnourished rural populations who may have limited access to commercially marketed fortified foods and supplements.

The biofortification strategy seeks to put the micronutrient-dense trait in those varieties that already have preferred agronomic and consumption traits, such as high yield. Marketed surpluses of these crops may make their way into retail outlets, reaching consumers in first rural and then urban areas, in contrast to complementary interventions, such as fortification and supplementation, that begin in urban centers. Biofortified staple foods cannot deliver as high a level of minerals and vitamins per day as supplements or industrially fortified foods, but they can help by increasing the daily adequacy of micronutrient intakes among individuals throughout the life cycle (Bouis et al. 2011).

Unlike the continual financial outlays required for supplementation and commercial fortification programs, a one-time investment in plant breeding can yield micronutrient-rich planting materials for farmers to grow for years to come. Varieties bred for one country can be evaluated for performance in, and adapted to, other geographies, multiplying the benefits of the initial investment. The nutritionally improved varieties will continue to be grown and consumed year after year. To be sure, recurrent expenditures are required for monitoring and maintaining these traits in crops, but these recurrent costs are low compared with the cost of the initial development of the nutritionally improved crops and the establishment, institutionally speaking, of nutrient content as a legitimate breeding objective.

Implementing biofortification

For biofortification to be successful, three broad questions must be addressed:

- Can breeding increase the micronutrient density in food staples to reach target levels that will have a measurable and significant impact on nutritional status?
- When consumed under controlled conditions, will the extra nutrients bred into the food staples be bioavailable and absorbed at sufficient levels to improve micronutrient status?

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[2] An important part of the overall solution is to improve the productivity of a long list of non-staple food crops. Because of the large number of foods involved, achieving this goal requires a very large investment, the dimensions of which are not addressed here.

- Will farmers grow the biofortified varieties and will consumers buy and eat them in sufficient quantities?

Much of the evidence available to address the above three questions has been generated under the HarvestPlus program. HarvestPlus leads a global interdisciplinary alliance of research institutions and implementing agencies in developing biofortified varieties of rice, wheat, maize, cassava, pearl millet, beans, and sweetpotato. Under HarvestPlus, breeding targets are set such that, for preschool children 4-6 years old and for non-pregnant, non-lactating women of reproductive age, the incremental amount of iron will provide approximately 30 percent of the Estimated Average Requirement (EAR); incremental zinc will provide 25 percent of the EAR; and incremental provitamin A will provide 50 percent of the EAR. Bioavailability of iron was originally assumed to be 5 percent for wheat, pearl millet, beans, and maize (10 percent for rice, cassava, and sweetpotato), that of zinc 25 percent for all staple crops, and for provitamin A 8.5 percent for all staple crops (12 micrograms of beta-carotene produce 1 micrograms of retinol, the form of vitamin A used by the body) (Hotz and McClafferty 2007).

Breeding and Release Progress

Conventional breeding research has thoroughly demonstrated that micronutrient density can be increased in food staples without negative effects on other farmer-preferred traits. Progress in breeding orange sweetpotato, provitamin A maize, provitamin A cassava, high zinc rice and high zinc wheat, and high iron beans and high iron pearl millet is reviewed below. As of 2013, released crop varieties are being disseminated through HarvestPlus and its partners in Uganda (OFSP), Zambia (maize), Nigeria (cassava), the Democratic Republic of the Congo (DRC) (cassava and beans), Rwanda (beans), and India (pearl millet) (Saltzman et al. 2013).

Orange-Fleshed Sweetpotato

After screening identified varieties that twice exceeded the target level of 30 ppm of provitamin A, varieties were improved by the International Potato Center (CIP) and National Agriculture Research and Extension System (NARES) scientists to suit local tastes and agronomic conditions. Mozambique and Uganda released high-provitamin A varieties in 2002 and 2007, respectively. Biofortified varieties are now being introduced in many parts of Africa and South America, as well as China. In 2009, CIP launched its Sweetpotato for Profit and Health Initiative (SPHI), which seeks to deliver OFSP in Africa to reach 10 million households by 2020. The project focuses on empowering women farmers, expanding market opportunities, diversifying the use of sweetpotato, and enhancing the breeding pipeline for OFSP varieties.

Maize

Provitamin A maize breeding is led by the International Maize and Wheat Improvement Center (CIMMYT) and International Institute of Tropical Agriculture (IITA) in conjunction with NARES in southern Africa. Germplasm screening discovered genetic variation for the target level (15 ppm) of provitamin A carotenoids in temperate maize, which was then bred into tropical varieties. Recent developments in marker-assisted selection technology have increased the speed and accuracy of identifying genes controlling the traits of interest in maize. Varieties that can provide 25 percent of the EAR for adult women and preschool children were released in Zambia (3 varieties) and Nigeria (2 varieties) in 2012. Varieties that can provide 50 percent of the EAR are in development.

