

The scientific body of evidence supporting biofortification spans over two decades. This document provides a summary of peer-reviewed research that has proven biofortification to be an efficacious, cost-effective, and scalable innovation that can play a pivotal role in transforming food systems to deliver affordable and accessible nutritious food for all.

Biofortification is the process of increasing the density of micronutrients in widely consumed staple crops through conventional plant breeding, agronomic practices, or genetic modification.\* Biofortification efforts have focused primarily on addressing vitamin A, iron, and zinc deficiencies, which collectively account for the greatest unaddressed burden of disease associated with "hidden hunger" in low- and middle-income countries (LMICs)<sup>1</sup>.

Biofortified crops are particularly advantageous for improving rural food systems in LMICs, where diets of farming families are heavily dependent on ownproduced or locally procured staple crops; where the prevalence of deficiencies in vitamin A, iron, and zinc is high; and where other year-around nutrition interventions including diverse diets, commercially fortified foods, or micronutrient supplements are often inaccessible, unaffordable or both. Young children, adolescent girls, and women are the priority target populations for biofortification. Their relatively high micronutrient needs, driven by rapid periods of growth and development, and menstruation for women, predispose them to hidden hunger.

For more information about biofortification and HarvestPlus, see pp. 8-9 in this brief.

#### The Scope of Biofortification Research

Multi-disciplinary research on biofortification follows an impact pathway from discovery to development, delivery, and scale-up. This research is conducted by crop, nutrition, food, and social scientists, and includes, among other themes:

- ex-ante analyses (forecasting) to identify target populations, geographies, staple crops, and micronutrients for biofortification;
- plant breeding approaches to develop biofortified staple crop varieties;

- nutrient retention, bioavailability and absorption, and efficacy and effectiveness studies to assess the impact of consuming biofortified varieties on nutrition and health outcomes;
- socio-economic studies to assess farmers', consumers' and other value chain actors' evaluation of biofortified varieties and willingness to adopt them;
- and program evaluations to understand the cost-effectiveness, inclusivity, and impact of the delivery models implemented.

<sup>\*</sup>All biofortified crops developed through the HarvestPlus program have been conventionally bred.

# Iron-Biofortified Crops

A meta-analysis has shown that daily consumption of iron-biofortified crops significantly improves iron status and cognition among multiple age groups and across geographies. Moreover, the impact of the additional iron from biofortification had the greatest impact on those with poor iron status—in other words, on those who needed it most<sup>2</sup>.

Studies also show that when biofortified beans and pearl millet are eaten as staples, the total amount of iron absorbed is higher than for conventional varieties and can meet between 75-90 percent of the daily average physiological iron requirement for women and children <sup>3-7</sup>.

#### Iron Beans

#### **Nutrition and Health Evidence**

- In Rwanda, iron-depleted female university students (18-27 years old) experienced a significant increase in iron status (hemoglobin, serum ferritin, and total body iron) after eating iron beans daily for 4.5 months<sup>8</sup>.
- In the same Rwanda study, this improvement in the women's iron status also led to significant improvements in their memory, attention, and ability to do every day physical tasks<sup>9-11</sup>—improving their likelihood of reaching their potential at work, school, and home.
- In Mexico, school-aged children (5-12 years old) who ate iron beans for six months experienced improvements in iron status (hemoglobin, serum ferritin, serum transferrin receptor (sTfR) and total body iron). However, differences in iron status between children eating iron beans versus conventional beans were not statistically significant except for sTfR (a measure of circulating iron). Improvements by both groups indicate the potential benefit of a food-based nutrition intervention in this population<sup>12</sup>.

#### **Socio-Economic Evidence**

- Farmer Adoption: In a 2015 study, a nationally representative sample of bean farming households in Rwanda found that after four years of iron bean delivery efforts, 28 percent of households had planted at least one iron bean variety in at least one of the past eight seasons, and in 2015 iron beans made up almost 12 percent of national bean production with 80 percent of iron beans produced being consumed on-farm. The study also found high awareness of iron beans (67 percent of bean farmer had heard about iron beans), significant farmer to farmer diffusion rates (with 40 percent of adopters getting the iron bean from their social networks), and adopting households allocating increasing proportions of bean area to iron beans (from 48 percent in season one to 70 percent in season six)13.
- Food and Nutrition Security: Data from the same Rwanda survey showed that adoption of an iron bush bean variety resulted in a yield gain of 20-49 percent over traditional bush bean varieties. This effectively increased the length of time farmers could eat beans grown from their own fields by almost three weeks (reducing the need to buy beans), and increased the probability of selling beans by 12 percent. These results indicate that iron bean production positively and significantly improved both food and nutrition security, as well as livelihood security, among adopting households.
- Reaching Target Populations: An outcome monitoring survey conducted in 2017 in Rwanda showed that 87 percent of the iron bean harvest was kept for home consumption. It was consumed by 98 percent of the women of childbearing age and 95 percent of the children under five who resided in these households. This showed that iron beans were reaching their intended primary beneficiaries, i.e., women and children in rural areas<sup>15</sup>. Iron bean delivery models

implemented by the HarvestPlus Rwanda program are documented<sup>16</sup>, as are lessons learned from the evaluation of the program activities<sup>17</sup>.

- Consumer Acceptance: Consumer acceptance studies conducted in rural Rwanda showed that even in the absence of nutrition information, consumers liked iron bean varieties, often more than local varieties, <sup>18</sup> with nutrition information having a positive effect on consumer valuation of iron beans. Similar studies conducted in the Latin America/Caribbean region (in Colombia<sup>19</sup> and Guatemala<sup>20–22</sup>), also revealed that consumers liked iron beans at least as much as their most popular local bean varieties.
- Livelihoods: The yield advantage of iron beans released and adopted in Rwanda resulted in an estimated USD 57-78 additional profit per hectare<sup>23</sup>. From 2010—when the iron bean program was established in the country—to 2018, the total value of benefits was estimated to be USD 25 million. USD 5 million of this was due to the reduction in the burden of iron deficiency, and the rest from the increased production levels<sup>23</sup>. The cost-benefit analysis showed that for the period (2010-2018) every dollar invested yielded USD 3 worth of benefits<sup>24</sup>.

