Improving Nutrition through Biofortification - A Systematic Review

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Abstract

Food and nutrients are important for human growth and development. However, malnutrition and hidden hunger continue to be a challenge globally. In most developing countries, access to adequate food and nutrients has been a challenge. Although hidden hunger is less prevalent in developed countries compared to developing countries, iron (Fe) and zinc (Zn) deficiencies are common. The 2nd Sustainable Development Goal was set to help eradicate malnutrition and hidden hunger. Hidden hunger has led to numerous cases of infant and maternal mortalities, and has greatly impacted growth, development, cognitive ability, and physical working capacity. This has influenced several countries to develop interventions that could help combat malnutrition and hidden hunger. Interventions such as dietary diversification and food supplementation are being adopted. However, fortification mainly biofortification has been projected to be the most sustainable solution to malnutrition and hidden hunger. Plant-based foods (PBFs) form a greater percentage of diets in certain populations hence; fortification of PBFs is relevant in combatting malnutrition and hidden hunger. Agronomic biofortification, plant breeding, and transgenic approaches are some currently used strategies in crops. Crops such as cereals, legumes, oilseeds, vegetables, and fruits have been biofortified through all these three strategies. The transgenic approach is sustainable, efficient, and rapid, making it suitable for biofortification programs. Omics technology has also been introduced to improve the efficiency of the transgenic approach.

1 Introduction

Food and nutrients are required in their right proportions by humans to ensure proper growth and development (Jha & Warkentin, 2020). The 2nd Sustainable Development Goal was set to eradicate extreme hunger and malnutrition whilst promoting food security (Dias et al., 2018; Olson et al., 2021; Saint Ville et al., 2019). However, population growth has led to extreme hunger in some parts of the world where there is insufficient food and nutrients to feed the entire population. Malnutrition has been defined as the condition where nutrients are present in unbalanced quantities in the human body, leading to adverse health effect (Wakeel et al., 2018). Hidden hunger, also known as micronutrient deficiency is an undernutrition condition that arises from consuming foods rich in calories but are limited in minerals and vitamins (Beenish et al., 2018; Wakeel et al., 2018). Hidden hunger is very common in developing countries, particularly Sub-Sahara Africa and Southern Asia due to over-consumption of staple foods, changes in dietary patterns and inability to access adequate foods due to poor political and economic status (Gödecke et al., 2018; Wakeel et al., 2018). Deficiencies in micronutrients such as Fe, iodine (I_2), vitamin D (VitD) and E (VitE) have also been reported in the USA, Canada and European countries (Cashman, 2018; Mantadakis et al., 2020). The effects of malnutrition and hidden hunger have been drastic. Malnutrition and hidden hunger have been devastating, particularly in infants, with an estimated 1.1 million out of 3.1 million infant deaths attributed to micronutrient deficiencies annually (Beenish et al., 2018; Wakeel et al., 2018). This has influenced various governments and stakeholders globally to devise strategies to tackle malnutrition and hidden hunger. These efforts include several initiatives such as the

New Alliance for Food Security and Nutrition, The Scaling Up Nutrition Movement and The Harvest Plus Challenge Program (Badiane et al., 2018; H. Bouis, 2018; Sriatmi et al., 2021).

Although dietary diversification and food supplementation have been used as intervention strategies, food fortification particularly biofortification has been projected to be the most sustainable intervention (H. E. Bouis et al., 2019; Garg et al., 2018; Wakeel & Labuschagne, 2021). Food fortification deals with the addition of selected nutrients to foods, naturally present in the foods or exogenous with the purpose of increasing the nutritional value of the food to help consumers reach the Recommended Dietary Allowances (RDAs) for those nutrients (Beenish et al., 2018; Lowe, 2021). Biofortification, a form of food fortification involves the increase in the quantities and bioavailability of nutrients in food crops during their growth (Lowe, 2021). Biofortification addresses the nutritional needs of both urban and rural populations and could be implemented at low costs. Multiple nutrients can be biofortified into foods without influencing the prices of foods (Olson et al., 2021). It does not require robust facilities; hence it is easy to implement and does not depend on the compliance of the consumer (Lowe, 2021). The Harvest Plus Program was initiated in 2003 to target Asia and African countries to ensure the availability and accessibility of high-quality biofortified varieties of staples and the bioavailability of nutrients after consumption. Common examples of biofortified crops through this program include orange-fleshed sweet potato (OFSP), golden rice, yellow and orange maize biofortified with VitA, wheat and rice biofortified with Zn and Fe, and beans biofortified with Fe (H. E. Bouis et al., 2019; Lowe, 2021). PBFs form a greater percentage of diets in certain populations hence their biofortification is relevant in combatting malnutrition and hidden hunger.

Agronomic biofortification, plant breeding and transgenic approaches are some currently used strategies (Garg et al., 2018; Jha & Warkentin, 2020). Agronomic biofortification involves the application of mineral fertilizers to soil or crops to increase the concentration and bioavailability of specific nutrients in the crops (Adu et al., 2018). Biofortification through plant breeding aims at improving the concentration and bioavailability of minerals in crops by utilizing the genetic differences between crops of similar species (Al-Khayri et al., 2016; Marques et al., 2021). There may be limited genetic variations among crops, making it impossible to biofortify certain crops via plant breeding. Alternatively, transgenic approach entails identifying and characterizing suitable genes which could be introduced into such crops to translate into desirable nutritional qualities (Garg et al., 2018). Crops such as cereals, legumes, oilseeds, vegetables, and fruits have been biofortified through these three strategies, with cereals being prominent. The limited genetic variability in oilseed lends itself to the transgenic approach (Garg et al., 2018).

Recently, omics technology has been introduced to improve the efficiency of transgenic approach as a strategy of biofortification (Nayak et al., 2021; Riaz et al., 2020). It involves identifying suitable genes through genomics; expressing a specific gene through transcriptomics; studying the role of proteins in nutrient synthesis, uptake and transport pathways through proteomics; assessing metabolic pathways that control the biosynthesis of natural metabolites through metabolomics; and assessing the response of minerals to environmental and genetic factors through ionomics (Carvalho & Vasconcelos, 2013; Riaz et al., 2020).

This review sought to comprehensively present current interventions and initiatives adopted in combatting malnutrition and hidden hunger in both developing and developed countries including the three main biofortification strategies and omics technology.

Methods

Search and selection of Studies

All articles were selected from the Google scholar database by using the specific search string “biofortification of crops”. An advanced search was done by introducing filters such that, all the articles should have the words “biofortification of crops”, with an exact phrase of “plant-based”, with at least one word of “malnutrition” OR “hidden hunger” OR “minerals” OR “vitamins” OR “fortification” OR “biofortification strategies” OR “biofortified” OR “bioavailability” OR “agronomic” OR “ transgenic” OR “engineering” OR “nutrition” OR “potential” OR “macronutrients” OR “released” OR “biotechnology” OR “gene” OR “current status”, and these filters with words can occur in any part of the article. In addition, the years of publications for the article was limited to custom years of 2016 to 2022 to get information on both traditional and modern biofortification strategies. No filters were applied for the authors, publication titles and the type of the articles. The last date for completing the search was August 31, 2022.

All the articles were downloaded, and two authors carefully read the abstracts of all the articles to pre - screen the selected articles. The rest of the selected articles were read fully by the same authors and the references cited in these articles but were not part of the main search and related to the scope of this review were assessed and included in this review if they met the eligibility criteria. All misunderstandings between the two authors with regards to the inclusion or exclusion of an article in the final review were sent to two additional authors for further verification.

Eligibility criteria: A total of 30,700 articles were obtained for the first search. This was reduced to 2,333 articles after applying the filters for the advanced search (Fig. 1). The screening of the abstracts to select suitable articles for this review was done such that, all abstracts which focus were on animal-based biofortification or improving plants traits such as grain yield and resistance to adverse conditions without including substantial information on improving micronutrient concentration or bioavailability were excluded.

Data extraction: After full reading of all the selected articles, data from the articles were categorized into subtopics. Data about each subtopic including micronutrient requirements in human life cycle, malnutrition and hidden hunger, current status of hidden hunger in developing and developed worlds, various interventions to hidden hunger, plant-based biofortification, micronutrient bioavailability and antinutritional factors, biofortification techniques, unreleased and released biofortified crops, and traditional and modern biofortification strategies were sourced from all selected articles. Also, the titles, year the studies were conducted, tables, and results of some of the articles were extracted and used in this review. Reported data from several articles were extracted to design complete tables and illustrations in this review. A meta-analysis was not performed due to the high degree of diversity among reported data.

Risk of bias assessment: The risk of bias was assessed based on 10 questions, which was answered as Yes, can't tell or No, according to the checklist provided by Critical Appraisal Skills Programme (CASP) for systematic reviews (CASP, 1994). An independent assessment of all articles was done by two authors and only articles which received a minimum of eight (8) Yes out of 10, indicating a good quality were included in the review.

2 Main Findings

It was observed that micronutrients play important roles in human health. However, in most developing countries, these micronutrients are limited in most diets. Among the interventions which have been utilized in improving micronutrient contents of foods, modern biofortification strategies such breeding and transgenic approaches have been the most effective in crops such as maize, rice, wheat, cassava and OFSP. The introduction of omics and gene editing techniques have enhanced the transgenic approach. Most research studies on biofortification of specific crops used in this review reported positive effects of biofortification on increasing micronutrient contents, bioaccesibility, and bioavailability. Although, political and economic influence, consumer acceptability and regulations have proven to be the limiting factors of biofortification, it is still considered as the best and sustainable strategy in tackling micronutrient deficiencies in plant-based foods.