Cassava

Biofortified cassava is being developed for Nigeria and the DRC. The initial breeding target was set at 15 ppm provitamin A. Screening research identified source germplasm from cassava populations in South America, and IITA and the International Center for Tropical Agriculture (CIAT) improved these varieties to be suitable to the African environment and resistant to cassava mosaic disease. Three varieties with sufficient provitamin A to provide 25 percent of the EAR for women and preschool children were released in Nigeria in 2011. Screening identified a variety with a similar level of provitamin A that was released in the DRC in 2008; it is now being disseminated to farmers.

Rice

In many Asian countries, rice provides up to 80 percent of the energy intake of the poor. High-zinc rice varieties for Bangladesh and India are developed by the International Rice Research Institute (IRRI) and the Bangladesh Rice Research Institute (BRRI). The breeding target has been set at 28 ppm zinc in polished rice, an increment of 12 ppm above the baseline zinc concentration of commercially available rice. High-yielding varieties with more than 75 percent of the target are in official registration trials in Bangladesh and India; release is expected in 2013. A high-zinc rice variety was identified in Brazil and registered for release in 2012 by Embrapa, and a high-iron rice variety was released in China in 2011; research to incorporate the high-zinc trait into this Chinese line continues.

Wheat

The development of high-zinc wheat for India and Pakistan is led by CIMMYT. The initial breeding target for whole wheat was set at 33 ppm zinc, an increment of 8 ppm above the baseline zinc concentration. It is expected that adoption of high-zinc wheat will be driven by its improved agronomic properties compared to current popular varieties, and breeding has focused on both zinc content and resistance to new strains of yellow and stem rust. Multilocation trials are underway in both India and Pakistan and the first release is expected in India in 2013.

Pearl Millet

Pearl millet is a regionally important staple in the Indian states of Maharashtra, Rajasthan, Gujarat, and Uttar Pradesh, the target area for biofortified pearl millet. The breeding target was set at 77 ppm iron, an increment of 30 ppm above the baseline. The International Crops Research Institute for the Semi-Arid Tropics (ICRISAT) carries out the pearl millet breeding research in collaboration with NARES and the private sector. The popular open pollinated variety (OPV) ICTP 8203 was improved to create the first biofortified variety, called ICTP 8203-Fe, which contains the full iron target and was officially released in 2013. Hybrid varieties with up to 100 percent of the iron target are in the development pipeline.

Beans

The target countries for high-iron bean are Rwanda and the DRC; CIAT and the Rwandan Agricultural Board (RAB) lead the breeding process to reach the initial breeding target of 94 ppm, 44 ppm above the baseline. Several “fast track” lines with more than 60 percent of the target level of iron are in delivery. Five varieties of biofortified beans with higher iron levels were released in Rwanda in June 2012. The breeding pipeline includes both large-seeded bush lines and mid-altitude adapted climbing beans.

TABLE 1. Schedule of product release of biofortified crops

Crop	Nutrient	Countries of first release	Agronomic trait	Release year
Sweetpotato	Provitamin A	Uganda, Mozambique	Disease resistance, drought tolerance	2007
Bean	Iron, zinc	Rwanda, DRC	Virus resistance, heat and drought tolerance	2012
Pearl millet	Iron, zinc	India	Mildew resistance, drought tolerance	2013
Cassava	Provitamin A	Nigeria, DR Congo	Disease resistance	2011
Maize	Provitamin A	Zambia, Nigeria	Disease resistance, drought tolerance	2012
Rice	Zinc, iron	Bangladesh, India	Disease & pest resistance, cold & submergence tolerance	2013
Wheat	Zinc, iron	India, Pakistan	Disease and lodging resistance	2013

Transgenic Projects

The Bill and Melinda Gates Foundation-funded Grand Challenges 9 is developing several transgenic crops, including golden and high-iron rice; cassava with increased levels of provitamin A and iron, bananas biofortified with provitamin A; and sorghum with elevated levels of provitamin A, reduced phytate, and an improved protein profile. Most of these crops are several years from release. Golden rice, expected to be one of the first released transgenic biofortified crops, will be required to pass biosafety tests prior to release; the data for this safety assessment are expected to be submitted to regulators in the Philippines in 2013 and in

Bangladesh after 2015. An efficacy trial is planned in the Philippines after biosafety approval is granted.

