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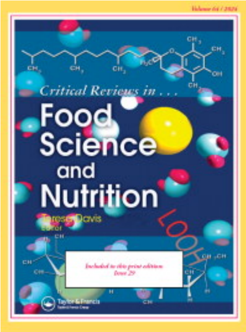

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REVIEW

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Biofortification as a food-based strategy to improve nutrition in high-income countries: a scoping review

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ABSTRACT

Biofortification (increasing the micronutrient content of food before harvest) has been successfully used to nutritionally improve staple foods in low- and middle-income countries. This approach could also help address micronutrient shortfalls in at-risk populations in high-income countries (HICs), however, the potential of biofortification interventions in this context is not well understood. The aim of this scoping review is to assess the nature and extent of available research evidence on biofortified foods in relation to human consumption in HICs. Literature searches were conducted in MEDLINE, WoS, ProQuest, CINAHL, AGRIS and Epistemonikos. Forty-six peer-reviewed articles were included. Most research was conducted in the USA ($n=15$) and Italy ($n=11$), on cereal crops ($n=14$) and vegetables ($n=11$), and on selenium ($n=12$) and provitamin A ($n=11$). Seven research domains were identified in the literature: *bioavailability* ($n=17$); *nutrient stability* ($n=11$); *opinions and attitudes* ($n=9$); *functionality* ($n=9$); *sensory properties* ($n=2$); *safety* ($n=1$); and *modeling* ($n=1$). Evidence from HICs in each domain is limited. There is a need for more research particularly in areas sensitive to the cultural and socio-economic context.

KEYWORDS
public health; nutrition; micronutrient deficiencies; food-based solutions

Introduction

Hidden hunger: a global challenge

Despite ongoing global efforts to end hunger (United Nations 2015), micronutrient malnutrition, or hidden hunger, is estimated to affect more than two billion people globally (Bailey et al. 2015, Lowe 2021; FAO et al. 2022). Micronutrient deficiencies and suboptimal status can arise from both under- and overnutrition and are associated with several noncommunicable diseases. For example, zinc deficiency is implicated in the pathophysiology of type II diabetes (Pompano and Boy 2020). Hidden hunger can lead to a range of debilitating conditions and increased likelihood of mortality and contribute to high healthcare costs and loss of human capital, placing a heavy burden on both affected individuals and society at large. The global economic burden of malnutrition, including both undernutrition and overnutrition, is estimated at $3.5 trillion per year, with micronutrient deficiencies playing a significant role in this (Nugent et al. 2020). The global cost of deficiency of vitamin A, iron, and iodine is estimated to be more than $60 billion annually in lost productivity and healthcare expenses (UNICEF et al. 2019). Thus, eliminating micronutrient malnutrition is a key part of achieving food security, and is a major global challenge. While women and young children in rural communities in low- and middle-income countries (LMICs), where there is a high degree of reliance on low-cost staples and the diversity of diets is limited, are the most vulnerable to hidden hunger, low micronutrient intakes and deficiencies also affect many people in high-income countries (HICs) (Ritchie and Roser 2017; Tulchinsky 2017; Von Grebmer et al. 2017; Lowe 2021; FAO et al. 2022). For example, in the UK, average intakes of several micronutrients, including iron, iodine, zinc, folate and vitamin D, are below the Reference Nutrient Intakes (RNIs) among certain socio-demographic groups, especially women, adolescents, and people on low incomes, in some cases correlating with critically low blood levels of these nutrients (Page et al. 2018). Suboptimal micronutrient intakes are similarly prevalent in other parts of the Global North, including the U.S. (Marriott et al. 2010; Reider et al. 2020), Europe (Mensink et al. 2013) and Australia (Australian Institute of Health Welfare 2018). This can largely be attributed to an increasing reliance on cheap, energy-dense but nutrient-poor highly processed foods across many HICs, particularly in low-income populations (Baker et al. 2020; Srour et al. 2022). The ongoing cost of living crisis is further contributing to existing issues of limited access to a nutritionally

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balanced diet, which is already estimated to cost 50% of the disposable income of the most deprived fifth of the UK population (The Food Foundation 2023). This means that some main sources of key micronutrients, such as green leafy vegetables for folate, and red meat and shellfish for iron and zinc (NHS 2020), are not accessible in adequate quantities for many people. Also underlying these issues is the continued primary focus of agriculture on yields with insufficient consideration of nutritional quality, and the often low and decreasing amounts of bioavailable mineral nutrients in soils. The adoption of intensive agricultural practices has led to declines in the micronutrient content of some major staples and horticultural crops in multiple countries (Yang et al. 2003; Davis, Epp, and Riordan 2004; White and Broadley 2005; Velu et al. 2014; Schiavon et al. 2020; Mayer, Trenchard, and Rayns 2022; Stangoulis and Knez 2022). Moreover, climate change is expected to negatively impact the micronutrient density of some important crops, posing a further threat to future nutrition security (Soares et al. 2019; Leisner 2020; Kumari et al. 2022; Semba et al. 2022).