#### Iron Pearl Millet

#### **Nutrition and Health Evidence**

- A study in rural Maharashtra, India showed that iron pearl millet was efficacious in improving the iron status and cognition of adolescent school children (12-16 years old). After only four months of eating flatbread (bhakri) and snacks (shev) made with iron pearl millet twice a day, iron deficiency was significantly reduced, and serum ferritin and total body iron were significantly improved. By six months, those who were iron deficient at the beginning of the study were 64 percent more likely to resolve their deficiency<sup>25</sup>.
- By the end of the same study, the adolescents also experienced significant functional improvements in perception, memory, and attention<sup>26</sup>, and spent less time sedentary and more time doing moderate physical activities<sup>27</sup>.

Improving the learning and physical capabilities of adolescents through increased iron intake can have lasting positive impacts on their ability to be successful at school or secure a job.

#### Socio-Economic Evidence

- conducted among iron pearl millet seed purchasers in rural Maharashtra in 2013, showed that 83 percent of pearl millet growers had replaced their traditional variety with a biofortified one; farmers liked the yield, input use and other production, processing, and consumption attributes of iron pearl millet more than the regular variety, and 84 percent of the iron pearl millet harvest was consumed by the household. A majority of the farmers were willing to plant iron pearl millet again next season, and plant more<sup>28</sup>.
- A more-recent outcome monitoring survey conducted in 2018, also in rural Maharashtra, showed that one in five pearl millet farming households planted iron pearl millet, with nutritional benefits and high yield being the key factors behind this decision. In almost all iron pearl millet adopting households, women and children were consuming iron pearl millet<sup>29</sup>.
- Consumer Acceptance: A study of bhakri made with iron pearl millet revealed that even in the absence of information about the nutritional benefits, rural Maharashtra consumers liked the sensory attributes of iron pearl millet grain and bhakri as much as, if not more than, grain and bhakri of the most popular variety. When nutrition information was provided, consumer acceptance and willingness to pay was even greater<sup>30</sup>.
- The operational cost of delivering biofortified pearl millet as part of a daily meal plan for children was evaluated as part of a randomized controlled feeding study in the urban slums of Mumbai. The delivery of nutrient-dense meals was shown to be highly cost-effective: over 15 months, nearly 100,000 meals were served at a total cost of USD 0.59/meal, which compares favorably to the costs of delivering national meal schemes<sup>31</sup>.

# Vitamin A-Biofortified Crops

Provitamin A carotenoids in biofortified vitamin A crops are efficiently converted into the active form of the vitamin (retinol)<sup>32</sup>.

# Vitamin A Maize Nutrition and Health Evidence

- Vitamin A maize improves numerous measures of good nutrition and health; it holds potential to confer protection against malnutrition-induced blindness<sup>33,34</sup>.
- In Zambia, a study among school-aged children (5-6 years old) found that replacing regular maize with vitamin A maize significantly improved the children's vitamin A status<sup>35</sup>.
- Another study in Zambia with children (4-8 years old) did not show significant improvements in serum retinol<sup>36</sup>; yet, among the children who were vitamin A deficient at baseline, those who ate vitamin A maize experienced significant improvements in their visual ability to see in dim (low) light conditions<sup>33</sup>.
- A short-duration (3 week) study with lactating mothers showed no increase in average breast milk vitamin A concentration among women who consumed vitamin A maize; however, a downward trend in the risk of low retinol concentration in milk warranted further investigation<sup>37</sup>.
- In a subsequent study, breastfeeding Zambian mothers who ate vitamin A maize twice a day for three months experienced improvements in the vitamin A content of their breast milk, and the prevalence of low vitamin A concentration in breast milk was reduced by over 50 percent<sup>38</sup>.

#### **Socio-Economic Evidence**

- survey 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. Nearly all farmers (97 percent) who participated in the study said that they would grow vitamin A maize in the next season, and on average, farmers were planning to plant four times more seed than they did in the previous (2014–2015) season<sup>39</sup>.
- found that almost all the farming households who had acquired vitamin A maize seed did plant it, and 87 percent of the harvest was kept for home consumption. Further, 97 percent of women and 96 percent of children in adopting households consumed this nutritious maize, on average for three days in the last seven days<sup>40</sup>. The survey also showed that 44 percent of the vitamin A maize growers also purchased vitamin A maize grain from the market, showing that adopting households liked the vitamin A maize grain.
- Consumer Acceptance: A study conducted in rural Zambia showed that consumers valued nshima (corn porridge) made with vitamin A maize more than nshima from white and yellow maize varieties, even in the absence of nutrition information. Nutrition information increased consumer valuation of vitamin A maize<sup>41</sup>.
- Another study, conducted in rural Ghana, found that consumers valued kenkey (maize dumpling) made with vitamin A maize less than kenkey made with either white or yellow maize, but the provision of nutrition information reversed this preference<sup>42</sup>.

#### Vitamin A Cassava Nutrition and Health Evidence

- In eastern Kenya, school-age children (5-13 years old) who ate boiled and mashed vitamin
   A cassava for 4.5 months experienced a modest
   but nutritionally significant improvement in their
   vitamin A status<sup>43</sup>.
- In Nigeria, eating vitamin A cassava twice daily improved the vitamin A and iron status (serum retinol) of pre-school children (3-5 years old) after 3.5 months<sup>44</sup>.
- In terms of retention, vitamin A cassava retains intermediate-to-high levels of provitamin A carotenoids when processed using traditional African recipes and methods such as boiling and frying. If boiled and eaten daily as a staple, it can provide young children with 100 percent of their average daily vitamin A needs. Yet, when processed as *fufu* or *chikwangue*—as is common in the Democratic Republic of the Congo—retention is much lower, demonstrating that local context and cooking practices influence the potential nutritional impact of biofortified crops<sup>45</sup>.