Nutrition Evidence on Bioavailability and Efficacy

Nutrition evidence increasingly shows that under controlled conditions, extra nutrients bred into the food staples are bioavailable and absorbed at sufficient levels to improve micronutrient status. Completed nutrition studies for each crop are briefly discussed below; the evidence for good bioavailability and efficacy is growing.

Provitamin A Carotenoids

A common concept applied in the calculation of the target level for provitamin A carotenoid concentrations is the bioconversion factor to retinol. This number is determined by evaluation of human studies and was set by the Institute of Medicine as 12 μg β-carotene and 24 μg for other provitamin A carotenoids to 1 μg retinol (IOM 2001). However, applying the established conversion factors to calculate a target level for provitamin A carotenoid content in staple crops without factoring in variations in the health status of individuals, the carotenoid content, or the food matrix in which it is packaged may not reflect what actually happens *in vivo* when provitamin A carotenoids are fed to different groups (Tanumihardjo 2013). Nonetheless, many studies use the Institute of Medicine's bioconversion number for predictions or calculate it based on experimental outcomes. In HarvestPlus, the experimental bioconversion factors were determined from human studies for sweetpotato, cassava, and maize.

Orange-fleshed sweetpotato

Many varieties of sweetpotato contain high levels of all-*trans*-β-carotene, and therefore reaching 100 μg β-carotene equivalents/g is easily accomplished in countries that wish to use these varieties or breed them into their popular white- or cream-fleshed varieties. The vitamin A value of β-carotene from sweetpotato was determined in Bangladeshi men to be approximately 13 μg β-carotene to 1 μg retinol using stable isotope methodology with deuterated vitamin A before and after a 60-d intervention study based on improvement in total body stores of vitamin A (Haskell 2004). A study in South Africa evaluated the impact of sweetpotato feeding to children for five months during the school year on their liver reserves of vitamin A. Children who ate OFSP had a positive change in liver reserves compared with those children eating white sweetpotatoes, measured using the modified relative dose response test (van Jaarsveld 2005), which is a semi-quantitative method to evaluate liver reserves (Tanumihardjo 2011). More recent work in Bangladeshi women who were fed OFSP 6 days/week over 10 weeks, however, did not result in a net gain of total body reserves of vitamin A over negative controls, but did contribute to higher circulating serum β-carotene concentrations (Jamil 2012).

Effectiveness studies are used to assess impact on nutritional status after the crop of interest has been broadly released for an extended period of time. A two-year integrated effectiveness study was undertaken in Mozambique that included the introduction of sweetpotato vines into households and monitoring for two agricultural cycles. Children in intervention households ate more OFSP and had higher dried-blood spot retinol concentrations than controls (Low 2007). However, after this study, many of the children still had low serum retinol concentrations, *i.e.* <0.7 µmol/L (WHO, 2011). In an effectiveness study in Uganda, vitamin A status was improved in children but only after making corrections and changing the currently recommended cutoff value for serum retinol from 0.7 to 1.05 µmol retinol/L (Hotz C 2012). This underscores the need to use more accurate biomarkers of vitamin A status in populations of interest, such as quantitative methods of liver reserves (Tanumihardjo 2011), when evaluating agriculture-based interventions.

Maize

Unlike the progression made with sweetpotato, studies with biofortified maize began with evaluation in animal models, which all showed very encouraging results. This progression was used because traditionally bred maize did not have high levels of provitamin A at the start of the HarvestPlus project (Pixley et al., 2013). Several animal studies with mid-target level provitamin A maize proved the feasibility of the method (Howe 2006, Davis 2008, 2008). Very favorable bioconversion factors for provitamin A carotenoids to retinol were obtained in these *in vivo* studies. Human studies were performed using chylomicron response and stable isotope evaluation to assess bioconversion. A conversion factor of 6.5 ± 3.5 µg β-carotene to 1 µg retinol was obtained in 6 young women in the US (Li 2010) and 3.2 ± 1.5:1 was obtained in 9 healthy Zimbabwean men (Muzhingi 2011). However, these values are single point estimates of bioconversion factors in healthy adults and may not reflect what would occur with longer feeding trials in target populations.

Long-term intake studies in children have been completed to determine whether these favorable bioconversion factors can translate into improved liver reserves of vitamin A. Using the stable ^{13}C-signature of maize, the change in natural abundance of ^{13}C in serum retinol was shifted in 3- to 5-year old children eating orange maize for 70 days when compared with the control children (Gannon and Tanumihardjo 2013). This shows that the β-carotene is bioavailable from the maize and contributing to the vitamin A pool of these children. Another study is evaluating the impact of 90 days of feeding orange maize to 5- to 7-year old children using the $^{13}C_2$-retinol isotope dilution test to measure the total body pool of vitamin A before and after the intervention in the same communities, with promising results (Tanumihardjo 2011, Gannon and Tanumihardjo 2013). A large efficacy trial with 6- to 8-year old children evaluating the effect of orange maize consumption on serum retinol, vitamin A deficiency prevalence, and dark adaptation is also underway in Zambia.