3 Micronutrient Requirements Through The Life Cycle

Food and nutrients are the chemical fuel utilized by the human body for metabolic activities, growth and development (Jha & Warkentin, 2020). Macronutrients including carbohydrates, proteins and lipids contribute greatly as the main sources of energy to the human body (Savarino et al., 2021; Singh et al., 2016). In contrast, micronutrients mainly minerals and vitamins, are required in smaller quantities to ensure proper functioning of the body (Godswill et al., 2020; Marcos, 2021; Savarino et al., 2021). At each stage of human development, these nutrients are required in acceptable quantities daily (Godswill et al., 2020) ensure maximum growth and development. Minerals such as Fe, Zn, iodine (I_2), calcium (Ca) and phosphorus (P) are required for growth in children, adolescents and adults (Savarino et al., 2021). Iron is important for the synthesis of haemoglobin and the functioning of the red blood cells in oxygen transport and energy production (Ilardi et al., 2021). Additionally, it aids in brain development, cellular metabolism and enzymatic functions (Cornelissen et al., 2019; Godswill et al., 2020; McCann et al., 2020). When children become deficient in Fe, the level of their physical activities, immune responses, brain and perception control reduces (Savarino et al., 2021). Adolescents have increased Fe requirements due to its relevance in muscle development and formation of new red blood cells especially in adolescent girls who experience menstruation (Savarino et al., 2021). Also, pregnant and lactating female adults have increased Fe requirements due to the need to deposit Fe for infants (Godswill et al., 2020; Ilardi et al., 2021). The recommended Fe intake for children, adolescents and adults are 7–11 mg/day, 13 mg/day and 18 mg/day, respectively (Godswill et al., 2020; Savarino et al., 2021). Zinc is essential for children due to its role in regulating growth hormones, promoting cellular immunity and gastrointestinal systems (Ilardi et al., 2021; Savarino et al., 2021). Growth occurs rapidly in adolescents, hence have higher Zn requirements (Savarino et al., 2021). It is also essential for enzymatic activities in the body of adolescents and adults (Godswill et al., 2020). Common symptoms of Zn deficiency include growth retardation, loss of appetite and weakened immune system (Savarino et al., 2021). The recommended intake of Zn for children, adolescents and adults are 2.9-4.3mg/day with upper intake levels of 7 mg/day, 11 mg/day and 11 mg/day, respectively (Chouraqui et al., 2020; Godswill et al., 2020; Savarino et al., 2021). Iodine plays an important role in the functioning of the thyroid gland in children, adolescents and adults (Andersson & Braegger, 2021; Godswill et al., 2020). Its deficiency is characterized by goitre and hypothyroidism especially in children (Savarino et al., 2021). Children require 90 µg/day of I_2 whilst adolescents and adults require 0.15 mg/day (Godswill et al., 2020; Savarino et al., 2021). Due to the physical activities of children, it is important to consume adequate amounts of Ca and P for bone development (Savarino et al., 2021). Adolescents have the highest Ca requirements due to rapid bone growth and increased physical activity within this phase of human development (Savarino et al., 2021). Adults require adequate levels of Ca for proper functioning of the muscles and digestive system, and P for energy production (Godswill et al., 2020). Children suffering from Ca and P deficiencies show symptoms of weak bones and rickets (Godswill et al., 2020). The recommended intake of Ca for children, adolescents and adults are 280–450 mg/day, 1150 mg/day and 1200 mg/day, respectively (Godswill et al., 2020; Savarino et al., 2021), and 160–250 mg/day and 700 mg/day, respectively, for children and adults for P (Godswill et al., 2020; Savarino et al., 2021).

Other minerals such as magnesium (Mg), selenium (Se), potassium (K), and silicon (Si) also contribute to human growth especially in adults. Mg is responsible for muscle contraction, enzyme functioning, synthesis of nuclear materials and transport of ions across membranes (Al Alawi et al., 2018; Godswill et al., 2020). The recommended intake of Mg for children and adults are 170 mg/day and 320–420 mg/day, respectively (Al Alawi et al., 2018; Chouraqui et al., 2020). Se promotes the activity of antioxidant enzymes and biological systems in the body (Sobolev et al., 2018). However, Se is required in extremely minute quantities in the body. The recommended intake of Se for adults is 0.055 mg/day (Godswill et al., 2020). K acts as electrolyte for the body and regulates ATP for energy production (Godswill et al., 2020). The recommended intake of K for adults is 4700 mg/day. The biochemical functions of Si have not been clearly defined and not considered as an essential mineral for growth (Nielsen, 2020). However, recent studies show that Si may be important for the functioning of bone and connective tissues (Nielsen, 2020). The recommended intake of Si has been set at 25 mg/day for adults (Nielsen, 2020).

Vitamin A (VitA) plays an important role in maintaining vision, regulating cell and tissue growth, and improving the immune system (Cabezuelo et al., 2020; Godswill et al., 2020). The recommended intake of VitA for children and adults are 300–600 mg and 700–900 mg of RAE/day (retinol activity equivalent), respectively (Cabezuelo et al., 2020). Vitamin D (VitD) is one of the essential vitamins for children due to its role in Ca absorption for bone tissue development (Savarino et al., 2021). Additionally, it provides anti-inflammatory and anti-microbial properties in adults (Marcos, 2021; Murdaca et al., 2019). The recommended intake of VitD for both children and adults is 15 μg/day (Godswill et al., 2020; Savarino et al., 2021). Vitamin K (VitK) promotes coagulation and prevents excessive bleeding in children (Savarino et al., 2021). Additionally, it aids in bone and muscle metabolism in adults (Bellone et al., 2022; Cozzolino et al., 2019). The recommended intake of VitK for children and adults are 12 μg/day and 120 μg/day, respectively (Godswill et al., 2020; Savarino et al., 2021). Vitamin C (ascorbic acid) plays a major role in enzymatic and non-enzymatic reactions, and acts as an antioxidant to improve the body's defensive mechanism against diseases in both children and adults (Jafari et al., 2019; Marcos, 2021; Savarino et al., 2021). Deficiency in VitC can be seen through symptoms such as tiredness, weight loss and scurvy (Savarino et al., 2021). The recommended intake of VitC for children and adults are 20 mg/day and 90 mg/day, respectively (Godswill et al., 2020; Savarino et al., 2021). The human body cannot synthesize folate therefore, it is essential to consume folate-rich foods (Savarino et al., 2021). Folate is one of the essential nutrients for all stages of human development. It promotes rapid growth through cell divisions and DNA replication (Rogers et al., 2018; Savarino et al., 2021). During pregnancy, folate deficiency results in neural tube defects in infants (Savarino et al., 2021), thus the highest amount is required during pregnancy. The recommended intake of folates for children are 120 μg/day, and 400 μg/day each for adolescents and adults (Godswill et al., 2020; Savarino et al., 2021). Vitamin B12 (VitB12) is essential for the synthesis of DNA and haemoglobin and may be deficient in adolescents and adults who consume exclusive plant-based diets (Savarino et al., 2021). The recommended intake of VitB12 for children, adolescents and adults are 1.5 μg/day, 3.5 μg/day and 2.4 μg/day, respectively (Godswill et al., 2020; Savarino et al., 2021).

4 Malnutrition And Hidden Hunger

Malnutrition is the generic term for the condition where food nutrients are present in excess (overnutrition) or limited quantities (undernutrition) in the body, leading to adverse health effect (Wakeel et al., 2018). As suggested by its name, hidden hunger denotes an undernutrition condition that arises from consuming foods rich in calories but is limited in minerals and vitamins with a sense of satisfaction to the consumer. Hidden hunger describes micronutrient deficiency unbeknownst to the consumer (Beenish et al., 2018; Gödecke et al., 2018).

Several factors synergistically contribute to malnutrition and hidden hunger, especially in developing countries (Gödecke et al., 2018; Wakeel et al., 2018). These factors include climate change which affects food production, spikes in food prices which affect the accessibility of foods to the low-income populace, economic status of the populace and diseases such as cancer and chronic renal failure, which increase the risk of malnutrition and hidden hunger in affected patients. Climate change has already affected food production by means of the effects of changes in weather patterns, drought, and flooding on crop yields. In 2020, a locust swarm devastated wheat crops, leading to food insecurity, particularly in the most disadvantaged communities in parts of South Asia and Sub-Saharan Africa (Lowe, 2021).

In both developing and developed countries, hunger, poverty, and malnutrition are interrelated challenges. Most people who suffer persistently from malnutrition are submerged in a vicious cycle; not being able to get nourishing meals regularly and consequently not being able to live an active and healthy life, not receiving adequate health care, hence not being able to produce or buy essential nutritious food. There is a close and complex relationship between hunger, malnutrition, and poverty. This phenomenon is described as the poverty trap, in which the poor are hungry, and their hunger traps them in poverty (Singh et al., 2016). On the other hand, the current COVID-19 pandemic has brought to light the vulnerability of the food system to which has resulted in disruptions in food production and distribution. The international border closures have also impacted the labor force, particularly seasonal migrant workers working in agricultural fields (Lowe, 2021). Movement restrictions have also had a negative impact on the transportation of food to marketplaces and limited consumers' access to those, particularly in situations where open marketplaces are the primary distribution channels. There has been an inevitable loss and waste of food due to the outbreak, with crops that could not be harvested or transported to the marketplaces sitting in the field to rot and milk being thrown away due to interrupted supply chains.

4.1 Trends in Malnutrition and Hidden Hunger in Developed and Developing Countries

The 2nd Sustainable Development Goal aimed at eradicating extreme hunger and malnutrition whilst promoting food security and sustainable agriculture (Dias et al., 2018; Lowe, 2021; Olson et al., 2021). This continues to be a big challenge globally but predominate in developing countries, particularly Sub-Saharan Africa, and Southern Asia. The Global Hunger Index (GHI) was updated in 2017 based on deficiencies in both calories and micronutrients using 119 countries as case studies (Grebmer et al., 2017). Reports showed that one country falls in the extremely alarming range, 7 countries fall within alarming range, 44 countries within the serious range, 24 countries within the moderate range, and 43 countries within the low range on the GHI severity scale. In addition, the remaining 13 countries did not have sufficient data for the studies. However, 9 of the 13 countries with no sufficient data showed significant levels of hunger. The countries who suffered greatly from all forms of hunger were Southern Asia and Sub Saharan African countries with Yemen, Central African Republic, Chad, Liberia and Madagascar among the predominant countries (Grebmer et al., 2017) The high occurrence of hidden hunger in developing countries has been attributed to their inability to access adequate diets due to their low income (Wakeel et al., 2018), over-reliance on staple foods that have limited micronutrient contents and changes in the type of diets from traditional less-processed foods to highly processed foods (Beenish et al., 2018) and to the inferior quality of foods consumed, poor economic status and political systems (Grebmer et al., 2017).

Although hidden hunger is not prevalent in developed countries compared to developing countries, Fe and Zn deficiencies can be found in most developed countries (Beenish et al., 2018). Surveys in the USA, Canada, Great Britain and other developed countries showed that the RDA for micronutrients such as Fe, iodine, VitD and VitE were not met by a certain percentage of the population (Cashman, 2018; Mantadakis et al., 2020; Singh et al., 2016). This was attributed to changes in the dietary lifestyle in those developed countries, which have had substantial effects on the consumption of balanced diets. This had intended to increase the occurrence of hidden hunger in those developed countries.

