

## Biofortification: The Evidence

A summary of research informing scaling up of biofortification to improve nutrition and health globally

HarvestPlus leads a global effort to improve nutrition by catalyzing the development and scaling up of staple food crops that are rich in essential vitamins and minerals, also known as micronutrients. This term is used because people need only very small amounts of micronutrients for good health, but in fact many people are micronutrient deficient, leading to serious health issues.

The process used to develop these nutritious crops is known as biofortification: a cost-effective, sustainable solution that uses conventional plant breeding and agronomic practices to increase the density of micronutrients such as vitamin A, iron, and zinc in staple crops consumed widely as part of everyday diets in Africa, Asia, and Latin America and the Caribbean (LAC). Micronutrient malnutrition is also called "hidden hunger" because of its often-invisible warning signs. Hidden hunger impairs the cognitive and physical development of children and adolescents, and the productivity of adults, thereby impairing their health and both short- and long-term livelihood potential.

Biofortification helps reduce the gap between micronutrient requirements and intake by increasing the content of dietary vitamins and minerals contained in staple foods. HarvestPlus focuses on tackling vitamin A, iron, and zinc deficiency, which contribute to the greatest burden of disease associated with "hidden hunger" worldwide. [1] Biofortified crops are particularly effective in delivering micronutrients to rural communities in low- and middle-income countries, where the majority of small-holder farming households who produce and eat staple food crops reside, and where year-around diverse diets, commercially fortified foods, or micronutrient supplements are often inaccessible or unaffordable, or both.

Women, young children, and adolescent girls are the primary targets of biofortification because they have relatively high nutrient needs that are often unmet because of dietary habits, cultural norms, insufficient micronutrient-dense foods, and other factors that increase their biological vulnerability to infections. These high nutrient requirements derive mostly from rapid prenatal and postnatal growth and menstrual blood loss. Interventions that improve nutrition in the preconception phase are key to preventing the intergenerational cycle of malnutrition [2].

Addressing malnutrition in young adults and women is key to ensuring the best start in life for future children and generations. A key advantage of delivering micronutrients through staple foods is that—unlike with micronutrient dense animal-sourced foods, fruits, and vegetables—discriminatory differential food allocation within a household does not usually happen [3]. Biofortified staple crops are therefore an equitable vehicle for improving micronutrient intake since staple foods are consumed by all members of a household as their primary, everyday source of food.

HarvestPlus works with more than 450 partners worldwide. It partners with crop breeding centers of the international agricultural research network known as the CGIAR to ensure conventionally bred varieties of nutritious, high-yielding, and climate smart staple crops are developed and available for testing and release by national agricultural research systems (NARS) in low- and middle-income countries. Through carefully designed studies, HarvestPlus and its partners measure the impact of biofortified crop consumption on women, adolescent girls, and children's nutritional status and functional outcomes, such as cognitive and physical performance. Delivery progress, in outcomes such as adoption and diffusion, as well as delivery program performance are captured through HarvestPlus' rigorous monitoring, evaluation and learning system. Assessments of the effectiveness, cost-effectiveness, and impact of various delivery strategies are tested, estimated or evaluated along staple crop value chains to capture and share lessons learned to catalyze scale-up.

Over the last 16 years, research conducted by HarvestPlus and its partners has demonstrated that:

- Conventional crop breeding can increase nutrient levels without compromising yield and other traits preferred by farmers and consumers.
- Additional nutrients in crops can measurably improve micronutrient status, health, and cognitive and physical abilities.
- Farmers are willing to grow biofortified crops and consumers are willing to eat them, and the costeffectiveness and impact of different delivery models are tested to inform scaling up of biofortification.
- When targeted correctly, biofortification can contribute to the improvement of food systems to deliver nutritious foods cost-effectively and with minimum behavior change.

Synthesis of the research on these questions have been regularly and systematically published as peer reviewed journal articles, book chapters, and discussion papers, [4-10] as well as in a special issue of the *Annals of the New York Academy of Sciences* [11]. Similarly, country programs, i.e., in country crop development and delivery efforts for biofortified crops, have been reviewed and documented in various publications [12, 13] in addition to a special issue of the *African Journal of Food, Agriculture, Nutrition, and Development* [14].