Effectiveness studies after biofortified maize is broadly introduced and disseminated are needed to measure its impact on vitamin A status under normal market conditions as well as the generational effects of feeding β-carotene enhanced staple crops to population groups (Tanumihardjo 2010). Effectiveness studies will best be interpreted if sensitive methodology, such as isotope dilution, is applied to a subset of the studied groups. Nutrition campaigns will likely improve acceptance and willingness to pay in target populations for orange biofortified maize (Meenakshi 2012).

Cassava

The progression of studies with biofortified cassava has mirrored those with maize. *In vitro* and animal studies were done in parallel. These studies support readily bioaccessible β-carotene from cassava, and breeding efforts should continue to enhance provitamin A concentration. *In vitro* studies with cassava showed that β-carotene content was proportional to uptake and genotype did not have an influence at the level of β-carotene currently available in the germplasm (Thakkar 2007). In studies conducted in animals, the bioconversion factor was 3.7 μg β-carotene to 1 μg retinol, despite 48% *cis*-β-carotene composition in processed cassava (Howe 2009). Follow-up studies with repeated dosing of *cis*-β-carotene isomers to animals are underway to determine the influence of isomeric orientation on bioefficacy (Bresnahan 2013). Human studies using chylomicron response were completed in women using biofortified cassava in porridge. The vitamin A equivalence of the β-carotene in the cassava was 2.80 ± 1.77 μg (Liu 2010) in one study and 4.2 to 4.5 ± 3.1 μg to 1 μg retinol with and without added oil in another study (La Frano 2013). Future larger human studies should consider stable isotope tests, especially during efficacy and effectiveness evaluations.

Rice

Golden Rice is the result of transgenic approaches to enhance provitamin A concentrations in the rice grain. Golden Rice β-carotene concentration has reached 37 μg/g dry weight (Paine 2005). Humans have been fed intrinsically deuterium-labeled rice with β-carotene concentrations of 5 and 20 μg/g. In 5 healthy adults, the conversion factor for Golden Rice β-carotene to retinol was 3.8 ± 1.7 μg to 1 μg with a range of 1.9–6.4 to 1 (Tang 2009). When fed to Chinese children, pure β-carotene, Golden Rice β-carotene, and spinach β-carotene to retinol bioconversion factors were 2.0, 2.1, and 7.3 μg to 1 μg, respectively. These favorable bioconversion factors likely reflect the low level of β-carotene in the rice as well as favorable bioaccessibility (Tang 2012).

Iron and Zinc in Staple Crops

Many studies have been done with *in vitro* methodology evaluating the bioaccessibility of minerals from staple crops. Moreover, in a more recent study, zinc bioavailability assessed in a Caco-2-cell model and rat pups with the radioactive isotope of zinc (^{65}Zn) were correlated (Jou 2012). However, due to whole body regulatory systems that come into play for mineral metabolism, the consensus was that human studies will ultimately be needed to assess the impact of biofortified crops on zinc and iron nutrition (Fairweather-Tait 2005). Several of the human studies are discussed below.

Iron

The first study to demonstrate the potential of iron biofortification used a rice variety bred for cool highlands that was aromatic and happened to have high iron content (Brooks, 2011). The randomized efficacy trial in Filipino women tested this variety, which contained 3.21 mg iron/kg, against a local rice variety which contained 0.57 mg/kg (Haas 2005). The study measured daily food intake and used traditional measures of iron status, such as hemoglobin and serum ferritin. After controlling for baseline iron stores in these women, computed body iron was higher in the biofortified rice group than the control group (Haas 2005). Considering the global prevalence of iron deficiency anemia and the billions of people who consume rice, iron-biofortified rice could make an impact, especially among groups who do not consume significant amounts of animal-source foods.