#### **Socio-Economic Evidence**

• Farmer Adoption: An outcome monitoring survey conducted in Akwa-Ibom, Anambra, Benue, and Ondo states of Nigeria in 2018 found 21 percent of the total cassava planting area was allocated to vitamin A cassava, and harvested vitamin A cassava roots constituted 25 percent of the cassava production, suggesting a significant yield advantage for vitamin A cassava varieties. Ninety-four percent of women and 85 percent of young children in vitamin A cassava-growing households were regularly consuming food made with this biofortified crop<sup>46</sup>.

- Consumer Acceptance: A study conducted in Oyo and Imo states of Nigeria found that regardless of the color of the commonly consumed local gari (cassava flour), consumers liked gari made with vitamin A cassava varieties albeit in varying degrees depending on the color difference between local and vitamin A cassava gari. Once consumers received information about the nutritional benefits of vitamin A cassava varieties, they preferred vitamin A cassava gari<sup>47</sup>.
- Another consumer acceptance study conducted in Nigeria compared traditional foods prepared with vitamin A cassava, fortified, or conventional foods, and found that consumers preferred food made with vitamin A cassava, associating the yellow color with improved eyesight and enhanced health<sup>48</sup>.
- Studies conducted in Eastern Africa found that school children and their caregivers in Kenya preferred vitamin A cassava to local (white) varieties<sup>49</sup>, while men and women farmers in Uganda favorably evaluated production traits of vitamin A cassava against popular varieties<sup>50</sup>.
- Livelihoods: Other studies conducted in Nigeria found vitamin A cassava production to be profitable<sup>51</sup>. Delivery models implemented for vitamin A cassava by HarvestPlus Nigeria program, and its partners are documented<sup>52,53</sup>, and lessons learned are summarized<sup>54</sup>.

#### Vitamin A Orange Sweet Potato Nutrition and Health Evidence

• Eating vitamin A orange sweet potato (OSP) significantly improves children's vitamin A status across age groups<sup>55–58</sup>, contributes to a healthy immune system, and can reduce the burden of diarrhea, the second leading cause of death of young children in LMICs<sup>59</sup>.

- In Uganda, a large-scale effectiveness study showed that the introduction of OSP to farming households significantly increased vitamin A intake among children (3-5 years old) and women, and improved the vitamin A status of children who were deficient at the start of the study (9.5 percent reduction in low serum retinol prevalence) after four growing seasons<sup>57</sup>.
- In Mozambique, another effectiveness study showed vitamin A intakes doubled among households accessing and growing OSP; almost all the vitamin A intake for children was provided by OSP<sup>58</sup>. Regular consumption of OSP also reduced child morbidity: in children under five, the likelihood of experiencing diarrhea was reduced by 39 percent, and duration of diarrhea episodes was reduced by more than 10 percent; in children under three, the reductions were by 52 percent and 27 percent, respectively<sup>59</sup>.
- Three years after the Mozambique study concluded, vitamin A intakes remained higher among women in the intervention households and their young children born after the trial demonstrating the long-term adoption and sustainability of biofortification as a food-based intervention<sup>60</sup>.

#### **Socio-Economic Studies**

- Delivery Models and Adoption: The effectiveness studies conducted 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 OSP adoption, vitamin A intake, and vitamin A status of participating households. The studies found no significant differences in these outcomes between the two delivery models, providing crucial evidence for cost-effective scaling<sup>57,58,61</sup>. Delivery models for OSP in several countries in Africa South of the Sahara are documented<sup>62</sup>, and lessons learned from these experiences are presented in several publications<sup>63,64,65,66</sup>.
- Consumer Acceptance: Consumer acceptance studies conducted in both rural and urban areas of several countries showed that consumers liked OSP and OSP food products<sup>67–70</sup>. As with other biofortified crops, nutrition information on the benefits of consuming OSP resulted in higher consumer valuation thereof in Uganda<sup>71</sup>. A study conducted in Uganda found that urban consumers' knowledge about this nutritious food increased significantly from 2014 to 2017, and consumers in all socioeconomic segments were consuming vitamin A sweet potato because of its increased availability<sup>67</sup>.

### **Zinc-Biofortified Crops**

Studies show zinc absorption from meals made with zinc-biofortified staple foods (polished rice, whole or refined wheat flour, or whole maize meal) is 8-25 percent higher than zinc absorption from meals made from conventional varieties<sup>72–75</sup>.

A meta-analysis on the effects of zinc supplementation on risk factors for non-communicable diseases showed that low-dose and long-duration supplementation—akin to how zinc is delivered by biofortified staples—reduces risk factors for type II diabetes and cardiovascular disease<sup>76</sup>. This provides a compelling case for a novel study to examine whether type II diabetes and cardiovascular disease could also be a target for food-based zinc interventions like biofortification.

#### **7inc Rice**

#### **Nutrition and Health Evidence**

- Zinc from biofortified rice is absorbed as well as zinc provided through commercial fortification and provides more bioavailable zinc than conventional rice<sup>77</sup>.
- In Bangladesh, eating zinc rice daily for nine months did not change the prevalence of zinc deficiency among young children (12-36 months old). However, by the end of the study, the children attained a greater height for age than the children consuming conventional rice<sup>78</sup>.
- Nutrient retention studies indicate parboiling rice lowers its zinc concentration, whether the rice is biofortified or not; yet, despite zinc losses during processing, biofortified rice retains a higher zinc concentration over non-biofortified rice and, when eaten as a staple, can provide over 50 percent of the daily zinc needs for children<sup>79,80</sup>.