By the end of 2018, 7.6 million farming households were growing biofortified planting material, benefiting about 38 million people. By the end of 2030, HarvestPlus aims for one billion people to consume biofortified foods globally. During its current program phase (2018–2022), HarvestPlus aims to catalyze scaling up of biofortification by investing in (1) expanding the scientific evidence on efficacy and effectiveness to stimulate advocacy and policy efforts; (2) mobilization of the knowledge on delivery models tested and (3) delivery in 30 priority countries selected based on their potential for the most significant impact on micronutrient deficiencies through biofortification.

## Conventional crop breeding can increase nutrient levels without compromising yield

From 2004 to the end of 2018, HarvestPlus has directly facilitated the release of 211 varieties of 11 biofortified crops, including iron beans and pearl millet; vitamin A cassava, maize, and sweet potato; zinc maize rice and wheat, in over 30 countries. Thousands of other varietal lines are in testing in these countries, and over 30 more. The biofortified varieties of staple crops are bred to fulfill a biologically important portion of the dietary requirements of vitamin A, iron, or zinc for women and children, in populations where these crops are consumed as staples. Based on usual eating patterns in these populations, it is estimated that for children 4 to 6 years old and for non-pregnant, non-lactating women of reproductive age, biofortified iron beans and iron pearl millet can provide up to 80 percent of the daily estimated average requirements (EARs); zinc wheat and zinc rice can provide up to 50 percent of average daily zinc needs; vitamin A maize can provide up to 50 percent of average daily vitamin A needs, and vitamin A cassava and sweet potato can provide up to 100 percent of average daily vitamin A needs, respectively.

These released varieties deliver at least 50 percent of the intended micronutrient level and the releases are approved by the official national release committees of these countries, demonstrating that it is possible to increase the micronutrient content of these crops using conventional crop breeding techniques without sacrificing other production and consumption attributes that farmers and consumers prefer. Crop improvement continues, with researchers developing varieties with ever-higher levels of vitamins and minerals that are adapted to a wide range of agroecological conditions and ensuring that the best germplasm for

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<sup>&</sup>lt;sup>1</sup>An overall total of more than 340 biofortified crop varieties of 11 crops were released from 2004 to the end of 2018 in over 40 countries. This includes varieties developed and released by other programs. Thousands of other varietal lines are in testing in these countries, and in over 20 more.

climate-adaptive as well as food quality traits is used in the breeding of biofortified crops. Biofortified germplasm and nutrient-rich breeding lines are made available as public goods to national governments, which can test and further improve these materials for subsequent official release as new crop varieties. Table 1 presents an overview of the numbers of biofortified varieties released, by crop and by region; a detailed map of releases and testing is available on <a href="HarvestPlus">HarvestPlus</a>' website.

Table 1. Numbers of Biofortified Crop Varieties Released, 2004-2018, by crop and by region

1				
Biofortified Crop	Region			Total
	Africa	Asia	LAC	TOTAL
Vitamin A sweet potato	7		7	14
Vitamin A maize	54		1	55
Vitamin A cassava	13		3	16
Vitamin A banana/plantain	10			10
Iron beans	39		21	60
Iron pearl millet	1	9		10
Iron and zinc lentil		9		9
Iron cowpea		5	3	8
Zinc wheat		10	1	11
Zinc rice		10		10
Zinc maize			7	7
All biofortified crops	124	44	43	211

# Additional nutrients in crops improve health, micronutrient status, and cognitive abilities

Nutrition researchers measure the loss and retention of micronutrients in crops under traditional storage, processing and cooking conditions to ensure sufficient levels of vitamins and minerals remain in biofortified foods that target populations eat [15-24]. The degree to which nutrients bred into crops are absorbed and utilized by the body, a prerequisite to improving micronutrient status, is also studied [25]. Randomized controlled efficacy trials are conducted to demonstrate the impact of biofortified crops on nutritional status and functional indicators of micronutrient status (e.g. visual adaptation to darkness for vitamin A crops; memory, attention, and physical activity for iron crops; and growth and immune competence for zinc crops), while randomized controlled effectiveness studies provide evidence that biofortified crops can improve the nutritional status of populations under typical (non-clinical) conditions. Results may vary across countries due

to differences in adoption rate, consumer preference, deficiency level of the target micronutrient(s) among target populations, or consumption rate of the crops, or a combination of several of these.