The most common iron isotope on Earth is ^{56}Fe (91.75%), and isotopes used for bioavailability studies include ^{57}Fe (2.12%) and ^{58}Fe (0.28%). Studies with iron stable isotopes are geared toward determining differences in bioavailability due to dietary components, among other factors. For example, high iron beans were studied in Rwandese women by determining the differences in bioavailability based on phytic acid and polyphenol content (Petry 2012) in mixed meals labeled with ^{57}Fe and ^{58}Fe. As indicated by incorporation of these isotopes into red blood cells, high iron beans did not seem to overcome the inhibitory effects of phytic acid and relatively low polyphenolic effect on bioavailability (Petry 2012). Such short-term bioavailability studies show that iron absorption from beans is low, due mainly to a high phytic acid level. However, the small difference in total iron absorbed from regular consumption of high iron beans over time could provide useful amounts of iron to populations consuming plant-based diets. Beans are a highly useful crop to biofortify with iron and emphasis in breeding programs should be placed on developing varieties with high iron and low to moderate phytic acid concentrations. This would explain the findings of a randomized controlled efficacy trial with rural Mexican school children who consumed biofortified or conventional black beans for 110 days. Children in the high iron group had a greater reduction in transferrin receptor from baseline to endline when compared with the control group (Haas 2011).

Pearl millet is consumed by populations in India and West Africa who reside in arid terrain where iron deficiency is prevalent. The fractional absorption of iron in biofortified pearl millet was found to be similar to a low iron variety when fed to young children in India (Hambidge et al. 2013) and adult women in Benin (Cercamondi, in press JN). Therefore, the biofortified pearl millet provided significantly more total iron to the individuals who consumed it. Consistent with these results, an efficacy trial completed recently with school children in rural India demonstrated that biofortified pearl millet is efficacious in improving iron status with 64% of the iron deficiency at baseline being resolved in the intervention group after 3 months of daily pearl millet consumption with respect to the low iron pearl millet group.

Zinc

Unlike iron and vitamin A, zinc does not have a measurable body store, and most studies use plasma zinc, which quickly responds to dietary intake or supplement usage (Wessells 2010). Therefore, most research on zinc-biofortified crops has used zinc isotopic bioavailability studies. The most common zinc isotope is ^{64}Zn (48.63%), and stable isotopes used for research include ^{67}Zn (4.10%), ^{68}Zn (18.75%), and ^{70}Zn (0.62%). For example, using this methodology, meals that included wheat tortillas made with zinc-biofortified wheat resulted in 0.5 mg/d higher absorption than control wheat (Rosado 2009). Bioavailability of zinc from rice-based diets that contained 4.8 mg Zn/d did not have any more absorbed zinc than a conventional rice-based diet at 3.8 mg Zn/d. This led the researchers to conclude that either zinc needs to be increased further or phytate needs to be decreased (Islam 2013).

As biofortification efforts move forward, developing cultivars that have multiple micronutrients should be pursued (Nuss 2010). For example, common beans and pearl millet already display simultaneous increases in zinc when bred for higher iron concentrations; and quality protein maize often has increased levels of zinc (Nuss 2011). The synergistic effects between vitamin A and zinc lead to enhanced overall nutrient metabolism (Tanumihardjo 2010). Therefore, maize that has quality protein, enhanced zinc, and increased provitamin A carotenoids may supply better nutrition than any single nutrient approach for populations that have high maize intakes. Simulations have demonstrated that adoption of zinc-biofortified rice could readily zinc intakes of women and children in Bangladesh (Arsenault 2010) and adults following a traditional eating pattern in China (Qin 2012). Manipulating both iron and zinc in rice may be feasible (Sperotto 2010). Further, depressed nutrient intakes occur in children who have repeated infections, such as endemic malaria, and therefore reevaluating target levels may be important in regions that adopt biofortified staple crops (Bresnahan 2013).

Delivery

The experience of delivering OFSP suggests that farmers will grow the biofortified varieties and consumers will buy and eat them, but food-based approaches in general have faced challenges in providing sufficient quality evidence that they can deliver nutrition improvements in a cost effective and timely manner (Bhutta et al. 2008). The characteristics of nutrition and health programs that have been successful at delivering at scale (e.g. micronutrient supplementation, immunization) include having a clearly defined biological pathway and largely vertical delivery strategies (Bryce et al. 2008). These characteristics, however, are not often associated with food-based interventions, which need to be context specific, promote horizontal linkages, and often require labor-intensive behavior change approaches. In light of these challenges, the section below reviews the different delivery systems that have been successfully used for taking biofortified OFSP to scale in sub-Saharan Africa, discusses lessons learned, and assesses key characteristics of partnerships that have been used to strengthen agriculture-nutrition linkages.