#### Socio-Economic Evidence

- Productivity: Field trials in several countries showed that agronomic biofortification of some varieties of both rice and wheat with zinc can be associated with enhanced grain yield/crop productivity<sup>54,81</sup>.
- Farmer Adoption: A nationally representative zinc rice adoption study conducted in 2018 in Bangladesh found that, despite the fact that zinc rice was in early stages of delivery, 16 percent of all farmers had heard about zinc rice varieties, while a quarter of a million farming households had already grown them. Zinc rice growing farmers liked zinc rice varieties' high yield82.
- Consumer Acceptance: In Bolivia and Colombia, consumer acceptance studies for zinc rice showed that consumers liked zinc rice varieties as much, if not more than, local rice varieties<sup>79</sup>.

## Zinc Wheat Nutrition and Health Evidence

- In New Delhi, India, over 3,000 preschool children (4-6 years old) and their mothers consumed either conventional wheat or agronomically biofortified wheat (i.e., wheat treated with zinc fertilizer) daily for six months. Biofortified wheat reduced time spent ill: children spent 17 percent fewer days sick with pneumonia and 40 percent fewer days vomiting than children who ate foods prepared with conventional wheat. Their mothers (nonpregnant, non-lactating) reported spending significantly fewer days (9 percent) with fever<sup>83</sup>.
- Studies show significantly more zinc is absorbed by the body from biofortified wheat than from conventional wheat<sup>72,73,84</sup>.

 In Pakistan, an effectiveness study is being implemented to assess the potential of zinc wheat for alleviating widespread zinc deficiency<sup>85,86</sup>. Results are expected in 2022.

#### **Socio-Economic Evidence**

• Livelihoods: An ex-ante cost-benefit analysis of a zinc wheat variety that is resistant to wheat blast and other diseases in Bangladesh, found a 5-8 percent higher yield when compared with popular varieties. Potential economic benefits of delivering this zinc wheat variety were found

- to far exceed the anticipated cost of the delivery, resulting in USD 0.23-1.6 million of net benefits even in a limited dissemination scenario<sup>87</sup>.
- Ex-ante impact assessment of scaling of zinc wheat and rice in Pakistan found that replacement of all wheat and rice varieties consumed in this country with zinc biofortified varieties by 2035 could result in a 12 percentagepoint reduction in inadequate zinc intake and 4.9 percent reduction in stunting<sup>88</sup>.

#### More on Biofortification

#### **How Biofortification Works**

The process of biofortification by conventional breeding methods begins by screening hundreds of thousands of staple crop varieties in CGIAR genebanks around the world to identify varieties that are high in vitamin A, iron, and zinc. Plant breeders spend five to seven years crossing these with the latest improved (i.e., high-yielding and climatesmart) varieties of the same crop to develop new varieties that can be adapted to grow in various agroecologies in LMICs.

These micronutrient-dense, high-yielding and climate-smart varieties are multiplied and made available to countries as public goods through their national agricultural research systems (NARS). NARS then test and develop these varieties further with farmers through multi-location trials and in farmers' fields for several planting seasons, comparing the performance of the biofortified varieties with the most popular varieties grown in each agro-ecology. The best-performing varieties are then officially released for planting by farmers in the country and are made available to the public and private sector for multiplication and delivery.

Crop development is an ongoing process. The next generations of biofortified varieties in the pipeline will not only have higher levels of micronutrients but will be higher yielding, better adapted to ever-changing climatic and other environmental conditions and meet preferences of value chain actors.

Equity benefits: Young children, adolescent girls, and women are the primary targets of biofortification. These populations' relatively high micronutrient needs from rapid periods of growth and development predispose them to deficiencies. These needs are often unmet because of dietary habits, cultural norms, lack of access to micronutrient-dense foods, and other factors that increase their biological vulnerability to infections.

Interventions that improve nutrition early in life are key to tackling the intergenerational cycle of malnutrition<sup>89</sup>. An advantage of delivering micronutrients through staple foods is that—unlike with micronutrient-dense animal-sourced foods, fruits, and vegetables—inequitable food allocation within a household does not usually occur with staple foods, which are consumed by all members of a household as their primary, everyday source of food<sup>90</sup>. Making biofortification of staples an inclusive solution for improving micronutrient intake.

Cost-effectiveness: The Copenhagen Consensus ranks interventions that reduce micronutrient deficiencies among the highest value-for-money investments for economic development; it estimated that every USD invested in biofortification yields an average of USD 17 of benefits in reducing disease burden associated with micronutrient deficiencies<sup>91</sup>.

Ex ante cost-effectiveness analyses of several biofortification interventions<sup>92,93</sup> as well as metaanalysis thereof<sup>94</sup> found most biofortification interventions to be highly cost-effective, according to the World Bank criteria of cost (in USD) per Disability-Adjusted Life Year (DALY) saved<sup>52</sup>. Many country-crop-micronutrient combinations ranked more cost-effective than supplementation and/or fortification programs for a given micronutrient<sup>92–94</sup>, for example for iron in India<sup>95</sup>, vitamin A in Zambia<sup>96</sup>, and zinc in Bangladesh<sup>97</sup>.

Climate resilience: Climate change is not only creating greater fluctuations and uncertainties in productivity (often resulting in local or national food insecurity), it is also affecting the nutrient content of commonly

consumed staples as increasing CO2 emissions decrease the nutrient density of most plants<sup>98-100</sup>. Coupled with changes in population and incomes, the gap between the demand for and supply of micronutrients is widening<sup>101</sup>. Biofortified staple crop varieties are developed by piggybacking on the CGIAR's latest varieties which are resilient to the effects of climate change (i.e., drought, and flood resistant, heat tolerant), and have high micronutrient density; there are plans to gradually increase this density to compensate for further nutrient losses resulting from CO2 emissions.

#### About HarvestPlus

As the global thought leader in biofortification science, technology, and policy, HarvestPlus provides strategic guidance, technical assistance, research expertise, and capacity strengthening to more than 600 partners worldwide in the public, private, NGO and humanitarian sectors. HarvestPlus is part of the global CGIAR and is based as the International Food Policy Research Institute (IFPRI), a CGIAR research center.