Biofortification: a food-based strategy to fight hidden hunger

One increasingly popular strategy aimed at combating micronutrient deficiencies is food biofortification (Bouis et al. 2011). Biofortification can be described as the process of improving the intrinsic nutritional value of food so that it has a higher bioavailable micronutrient content than its standard equivalent, prior to harvest (as opposed to conventional fortification, which involves the addition of vitamins or minerals post-harvest and during food processing (Lowe 2021)). Biofortification can improve the nutritional value of crops through increased mineral uptake from the soil, enhanced synthesis of secondary metabolites, or altered transport or metabolism of micronutrients, or other substances that affect micronutrient bioavailability. Biofortification has the combined advantage of being a low-agency approach that addresses the root cause of deficiencies that can be cost-effective and sustainable in the long term, and thus represents a promising alternative to other strategies aimed at improving nutrition at the population level, such as the use of supplements, industrial food fortification, or nutritional education campaigns (Bouis and Saltzman 2017; Jha and Warkentin 2020; Van Der Straeten et al. 2020).

Crops can be biofortified using various methods, which can be broadly classified as genetic or agronomic approaches (Garg et al. 2018; Connorton and Balk 2019; Jha and Warkentin 2020; Van Der Straeten et al. 2020). Genetic biofortification can be achieved through selective breeding, which is the most widely used approach to biofortification, or through genetic engineering. Both genetic engineering and conventional breeding produces organisms with improved traits by changing their genetic makeup. However, while genetic engineering achieves this by adding a new gene (or genes) to the genome of a plant (or animal), conventional breeding achieves it by crossing together plants (or animals) with relevant traits and selecting the offspring with the desired characteristics resulting from particular combinations of genes inherited from both parents. Using biotechnology could help overcome some of the limitations of conventional breeding, e.g., enabling the uptake of higher levels of micronutrients, multiple micronutrients or novel micronutrients not naturally found in particular edible plant species, but such approaches are facing major barriers in terms of regulation and public acceptance. For example, the genetically engineered provitamin A enriched Golden Rice developed over 20 years ago is yet to gain regulatory approval (De Steur, Stein, and Demont 2022). Currently no biofortified crops or animals produced via traditional genetic engineering are available on the market anywhere in the world. However, certain new genetic technologies are becoming increasingly accepted, with precision gene edited GABA enriched tomatoes and high-oleic soybeans already commercialized in Japan and the United States, respectively (Voigt 2020; Waltz 2022). The other main approach, agronomic biofortification, can involve the use of micronutrient-rich fertilizers, nutrient solutions, or beneficial microorganisms. In addition, foods of animal origin (including dairy products, eggs, fish and meat) can be biofortified through supplementing the diets of animals with micronutrients (Barbosa et al. 2022; Neill et al. 2023b), and in the case of vitamin D in mushrooms and animal products, using UVB irradiation (Pinto et al. 2020; Neill et al. 2023a). There is also increasing attention on the potential role of regenerative agriculture in the nutritional improvement of foods (Manzeke-Kangara et al. 2023). As there is a lack of general consensus regarding the exact definition of biofortification, for the purposes of this review we define a biofortified food as any item intended for human consumption that had been intentionally developed, using any method, to have a higher bioavailable amount of one or more micronutrients (including vitamins, minerals and other health-promoting bioactive compounds) than its standard equivalent pre-harvest, as well as products made from biofortified ingredients.

Biofortified foods in the Global North

A large number of biofortified crops have already been developed, tested and distributed in several countries, with the nonprofit organization HarvestPlus leading international efforts, focusing on enriching staple crops that form the basis of many people's diets in LMICs with iron, zinc or provitamin A, which are among the micronutrients deemed to be of most concern globally (Bouis and Welch 2010, www.harvestplus.org). As of 2020, 393 biofortified crop varieties developed by HarvestPlus using targeted breeding (the most widely used approach to biofortification to date) had been released or were in testing in 63 countries, potentially benefitting over 48 million people (Virk et al. 2021). This number only captures those involved in the HarvestPlus and CGIAR programs and increases on a weekly basis.