Delivery Systems to Strengthen Agriculture-Nutrition Linkages

The “Towards Sustainable Nutrition Improvement in Rural Mozambique” (TSNI) research project sought to use OFSP as an entry point for improving dietary habits and child caring behaviors among resource-poor households with high levels of child malnutrition. The project was implemented over four growing seasons between 2003 and 2005 in a drought-prone area in northern Mozambique. This integrated agriculture-nutrition-marketing approach aimed to improve access to OFSP planting material or seed; increase demand and enhance knowledge and practices through extension; and increase income through market development and expanded production (Low et al. 2005). Explicit communication for behavior change (CBC) strategies were used, including an adaptation of the trials for improved practices (TIPs) approach that was used with mothers of young children. Easily understood messages for improved dietary practices, including how to effectively use OFSP, were developed with individual mothers and then promoted in group sessions with 25-30 caregivers. A market communication strategy was used with murals at markets depicting the benefits of OFSP and kiosks where OFSP vines were available, and was supported by radio programs, theatre, and promotion materials, as well as the development of new products such as “golden bread” (Low et al. 2005). Horizontal linkages and coordination between nutrition and agricultural community workers were achieved through joint monthly meetings to share progress, discuss challenges, and receive refresher trainings, which were critically important to ensure continuity and consistency in messaging across both sectors and over time.

The evidence from this project has since supported the expanded implementation of food-based approaches using OFSP to improve vitamin A status. However, a key challenge with demand creation strategies is to match the increased awareness about the benefits of the novel product with increased availability of the roots. This challenge is particularly pertinent in countries with a long dry season (> 4 months), and is in turn dependent on an effective seed system that can ensure that sufficient quantities of quality planting material (*i.e.*, seed) of the novel varieties are available at the right time and place. This is more difficult for sweetpotato compared to seed for grain, legume, or vegetable crops, because the “seed” is a vegetatively propagated cutting, which is both perishable and bulky.

Building on the findings from the TSNI project, the HarvestPlus Reaching End Users project in Mozambique and Uganda (2006-2009) used an integrated model to reach 24,000 households (HarvestPlus 2010). The model included:

1. Developing an OFSP vine distribution system including subsidized vines to households,

2. Providing extension to men and women in farm households on OFSP production practices and marketing opportunities,

3. Providing nutritional knowledge, in particular about vitamin A deficiency, to women in these same households, and

4. Developing markets for OFSP roots and processed products made from OFSP roots.

In both countries, two dissemination strategies (with different intensities of extension visits) were implemented: a more intensive and costly "Model One", as compared with a "lighter" "Model Two." In the lighter model, there were no community-level nutrition activities in the second year, and this less intensive model cost about 30% less to implement. Yet, importantly, no differences in impact were found in either country between Model One and Model Two on rate of adoption of OFSP, increase in vitamin A intakes, or other key metrics. This finding raises the question as to what intensity and coverage of demand creation is required to achieve a sufficient mass of adopters for internal or existing diffusion practices to take over (HarvestPlus 2010; Hotz et al. 2012a; Hotz C et al. 2012b).

In 2009, a component of the SASHA project in Western Kenya called "Mama SASHA" was initiated with the objective of targeting pregnant women and encouraging them to attend ante-natal clinics early and on a regular basis and to increase the consumption of vitamin A-rich foods. At the ante-natal clinics, women receive nutrition education and a voucher entitling them to collect planting material for beta-carotene rich OFSP varieties (SASHA 2012). Monthly feedback meetings at the facility level among community-based agriculture and health workers have strengthened coordination and communication between the two sectors, which is reinforced by quarterly partners' meetings that include a wider range of stakeholders. In northern Uganda, the trained birth attendants supported by the NGO Earth Birth are also being trained on the benefits of OFSP and how to multiply planting material and produce roots for consumption. The trained birth attendants are respected older women who are in a good position to pass on skills and knowledge to the expectant mothers in their communities. To encourage fathers to participate and learn as well, the family can offset health facility fees through contributing labor for the facility's sweetpotato vine multiplication plot (CIP and ASARECA 2013).

In East and Central Africa, innovation platforms for technology adoption (IPTAs) have been used for the promotion of OFSP. The platforms are comprised of sweetpotato value chain actors from vine multipliers to consumers. In Rwanda, groups supporting people living with HIV are also members of the platforms. The platform facilitates linkages to help them source quality planting material, agronomic information on the production of sweetpotato, knowledge about the nutritional benefits of the crop, and different options for preparation and utilization. In Lake Zone, Tanzania, similar IPTAs have incorporated medical doctors from the local hospital who have now established a business producing OFSP-based porridge as they are convinced of its benefit to their patients (CIP and ASARECA 2013).

Lessons Learned

Implementation

Across these OFSP interventions, two issues were identified that must be integrated into behavior change strategies: color and status. First, the color: in contrast to the Americas, most sweetpotato varieties grown in sub-Saharan Africa (SSA) are white or cream-fleshed (completely lacking or low in beta-carotene). The visible trait must be addressed as part of the introduction of OFSP to producers and consumers. Social marketing and branding techniques at market kiosks, health centers, and bus shelters using product names and promotional materials have emphasized the color orange and have brought attention to the novel crop. Subsequently, context-specific messaging has been used to associate the color orange with improved nutrition, health, vitamin A specifically, and income generation for particular population groups, *e.g.* children under five years, pregnant and lactating women. The visible orange trait has become a selling point, in particular in the baked product and snack market, where the golden color is attractive to consumers.