Worldwide, nearly 400 biofortified varieties of 12 staple crops have been released for planting in 41 countries. As a result of HarvestPlus-led delivery efforts, at the end of 2020, an estimated 9.7 million households (comprising 48.5 million household members) were growing and consuming biofortified crops across 19 countries in Africa, Asia and Latin America and the Caribbean.

The goal of HarvestPlus and its partners is to rapidly scale up production and consumption of biofortified crops and foods, to reach hundreds of millions more people who can benefit from them. The HarvestPlus strategy for enabling rapid scale includes:

- mainstreaming biofortification in global and national crop breeding programs;
- working with value chain actors to facilitate the "biofortification" of seed-to-food value chains for key staples;
- providing technical assistance and evidencebased advocacy for the integration of biofortification in international finance institutions' loans and national/regional policies and programs;
- and facilitating a global platform for knowledge exchange and learning among stakeholders – while also continuing current efforts to expand the evidence base and product portfolio.

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#### References

- Victora, C. G. et al. Revisiting maternal and child undernutrition in low-income and middle-income countries: variable progress towards an unfinished agenda. Lancet 397, 1388–1399 (2021).
- Finkelstein, J. L., Fothergill, A., Hackl, L. S., Haas, J. D. & Mehta, S. Iron biofortification interventions to improve iron status and functional outcomes. *Proc. Nutr. Soc.* 78, 197–207 (2019).
- Petry, N. et al. Phytic Acid concentration influences iron bioavailability from biofortified beans in rwandese women with low iron status. J. Nutr. 144, 1681–1687 (2014).
- Kodkany, B. S. et al. Biofortification of pearl millet with iron and zinc in a randomized controlled trial increases absorption of these minerals above physiologic requirements in young children. J. Nutr. 143, 1489–1493 (2013).
- Cercamondi, C. I. et al. Total Iron Absorption by Young Women from Iron-Biofortified Pearl Millet Composite Meals Is Double That from Regular Millet Meals but Less Than That from Post-Harvest Iron-Fortified Millet Meals. J. Nutr. 143, 1376–1382 (2013).
- Bechoff, A., Taleon, V., Carvalho, L. M. J., Carvalho, J. L. V. & Boy, E. Micronutrient (provitamin A and iron/zinc) retention in biofortified crops. *African J. Food, Agric. Nutr. Dev.* 17, 11893–11904 (2017).
- Council for Agricultural Science and Technology. Food Biofortification—Reaping the Benefits of Science to Overcome Hidden Hunger. CAST Issue Pap. 69, (2020).
- 8. Haas, J. D. *et al.* Consuming Iron Biofortified Beans Increases Iron Status in Rwandan Women after 128 Days in a Randomized Controlled Feeding Trial. *J. Nutr.* **146**, 1586–1592 (2016).
- Murray-Kolb, L. E. et al. Consumption of iron-biofortified beans positively affects cognitive performance in 18- to 27-year-old Rwandan female college students in an 18-week randomized ontrolled efficacy trial. J. Nutr. 147, 2109–2117 (2017).
- 10. Wenger, M. J. et al. Changes in iron status are related to changes in brain activity and behavior in Rwandan female University students: Results from a randomized controlled efficacy trial involving iron-biofortified beans. J. Nutr. 149, 687–697 (2019).
- 11. Luna, S. V, Pompano, L. M., Lung'aho, M., Gahutu, J. B. & Haas, J. D. Increased iron status during a feeding trial of iron-biofortified beans increases physical work efficiency in Rwandan women. J. Nutr. Jan 31, (2020).
- 12. Finkelstein, J. L. *et al.* A randomized feeding trial of ironbiofortified beans in school children in Mexico. *Nutrients* 11, 381 (2019).

- 13. Asare-Marfo, D. et al. Assessing the adoption of high iron bean varieties and their impact on iron intakes and other livelihood outcomes in Rwanda. Main Survey Report. Available upon request. (2016).
- Vaiknoras, K. & Larochelle, C. The impact of iron-biofortified bean adoption on bean productivity, consumption, purchases and sales. World Dev. 139, (2021).
- 15. HarvestPlus. Rwanda Outcome Monitoring Survey Report. Available upon request. (2018).
- Mulambu J, Andersson M & Palenberg M. Chapter 10: Iron Beans in Rwanda: Crop Development and Delivery Experience. Afr. J. Food Agric. Nutr. Dev 17, 12026–12050 (2017).
- Vaiknoras, K., Larochelle, C., Birol, E., Asare-Marfo, D. & Herrington, C. Promoting rapid and sustained adoption of biofortified crops: What we learned from iron-biofortified bean delivery approaches in Rwanda. *Food Policy* 83, 271–284 (2019).
- 18. Oparinde, A., Murekzi, A., Birol, E., Katsvairo, L. & 26, N. Demand-Pull Creation, Public Officer's Endorsement, and Consumer Willingness-to-Pay for Nutritious Iron Beans in Rural and Urban Rwanda. *HarvestPlus Working Paper.* (2017).
- Beintema, J. J. S., Gallego Castillo, S., Londoño Hernandez, L. F., Talsma, E. F. & Restrepo Manjarres, J. Scaling up biofortified beans high in iron and zinc through the school feeding program: A sensory acceptance study with schoolchildren from two departments in southwest Colombia. Food Sci. Nutr. 6, 1138–1145 (2018).
- Pérez, S. et al. Identifying socioeconomic characteristics defining consumers' acceptance for main organoleptic attributes of an iron-biofortified bean variety in Guatemala. Int. J. Food Syst. Dyn. 8, 222–235 (2017).
- 21. Pérez S, Gonzalez C, Oparinde, A., Birol, E. & Zeller, M. The Role of Respondents' Market Participation in Consumer Acceptance of Seeds and Grains of an Iron-Enriched Bean Variety in Guatemala. *J. Agric. Stud.* **6**, 36–53 (2018).
- Pérez, S., Oparinde, A., Birol, E., Gonzalez, C. & Zeller, M. Consumer acceptance of an iron bean variety in Northwest Guatemala: the role of information and repeated messaging. Agric. Food Econ. 2018 61 6, 1–23 (2018).
- 23. Lividini, K. & Diressie, M. Outcomes of biofortification: High iron beans in Rwanda. Available upon request. (2019).
- 24. HarvestPlus. Innovative Delivery Models for Iron Beans Resulted in Adoption by an Estimated 442,000 Households in Rwanda. CGIAR Outcome Impact Case Reports, 2019: Study #3293. (2019).
- 25. Finkelstein, J. L. *et al.* A Randomized Trial of Iron-Biofortified Pearl Millet in School Children in India. *J. Nutr.* **145**, 1576–1581 (2015).