There is mounting evidence that biofortification can be an impactful strategy for fighting hidden hunger in farming communities in LMICs due to the poor dietary diversity and over-reliance on staple foods that typically characterize these populations (Bouis and Saltzman 2017). However, so far relatively little research attention has been paid to the potential of biofortification interventions to improve nutrition-related public health in HICs, where biofortified foods are not so widely introduced, and, to the best of the authors' knowledge, no work exists that comprehensively reviews current knowledge in this area. There may be differences between countries in the prevalence of micronutrient deficiencies in different socio-demographic groups, typical diets, environmental factors affecting agriculture, and the wider socio-political and regulatory contexts in which food systems operate. Thus, to be successful, new biofortification interventions must be devised based on an understanding of the local context. In addition, due to the generally greater dietary diversity, in HICs a wider food basket approach would likely be required with multiple commonly consumed foods targeted. Therefore, in this review, we sought to understand the extent of the available evidence focusing on biofortified foods in relation to human consumption in HICs, to identify key knowledge gaps to inform future biofortification-related research and policy. The specific objectives of the review were: (1) to determine the extent, range and nature of existing research on biofortified foods in relation to human consumption in HICs, and (2) to summarize current knowledge on different aspects of biofortification in this context.

Materials and methods

Approach

Given the broad objectives of this review, which were to identify, quantify and map the types of available evidence, and to identify gaps in existing research, a scoping review was conducted. The framework developed by Arksey and O'Malley and refined by Colquhoun et al. (Arksey and O'Malley 2005; Colquhoun et al. 2014) and further detailed in the Joanna Briggs Institute Reviewers Manual: Scoping Reviews (Peters et al. 2015) were used as a guide. The review was reported following the PRISMA scoping reviews (PRISMA-ScR) checklist (Tricco et al. 2018). The review was pre-registered on the Open Science Framework (Gulyas, Caton, and Mogeni 2024).

Databases and search strategy

A detailed search strategy was developed by the research team and an information specialist to capture relevant published studies (see Supplementary Table S1 for the query strings used). Search terms were developed based on titles and abstracts of key studies in preliminary searches, identifying synonyms related to biofortification and including countries within the Global North (as defined below). We developed our primary query in MEDLINE, then adapted this to other databases based on available search fields and operators. No limit on publication date was applied to maximize the amount of literature captured. Using the defined search terms, searches were conducted on 18th July 2023, in six databases: MEDLINE (Ovid), Web of Science Core Collection (Clarivate), ProQuest (Clarivate), CINAHL, AGRIS and Epistemonikos. The reference lists of included papers were also screened manually for relevant studies not identified in the primary searches.

Eligibility criteria

Primary quantitative and qualitative, published, English full-text only, studies focusing on biofortified foods with relevance to human consumption were included in the review. Relevance to human consumption was defined as studies focusing on the assessment of micronutrient bioavailability, bioefficacy or functionality (*in vitro* or *in vivo*), effects of storage or processing on micronutrient content or bioavailability, consumption safety, consumer understanding and attitudes, sensory evaluations and dietary and/or economic modeling. Studies focusing on the development of biofortified foods were not included and considered beyond the scope of this review. Only studies focusing on high-income developed countries were included, which were identified using a two-stage approach. First, we used the United Nations' Human Development Index (HDI) to identify all countries with very high human development (HDI ≥ 0.80), based on 2021 HDI data (United Nations Development Programme 2023; Global North countries 2023) to identify potentially relevant studies. Secondly, during the screening process we then removed any studies that did not meet the high-income country criteria, according to the Organization for Economic Co-operation and Development (OECD 2022), to ensure that the socio-economic context was sufficiently similar among studies.

Selection of studies

The full screening process is shown in the PRISMA flow diagram (Figure 1). Studies identified in the literature search were screened for relevance, guided by the inclusion/exclusion criteria. Titles, abstracts and full papers were initially screened by one researcher (BZG). Papers were included if they met all of the inclusion criteria and none of the exclusion criteria. Full-text review was conducted independently by two researchers (BZG and SJC). Disagreement was resolved by discussion where necessary.

Data extraction and synthesis

The first reviewer (BZG) developed and piloted a data extraction table. Data were extracted under the following headings: author(s); year of publication; study location or geographic focus; type of biofortified food(s); target micronutrient(s); method(s) of biofortification; study type (e.g., human feeding trial, questionnaire survey, modeling study); study population and sample size (where applicable); main findings. A second reviewer (BM) completed data extraction for 10% of the papers and no disagreements were noted. A narrative review of the data was synthesized under seven research domains, which were defined after identifying relevant literature and agreed upon by the research team: 1. *bioavailability:* including bioaccessibility, bioavailability, nutritional equivalency or bioefficacy (i.e., availability of a