Second, sweetpotato has an image problem: it is widely grown as a secondary staple throughout sub-Saharan Africa, and in a few countries (Uganda, Rwanda, Burundi, and Malawi) it is a primary staple with over 80 kilograms per capita consumed (Low et al. 2009). However, its image is that of a food security crop - available for when the maize fails and a crop of the poor, grown mostly by women, for subsistence and not for sale. Hence, it has often received little attention from national research and development programs. Improving the image of sweetpotato has been tackled in three ways: by changing how roots are marketed, by changing how roots are processed and consumed, and by investing in sweetpotato research and advocacy capacity.

First, efforts have been made to change how fresh sweetpotato roots are marketed. For example, they are often sold in piles on the ground and sweetpotato sellers occupy the least attractive positions in informal markets. To improve the image of OFSP, the roots have been “raised up” onto tables or stalls, which are painted orange, have good signage and decorated with nutrition messaging. Second, investments have been made into diversifying the utilization of OFSP through semi-processed and processed products suitable for small- to medium-scale food production. This has contributed to changes in perception where sweetpotato was only consumed in its boiled form to a “five star hotel food.” Third, since 2009, significant new global investment has been made into sweetpotato research and development, orientated towards re-building national human and infrastructure technical research capacity after a generation lost to structural adjustment in the 1990s and 2000s (CIP and BMGF 2009). These investments have increased capacity, created a new dynamic, and sparked additional regional and national investment in the crop. Additionally, specific efforts have been made to build capacity for sustained advocacy for OFSP to “reach agents of change” and tap into the renewed national, regional and global commitment to address nutrition (International Potato Center and Helen Keller InternationaI 2012).

Partnership strategies

The delivery systems for promotion and utilization of OFSP vary by country, but all have shown the need for and benefit of bringing together stakeholders from multiple sectors. Historically, the implementation of integrated or cross-sectoral nutrition sensitive programs has been plagued with challenges. Von Braun et al (2011) have explored bridging the gap between the agricultural and health sectors, particularly in the context of promoting greater synergies among the MDGs, noting that these are “researchable issues” in themselves. More recent work examines how partnerships influence agriculture for development outcomes (Horton et al. 2009). Disciplinary paradigms and organizational cultures influence partnership efforts for improved nutrition outcomes (McEwan et al. 2013), and an “invisible firewall” often separates the agriculture, health, and nutrition sectors (Pinstrup-Andersen 2011). The experience to date on developing delivery systems for the promotion of OFSP has highlighted a number of challenges to work together across sectors to make agriculture-nutrition linkages, which are relevant to other biofortified crops and food-based approaches.

Delivery systems for biofortified crops require strong partnerships and effective partnering practices. Barriers to cooperation that must be overcome include information overload, differing target groups, and marketing issues. Additionally, capacity constraints, particularly in sub-Saharan Africa, are very serious and exacerbate the difficulties of cross-sectoral cooperation.

Behavioral change studies consistently reveal that fewer messages reinforced by presentation in different ways or through different channels are more effective at achieving the desired change. For program participants, there is the danger of information overload. However, partners often hold tight to their own disciplinary perspective, insisting that their “key messages” are the most critical to include. Integrated projects, in an effort to be inclusive, tend to end up with too many messages, and fail to be successful in attaining the looked-for behaviors. Thus, partners need to find ways to move from complex multi-causal analysis to reach consensus on simple “doable” messages.

Second, historically the agriculture and health sectors have worked with different target groups. Members of established farmer groups tend to be men (and sometimes women) who are oriented towards commercial opportunities and who are more advanced in their life cycle. Younger households, especially those with young women and children, tend not to belong to farmer groups unless specifically recruited. In contrast, the health sector has long focused on infant and young child survival and ante-natal care with an emphasis on vertically driven programs such as immunization and monitoring of child growth. Nutrition promotion and education is considered time consuming and challenging: “eating well” is regarded as requiring additional resources to purchase special foods. However, a link with agriculture can be beneficial to health-sector workers in that locally and seasonally available foods can be identified and promoted. Through providing tangible options such as planting material for OFSP varieties together with nutrition information, the credibility of both agriculture and health community workers can be strengthened.