Rigorous external reviews of the impact of biofortification are also taking place. For example, a systematic review of three randomized efficacy trials on iron-biofortified crops reinforced the conclusion that iron-biofortified interventions significantly improve iron status—particularly among women and children in low-income communities who need it most [26, 27]. In addition, a World Health Organization (WHO) and FAO guidelines review committee was assembled in 2016 to review the scientific evidence and country experiences of scaling up biofortification; a joint recommendation on biofortification is expected in 2020.

#### Vitamin A sweet potato

Consumption of vitamin A sweet potato significantly increases body stores of vitamin A across age groups [28–30]. Following promising results from randomized controlled efficacy trials for vitamin A sweet potato [29, 30], two randomized controlled effectiveness trials were conducted in Uganda and Mozambique, with vitamin A sweet potato adoption rates reaching over 60 percent among intervention households after four subsequent growing seasons. In Uganda delivery of vitamin A sweet potato significantly increased vitamin A intake among children and women in intervention households, and measurably improved vitamin A status among some children, with a 9.5 percent reduction in the prevalence of low serum retinol [31]. In Mozambique, the delivery of vitamin A sweet potato doubled vitamin A intakes among intervention households, with vitamin A sweet potato providing almost the entire total vitamin A intake for children [32]. Also, in Mozambique, consumption of vitamin A sweet potato by children under five significantly reduced the burden of diarrhea, the second leading cause of death in this age group globally; the likelihood of experiencing diarrhea was reduced by 39 percent and duration of diarrhea episodes was reduced by more than 10 percent and by 52 percent and 27 percent respectively in children under three [33].

#### Vitamin A cassava

A randomized controlled efficacy study conducted in Eastern Kenya demonstrated a modest but significant improvement in vitamin A status among five- to 13-year-old children who consumed boiled and mashed vitamin A cassava [34]. When retention of provitamin A carotenoids (pVACs) in biofortified cassava varieties was tested using traditional African cooking methods, it was shown that boiled vitamin A cassava retained very high pVAC levels and could provide young children who consume it as a staple with 100% of their daily average vitamin A needs. When processed as *gari*—as is common in Nigeria—retention was lower yet sufficient to provide 50 percent of daily average needs. When processed as *fufu* or *chikwangue*—as is common in DRC—retention was much lower still, demonstrating that local context and cooking practices influence the potential nutrition impact of biofortified crops [24].

#### Vitamin A maize

A randomized controlled efficacy study conducted in rural Zambia showed that after three months, beta carotene concentrations and total body stores of vitamin A in five to six-year-old children eating vitamin A maize increased to a significant extent compared to the control group [35]. A larger trial with over 1,000 marginally malnourished four to eight year-old children in another farming district of Zambia demonstrated that vitamin A maize consumption significantly increased serum beta-carotene concentrations but did not improve serum retinol [36]; significant improvements in other carotenoids ( $\alpha$ -carotene,  $\beta$ -cryptoxanthin, and zeaxanthin) were also detected, indicating the potential of vitamin A maize to effect health benefits beyond improvements in vitamin A status, such as protection from oxidative stress, chronic diseases, and age-related retinal degeneration [37]. In this same trial, visual adaptation to darkness was assessed; among children who were vitamin A deficient at baseline, those who consumed vitamin A maize had greater improvement in

pupillary responsiveness than those in the control group, improving their ability to see in dim light [38]. Another shorter duration study with the lactating mothers of these children showed no increase in mean breast milk retinol concentration among women who consumed vitamin A maize; however, the plausible downward trend in the risk of low milk retinol warrants further investigation [39].