The major micronutrient deficiencies in most developing countries include Fe, I_2, Ca, Zn, folic acid and VitA deficiencies (Singh et al., 2016; Wakeel et al., 2018). These deficiencies have had adverse effects on more than an average percentage of the world's population (Wakeel et al., 2018). An estimated two billion people have suffered from hidden hunger globally (Gödecke et al., 2018; Sheoran et al., 2022; Stangoulis & Knez, 2022). Among all the other micronutrient deficiencies, Fe deficiency is said to have affected a greater percentage of the human population worldwide (Mantadakis et al., 2020; Wakeel et al., 2018). Iron and other micronutrient deficiencies have direct relationships with mortality rates in infants and reproductive women (Mantadakis et al., 2020). These micronutrient deficiencies are highly fatal, particularly in infants, with an estimated 1.1 million out of 3.1 million infant deaths attributed to micronutrient deficiencies annually (Beenish et al., 2018). Aside infant and maternal deaths, malnutrition and hidden hunger also hinder growth, development, cognitive ability and physical working capacity (Wakeel et al., 2018). Furthermore, hidden hunger decreases the productivity of labor of the affected population which intend affect the economy (Beenish et al., 2018; Wakeel et al., 2018) (Fig. 2). These adverse effects of malnutrition and hidden hunger comprehensively explain why there is the need to find suitable ways of addressing them.

Undernutrition persists throughout life. A baby born with low birth weight grows up as a stunted adolescent and later becomes an under nutrient adult increasing the risk of chronic diseases, besides other adverse effects, including reduction of productivity. In parallel, malnourished women during pregnancy gain less weight, which increases their risk of delivering small infants. It has been demonstrated that this cycle extends over more than two generations through changes in DNA. Pregnant women, children, and adolescents are often the most cited as affected by hidden hunger; however, it adversely impacts people of all ages and stages (ACC/SCN, 2000).

Additionally, in some countries in Latin America and the Caribbean, there is a lack of data related to malnutrition (Batis et al., 2020). Many countries are usually not included in analysis, either because research teams are unwilling to participate or because there is no actual data to analyze. Moreover, anemia remains a public health issue among children under six years old and women in most countries for which data are available (Galicia et al., 2016). Finally, other studies indicated that there is a high prevalence of Zn deficiency in children less than six years of age and girls and women from twelve to forty-nine years of age. High rates of both estimated Zn dietary inadequacy and stunting were also reported in most Latin American and Caribbean countries (Batis et al., 2020; Cediel et al., 2015; Galicia et al., 2016).

It is important to add that to successfully combat hidden hunger through biofortification, even after the development of biofortified varieties, it will be essential to address various socio-political and economic challenges to promote their cultivation and finally their consumption by customers. For future actions, an integrated approach is required, not only politicians and citizens need to be included but there is also a need to involve farmers, food product developers, dietitians, and educators. These stakeholders can impact population eating habits and contribute to increase the consumption of the target PBFs (Buturi et al., 2021).

5 Interventions To Alleviate Malnutrition And Hidden Hunger

The adverse effect of malnutrition and hidden hunger has been a global concern for several years with several countries developing interventions. The Copenhagen Consensus, 2008 highlighted that governments and other agencies should prioritize the provision of micronutrients to their populace to serve as one of the best underlying factors for development (Osendarp et al., 2018). This has influenced several global initiatives including the New Alliance for Food Security and Nutrition formed in 2012 to help promote agricultural growth in Sub-Sahara Africa (Badiane et al., 2018) and the Scaling Up Nutrition Movement sought to fight malnutrition around the globe (Sriatmi et al., 2021). Several countries have added laws regarding nutrition and health to their constitutions (Lopez Villar, 2015; Osendarp et al., 2018). Generally, there are four interventions that have been adopted in curbing malnutrition and hidden hunger. These include dietary diversification, food supplementation, food fortification and biofortification (Cominelli et al., 2020; Jha & Warkentin, 2020).

5.1 Dietary Diversification

Micronutrients such as Fe, Zn, I_2 and vitamins are limited in most staples but can be found in certain types of foods (Ul-Allah, 2018; Wakeel et al., 2018). Therefore, consuming a narrow range of foods and more staples with insufficient quantities of micronutrient-rich foods may result in hidden hunger. This makes dietary diversification a vital strategy that can be used in curbing malnutrition and hidden hunger (Malik & Maqbool, 2020). Dietary diversification or modification pertains to the consumption of different varieties of foods with sufficient quantities of macro and micronutrients that synergistically contribute to meeting the RDA over a specific period (Beenish et al., 2018; H. Bouis, 2018; Lowe, 2021).

Dietary diversification helps alleviate all forms of deficiencies, aids in boosting the immune system, culturally acceptable and sustainable as compared to other interventions used in alleviating malnutrition and hidden hunger (Jha & Warkentin, 2020; Nair et al., 2016). Major disadvantages of dietary diversification as a strategy of alleviating malnutrition and hidden hunger include the obligation of nutrition education, change in dietary patterns, the need for accurate food data and presence of anti-nutrients in foods consumed, which impact nutrient absorption (Beenish et al., 2018). Also, one of the main disadvantages of dietary diversification is the financial commitment involved in purchasing and producing high-quality varieties of foods (Farsi Aliabadi et al., 2021; Kiran et al., 2022; Wakeel et al., 2018). Therefore, dietary diversification is very difficult to implement in developing countries; hence other interventions such as food supplementation, food fortification and biofortification are preferred in developing countries (Beenish et al., 2018; Wakeel et al., 2018).

5.2 Food Supplementation

Food supplementation involves the intake of additional nutrients in the form of capsules, syrups or tablets to add to the nutrients that are obtained from the consumption of foods to meet the RDA for nutrients (Beenish et al., 2018; Tam et al., 2020). Food supplements include vitamins, herbals, amino acids and proteins, bodybuilding, essential fatty acids and omega-3, mineral, fiber and calorie supplements (Ghosh et al., 2018; Tam et al., 2020). In most developing countries, vitamin supplements are the most commonly used in combating hidden hunger whilst mineral supplements such as folic acid, Zn, Fe, and amino acid supplements are less common (Beenish et al., 2018; Buturi et al., 2021; Wakeel et al., 2018). Food supplements are usually targeted to small populations with acute nutrient deficiencies in developing countries. Food supplementation is also a short-term strategy. It is direct and controllable and can be tailored to meet the specific needs of a targeted population. It yields positive results rapidly and is cost-effective as compared to other interventions such as dietary diversification (Beenish et al., 2018; Tam et al., 2020). A population-based study in Ceará, Brazil was conducted to assess the association between VitA supplementation and child development using 1,232 children between the age of 0 to 35 months in 8,000 households (Correia et al., 2019). It was reported that children supplemented with VitA showed over 40% lower probability each for delay in development of cognitive and motor abilities, as compared to children without VitA supplements. One of the key messages of the study was that VitA supplementation had positive effects on child development; indicating food supplementation can be used to improve the nutritional status of a population with micronutrient deficiencies.

Zinc supplementation in infancy increases specific growth outcomes, especially after age 2 (Lowe, 2021). Nevertheless, identifying those at risk of Zn deficiency is challenging due to the lack of a reliable diagnostic tool. Another challenge can be reaching rural population as it needs continuous distribution of the supplements (Kiran et al., 2022). Other disadvantages of food supplementation include its reliance on the compliance of the targeted population, require well-defined structures to successfully implement in targeted populations and is highly unsustainable, especially in developing countries (Jha & Warkentin, 2020; Lowe, 2021; Wakeel et al., 2018). Food supplementation may also cause toxicity, which has severe effects on the health of targeted populations (Ghosh et al., 2018).

5.3 Food Fortification

Food fortification involves the addition of selected nutrients to foods, whether they are naturally present in the foods or not with the purpose of increasing the nutritional value of the foods to help consumers reach the RDA for those nutrients (Beenish et al., 2018; Das et al., 2019). Both food fortification and food enrichment contribute to increasing the nutritional value of foods, but there is a major difference between them (Nwadi et al., 2020). Food enrichment only involves replacing the nutrients lost during the processing of the food, whilst food fortification considers restoring lost nutrients and adding to nutrients that are already present in the food in insufficient amounts. There are several forms of food fortification; voluntary fortification, mass fortification, mandatory fortification, and target fortification (Olson et al., 2021). Voluntary fortification occurs when food processing companies optionally add nutrients to processed foods as it not mandated by the government (Olson et al., 2021). A typical example of voluntary fortification is the addition of nutrients such as Fe and VitA to breakfast cereals and wheat flours as seen in countries such as Gambia, Qatar and United Arab Emirates (Olson et al., 2021; Osendarp et al., 2018). Mass fortification involves the addition of selected nutrients to commonly-consumed foods of a specific population with the aim of preventing specific nutrient deficiencies (Das et al., 2019; Saghir Ahmad, 2015). An example of mass fortification is the fortification of rice which is usually consumed by greater percentage of the population of Asian countries like China (Das et al., 2019; Jan et al., 2019; Saghir Ahmad, 2015). As suggested by its name, mandatory fortification deals with the addition of nutrients to foods as demanded by the laws and regulations of the government (Olson et al., 2021; Saghir Ahmad, 2015). It is the most common among all forms of fortification. Most governmental regulations demands the addition of iodine to salts, Fe and folic acid to wheat flour, and VitA to edible oils (Olson et al., 2021; Osendarp et al., 2018). Target fortification has been described as a form of fortification designed specifically for a particular group within a targeted population to reduce a particular nutrient deficiency (Saghir Ahmad, 2015). An example of target fortification is the addition of nutrients such as Fe to infant formulas (Jan et al., 2019; Saghir Ahmad, 2015).

Food fortification has become relevant in both developing and developed countries due to the changes in dietary patterns with increases in the consumption of processed foods (Beenish et al., 2018; Olson et al., 2021). Extensive food processing and storage conditions tend to reduce nutrients such as water-soluble vitamins and minerals of foods (Martínez et al., 2020). Food fortification acts as the medium through which these lost nutrients are restored after processing whilst complementing insufficient nutrients. Common examples of fortified processed foods include iodized salts, Fe and folic acid-fortified wheat, VitD and calcium-fortified milk and, VitA-fortified rice and edible oil (Beenish et al., 2018; Olson et al., 2021; Osendarp et al., 2018). In some contexts, implementation of food fortification is limited due lack of well-structured processing and distribution networks (Buturi et al., 2021; Lowe, 2021; Wakeel et al., 2018). Food fortification also tends to favor urban areas rather than rural regions, where there are often communities with higher socioeconomic status, combined with higher levels of health education (Kiran et al., 2022; Lowe, 2021).