- Scott, S. P. et al. Cognitive Performance in Indian School-Going Adolescents Is Positively Affected by Consumption of Iron-Biofortified Pearl Millet: A 6-Month Randomized Controlled Efficacy Trial. J. Nutr. 148, 1462.
- 27. Pompano, L. M. *et al.* Iron-biofortified pearl millet consumption increases physical activity in Indian adolescent schoolchildren after a 6-month randomised feeding trial. *Br. J. Nutr.* 1–8 (2021).
- 28. Karandikar, B., Birol, E. & Tedla-Diressie, M. Farmer feedback study on high iron pearl millet delivery, distribution and diffusion in India. in AAEA & CAES Joint Annual Meeting (2013).
- 29. HarvestPlus. India Iron Pearl Millet Outcome Monitoring Survey Report. Available upon request. (2018).
- 30. Banerji, A., Birol, E., Karandikar, B. & Rampal, J. Information, branding, certification, and consumer willingness to pay for high-iron pearl millet: Evidence from experimental auctions in Maharashtra, India. *Food Policy* **62**, 133–141 (2016).
- 31. Huey, S. *et al.* Nutrient-Dense Meal Delivery in Partnership with Small-Scale Producers in Mumbai Urban Slums: Implementation Considerations Within a Randomized Controlled Feeding Trial. *Curr. Dev. Nutr.* **4**, 844–844 (2020).
- 32. Bouis, H. E. & Saltzman, A. Improving nutrition through biofortification: A review of evidence from HarvestPlus, 2003 through 2016. *Glob. Food Sec.* 12, 49–58 (2017).
- Palmer, A. C. et al. Provitamin A carotenoid-biofortified maize consumption increases pupillary responsiveness among Zambian children in a randomized controlled trial. J. Nutr. 146, 2551–2558 (2016).
- 34. Palmer, A. C. *et al.* Impact of biofortified maize consumption on serum carotenoid concentrations in Zambian children. *Eur. J. Clin. Nutr.* **72**, 301–303 (2018).
- 35. Gannon, B. *et al.* Biofortified orange maize is as efficacious as a vitamin A supplement in Zambian children even in the presence of high liver reserves of vitamin A: A community-based, randomized placebo-controlled trial. *Am. J. Clin. Nutr.* **100**, 1541–1550 (2014).
- 36. Palmer, A. C. *et al.* Provitamin A-biofortified maize increases serum -carotene, but not retinol, in marginally nourished children: A cluster-randomized trial in rural Zambia. *Am. J. Clin. Nutr.* **104**, 181–190 (2016).
- Palmer, A. C. et al. Short-Term Daily Consumption of Provitamin A Carotenoid-Biofortified Maize Has Limited Impact on Breast Milk Retinol Concentrations in Zambian Women Enrolled in a Randomized Controlled Feeding Trial. J Nutr 146, 1783–1792 (2016).

- 38. AC, P. et al. Biofortified and fortified maize consumption reduces prevalence of low milk retinol, but does not increase vitamin A stores of breastfeeding Zambian infants with adequate reserves: a randomized controlled trial. Am. J. Clin. Nutr. 113, 1209–1220 (2021).
- Tedla Diressie, M., Zulu, E., Smale, M., Simpungwe, E. & Birol, E. An assessment of the vitamin A maize seed delivery efforts to date: Agro-dealer sales and farmer production in Zambia. SUNFUND Project Report. (2016).
- 40. HarvestPlus. Zambia Outcome Monitoring Survey Report. Available upon request. (2018).
- 41. Meenakshi, J. V. *et al.* Using a discrete choice experiment to elicit the demand for a nutritious food: Willingness-to-pay for orange maize in rural Zambia. *J. Health Econ.* **31**, 62–71 (2012).
- 42. Banerji, A. *et al.* Eliciting Willingness-to-Pay through Multiple Experimental Procedures: Evidence from Labin-the-Field in Rural Ghana. *Can. J. Agric. Econ. Can. d'agroeconomie* **66**, 231–254 (2018).
- 43. Talsma, E. F. *et al.* Biofortified yellow cassava and vitamin A status of Kenyan children: A randomized controlled trial. *Am. J. Clin. Nutr.* **103**, 258–267 (2016).
- 44. Afolami, I. *et al.* Daily consumption of pro-vitamin A biofortified (yellow) cassava improves serum retinol concentrations in preschool children in Nigeria: a randomized controlled trial. *Am. J. Clin. Nutr.* **113**, 221-231 (2021).
- 45. Taleon, V., Sumbu, D., Muzhingi, T. & Bidiaka, S. Carotenoids retention in biofortified yellow cassava processed with traditional African methods. *J. Sci. Food Agric.* **99**, 1434–1441 (2019).
- 46. HarvestPlus Monitoring and Evaluation Team. *Nigeria* outcome monitoring: Main survey report 2018. Available upon request. (2018).
- 47. Oparinde, A., Banerji, A., Birol, E. & Ilona, P. Information and consumer willingness to pay for biofortified yellow cassava: Evidence from experimental auctions in Nigeria. *Agric. Econ. (United Kingdom)* 47, 215–233 (2016).
- 48. Bechoff, A., Chijioke, U., Westby, A. & Tomlins, K. I. 'Yellow is good for you': Consumer perception and acceptability of fortified and biofortified cassava products. *PLoS One* 13, (2018).
- 49. Talsma, E. F. et al. Biofortified cassava with pro-vitamin A is sensory and culturally acceptable for consumption by primary school children in Kenya. PLoS One 8, e73433 (2013).
- 50. Esuma, W., Nanyonjo, A. R., Miiro, R., Angudubo, S. & Kawuki, R. S. Men and women's perception of yellow-root cassava among rural farmers in eastern Uganda. *Agric. Food Secur.* **8**, 10 (2019).