Vitamin A biofortification may also help defend against exposure to aflatoxin. Aflatoxins are naturally found toxins, produced by molds. They can contaminate food crops including maize and can cause an estimated 25 percent of crops loss during production and severe health problems such as congenital disabilities in children or liver cancer when consumed and exposed long-term [40]. The stunting effect on children is another potential impact that has been investigated [41]. Farmers may be exposed when handling contaminated crops [42]. A study conducted in Mexico showed that breeding vitamin A into maize significantly reduced aflatoxin contamination in the crop [43].

#### Iron beans

Iron-biofortified beans have been demonstrated to be efficacious in Rwanda, where a randomized controlled efficacy study conducted with iron-deficient young women (ages 18–27) showed that regular consumption of iron beans can significantly increase hemoglobin, ferritin, and total body iron after only 4.5 months [44]. Iron beans also had a profound effect on cognition: iron-deficient women who ate iron-biofortified beans experienced improved memory and ability to pay attention [45], key skills for optimal performance at school and work. Consumption of iron beans also significantly improved behavioral performance in the same population of young Rwandan women, including better reaction time and efficiency of memory retrieval [46]; this is the first evidence to implicitly show the link between consumption of iron beans, improved iron status, positive changes in brain activity, and improved cognitive performance. The same study also measured physical performance, and preliminary results suggest that the improvements in iron status were accompanied by a reduction in time spent in sedentary activity [47]. Another randomized controlled efficacy study conducted for six months with school-aged children in Mexico showed no difference in measures of iron status among children who were fed iron beans compared to children who were fed conventional beans [48].

#### Iron pearl millet

Iron pearl millet was demonstrated to be an efficacious approach to improve iron status in adolescent children through a six-month randomized controlled efficacy study conducted in rural Maharashtra, India. After only four months, iron deficiency was significantly reduced, and serum ferritin and total body iron were significantly improved in secondary schoolchildren who consumed iron pearl millet flat bread twice daily. Children who were iron deficient at the beginning of the study were 64 percent more likely to resolve their deficiency by the end of the six months [49]. Results from the same trial indicate that iron-biofortified pearl millet consumption also improved the children's performance in attention and memory tests [50].

#### Zinc rice

A zinc absorption trial is in progress in Bangladesh, where a randomized controlled efficacy study is also underway to determine the impact of zinc-biofortified rice consumption on the nutrition outcomes of young children aged 12–36 months. A previous study compared the absorption of zinc from a biofortified rice variety to commercially fortified rice in 16 healthy adults; the findings indicated that rice biofortification is as good a source of bioavailable zinc as postharvest zinc fortification [51].

#### Zinc wheat

A large randomized controlled efficacy study including over 3,000 mother-child pairs was conducted in New Delhi, India. This study demonstrated that when preschool children aged four to six, consumed agronomically biofortified (i.e., treated with zinc fertilizer) zinc wheat for six months, morbidity outcomes were significantly reduced: children spent 17 percent fewer days sick with pneumonia and 40 percent fewer days vomiting than children who consumed foods prepared with conventional wheat. Mothers (non-pregnant, non-lactating) who consumed foods prepared with zinc-biofortified wheat spent significantly fewer days (9 percent) with fever than mothers in the control group [52]. Previous studies in Switzerland and Mexico have shown that absorption of zinc from zinc-biofortified wheat is significantly greater than from conventional wheat, and as well absorbed as zinc in fortified wheat [53, 54].

#### Farmers are willing to grow biofortified crops and consumers are willing to eat them

Economists conduct farmer field day evaluations, monitoring surveys, and adoption studies to understand farmers' willingness to grow biofortified crops [55]; consumer acceptance studies to understand consumers' preferences—expressed in terms of their willingness to pay—for biofortified crops and foods, and program evaluations to understand the cost-effectiveness and impact of the delivery programs implemented [56, 57]. The aim of these studies is to inform the development of biofortified products (both planting material and food), and delivery models that are acceptable, effective, and scalable.