Food fortification is measurable, sustainable in developed countries, and implemented at low costs (Beenish et al., 2018; Osendarp et al., 2018). Fortifying foods with nutrients such as Fe, I_2 and vitamins in developing countries has greatly reduced the prevalence of diseases associated with nutrient deficiencies (Mkambula et al., 2020). However, in developing countries, the higher prices of fortified foods makes it less appealing to consumers (Chadare et al., 2019; Kiran et al., 2022). Thus, in developing countries, biofortification is considered as a complementary intervention in alleviating malnutrition and hidden hunger.

5.3.1 Biofortification

Biofortification seeks to increase the quantities and bioavailability of nutrients in food crops during their growth (Sushil Kumar et al., 2019; Malik & Maqbool, 2020). It focuses on producing crops with characteristics of high levels of micronutrients in addition to agronomic characteristics such as high yield and disease resistance (Kiran et al., 2022; Umar et al., 2019). Biofortification differs from food fortification in that the former involves the addition of nutrients to food crops prior to harvesting whilst the latter adds nutrients to foods during post-harvest processing (J. L. Finkelstein et al., 2019; Olson et al., 2021). Food fortification repeatedly adds nutrients to foods whilst biofortification of varieties of food crops occurs once (J. L. Finkelstein et al., 2019; Saghir Ahmad, 2015).

Biofortification has been projected to be the most sustainable solution to malnutrition and hidden hunger (H. E. Bouis et al., 2019). At present, Harvest Plus, the Biocassava project, and the National Agricultural Research Organization (NARO) are the major projects initiated for nutritional security via the development of biofortified varieties (Sheoran et al., 2022). The initiation of The Harvest Plus Program in 2003, aimed to improve the quality (nutritional value) of food crops through biofortification (H. Bouis, 2018). The Harvest Plus Program targeted Asia and African countries to ensure the availability and accessibility of high-quality biofortified varieties of staples and the bioavailability of nutrients after consumption (H. Bouis, 2018; H. E. Bouis et al., 2019). Interventions such as food supplementation and industrial food fortification usually benefit the populace of developed and industrialized countries with little to no impact in most developing countries. On the other hand, biofortification targets the developing and rural world and extends greatly to the developed world as well (Beenish et al., 2018; Wakeel et al., 2018). To fully implement biofortification, there is the need to assess the bioavailability of the nutrients, set targeted nutrient levels, assess the nutritional requirement of the targeted population, and enhance the absorption and retention levels of nutrients when subjected to processing and storage conditions (H. E. Bouis et al., 2019; Saltzman et al., 2016).

Table 1
Adapted biofortified crops (Lowe, 2021)

Biofortified Crop	Target Micronutrient	Countries where crop has been tested	References
Orange sweet potato	Vitamin A	Uganda; Zambia	(Hotz et al., 2012; Tanumihardjo et al., 2017)
Beans	Iron	Uganda; Zimbabwe; Rwanda	(J. Finkelstein et al., 2017; Haas et al., 2016)
Cassava	Vitamin A	Nigeria; Democratic Republic of Congo; Kenya	(Afolami et al., 2021; Talsma et al., 2016)
Maize	Vitamin A	Nigeria; Democratic Republic of Congo; Zambia; Zimbabwe	(Gannon et al., 2014)
Pearl millet	Iron	India	(J. Finkelstein et al., 2017; Scott et al., 2018)
Wheat	Zinc	India; Pakistan	(Signorell et al., 2019; Zia et al., 2020)
Rice	Zinc	Bangladesh	(Sanjeeva Rao et al., 2020)

In 2017, a total of 33 million people across Africa, Asia, Latin America, and the Caribbean consumed biofortified crops (Heidkamp et al., 2021). Common examples of biofortification include OFSP, golden rice, yellow and orange maize biofortified with VitA, Zn and Fe biofortified-rice and wheat, and beans (H. E. Bouis et al., 2019; Lowe, 2021). Biofortification programs implemented in most countries have yielded positive results. In Nigeria, it was reported that two groups of 176 pre-school children aged from 3–5 years were fed with foods prepared using biofortified (yellow) cassava and white cassava, respectively, twice daily and for 93 days. It was further reported that the status of VitA (determined using serum retinol and hemoglobin concentrations) of the group that consumed the biofortified cassava significantly improved in relation to the other group (Afolami et al., 2021). While in Rwanda, haemoglobin, serum ferritin, and body Fe levels increased among reproductive women after consuming beans biofortified with Fe (Haas et al., 2016) (Table 1). Biofortification has certain advantages over other interventions to alleviate malnutrition and hidden hunger. It addresses the nutritional needs of both urban and rural populations and could be implemented at low costs after the initial developmental stages (Lowe, 2021). Multiple nutrients can be biofortified into foods without influencing the prices of foods (Olson et al., 2021). It is the most sustainable method among other intervention (Beenish et al., 2018). Nutrients in biofortified crops are bioavailable hence have no impacts on the organoleptic properties of the food (Lowe, 2021; Singh et al., 2016). The main disadvantage associated with biofortification is its inability to expediently improve the nutritional status of populations who are highly deficient in nutrients (Beenish et al., 2018).

6 Biofortification Of Plant-based Foods

Global production, consumption, and sales of PBFs have significantly increased (Alcorta et al., 2021). Additionally, vegetables can contribute to combating undernutrition, poverty, and hunger, since they can be locally cultivated and consumed (Buturi et al., 2021). Many consumers opt for exclusive PBFs due to the established relationships with health improvement, reduction in environmental impacts, and promoting food security (Alcorta et al., 2021; Siegrist & Hartmann, 2019). PBFs have also been shown to provide nutritional benefits, specifically increased fiber, VitK and VitC, folate, magnesium, beta-carotene, and potassium consumption (Medawar et al., 2019). Additionally, Ca, I_2, and Se present in vegetable-rich diet, are beneficial for optimal bone strength, blood pressure, hormone production, heart, and mental health (Buturi et al., 2021). However, it is important that consumers of exclusive plant-based diets select and combine PBFs to help prevent the risk of micronutrient deficiencies (Alcorta et al., 2021); particularly vitamin B12 (needed for neurological and cognitive health), a mainly animal-derived nutrient, unless supplemented or provided in B12-fortified products (Medawar et al., 2019). PBFs also contain high amounts anti-nutritional factors such as phytates and tannins known to reduce the bioavailability of minerals by preventing their absorption in the intestine (Popova & Mihaylova, 2019). Additionally, processes like polishing, milling, and pearling of cereals can reduce their nutritional value (Rawat et al., 2013). Biofortification of PBFs presents a way to reach populations where supplementation and conventional fortification activities may be challenging (Meena et al., 2018) and may serve as an essential step in preventing nutrient deficiencies, especially among consumers of exclusive PBFs.

Biofortification of PBFs involves increasing the levels of nutrients and their bioavailability. This is dependent on enhancing the bioavailability of the nutrients, uptake and transportation of the nutrients through the plant tissues, and their accumulation in non-toxic quantities in edible parts of the plants (Carvalho & Vasconcelos, 2013; Umar et al., 2019). Biofortification of PBFs addresses two main challenges; the inability of the plants to synthesize certain nutrients and the uneven distribution of nutrients in different parts of the plant (Carvalho & Vasconcelos, 2013; Umar et al., 2019). For example, the grains of rice are the consumed portion of the rice plant, however, pro-VitA synthesis and accumulation occurs in the leaves hence limited in quantities and bioavailability in the edible portion. Therefore, biofortifying the rice plant with pro-VitA would enhance its accumulation and bioavailability in the grains (Sheoran et al., 2022).The Harvest Plus Program has designed suitable steps involved in biofortification of PBFs. These steps (Fig. 3) can be grouped into four categories; breeding, nutrition and food technology, impact and socioeconomics, and consumer response (H. Bouis, 2018; H. E. Bouis et al., 2019; Pfeiffer & McClafferty, 2007).

Although increasing concentration of nutrients is an important factor in PBFs biofortification, it is relevant to prevent over-accumulation of these nutrients due to its tendency to adversely affect the edible part of the crop and enhance the accumulation of undesirable metals, which could affect consumer’s health (Carvalho & Vasconcelos, 2013; Sheoran et al., 2022). For example, Se play important roles and is required in extremely minute quantities in the human body with recommended level of Se intake for adults being 0.055 mg/day (Godswill et al., 2020). Excessive intake of Se causes toxicity which is characterized by adverse health effects such as muscle soreness, intestinal complications, cardiovascular diseases and can extend to extreme cases of mortalities (Hossain et al., 2021). The consumption of biofortified foods should help consumers meet their nutritional needs without any risk of toxicity.

Both bioavailability (fraction of nutrient that is stored or available for physiological functions) and bioaccessibility (fraction of the total nutrient that is potentially available for absorption) (Umar et al., 2019) are important in PB biofortified foods. In a study reported by (Coelho et al., 2021) significant improvement in contents, bioaccessibility and bioavailability of Fe- and Zn-biofortied cowpea cultivars were shown. The values obtained for Fe bioaccessibility (18.5–32.3 mg/kg (2.5-fold higher)) and bioavailability (> 3.0% (2.6-fold higher)) in Fe-biofortified cowpea seeds were found to be higher compared to common beans (7.3–15.4 mg/kg) and (1–2%), respectively. Zn bioaccessibility in the biofortified cowpea cultivars was also about 25% higher than in the common beans, while Zn bioavailability in the biofortified cowpea was slightly higher compared to the common beans. In another study, increasing doses of selenate during wheat biofortification enhanced both Se content (0.18–0.45 mg/kg) and bioaccessibility (63.3–93.8%). However, its effect on bioavailability was minimal with only 19.6% being absorbed (Delaqua et al., 2022).