- Ayodeji Sunday, O. Profitability of investment and farm level efficiency among groups of vitamin A cassava farmers in Oyo State Nigeria. *Economics* 8, 14 (2019).
- 52. Olaosebikan, O. *et al.* Gender-based constraints affecting biofortified cassava production, processing and marketing among men and women adopters in Oyo and Benue States, Nigeria. *Physiol. Mol. Plant Pathol.* **105**, 17–27 (2019).
- Ilona, P., Bouis, H. E., Palenberg, M., Moursi, M.
   Oparinde, A. Vitamin A cassava in Nigeria: Crop development and delivery. *African J. Food, Agric. Nutr. Dev.* 17, 12000–12025 (2017).
- 54. Bouis, H. E., Saltzman, A. & Birol, E. Improving Nutrition Through Biofortification Introduction: Exploring the Potential of Biofortification. In Agriculture for improved nutrition: Seizing the momentum. 47–57, International Food Policy Institute (IFPRI) and CABI. (2019).
- 55. Van Jaarsveld, P. J. *et al.* -carotene-rich orange-fleshed sweet potato improves the vitamin A status of primary school children assessed with the modified-relative-dose- response test. *Am. J. Clin. Nutr.* **81**, 1080–1087 (2005).
- 56. Low JW Osman N, Cunguara B, Zano F, Tschirley D, A. M. A food-based approach introducing orange-fleshed sweet potatoes increased vitamin A intake and serum retinol concentrations in young children in rural Mozambique. *J Nutr* 137, 1320–1327 (2007).
- 57. Hotz, C. *et al.* Introduction of -carotene-rich orange sweet potato in rural Uganda resulted in increased vitamin A intakes among children and women and improved vitamin A status among children. *J. Nutr.* **142**, 1871–80 (2012).
- 58. Hotz, C. *et al.* A large-scale intervention to introduce orange sweet potato in rural Mozambique increases vitamin A intakes among children and women. *Br. J. Nutr.* **108**, 163–176 (2012).
- 59. Jones, K. M. & de Brauw, A. Using agriculture to improve child health: Promoting orange sweet potatoes reduces diarrhea. *World Dev.* **74**, 15–24 (2015).
- 60. De Brauw, A., Moursi, M. & Munhaua, A. B. Vitamin A intakes remain higher among intervention participants 3 years after a biofortification intervention in Mozambique. *Br. J. Nutr.* 122, 1175–1181 (2019).
- 61. De Brauw, A. *et al.* Biofortification, crop adoption and health information: Impact pathways in Mozambique and Uganda. *Am. J. Agric. Econ.* **100**, 906–930 (2018).
- 62. Arimond, Mary; Ball, Anna-Marie; Bechoff, Aurelie; Bosch, Diane; Bouis, H. Reaching and Engaging End Users (REU) Orange Fleshed Sweet Potato (OFSP) in East and Southern Africa. (2010).
- 63. Low, J. et al. Sweet potato development and delivery in Sub-Saharan Africa. Afr. J. Food Agric. Nutr. Dev 17, 11955–11972 (2017).

- 64. HarvestPlus. Developing and delivering biofortified crops in Uganda: Annual report 2015-Achievements, Lessons learned, and Way forward. Available upon request. (2015).
- 65. Low, J. W., Mwanga, R. O. M., Andrade, M., Carey, E. & Ball, A. M. Tackling vitamin A deficiency with biofortified sweetpotato in sub-Saharan Africa. *Glob. Food Sec.* 14, 23–30 (2017).
- Okello, J. J., Kwikiriza, N., Muoki, P., Wambaya, J. & Heck, S. Effect of Intensive Agriculture-Nutrition Education and Extension Program Adoption and Diffusion of Biofortified Crops. J. Agric. Food. Info. 20, 254–276 (2019).
- 67. Birol, E., Meenakshi, J. V., Oparinde, A., Perez, S. & Tomlins, K. Developing country consumers' acceptance of biofortified foods: a synthesis. *Food Secur.* **7**, 555–568 (2015).
- 68. Brouwer, R. Adoption of orange-fleshed sweetpotato varieties by urban consumers in Maputo, Mozambique. *African J. Agric. Food Secur.* (2019).
- 69. Hummel, M. et al. Sensory and cultural acceptability tradeoffs with nutritional content of biofortified orange-fleshed sweetpotato varieties among households with children in Malawi. PLoS One 13, e0204754 (2018).
- Naico, A. T. A. & Lusk, J. L. The value of a nutritionally enhanced staple crop: Results from a choice experiment conducted with orange-fleshed sweet potatoes in Mozambique. J. Afr. Econ. 19, 536–558 (2010).
- 71. Chowdhury, S., Meenakshi, J. V., Tomlins, K. I. & Owori, C. Are consumers in developing countries willing to pay more for micronutrient-dense biofortified foods? Evidence from a field experiment in Uganda. *Am. J. Agric. Econ.* **93**, 83–97 (2011).
- 72. Rosado, J. L. *et al.* The quantity of zinc absorbed from wheat in adult women is enhanced by biofortification. *J. Nutr.* **139**, 1920–1925 (2009).
- 73. Signorell, C. *et al.* Zinc absorption from agronomically biofortified wheat is similar to post-harvest fortified wheat and is a substantial source of bioavailable zinc in humans. *J. Nutr.* **149**, 840–846 (2019).
- 74. Chomba, E. *et al.* Zinc absorption from biofortified maize meets the requirements of young rural zambian children. *J. Nutr.* **145**, 514–519 (2015).
- Zyba, S. J. et al. A moderate increase in dietary zinc reduces DNA strand breaks in leukocytes and alters plasma proteins without changing plasma zinc concentrations. Am. J. Clin. Nutr. 105, 343-351 (2017).
- Pompano, L. M. & Boy, E. Effects of Dose and Duration of Zinc Interventions on Risk Factors for Type 2 Diabetes and Cardiovascular Disease: A Systematic Review and Meta-Analysis. Adv. Nutr. (2020).