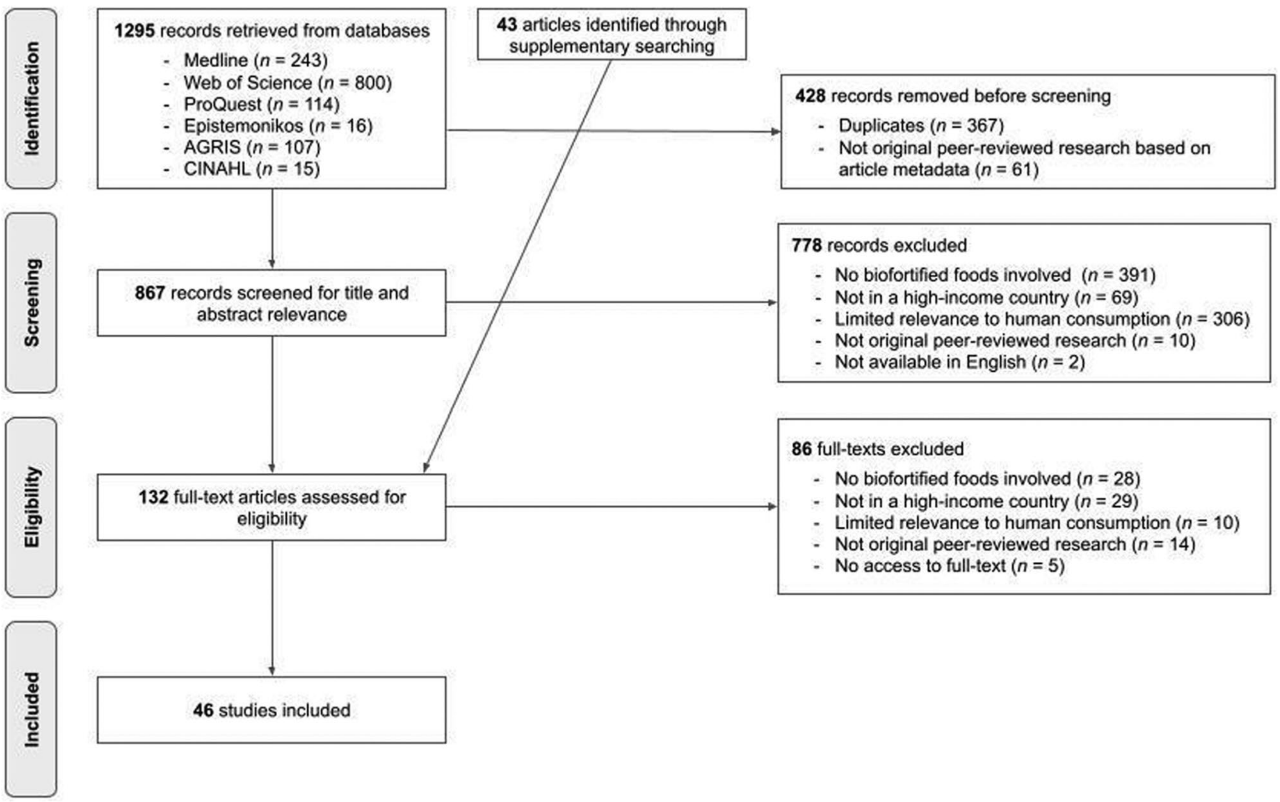

Figure 1. PRISMA flow diagram of the literature search and screening process showing the number of studies included and excluded at each stage.

nutrient × its bioconversion to the active form) of target micronutrients in biofortified foods, using *in vitro* or *in vivo* (humans or animal models) methods; 2. *functionality:* assessments of nutrition-related health outcomes, including biomarkers of disease risk and indicators of health status, upon consumption of biofortified foods, using *in vitro* or *in vivo* (humans or animal models) methods; 3. *nutrient stability:* retention of target micronutrients in biofortified foods upon processing, cooking or storage; 4. *opinions and attitudes:* studies of consumers' attitudes toward, understanding or acceptance of, willingness to buy, or willingness to pay for biofortified foods; 5. *sensory properties:* evaluations of sensory attributes, including taste, smell, and texture, of biofortified foods; 6. *safety:* tests of safety for human consumption of newly developed biofortified products; and 7. *modeling*: assessments of the potential impact of biofortification interventions on population micronutrient intakes or nutrition-related health status, using mathematical tools. Since the aim of this review was to quantify and map existing literature, quality assessment was not undertaken (Colquhoun et al. 2014).

Results

The primary database searches yielded 867 studies, after the removal of duplicates ($n = 367$) and results of the wrong type (e.g., conference abstracts or data only) based on article metadata ($n = 61$) (Figure 1). Of these, 89 studies passed the title and abstract screening and were evaluated against the eligibility criteria at the full-text level, which resulted in the inclusion of 31 articles. A manual search of the reference lists of these 31 studies identified a further 43 articles to be screened, of which 15 passed full-text screening, resulting in a total of 46 studies included in the review. The number of items excluded for different reasons at each stage are shown in the PRISMA diagram (Figure 1).