In presence of antinutrients, biofortified crops showed limited improvement in the bioavailability of certain nutrients (Hummel et al., 2020; R. R. Kumar et al., 2022). Antinutrients such as phytic acid/phytate, tannins, lectins, saponins and oxalic acid can limit the absorption of certain essential nutrients (Ram et al., 2020; Singh et al., 2016). These include phytic acid/phytate mostly found in PBFs such as wheat, rice, barley and beans (Ram et al., 2020). Phytate/phytic acid accumulate in the seed during ripening and forms complexes with Fe, Zn, Ca, Cu and Zn to reduce the solubility and absorption of these minerals (Hamid et al., 2017). It also binds with proteins to form complexes which decrease their solubility, limiting nutrient digestion, release and absorption (Shishir Kumar & Pandey, 2020; Singh et al., 2016). To overcome this problem phytase may be added to degrade phytic acid, reducing its ability to form complexes and, enhance micronutrient absorption (Ram et al., 2020). Ascorbic acid forms complexes with Fe^{3+} and reduce it to soluble Fe^{2+} which is more bioavailable (Shishir Kumar & Pandey, 2020). Tannins, a polyphenol is mostly found in legumes, berry fruits and cocoa beans, and reduce Fe bioavailability by forming tannin-Fe complexes which reduces the absorption of Fe (Ram et al., 2020; Samtiya et al., 2020; Singh et al., 2016). Lectins are common in legumes, cereals and fruits with adverse effect of damaging the cells of the gut epithelium to limit its efficiency in nutrient absorption (Ram et al., 2020; Samtiya et al., 2020). Saponins are commonly found in crops such as legumes, tea leaves and oats, and have the potential to form complexes with sterols which affect the absorption of fat-soluble vitamins such as VitA and VitE (Samtiya et al., 2020).

Oxalic acids form strong bonds with Ca, Mg, K and Na to form soluble or insoluble oxalate salts, which prevent the absorption of these nutrients for metabolic activities (Hamid et al., 2017; Thakur et al., 2019). Pre-processing and processing conditions such as soaking, germination, cooking, extrusion, milling, and chemical treatments have been used to reduce the antinutrient contents in foods (Hamid et al., 2017;

Hummel et al., 2020; Samtiya et al., 2020). Although these antinutrients negatively affect the absorption of essential nutrients, they have health-promoting properties which could be beneficial to the body (Praharaj et al., 2021). Phytate has been shown to have hypoglycaemic, anti-inflammatory and anti-carcinogenic properties (Praharaj et al., 2021; Singh et al., 2016). Polyphenols aid in removing free-radicals and limiting low density lipoproteins (Ram et al., 2020; Sharma et al., 2021). Lectins promote mitotic cell divisions and destruct cancer-affected cells (Thakur et al., 2019). Saponins have great antimicrobial, cancer-prevention and cholesterol-reducing properties which reduce the risk of cancer and heart diseases (Shishir Kumar & Pandey, 2020; Thakur et al., 2019). Therefore, a balance of these antinutrients/bioactive compounds may offer beneficial effects (Praharaj et al., 2021).

Three biofortification strategies for PBFs - agronomic intervention, conventional plant breeding and genetic engineering has been described (Jha & Warkentin, 2020). These three strategies have been applied to cereals, legumes, oilseeds, vegetables and fruits, with cereals having the largest number of biofortified crops. Due to the limited genetic variability in oilseeds, the transgenic approach is well-suited (Garg et al., 2018; Sheoran et al., 2022).

7 Strategies For Plant-based Foods Biofortification

7.1 Agronomic Biofortification

Agronomic biofortification involves the application of mineral fertilizers to soil or crops to increase the concentration and bioavailability of specific nutrients in the crops (Adu et al., 2018). Initially, agronomic practices were done to improve the health of crops and increase yield. However, the importance of nutrition has been highlighted over the years; hence agronomic practices have been expanded to improve the nutritional qualities of crops (de Valença et al., 2017; Malik & Maqbool, 2020; Wakeel et al., 2018). Changes in climate conditions and rapid depletion of soil nutrients is an indication of the need to improve and expand agronomic practices to include improving the nutritional qualities of crops (Siwela et al., 2020). Agronomic biofortification focuses on improving solubilization and mobilization of minerals (de Valença et al., 2017; Sheoran et al., 2022). The effectiveness of agronomic interventions depends on the soil composition, the solubility and mobility of minerals, the ability of crops to absorb minerals, and the accumulation of bioavailable minerals in non-toxic levels in the edible parts of the crops (Sheoran et al., 2022; Singh et al., 2016; Umar et al., 2019). Agronomic biofortification mainly covers minerals and not vitamins because vitamins are synthesized in the crops. Hence, agronomic biofortification cannot be used as a single strategy in eliminating micronutrient deficiencies and should complement other strategies for effective biofortification (Jha & Warkentin, 2020; Sheoran et al., 2022; Wakeel et al., 2018). The use of fertilizers for agronomic biofortification must be performed carefully as an improper application of fertilizer can have unanticipated, and sometimes severe, consequences for the environment and crops. By contrast, a balanced fertilization strategy is both economically more beneficial and environmentally more sustainable. Additionally, soil microorganisms play a crucial role in the soil ecosystem and are highly sensitive to fertilization. A deficient fertilization regime results in nutrient deficiency and subsequent modifications of the microbial community of the soil. Unbalanced fertilizations can have detrimental effects on soil biological health over the long-term (Shahzad Aslam et al., 2012; Sheoran et al., 2022).

Mineral fertilizers are mostly applied to the soil or leaf of crops where the former is more common and applicable and when nutrients are required in higher amounts. Foliar application is more economical and applicable when symptoms of nutrient deficiencies in crops are visible (de Valença et al., 2017; Singh et al., 2016), when mineral elements are not translocated and accumulated in adequate amounts in the edible parts of the crop (de Valença et al., 2017; Jha & Warkentin, 2020). Foliar application tends to be more effective than soil applications by increasing micronutrient contents rather than just promoting yield (de Valença et al., 2017; Melash et al., 2016; Singh et al., 2016), whilst the latter promote yield with minimal effects on improving nutritional quality. Foliar application is dependent on several factors including the type of fertilizer, characteristics of crops, time of application and environmental conditions (Alshaal & El-Ramady, 2017; Praharaj et al., 2021). Agronomic biofortification of crops with minerals such as Fe and Zn require certain adjustments. Due to their low mobility, adding metal chelators to the fertilizer is essential (Wakeel et al., 2018). Foliar application of $FeSO_4$ has proven effective for Fe biofortification (Dodake et al., 2022; Pal et al., 2021). For I_2, potassium iodate has been effective as seen as in countries like China (Krzepiłko et al., 2019; Mao et al., 2014; Wakeel et al., 2018). Inorganic fertilizers such as $ZnSO_4$, ZnO and Zn-oxy-sulphate are suitable for Zn agronomic biofortification. Just like Fe, foliar application of Zn chelators such as ZnEDTA is highly effective (Bruulsema et al., 2012; Cakmak & Kutman, 2018; Rehman et al., 2020). Se is agronomically fortified as selenate which is converted into organic selenomethionine in the crop. Both foliar and soil applications are suitable for Se biofortification, but dependent on soil type and timing of the application (Galić et al., 2021). However, foliar applications are costly and could easily be rinsed off by raining water (de Valença et al., 2017; Galić et al., 2021). The characteristics of the leaf play an important role in absorbing nutrients during foliar applications. Nutrients from foliar application penetrate the cuticle to leaf cells and are transported to other parts through the plasmodesmata. The age, structure and permeability of the leaf affect nutrients absorption (Alshaal & El-Ramady, 2017). Foliar application is mostly effective during the flowering and early milk phases than booting and elongation phases of the developmental stages of crops. The flowering and early milk stages are among the earliest phases where absorption of nutrients for fruit formation begins hence, foliar application of nutrients at this stage would contribute greatly to increasing the micronutrient contents of the fruits (Melash et al., 2016; Zaman et al., 2018). This was experienced during Zn agronomic biofortification of wheat using foliar application; and it was attributed to enhanced phloem mobility and active photo-assimilation allocation to reproductive silk organs that enhanced remobilization of nutrients (Melash et al., 2016; Praharaj et al., 2021; Zaman et al., 2018). Also, environmental conditions such as time of the day, humidity, temperature and wind speed affect the efficiency of foliar applications (Alshaal & El-Ramady, 2017). Warm and moist conditions in the early morning and late evening promote permeability of nutrients whilst low relative humidity and high temperature evaporate water from sprayed solution, leading to concentration of minerals on surfaces and intend reduces permeability (Alshaal & El-Ramady, 2017). Other strategies that are used for agronomic biofortification include coating and priming of seed with mineral fertilizers. These strategies aid in promoting crop yield and development but have minimal effects on the nutritional qualities of crops (de Valença et al., 2017; Sheoran et al., 2022).

Agronomic biofortification has been used effectively in several countries to combat micronutrient deficiencies and promote agricultural productivity. The effect of agronomic biofortification of selected underutilized vegetables in Ghana has been assessed (Adu et al., 2018). Increasing application rate of K fertilizer increased fruits and vegetables weight. Also, the application rate of K fertilizer and the type of K fertilizer synergistically affected K concentration in the fruit. The highest fruit K concentration was reported to be 2316 mgK/kg DW and this was a 140% increase with respect to the control (no K fertilizer application). In another study that assessed the influence of irrigation and fertilizer application on β-carotene yield and productivity of OFSP in South Africa (Laurie et al., 2012), the total storage root yield increased by 2–3 folds and β-carotene content increased from 133.7 μg/g to 151.0-153.1 μg/g when 50–100% fertilizer was applied, compared to no fertilizer application.

Agronomic biofortification is simple and yields results rapidly in the short term (Galić et al., 2021; Wakeel et al., 2018). However, mineral fertilizers used in agronomic biofortification is costly which increases the prices of biofortified crops making it inaccessible to poorer populations (Cakmak & Kutman, 2018). Also, agronomic biofortification is highly dependent on farmers. Application of mineral fertilizers is a regular activity hence may be omitted by farmers if they do not gain profits from the process (de Valença et al., 2017; Singh et al., 2016; Umar et al., 2019). Application of mineral fertilizers repeatedly may also cause accumulation, leading to toxicity (de Valença et al., 2017; Jha & Warkentin, 2020). In addition, increasing demand for mined minerals such as Se may cause exhaustion and negative impact on the environment (de Valença et al., 2017; Umar et al., 2019).