- 77. Brni , M. *et al.* Zinc absorption by adults is similar from intrinsically labeled zinc-biofortified rice and from rice fortified with labeled zinc sulfate. *J. Nutr.* **146**, 76–80 (2016).
- Jongstra, R. et al. The effect of zinc-biofortified rice on zinc status of Bangladeshi pre-school children: a randomized, double-masked, household-based controlled trial. Am. J. Clin. Nutr. (In press).
- 79. Taleon, V., Gallego, S., Orozco, J. C. & Grenier, C. Retention of Zn, Fe and phytic acid in parboiled biofortified and non-biofortified rice. *Food Chem. X* **8**, 100105 (2020).
- 80. Taleon, V., Hasan, M. Z., Jongstra, R., Wegmüller, R. & Bashar, M. K. Effect of parboiling conditions on zinc and iron retention in biofortified and non-biofortified milled rice. *J. Sci. Food Agric.* (2021).
- 81. Rehman, A. *et al.* Agronomic Biofortification of Zinc in Pakistan: Status, Benefits, and Constraints. *Front. Sustain. Food Syst.* **4**, 276 (2020).
- 82. HarvestPlus. Bangladesh zinc rice adoption study. Available upon request. (2018).
- 83. Sazawal, S. *et al.* Efficacy of high zinc biofortified wheat in improvement of micronutrient status, and prevention of morbidity among preschool children and women a double masked, randomized, controlled trial. *Nutr. J.* 17, 86 (2018).
- 84. Hussain, S., Maqsood, M. A., Rengel, Z., Aziz, T. & Abid, M. Estimated Zinc Bioavailability in Milling Fractions of Biofortified Wheat Grains and in Flours of Different Extraction Rates. *Int. J. Agric. Biol. Int. J. Agric. Biol* 15, 921–926 (2013).
- 85. Ohly, H. *et al.* The BiZiFED project: Biofortified zinc flour to eliminate deficiency in Pakistan. *Nutr. Bull.* **44**, 60–64 (2019).
- 86. Lowe, N. M. *et al.* Biofortification of wheat with zinc for eliminating deficiency in Pakistan: study protocol for a cluster-randomised, double-blind, controlled effectiveness study (BIZIFED2). *BMJ Open* **10**, e039231 (2020).
- 87. Mottaleb, K. A. *et al.* Economic benefits of blast-resistant biofortified wheat in Bangladesh: The case of BARI Gom 33. *Crop Prot.* **123**, 45–58 (2019).
- 88. Zeller., L. K. and M. Reductions in inadequate zinc intake with zinc biofortification of rice and wheat. HarvestPlus, International Food Policy Research Institute. Available upon request. (2015).

- 89. Barker, M. *et al.* Intervention strategies to improve nutrition and health behaviours before conception. *Lancet* **391**, 1853–1864 (2018).
- 90. Gittelsohn, J. & Vastine, A. E. Sociocultural and household factors impacting on the selection, allocation and consumption of animal source foods: current knowledge and application. J. Nutr. 133, (2003).
- 91. Horton, S., Alderman, H. & Rivera, J. A. copenhagen consensus 2008 malnutrition and hunger.
- 92. Meenakshi, J. V. et al. How Cost-Effective is Biofortification in Combating Micronutrient Malnutrition? An Ex ante Assessment. World Dev. 38, 64–75 (2010).
- 93. Birol, E., Asare-Marfo, D. & Fieldler, J. Cost-effectiveness of biofortification. Biofortification Progress Briefs: Progress Brief #25. (2014).
- 94. Lividini, K., Fiedler, J. L., De Moura, F. F., Moursi, M. & Zeller, M. Biofortification: A review of ex-ante models. *Glob. Food Sec.* 17, 186–195 (2018).
- 95. Fiedler J, and L. K. An Analysis of Rajasthan's Iron Program Portfolio Options, 2014-2043. Available upon request. (2015).
- 96. Fiedler, J. L. & Lividini, K. Managing the vitamin A program portfolio: a case study of Zambia, 2013-2042. *Food Nutr. Bull.* **35**, 105–125 (2014).
- 97. HarvestPlus. Assessing Bangladesh's Zinc Program Portfolio Options, 2013-2042. Available by HarvestPlus upon request. (2014).
- 98. Debela, C. & Tola, M. Effect of Elevated CO2 and Temperature on Crop-Disease Interactions under Rapid Climate Change. *Int. J. Environ. Sci. Nat. Resour.* 13, 1–7 (2018).
- 99. Smith, M. R. & Myers, S. S. Impact of anthropogenic CO2 emissions on global human nutrition. *Nat. Clim. Chang.* **8**, 834–839 | (2018).
- 100. Loladze, I. Hidden shift of the ionome of plants exposed to elevated CO2 depletes minerals at the base of human nutrition. *Elife* **2014**, (2014).
- 101. Nelson, G. *et al.* Income growth and climate change effects on global nutrition security to mid-century. *Nat. Sustain.* **1**, 773–781 (2018).