Study characteristics

The key characteristics of articles included in this scoping review ($N = 46$) are presented in Table 1. Studies were published between 1994 and 2023 (Supplementary Figure S1), in 27 academic journals with focal topics mainly around nutrition, agriculture and food science (see Supplementary Figure S2). Articles came from 13 different high-income countries, predominantly in Europe ($n = 26$) and North America ($n = 16$), with a smaller number of studies from Australia ($n = 3$) and Asia ($n = 1$). By country, the largest amount of research conducted was in the USA ($n = 15$), Italy ($n = 11$) and Germany ($n = 5$), followed by Australia ($n = 3$), the UK ($n = 3$), Spain ($n = 2$), and Poland, Denmark, Canada, Romania, Finland, Saudi Arabia and Norway ($n = 1$ each) (Table 1). The majority of studies ($n = 36$) involved actual biofortified foods, while a smaller number ($n = 10$) had these as the subject of a theoretical investigation. Research looked at over 20 different foods, which can be grouped into seven food types: cereal grains ($n = 17$; wheat, maize, rye, rice), non-leguminous vegetables ($n = 13$; lettuce, tomatoes, cabbage, carrots, broccoli, tatsoi, mizuna, purslane, Swiss chard, chicory), fruits ($n = 4$; apples, pears), legumes ($n = 2$; beans), starchy tubers ($n = 4$; potatoes, cassava), animal products ($n = 7$; eggs, milk, pork, lamb), and other ($n = 3$; baker's yeast,

Table 1. Characteristics of studies ($N = 46$) included in the scoping review, ordered by research domain.

Author(s) & year	Country	Food a	**Nutrienta**	**Biofortification methoda**	Study design	Participants	**Research domainb**
Campion et al. (2013)	Italy	beans	Fe (low phytic acid lectin free)	breeding	*in vitro* (Caco-2 cell system) bioavailability assessment in bean lines with different seed color	n/a	BA
D'Imperio et al. (2016)	Italy	tatsoi, mizuna, purslane, basil, Swiss chard, chicory	Si	fertilization	*in vitro* (chemical digestion) bioaccessibility assessment	n/a	BA
Davis et al. (2008)	USA	maize	PVA	breeding	animal (Mongolian gerbil) feeding trial evaluating the vitamin A value of β-cryptoxanthin and β-carotene biofortified maize varieties compared to equivalent vitamin A and β-carotene supplements	n/a	BA
Howe, Maziya-Dixon, and Tanumihardjo (2009)	USA	cassava	PVA	breeding	animal (Mongolian gerbil) feeding trial assessing bioefficacy of PVA in biofortified cassava varieties vs β-carotene or vit A supplementation	n/a	BA
Itkonen et al. (2016)	Finland	"BreaD" made with biofortified yeast	Vit D	UV-B irradiation	randomized-controlled feeding trial comparing efficacy of consuming bread made with vit D2 biofortified yeast with vit D2 or D3 supplements	healthy women 20–37 y ($N = 33$)	BA
Jou et al. (2012)	USA	rice	Zn	breeding	*in vitro* (Caco-2 cell system) and animal (rat) feeding trial	n/a	BA
Kirby, Lyons, and Karkkainen (2008)	Australia	wheat (as wafer biscuits)	Se	fertilization	6-month human feeding trial assessing Se bioavailability in biofortified vs fortified biscuits	men 40–70 y ($N = 75$)	BA
La Frano et al. (2013)	USA	cassava	PVA	breeding	randomized cross-over feeding trial assessing nutritional efficacy of β-carotene biofortified cassava porridge, with or without added (peanut or rapeseed) oil	healthy women 21–44 y ($N = 10$)	BA
Li et al. (2010)	USA	maize	PVA	breeding	human feeding trial assessing vitamin A equivalency of β-carotene biofortified maize porridge and white maize porridge with added β-carotene or with added retinyl palmitate	healthy women 18–30 y ($N = 6$)	BA
Schmaelzle et al. (2014)	USA	maize and carrots	PVA	breeding	animal (Mongolian gerbil) feeding trial measuring carotenoid vit A equivalency in biofortified maize; and β-carotene bioefficacy in freeze-dried biofortified carrots added to staple-based feeds (potato, rice, banana, maize) vs standard diets and *in vitro* bioaccessibility	n/a	BA
Tako, Blair, and Glahn (2011)	USA	beans, common	Fe	breeding	*in vitro* (Caco-2 cell system) and *in vivo* (chicken) comparison of standard vs Fe rich beans to deliver Fe for hemoglobin synthesis and improve Fe status	n/a	BA
Tang et al. (2009)	USA	rice	PVA	GM, transgenic	36-day human feeding trial assessing vitamin A equivalency of β-carotene biofortified rice	healthy adults ($N = 5$; 3 females, 2 males)	BA

(*Continued*)

Table 1. Continued.