7.2 Plant Breeding

Plant breeding involves producing genetically different or new varieties of crops with improvements in essential micronutrients (Dhaliwal et al., 2022; Shahzad et al., 2021; Sheoran et al., 2022). Biofortification through plant breeding aims at improving the concentration and bioavailability of minerals in crops by utilizing the genetic differences between crops of similar species (Marques et al., 2021; Sheoran et al., 2022). Plant breeding initially focused on promoting yield and improving agronomic traits of crops however, recent plant breeding techniques have been geared towards promoting both the nutritional quality and agronomic traits of crops (Dhaliwal et al., 2022; Stangoulis & Knez, 2022). Plants breeding techniques should focus on introducing genotypes that would enhance the uptake, transport and redistribution of minerals to improve the efficacy of the biofortification (Lal et al., 2020). In order to achieve this goal, there is the need to enhance mineral mobility in the phloem vessels responsible for redistributing and remobilizing these minerals (Lal et al., 2020). The translocation and redistribution of Zn from the shoot to fruits or edible portions of crops has been a challenge due to the low mobility of Zn in phloem vessels, leading to lower Zn concentrations in the edible portions as compared to the leaves or root system (Buturi et al., 2021; Lal et al., 2020). Plants have been bred using three main techniques - conventional, molecular and mutation breeding techniques (Sheoran et al., 2022; Singh et al., 2016).

Conventional breeding is the most common and accepted form of plant breeding biofortification (Garg et al., 2018; Sheoran et al., 2022). Conventional breeding enhances improvement in the nutritional qualities of crops without compromising the other agronomic traits of the crop (Dhaliwal et al., 2022; Sheoran et al., 2022; Stangoulis & Knez, 2022). Biofortification through conventional breeding involves crossing crops with genotypic characteristics of high nutrient density and other agronomic traits to produce new varieties with desirable nutrient and agronomic traits (Garg et al., 2018). It requires identifying the biodiverse varieties of crops, assessing traits and amounts of target nutrients in these varieties, and determining the effects of growing conditions on the stability of these traits (Shelenga et al., 2021). Currently, about 299 varieties of biofortified cops via conventional breeding have been released in over 30 countries (Dhaliwal et al., 2022). A typical crop biofortified through conventional breeding is OFSP which has been biofortified with pro-VitA and with increased yield traits (Dhaliwal et al., 2022; A. Kumar et al., 2021; Marques et al., 2021). Quality Protein Maize (QPM) is also a product of conventional breeding (Sheoran et al., 2022; Singh et al., 2016). Other recent examples of conventionally-bred biofortified PBFs include biofortified wheat varieties, “Zincol” and “Akbar-2019” released in 2015 and 2019, with enhanced Fe and Zn contents, Fe-biofortified beans and, pro-VitA-biofortified cassava and maize (Marques et al., 2021; Shahzad et al., 2021; Van Der Straeten et al., 2020).

Mutation breeding differs from conventional breeding such that, differences in genetic traits among crops are created by introducing mutations through chemical treatments or physical methods such as irradiation (Sheoran et al., 2022; Singh et al., 2016). Mutation breeding has been recently adapted to biofortify resistant chickpea mutants like Pusa-408 (Ajay), Pusa-413 (Atul), Pusa-417 (Girnar), and Pusa-547, developed at I.A.R.I., India. Crop improvements *via* mutation in Pusa-547 include: thin testa, attractive bold seeds, better cooking quality and high yield performance (Zakir, 2018). Unlike conventional breeding, differences in genetic traits among crops are created by introducing mutations through chemical treatments or physical methods such as irradiation (Sheoran et al., 2022; Singh et al., 2016).

Biofortification through molecular breeding involves the identification of the location of a gene responsible for improving the nutritional quality of crops and attaching markers to that specific gene. With the aid of the marker, the desirable traits can then be bred into generations of the crop using conventional breeding (Jha & Warkentin, 2020; Sheoran et al., 2022). Molecular breeding can be used to determine if a desirable trait is present or absent in a specific crop during developmental stages. Hence, it is more rapid as compared to other forms of plant breeding (Sheoran et al., 2022; Singh et al., 2016). Molecular or marker-assisted breeding has been used to develop several varieties of maize with improved pro-VitA contents which can provide 25–50% of the estimated average requirements for VitA for women and children (Saltzman et al., 2013; Sheoran et al., 2022). These varieties have been released in countries such as Zambia, Nigeria and India. Also, it has been reported that several rice varieties have been bred to produce a variety with high Fe and Zn contents and improved agronomic traits (Garg et al., 2018).

Plant breeding is sustainable and less costly as compared to other biofortification strategies (Garg et al., 2018; Jha & Warkentin, 2020), and financial investments occur only at the research and development stages. Also, unlike agronomic biofortification, plant breeding has little to no impacts on the environment (Marques et al., 2021). Consumers generally accept crops that are biofortified through conventional plant breeding and easy to obtain regulatory approval as compared to genetically modified (GM) foods (Marques et al., 2021). Plant breeding may take a longer time to develop varieties with both desirable nutrient densities and agronomic traits (Carvalho & Vasconcelos, 2013; Marques et al., 2021). Also, there may be limited genetic variations among crops, making it impossible to biofortify these crops via plant breeding (Garg et al., 2018; Sushil Kumar et al., 2019; Shahzad et al., 2021) and may not be successful for all nutrients. For instance, breeding varieties of rice with improved VitA content initially proved to be challenging, but recent advances in omics technologies have provided the opportunity to practically biofortify varieties of rice with pro-VitA (Sushil Kumar et al., 2019). Also, crops such as banana that are propagated by vegetative means are not suitable for conventional plant breeding (Sushil Kumar et al., 2019).

7.3 Genetic Engineering/Transgenic Approach

Plant breeding relies heavily on the genetic variations among crops and this may prove to be a hindrance to biofortification through plant breeding when genetic variations are limited (Dhaliwal et al., 2022). Unlike plant breeding, genetic engineering is not limited to crops of related species. Genetic engineering has demonstrated to be a viable solution to this problem (Garg et al., 2018; Malik & Maqbool, 2020) and has been shown to effectively biofortify crops such as banana and rice, which cannot be subjected to conventional plant breeding (Dhaliwal et al., 2022; Kawakami & Bhullar, 2018; Sushil Kumar et al., 2019). Genetic engineering provides the platform for introducing nutrient or agronomic traits new to specific crop varieties by applying plant breeding and biotechnology principles (Melash et al., 2016; Mir et al., 2020) and when employed in biofortification, it identifies and characterizes suitable genes which could be introduced into crops to translate into desirable nutritional qualities (Garg et al., 2018). It utilizes genes from vast array of species, including bacteria, fungi and other organisms. Certain microorganisms enhance the uptake of nutrients by plants. Genes from these microorganisms can be genetically engineered into crops to enhance nutrient absorption, transportation, concentration and bioavailability (Mir et al., 2020; Singh et al., 2016). Fluorescent pseudomonas is a bacterium that enhances plant Fe uptake. Plants growth-promoting rhizobacteria and mycorrhizal fungi enhance the absorption of minerals from the soils and promote plants growth. Genes from bacteria and *Aspergillus* species have been used to adjust the lysine and phytate contents of crops such as rice and wheat, respectively (Sheoran et al., 2022; Singh et al., 2016).

Genome editing, also known as gene editing, corrects, introduces or deletes almost any DNA sequence in many different types of cells and organisms (Khalil, 2020). Gene editing provides an opportunity to develop GMOs without the use of transgenes; in addressing regulatory challenges associated with transgenic crops (K. Kumar et al., 2020; Mir et al., 2020). Methods such as Mega-nucleases, Zinc-finger nucleases (ZFNs), transcription activator-like effector nucleases (TALENs), and Clustered regularly interspaced short palindromic repeats (CRISPR/Cas9) have been exploited in genome editing to produce β-carotene biofortified rice and zinc-rich wheat varieties (Jaganathan et al., 2018; Malik & Maqbool, 2020). Except for the CRISPR/Cas9 technique, these genome editing methods are complex, expensive, and labor-intensive (Malik & Maqbool, 2020). Although CRISPR/Cas9 is flexible, cost-effective, and precise, it can sometimes lead to undesired mutations when untargeted regions in the genome are involved in the editing process (K. Kumar et al., 2020; Malik & Maqbool, 2020). These off-targets can be overcome by the dimeric nuclease method, which is highly precise and specific (K. Kumar et al., 2020). According to (Gatica-Arias et al., 2019), low levels of knowledge about gene editing occur because information generated in scientific studies has not been communicated effectively to consumers (Vasquez et al., 2022).

Biofortification through transgenic approach has been greatly explored in most developed countries. The most notable example is golden rice which was developed by biofortifying rice with pro-VitA (Jha & Warkentin, 2020). This was done by expressing genes encoding phytoene synthase and carotene desaturase which are responsible for β-carotene pathway (Siwela et al., 2020). In golden rice, the expression of these genes caused an increase in pro-VitA levels by 1.6 to 3.7 μg/g DW (Siwela et al., 2020). The overexpression of *Arabidopsis thaliana* vacuolar Fe transporter VIT1 in cassava caused three-seven fold increase in Fe contents in the storage roots (Narayanan et al., 2019). The overexpression of Zn transporters and expression of the gene responsible for phytase activity in barley enhances the levels and bioavailability of Zn (Sushil Kumar et al., 2019; Sheoran et al., 2022).

In order to improve the efficiency of the transgenic approach as a biofortification strategy, omics technology has been introduced (Nayak et al., 2021; Riaz et al., 2020). Omics technology explains the interrelationship between genes, proteins, transcripts, metabolites and nutrients (Carvalho & Vasconcelos, 2013; Nayak et al., 2021; Riaz et al., 2020). Specific genes control the uptake, transport, concentration, and bioavailability of nutrients by crops. Hence, genomics (omics technology of genes) is important since it presents the opportunity to study these specific genes and design suitable ways of improving and inducing them into crops (Ali & Borrill, 2020; A. Kumar et al., 2021). Transcriptomics (omics technology of transcripts) aids in conducting full-spectrum analysis to identify a specific expressed gene (Lai et al., 2012; Nayak et al., 2021; Roda et al., 2020). Proteomics (omics technology of proteins) helps to understand the role of proteins in nutrient synthesis, uptake and transport pathways (Carvalho & Vasconcelos, 2013; Riaz et al., 2020). Metabolomics (omics technology of metabolites) aids in assessing metabolic pathways that control the biosynthesis of natural metabolites (Hall et al., 2008; Ranilla, 2020), while ionomics considers how minerals present in crops undergo changes in response to genetic and environmental factors (Carvalho & Vasconcelos, 2013). These omics technologies have been used in studies involving biofortification of lysine, Ca, Zn and Fe, and VitC in PBFs such as maize, finger millet, wheat and tomatoes, respectively (Jain et al., 2019). PBFs such as cauliflower, cassava, and banana have been biofortified by both transgenic and breeding approaches while barley, soybean, lettuce, canola, carrot, and mustard have been biofortified with transgenic and agronomic approaches (Garg et al., 2018). The transgenic approach has been shown to be sustainable and rapid when introducing desired traits into crops (Mir et al., 2020; Singh et al., 2016). Table 2 summarizes a selection of biofortified crops developed by transgenesis.