#### Vitamin A sweet potato

The above mentioned randomized controlled effectiveness trials in Mozambique and Uganda evaluated the impact of two delivery models (one providing more intensive training on nutrition and best agronomics practices than the other) on vitamin A sweet potato adoption, vitamin A intake, and vitamin A status of participating households. The study found that 61 percent and 68 percent of participating households adopted vitamin A sweet potato in Uganda and Mozambique, respectively. No significant differences in the adoption, vitamin A intake, and vitamin A status outcomes resulted from the two delivery models [58] and the impact of nutritional training on these outcomes [59]. A follow-up study conducted in Uganda found that adoption rates remained high in two of the three study areas and that nutrition information was well retained. The area with the lower adoption rates became a major supplier, but not consumer, of vitamin A sweet potato [60]. These impact evaluations provided a crucial evidence-base for donors and helped inform the scaling up of biofortified crops in Uganda [61]. Development and delivery experiences for vitamin A sweet potato in several countries in Africa South of the Sahara are documented [62] and lessons learned from these experiences are presented in several publications [63-67].

Sensory evaluation studies conducted in both rural and urban areas of several countries (e.g., Uganda, Tanzania, Malawi, Mozambique, and South Africa) showed that consumers liked the sensory attributes, such as appearance, odor, taste and texture, of vitamin A sweet potato, as well as those of various products made with vitamin A sweet potato such as bread [56, 68, 69]. Studies in rural Uganda revealed that when nutrition information on the benefits of vitamin A sweet potato was provided, consumers valued the vitamin A-rich varieties more than white, conventional sweet potatoes [70]. Another study conducted in Mozambique also found that consumers valued vitamin A sweet potato and that the value was influenced by information on nutritional benefits [71]. Collectively, these studies highlight the importance of information campaigns in driving demand for vitamin A sweet potato.

#### Vitamin A cassava

A consumer acceptance study conducted in two states of Nigeria tested vitamin A cassava *gari* against local *gari*. In the state of Oyo, the local *gari* tested was made with white cassava, and in the state of Imo it was

yellow (white cassava mixed with red palm oil), in accordance with regional preferences. In Oyo, consumers preferred *gari* made with light-colored vitamin A yellow cassava even in the absence of nutrition information. Once consumers received information about the nutritional benefits of vitamin A cassava varieties, light-colored vitamin A yellow cassava remained the most popular, but *gari* made with deeper-colored vitamin A yellow cassava was preferred over the local variety. In Imo, on the other hand, in the absence of nutrition information, local *gari* was preferred to the *gari* made with either light- or deeper-colored vitamin A yellow cassava varieties; however, once consumers were told about the nutritional benefits of vitamin A cassava, *gari* made with the deeper-colored yellow cassava was preferred, another example of the importance of information campaigns in areas where biofortified crops are introduced [72].

A study on vitamin A cassava, this time in Kenya, found that both the caregivers (18- to 45-year-olds) and children (7- to 12-year-olds) preferred yellow cassava over white cassava because of its soft texture, sweet taste, and attractive color [73]. A recent study on vitamin A cassava acceptability in Nigeria, compared traditional West African foods prepared with biofortified, fortified, or conventional products. It showed that consumers prefer biofortified products. They associated the yellow color with improved eyesight and enhanced health [74]. A study in Uganda, this time evaluating mainly production traits of this crop, found vitamin A cassava be favorably evaluated by both men and women farmers [75]. A study in Nigeria published in 2019 showed that production, processing, and marketing of vitamin A cassava products are affected by gender-based constraints, such high cost of labor, inputs, transporting, and exploitation by middle men. These results highlighted the importance of having gender-responsive strategies in place to ensure equitable impact and delivery for both men and women, a critical step in the successful scaling up of biofortified crops [76]. Another study conducted in Nigeria's Oyo state with cassava farmers showed vitamin A cassava production to be highly profitable [77]. Development and delivery experiences for vitamin A cassava in in Nigeria is documented [78] and lessons learned were summarized [12].