Author(s) & year	Country	Food a	**Nutrienta**	**Biofortification methoda**	Study design	Participants	**Research domainb**
Zhu et al. (2015)	USA	cassava	PVA	breeding	randomized cross-over feeding trial (3 treatments separated by 2-week washout) comparing effectiveness of β-carotene biofortified vs red palm oil fortified gari in improving vit A status	healthy women (*N* = 8)	BA
Baldassano et al. (2022)	Italy	lettuce	Mo	fertilization	12-day placebo-controlled feeding trial assessing effects of Mo-enriched lettuce on Fe and lipid metabolism, blood parameters, and liver function	healthy adults (*N* = 24; 12 males, 12 females)	BA, FU
Bryszewska et al. (2007)	Poland	rye (dry seedling powder in bread)	Se	fertilization; germination in Se rich environment	4-week human feeding trial assessing nutritional efficacy of daily consumption of Se-enriched bread vs non-enriched bread	females 24–25 y (*N* = 24)	BA, FU
D'Imperio et al. (2017)	Italy	tatsoi, mizuna, purslane, Swiss chard, chicory	Si	fertilization	*in vitro* bioavailability (chemical digestion and Caco-2 cell system); *in vitro* (human osteoblast cells) effect on bone mineralization, comparison to Si supplement	n/a	BA, FU
Hohman et al. (2011)	USA	bread made with vitamin D2-rich yeast	Vit D	UV-B irradiation	animal (rat) feeding trial assessing vit D2 bioavailability in bread made with biofortified yeast & its effect on bone properties, vs vit D3 supplements	n/a	BA, FU
Oancea et al. (2015)	Romania	cabbage	Se	fertilization + biostimulants	*in vitro* (Caco-2 human carcinoma cells) assessment of antitumoral activity of Se biofortified cabbage	n/a	FU
Ravn-Haren et al. (2008)	Denmark	yeast and cow's milk	Se	(fermentation in Se rich environment / animal feed with Se-yeast)	randomized cross-over human feeding trial (4 × 1 week) measuring acute effects of dietary supplementation with high doses of different forms of Se (organic from biofortified yeast or milk; inorganic selenate) on oxidative defense and risk factors for cardiovascular disease	healthy men 18–40 y (*N* = 20)	FU
Vasto et al. (2022)	Italy	lettuce	Mo	fertilization	12-day randomized control feeding trial assessing effects of consuming Mo biofortified lettuce on glucose homeostasis	healthy adults (*N* = 24; 12 males, 12 females)	FU
Vasto et al. (2023)	Italy	lettuce	Mo	fertilization	12-day randomized control feeding trial assessing effects of consuming Mo biofortified lettuce on bone remodeling and metabolism, vs Mo supplements	adults 23–54 y (*n* = 42; 25 males, 17 females) and 55–73 y (*n* = 42; 24 males, 18 females), (*N* = 84)	FU
Wu et al. (2009)	Australia	wheat	Se	fertilization	24-week placebo-controlled feeding trial measuring markers of cancer and cardiovascular disease risk, oxidative stress, and immune function upon consuming Se enriched wheat biscuits	healthy older men with lower Se status (*N* = 62)	FU

(*Continued*)

Table 1. Continued.