Table 2
Some examples of biofortified crops produced by transgenesis

Crop	Gene/Protein	Target and Country	Status[1]	Reference
Soybean	Phytoene synthase c*rtB*	β-carotene	Released	(Mir et al., 2020; Pierce et al., 2015)
	FATB1-A and FAD2-1A	Reduced linoleic acid, Vistive Gold® (USA)		Monsanto (K. Kumar et al., 2020)
Maize	*Aspergillus niger phy*A2	Phytate degradation; BVLA4 3010 (China)	Released	Origin Agritech (Chen et al., 2008)
	Corynebacterium glutamicum cordapA	Lysine; Mavrea™ YieldGard (Japan and Mexico)		Monsanto Renessen LLC (K. Kumar et al., 2020)
		Lysine; Mavrea™ Maize (LY038) (Australia, Colombia, Canada, Japan, Mexico, New Zealand, Taiwan, USA)		
	Ferritin and lactoferrin	Iron	Research	(Drakakaki et al., 2005; Malik & Maqbool, 2020)
Rice	*C1* and *R-S* *PAL, F3'H, ANS, CHS* and *DFR*	Flavonoids	Research	(Ogo & Takaiwa, 2017; Shin et al., 2006)
	OsIRT1	Zinc		(Lee & An, 2009; Mir et al., 2020)
	Maize *psy*1, *Pantoea ananatis* bacterium *crtI*, and *E coli* strain K-12 *pmi*	Provitamin A rice line GR2E (Australia, New Zealand, Canada, USA)	Released	ISAAA Database 2019 (K. Kumar et al., 2020)
Cassava	Ferritin and *FEA1*	Iron	Released	Biocassava Plus (Sayre et al., 2011)
	Arabisopsis ZAT and ZIP	Zinc		
	Phytoene synthase c*rtB* and DXS	β-carotene		

[1]Status: Released means products are available in the marketplace; research means laboratory investigations are ongoing

Crop	Gene/Protein	Target and Country	Status[1]	Reference
	ASP1 and Zeolin	Protein		
Sweet potato	*Crtl, CrtB, CrtY, LCYe*	β-carotene (South Africa, Mozambique, Bangladesh and other African countries)	Released	(Malik & Maqbool, 2020; Mir et al., 2020; Tumuhimbise et al., 2013)
	IbMYB1	Antioxidants	Research	(Park et al., 2015)
Banana	Phytoene synthase PSY2a	β-carotene	Research	(Waltz, 2014)
Alfalfa	MtIFS1	Isoflavonoids	Research	(Deavours & Dixon, 2005)
Wheat	Ferritin *TaFer*	Iron	Released	(Borg et al., 2012; Mir et al., 2020)
	Silencing *SBEIIa*	Amylose	Research	(Sestili et al., 2010)
	PSY, *Crtl, CrtB*	Provitamin A, carotenoids		(Sumanth et al., 2022; Wang et al., 2014)
Potato	nptII	Amylopectin component of starch; AM 04-10200 (USA)	Released	ISAAA Database (Tilocca et al., 2014)
		Amflora ™ (EH 92-527-1 (European Union)		
Tomato	HMT, S3H and SAMT	Iodine	Research	(Halka et al., 2019; Malik & Maqbool, 2020)
	GDP-l-galactose phosphorylase	VitC		(Bulley et al., 2012; Malik & Maqbool, 2020)
Barley	AtZIP1	Iron, Zinc	Research	(Malik & Maqbool, 2020; Ramesh et al., 2004)

[1]Status: Released means products are available in the marketplace; research means laboratory investigations are ongoing

Biofortification through the transgenic approach has its limitations. The transgenic approach requires huge investments in financial, time and human resources at the research and developmental stages (Jha

& Warkentin, 2020; Singh et al., 2016; Wakeel et al., 2018). Transgenic crops are not generally accepted due to concerns over GMOs (Carvalho & Vasconcelos, 2013; Wakeel et al., 2018). Also, there are several regulations governing the production of transgenic crops (Shelenga et al., 2021). Interactions among genes introduced into crops during genetic engineering may reduce the efficacy of the biofortification process (Carvalho & Vasconcelos, 2013; Garg et al., 2018). Agronomic biofortification, plant breeding and genetic engineering, including omics technology, are suitable strategies that could be used for plant-based biofortification to help reduce the occurrence of malnutrition and hidden hunger.

8 Regulations, Consumer Acceptance, Opportunities And Future Prospects

The successful implementation of biofortification programs depends on the acceptance of biofortified crops by farmers and consumers (Mir et al., 2020). The acceptance of GM crops is different for customers and farmers. In general, consumers have expressed a lower level of acceptance of GM crops and foods, because they are skeptical about the risks and benefits associated with these products (Ashokkumar et al., 2020; Sendhil et al., 2022). Many factors influence consumer attitudes, including information, trust, beliefs, perceptions of benefits and risks. Several concerns have been raised about the human health implications from gene flow and transfer, environmental impacts from possible development of resistant weeds and crops, impacts on conventional methods, artificial-like methods, toxicity, and allergenicity of GM crops (K. Kumar et al., 2020; Sumanth et al., 2022). It is because of this that genetically engineered plants and their products are often rejected based on unclear grounds. The overall inclination toward avoidance have been directed toward GM crops, even though several scientific reports have shown that GM crops are safe to consume (Sendhil et al., 2022; Sumanth et al., 2022). Therefore, it may be necessary to create adequate informational programs which would highlight the importance of biofortified-genetically engineered plants and quell misconceptions about GM crops (Mir et al., 2020). In many parts of the world where biotech seeds are available, farmers are highly embracing and accepting biotech seeds because of the benefits they receive from GM crops (Lucht, 2015).

Globally, GM crops are governed by different regulations (Lobato-Gómez et al., 2021). These regulations and legislations have huge effects on the commercialization and adoption of GM crops (Gu et al., 2021). Strict labeling rules of GM crops have been set by over 40 countries (Sumanth et al., 2022). The European Union introduced a very strict authorization system for GM crops and foods over a decade ago, as a precaution. All food derived from GM plants were required to be labeled based upon the process, even if no traces of the genetic modification could be detected in the purified end-product. Accordingly, recent trends in many European countries have created an environment that makes the cultivation of GM crops and foods extremely difficult. The US legislation is more lenient in that novel GM foods do not have to be labeled if they do not differ in composition from established non-GM foods. As with Europe, China has been requiring the labeling of foods derived from GM crops for more than a decade (Hartung & Schiemann, 2014; Lucht, 2015). It was estimated that it can take about 13 years to develop and commercialize GM crops, and the average cost of acquiring authorization for commercialization of GM crops was about $35 million USD (K. Kumar et al., 2020). Also, most agri-business companies patent newly developed GM crops, monopolizing the commercialization of the GM crops. Several debates have been raised about the motive for developing GM crops - for privatization and profit-making or for the purpose of promoting food security (Sumanth et al., 2022)? Therefore, regulations and legislations governing GM crops should be adjusted, especially in developing countries, to be rigorous and cost and time-effective to promote the adoption of GM crops (K. Kumar et al., 2020; Sumanth et al., 2022).

In many countries, researchers and seed companies are predicting that new breeding techniques such as intragenesis and cisgenesis, which transfer only genetic information from the same species without transferring foreign genes, could provide smoother routes to market for plants with improved traits, thereby avoiding the roadblocks presented by transgenic GMOs (Hartung & Schiemann, 2014; K. Kumar et al., 2020). These newly developed breeding techniques do not fit within the traditional definition of GMOs, and a debate is taking place in many areas regarding how they should be regulated. In view of this regulatory uncertainty, it is possible for GM products to be distributed differently in the market and for customer acceptance to differ globally (Sendhil et al., 2022). What does the future hold for GM crops? Can there be a universal labeling system for GM crops? Should there be a change in regulations governing Intellectual property rights of GM crops? The adaptation of GM crops in the production of biodegradable polymers has been discussed. Does that indicate GM crops have strong positive environmental impacts in the future (K. Kumar et al., 2020; Sumanth et al., 2022)? The possibility of using transgenic crops as means of providing vaccines and medications can be exploited in the future (Sumanth et al., 2022). Can GM crops be adapted to have other desirable traits aside agronomic and nutritional traits? These questions could be the focal points of future research in promoting the development and commercialization of GM crops.

9 Conclusion

Malnutrition and hidden hunger are both present in developed and developing countries and have devastating effects globally. The recent implications of the global pandemic have shown that food systems need to be adapted to advance global changes that can limit deficiencies in our food supply. Furthermore, climate change projections predict higher inequality and poverty for developing countries and hence, the need to augment the nutritional content in PBFs. Biofortification is the most sustainable and cost-effective method for alleviating malnutrition. Biofortification of PBFs has been used to produce crops with adequate nutrient density and bioavailability and help to combat hidden hunger. Through plant breeding, transgenics, and mineral fertilizer applications, biofortification micronutrient malnutrition can potentially be tackled. It is important to add that to successfully combat hidden hunger through biofortification, even after the development of biofortified varieties, it will be essential to address various socio-political and economic challenges to promote their cultivation and finally their consumption by customers. For future actions, an integrated approach is required, where politicians, farmers, food product developers, genetic engineers, dietitians, and educators need to be included in the developing efforts. One of the biggest challenges of biofortification aside from the methods to strengthen the nutritional value of crops is the public acceptance. Especially for the transgenic techniques more education and marketing should be invested for the success of biofortified products in the market as only few cultivars are finally released for costumers. Globally, the specificity of biofortification techniques should tackle regional nutritional challenges and should be chose based on the likelihood of acceptance of cultural difference in consumers. Overall, biofortification represents a promising group of techniques that can improve the global nutritional wellbeing and lead us closer to minimize hunger and malnutrition.

Declarations

Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Author Contributions: ANAA conceptualized the manuscript, crafted the outline and led the manuscript writing. KFO and SA wrote the initial draft. SA prepared illustrations. ANAA and ME reviewed and edited the manuscript. ANAA formatted the final version of the manuscript. All authors approved the submitted version of the manuscript.