#### Vitamin A maize

In Zambia, farmer field day surveys conducted in 2012 and monitoring surveys conducted in 2015 confirmed a strong preference by farmers for both the production and consumption attributes of vitamin A maize varieties compared with conventional white maize varieties. Farmers appreciated the yield, cob size, and cob-filling characteristics of the new varieties, as well as the taste and aroma of vitamin A maize preparations. Nearly all farmers (97 percent) said they would grow vitamin A maize in the next season and that they were planning to plant four times more seed than they did in the previous (2014–2015) season [79]. A more recent monitoring survey conducted in 2017 found that almost 100 percent of the farming households who had acquired vitamin A maize seed planted it, and 87 percent of the harvest was kept for home consumption, and was consumed by almost all (97 percent) of the women of childbearing age and 96 percent of the children under five residing in these households, on average on three days in the last seven days. Another promising finding from this survey was that almost half (44 percent) of the households who grew vitamin A maize, also purchased the grain of this variety from the market [80].

A consumer acceptance study conducted in rural Zambia showed that consumers valued *nshima* made with vitamin A maize more than *nshima* from white and yellow maize varieties, even in the absence of nutrition information [81]. When nutrition information was delivered by radio or community leaders, it translated into even greater acceptance of vitamin A maize. The increases in acceptance were similar regardless of the media source, implying that radio—which is significantly less costly than face-to-face messaging—can be used to effectively convey nutrition information. Another study, conducted in rural Ghana, found that consumers valued *kenkey* made with vitamin A maize less than *kenkey* made with either white or yellow maize, but the provision of nutrition information reversed this preference. An information campaign will be key to driving consumer acceptance of vitamin A maize in Ghana [82].

#### Iron beans

An adoption study conducted in Rwanda in 2015 assessed the adoption and diffusion rates of iron bean varieties after eight seasons of intensive delivery efforts by HarvestPlus and its partners. Data from this nationally representative study revealed that 28 percent of rural bean-producing households—about half a million households—had planted at least one iron bean variety in at least one of the past eight seasons. In the study season (the first bean-growing season of 2015), an estimated 20 percent of all bean growers in Rwanda (more than 300,000 rural households) were found to grow iron beans. Further analysis revealed several encouraging findings: awareness of iron beans is high among bean growers in Rwanda, with over two-thirds having heard of iron varieties; diffusion levels are high, with four out of ten farmers receiving planting material from a farmer in their social network; and, the proportion of land farmers allocate to iron beans increases over time (from 48 percent in season one to 70 percent in season six). Additionally, during the study season, iron bean varieties made up almost 12 percent of the national bean production, and within households, 80 percent of iron beans produced were used for household consumption [83]. A monitoring survey conducted in 2017 found that 87 percent of the harvest was kept for home consumption, being consumed by almost all (98 percent) of the women of childbearing age and (95 percent of the) children under five who reside in these households, while almost one in every five iron bean growing households (i.e., 17 percent) also purchased iron bean grain from the market for home consumption [84]. Another study investigated the effect of iron bean adoption on socio-economic welfare of farmers in Eastern Rwanda. In this study, the yield was found to be significantly enhanced, which indicated potentially higher incomes, and the authors suggested to increase the efforts towards creating awareness for and facilitating the access to iron beans [85]. Development and delivery experiences for iron beans in Rwanda is documented [86] and lessons learned from the evaluation of the program activities can be found in here [87].

Consumer acceptance studies conducted in rural Rwanda showed that even in the absence of nutrition information, consumers in the Northern Province liked the sensory attributes of a red iron-biofortified bean variety more than a white iron bean or local bean variety [88]. Nutrition information had a positive effect on the premium consumers in urban wholesale and retail markets were willing to pay for iron beans: when provided, both iron bean varieties were preferred to the local variety. When compared across regions, consumers in the rural Western Province and urban wholesale market also had similar preferences for one of the iron bean varieties tested, suggesting potential for linking demand and supply [89]. Another analysis of multiple sensory attributes revealed several opportunities for marketing of iron beans in both rural and urban markets [90]. Similar studies conducted in the LAC region, (in Colombia [91] and Guatemala [92, 93]), also revealed positive results for consumer acceptance of iron beans.