Author(s) & year	Country	Food a	**Nutrienta**	**Biofortification methoda**	Study design	Participants	**Research domainb**
Budke et al. (2021)	Germany	apples and pears	I	fertilization	nutrient retention upon washing and cold storage of I enriched fruits	n/a	NS
Burt et al. (2010)	Canada	maize	PVA	breeding	nutrient retention in three drying and storage regimes (freeze-dried & −80 °C storage; room temp. drying & storage; 90 °C drying & room temp. storage) in carotenoid biofortified maize kernels	n/a	NS
Cerretani et al. (2014)	Italy	potatoes	I	fertilization	nutrient retention upon cooking (dumplings, vegetable pie, focaccia) of I biofortified potatoes	n/a	NS
Comandini et al. (2013)	Italy	potatoes, carrots and tomatoes	I	fertilization	I retention in biofortified potatoes and carrots during boiling or baking, and in tomatoes upon pasteurization (whole or homogenized); in non-biofortified potatoes and carrots boiled or baked with iodized salt	n/a	NS
Hart et al. (2011)	UK	wheat, bread	Se	fertilization	nutrient retention and speciation in flour and bread made from Se biofortified wheat	n/a	NS
Ortiz, Rocheford, and Ferruzzi (2016)	USA	maize	PVA	breeding	nutrient retention in carotenoid biofortified maize kernels upon drying and controlled condition storage for 12 months	n/a	NS
Poblaciones, Rodrigo, et al. (2014)	Spain	wheat, durum	Se	fertilization	nutrient retention during milling, pasta making and cooking of Se biofortified durum wheat	n/a	NS
Poblaciones, Rodrigo, et al. (2014)	Spain	wheat, bread	Se	fertilization	nutrient retention during milling of Se biofortified bread wheat	n/a	NS
Puccinelli et al. (2020)	Italy	basil	Se	fertilization	effect of Se biofortification at varying rates on basil after 5 days storage	n/a	NS
Rodrigo et al. (2015)	UK	beer from biofortified wheat	Se	fertilization	nutrient retention during beer making from Se biofortified wheat	n/a	NS
Sowa et al. (2017)	USA	maize and eggs	PVA	breeding / animal feed	nutrient retention during storage and cooking of β-cryptoxanthin biofortified maize flour (making muffins, tortillas, porridge, fried puffs) and eggs (frying, scrambling, boiling, microwaving)	n/a	NS
Colson, Huffman, and Rousu (2011)	USA	(broccoli, tomatoes, potatoes)	("Antioxidant + Vit C")	("GM Free" vs "Intragenic GM" vs 'Transgenic GM" vs "Plain")	auction market mechanism; willingness to pay for vegetables biofortified with vitamins and antioxidants using different genetic methods	adults in Pennsylvania and Iowa (*N* = 190)	OA
Cox and Bastiaans (2007)	Australia	(meat, dairy, wheat)	(Se)	(agronomic)	quantitative questionnaire survey of consumer acceptance of different methods of increasing Se intake	Australian residents (*N* = 274)	OA
Foti et al. (2021)	Italy	(tomatoes)	(Lycopene)	(multiple)	quantitative and qualitative, in person and online questionnaire survey and interviews assessing knowledge, attitudes and willingness to pay for lycopene biofortified tomatoes	consumers (*N* = 500)	OA

(*Continued*)

Table 1. Continued.

Author(s) & year	Country	Food a	Nutrienta	Biofortification methoda	Study design	Participants	Research domainb
Kleine-Kalmer et al. (2021)	Germany	(apples)	(Se and I)	(fertilization)	Discrete Choice Experiment; online questionnaire assessing acceptance of, and willingness to purchase, Se and I biofortified apples	apple consumers (N = 1042)	OA
Marshall et al. (1994)	USA	eggs	Omega-3	animal feed	questionnaire survey assessing consumer acceptability and willingness to pay for omega-3-enriched eggs	consumers in five Texas cities (N = 500)	OA
Timpanaro et al. (2020)	Italy	(tomatoes)	(Lycopene)	(multiple)	quantitative and qualitative, in person and online questionnaire survey and interviews assessing knowledge, attitudes and willingness to pay for lycopene biofortified tomatoes	consumers (N = 500)	OA
Welk et al. (2021)	Germany	(apple, lettuce, tomato, basil)	(I)	(multiple)	quantitative, online, fully structured questionnaire assessing reasons for purchase, perceptions of different forms of biofortification and willingness to pay for I biofortified fruits and vegetables	fruit and vegetable consumers (N = 1016)	OA
Welk et al. (2023)	Germany	(bell pepper, spinach, broccoli, arugula, kohlrabi)	(Fe)	("special cultivation")	quantitative, online questionnaire survey of consumer acceptance and willingness to pay for Fe biofortified vegetables	vegetable consumers (N = 1000)	OA
Wortmann, Enneking, and Daum (2018)	Germany	(apples)	(Se)	(multiple)	quantitative and qualitative, interviews, focus groups and questionnaire survey assessing acceptance of Se biofortified apples	adults (N = 356)	OA
Grabez et al. (2022)	Norway	lamb meat	I and Se	animal feed (seaweed in finishing diet)	sensory analysis of odor intensity, taste and texture attributes of I and Se biofortified dry-cured lamb leg	semi-trained panel (N = 12; 3 males, 9 females)	SP
Khan et al. (2017)	Saudi Arabia	eggs	Omega-3	animal feed (flaxseed or fish oil)	sensory analysis (flavor, taste, mouth feel, yolk color, smell, texture, overall acceptability) of omega-3 enriched eggs produced by addition of flaxseed or fish oil to laying hen diets	adults 18–35 y (N = 37; 19 males and 18 females)	SP
Oliva et al. (2020)	USA	rice	PVA	GM, transgenic	animal (mice) feeding trial, acute oral toxicity test of biofortified rice	n/a	SA
Neill et al. (2021)	UK	(pork meat)	(Vit D)	(animal feed)	dietary modeling of impact of vit D biofortification of pork and pork products on population vit D intakes	n/a	MO

[a]Parentheses around items indicate theoretical/conceptual involvement of biofortified foods only (e.g., in surveys or modeling studies).
[b]Abbreviations of research domains: BA = bioavailability; NS = nutrient stability; OA = opinions and attitudes; FU = functionality; SP = sensory properties; MO = modeling; SA = safety.