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Figures

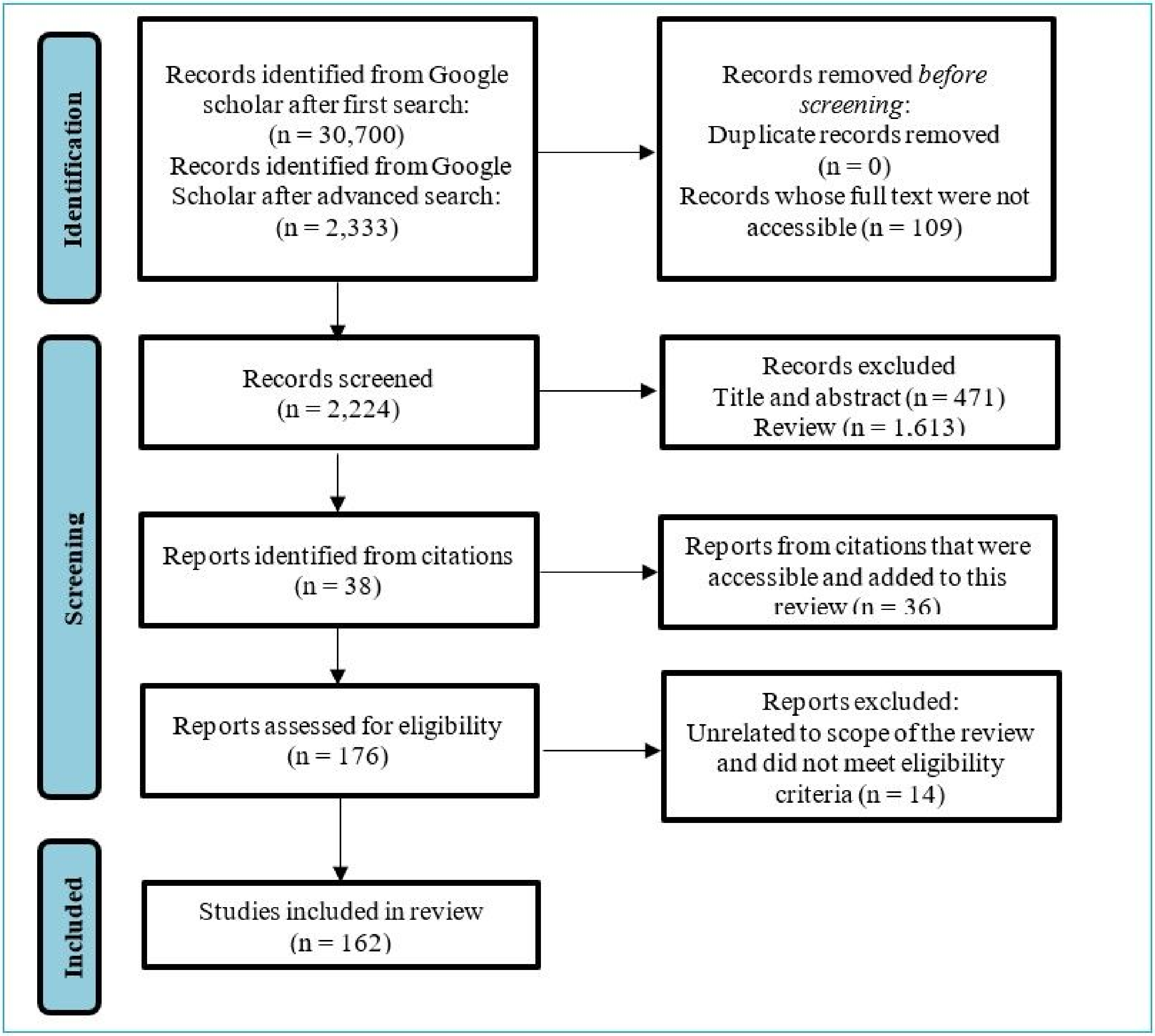

Figure 1

Flow diagram of information search for the systematic review (PRISMA, 2020)

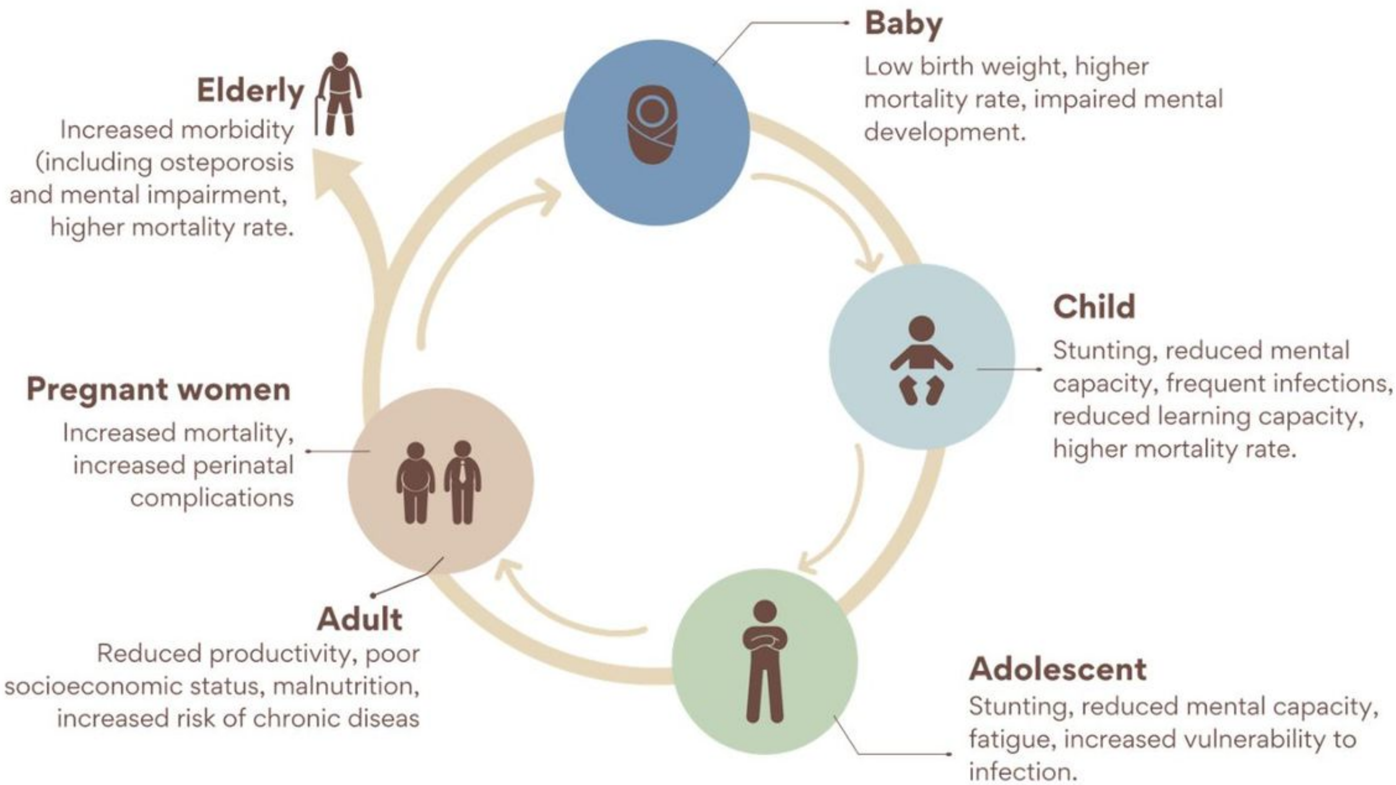

Figure 2

Consequences of micronutrient deficiency through the life cycle (Modified from (ACC/SCN, 2000))

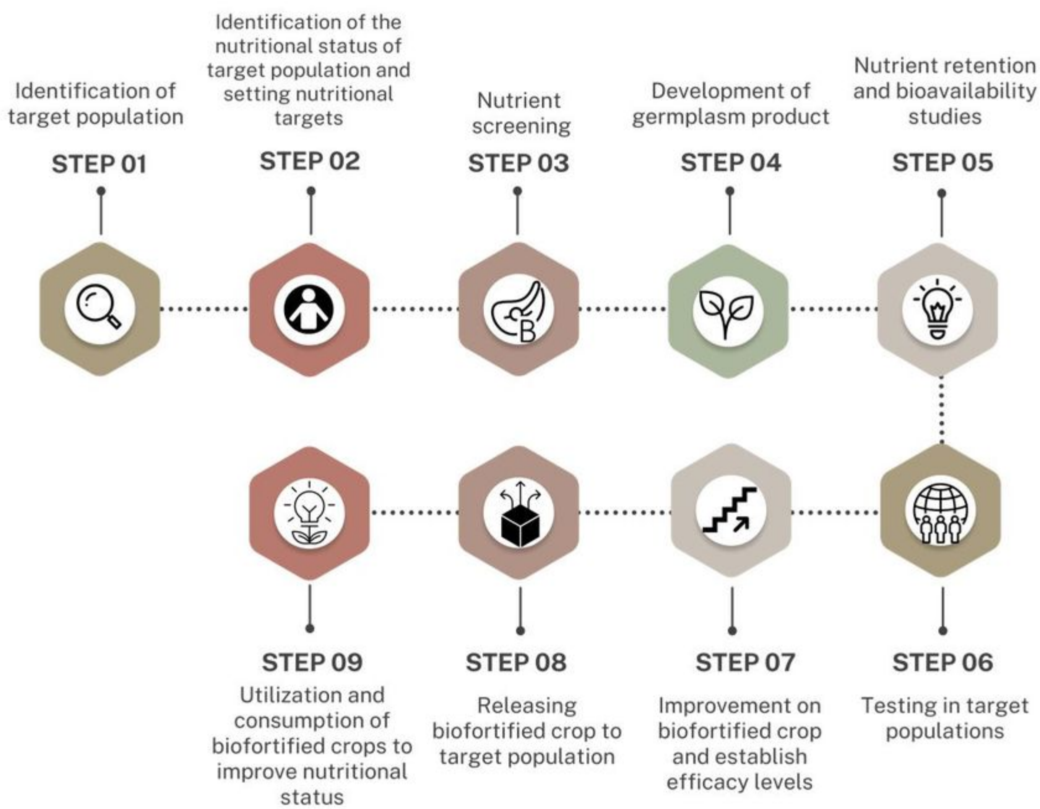

Figure 3

Harvest plus impact pathway - Plant-based biofortification steps (Modified from (Pfeiffer & McClafferty, 2007))