Finally, it should be recognized that building a market component into integrated agriculture-nutrition programs is complicated and takes time, but is essential for long-term sustainability. Nutrition interventions are often targeted to marginal agro-ecological areas, which are more vulnerable to food insecurity. In these areas, however, there may not be surplus production, and the transport and communication infrastructure needed to ensure linkages between production areas and markets may not be developed. Furthermore, messaging for a market component needs different timing and greater flexibility and local adaptation than nutrition messaging, and requires a skilled communications team.

As agriculture-nutrition programs move to scale, they face the issue of capacity. There is a dearth of community-level personnel trained in basic nutritional knowledge. Already overworked health workers are not keen to take on the additional task of nutrition counseling. In many sub-Saharan countries, public sector investment in agriculture and health extension services has been curtailed, and donors have shifted support from state provided services to NGO or private sector service provision. Consequently it may be necessary to work with a multitude of NGO and CBO partners in addition to the public extension providers, with each organization having its own mode of operation and institutional vision. Therefore ensuring true buy-in to new cross-sectoral ways of working and common monitoring systems is difficult, particularly when there may be limited resources to facilitate training and implementation of the new practices.

OFSP has been scaled-up through variations on two broad approaches: OFSP led and integrated programs. Integrating OFSP (or other biofortified crops) into existing programs, either through

NGOs or government departments, can be more cost-effective, but still has high transaction costs. Adopting good institutional partnering practices and identifying good partners is a learning process. The early scoping stage in a potential partnership is critical to ensuring mutual understanding and leveling of expectations. This process is made even more challenging when dealing with the multi-lateral partnerships needed for agriculture-nutrition interventions. In the different cases briefly highlighted above, the importance of regular face-to-face review and planning meetings at the field level cannot be over-emphasized. Process review is as important as technical review. In 2010, a rapid self-assessment tool was developed to assess the "health" of our partnerships. The tool covers the key elements which are considered essential for good partnerships: *i.e.*, common objective, clear understanding of roles, internal and external communication, and conflict resolution mechanisms. The informal "partnership health" check-up is conducted once or twice a year, opening a neutral "space" to raise and discuss "hidden" issues that may be hindering the program's implementation.

Partnerships around nutrition sensitive agricultural interventions must be clear about their objectives (e.g. advocacy, information sharing, implementation) and what types of capacity strengthening are needed to make that agriculture-nutrition partnership work. Due to the high transaction costs associated with cross-sectoral partnerships, incentives, added value, and goals of multi-stakeholder partnerships and individual organizational objectives must be fully analyzed.

Concluding remarks

Policies to support cross-sectoral implementation at all levels, as well as increasing the evidence base, will contribute to ensuring that biofortification is a cost-effective investment in community nutrition. Specific recommendations for participants in the ICN+21 conference include:

- Make enhanced mineral and vitamin content of the edible portions of new crop varieties core breeding objectives at agricultural research centers, in addition to yield and other agronomic characteristics
- Invest in developing cultivars with multiple micronutrients to capitalize on the synergistic effects between micronutrients
- Develop further efficacy trial evidence for biofortified crops, in particular with respect to the nutritional status of mothers going into pregnancy and for young children less than 24 months
- Through effectiveness studies and other evidence, demonstrate that deployment of biofortified crops can be scaled-up cost-effectively in selected target countries
- Identify and engage private sector entities, such as seed and food companies, to incorporate biofortified crops into their core business activities
- Integrate biofortification into selected global frameworks that heavily influence national governments, including *Codex Alimentarius*, the Scaling Up Nutrition framework (SUN), and the Comprehensive Africa Agriculture Development Program (CAADP)
- Incorporate biofortification into WHO evidence-based guidelines for nutrition interventions in its e-Library of Evidence for Nutrition Actions (eLENA)
- Identify opportunities to integrate biofortification within existing funding mechanisms and platforms, such as the Global Agriculture and Food Security Program (GAFSP), Global Donor Platform for Rural Development (GDPRD), Global Alliance for Improved Nutrition (GAIN), AgResults, the World Bank and regional development banks, and others

- Expand the number of nutrition and health professionals within multilateral institutions, including the CGIAR and FAO, and invest in and reward efforts to work collaboratively across disciplinary divisions
- Engage health and agricultural ministries to achieve a joint understanding of how agricultural policies can hinder or help achieve nutrition and health goals
- Consider dietary quality in economic policy analysis related to food security, not just energy intake
- Invest at higher rates in sustained productivity increases for a range of non-staple foods as well as biofortified foods

Biofortification is yet to be fully scaled-up in a single country, but much evidence and experience has been assembled to support its eventual effectiveness. As evidence continues to mount, it should be included in the policy framework to address today's major nutrition challenges and considered a priority area for enhanced international cooperation on nutrition.

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