#### Iron pearl millet

A consumer acceptance study of *bhakri* made with iron pearl millet, conducted in rural Maharashtra, India, revealed that even in the absence of information about the nutritional benefits, consumers liked the sensory attributes of iron pearl millet grain and the *bhakri* made from it as much as, if not more than, conventional pearl millet grain and *bhakri*. When nutrition information was provided, consumer acceptance and willingness to pay was even greater [94].

### Targeting biofortification interventions for cost-effectiveness and impact

The Copenhagen Consensus ranked interventions that reduce micronutrient deficiencies, including biofortification, among the highest value-for-money investments for economic development. As per their analysis, for every USD invested in biofortification, as much as 17 USD of benefits may be gained [95].

Other ex-ante (before intervention) analysis conducted for several micronutrient-crop and country scenarios (see e.g., 96, 97), as well as a recent review of such analyses [98] pointed out that biofortification is highly cost-effective according to the World Bank criteria of cost (in USD) per Disability-Adjusted Life Year (DALY) saved [76]. These analyses not only revealed the most cost-effective biofortification interventions (which country and which biofortified crop), but also compared cost-effectiveness of biofortification with those of other interventions, such as supplementation and fortification, to inform policies and programs [96, 97]. The results revealed biofortification to be cost-effective in most cases, and exceptions typically involved scenarios with low substitution and/or consumption of the staple crop [98]. More-in-depth studies modelling the micronutrient program portfolios looking at biofortification, fortification, and supplementation for iron in India (Rajasthan) [99], vitamin A in Zambia [100, 101] and zinc in Bangladesh [102], all found biofortification of the key staples to be one of the most cost-effective strategies for tackling the deficiency of the micronutrient which can be addressed through biofortification.

Another *ex-ante* tool that informs targeting of the most impactful biofortification interventions across micronutrient-crop and country contexts is the <u>Biofortification Priority Index (BPI)</u> [103, 104]. For each micronutrient-crop combination, the BPI ranks countries in Africa, Asia, and LAC, according to the biofortified crops' potential impact for alleviating micronutrient deficiency (based on national-level data on production and consumption of the biofortifiable crop, and the rate of micronutrient deficiency which can be addressed by the biofortified version of that crop. In this context, BPI implies a high potential for cost-effectiveness in the priority countries. For large countries with diverse staple food production and consumption patterns, and with significant regional differences in micronutrient deficiency rates, sub-national (i.e., within country) BPIs are developed to inform better targeting of biofortification interventions (see e.g. 105, 106).

Ex post (after intervention) cost-effectiveness of mature biofortification programs, as well as cost figures per beneficiary reached with biofortified planting material across delivery models, are currently being analyzed. An available ex-post cost-effectiveness figure is from the above mentioned randomized controlled effectiveness trial conducted to deliver vitamin A orange sweet potato in Uganda. That study demonstrated that biofortification costs 15-20 USD per DALY saved [58], which is highly cost-effective per World Bank criteria [107].

Sustainable Development Goal 2 calls for ending all forms of malnutrition, including micronutrient deficiencies, by 2030. More than two billion people in the world are currently micronutrient deficient. There are no silver bullets to achieve this goal, though an understanding of which intervention(s) are most cost-effective, impactful, and scalable, and in which context, is paramount to developing and implementing targeted, efficient, and effective policies and programs. Current food systems should and could provide the most sustainable means to add essential vitamins and minerals into the diet. However, the potential of current food systems, especially of staple food-based food systems in rural areas of developing countries, for providing sufficient micronutrients is decreasing at an accelerating rate as a result of climate change [108], while the gap between the demand and supply of micronutrients is increasing [109]. As the evidence summarized above can attest, biofortification is scientifically proven to be a feasible, efficacious, acceptable, and cost-effective agricultural-nutrition intervention which, once scaled, can help close at least some of this gap [110].

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