basil). Five methods of biofortification were studied in the literature: use of micronutrient-rich fertilizers ($n = 22$), selective breeding ($n = 10$), animal feed supplementation ($n = 5$), genetic engineering ($n = 4$), and UV-irradiation ($n = 2$), with four additional theoretical papers studying multiple methods of nutrient enrichment. Foods in the literature were biofortified with 11 micronutrients: selenium (Se) ($n = 14$), provitamin A (PVA) ($n = 11$), iodine (I) ($n = 6$), iron (Fe) ($n = 3$), molybdenum (Mo) ($n = 3$), vitamin D ($n = 3$), omega-3 fatty acids ($n = 2$), silicon (Si) ($n = 2$), lycopene ($n = 2$), zinc (Zn) ($n = 1$), and vitamin C ($n = 1$), with lycopene and vitamin C only occurring in theoretical studies of consumer opinions. Study types in the identified literature include human feeding trials ($n = 12$), animal feeding trials ($n = 6$), *in vitro* analyses ($n = 18$), surveys ($n = 9$; including questionnaires and interviews), sensory analyses ($n = 2$), and modeling ($n = 1$), with some studies using both *in vitro* and *in vivo* methods (Table 1).

Current knowledge on biofortified foods in HICs

We identified studies representing seven research domains among the articles included in this review ($N = 46$): nutrient *bioavailability* ($n = 17$, Table 2); physiological *functionality* of nutrients ($n = 9$, Table 3); *nutrient stability* ($n = 11$, Table 4); consumer *opinions and attitudes* ($n = 9$, Table 5); *sensory properties* of biofortified products ($n = 2$, Table 6); consumption *safety* of new biofortified foods ($n = 1$, Table 7); and *modeling* of the potential impact of interventions ($n = 1$, Table 8) (Figure 2 and Supplementary Table S2). Key findings of studies in each of these areas are discussed herein in turn. Four studies assessed both nutrient bioavailability and functionality (Bryszewska et al. 2007; Hohman et al. 2011; D'Imperio et al. 2017; Baldassano et al. 2022); the findings of these studies in each of these domains are discussed separately under the corresponding subheadings.

Bioavailability

Seventeen studies investigated the bioaccessibility, bioavailability, or nutritional equivalency of target micronutrients in biofortified foods. Eight of these involved a human feeding trial, six used an animal model, and six used *in vitro* methods, with some studies using a combination of these (Table 2).

Provitamin A (PVA) maize, cassava and rice. The majority ($n = 7$) of studies in this research domain focused on PVA enriched crops and were conducted in the USA (Davis et al. 2008; Howe, Maziya-Dixon, and Tanumihardjo 2009; Tang et al. 2009; Li et al. 2010; La Frano et al. 2013; Schmaelzle et al. 2014; Zhu et al. 2015). These include four human studies, including a cross-over feeding trial in women ($N = 10$) by La Frano et al. (2013), which

Table 2. Key findings of studies assessing bioavailability ($n = 17$).

Author(s) & year	Study type	Key findings
Baldassano et al. (2022)	Human feeding trial	Supplementation with Mo lettuce increased serum Mo concentration by 42%.
Bryszewska et al. (2007)	Human feeding trial	Changes in plasma Se were different between the standard and Se bread groups, increasing from 56.3 ± 6 to 63.1 ± 7 μg L^{-1} in the treatment group, but not in the control. Two weeks after feeding cessation plasma Se in the Se bread group was still elevated.
Campion et al. (2013)	*In vitro*	Fe bioavailability in low phytic acid and lectin free (lf + lpa) brown and black beans was not significantly different from wild type colored parents but was on average twelve times higher in lf + lpa white beans.
Davis et al. (2008)	Animal model	Liver β-Carotene concentrations in the β-carotene supplement and maize groups did not differ. Liver retinol was higher in the vitamin A supplement (1.17 (SD 0.19) μmol) and maize (0.71 (SD 0.18) μmol) groups compared to control (0.42 (SD 0.16) μmol) and β-carotene supplement (0.57 (SD 0.21) μmol) groups. β-carotene in biofortified maize was converted to vitamin A more efficiently than β-carotene in supplements (2.4 mg vs 4.6 mg β-carotene to 1 mg retinol).
D'Imperio et al. (2016)	*In vitro*	Bioaccessibility of Si in biofortified leafy vegetables ranged from 23% (basil) to 64% (chicory). On average, biofortified vegetables had more bioaccessible Si than their non-biofortified equivalents.
D'Imperio et al. (2017)	*In vitro*	Si Swiss chard released the most Si (4.7 mg/L), followed by chicory (4.5 mg/L), mizuna (3.9 mg/L), tatsoi (3.7 mg/L), and purslane (3.30 mg/L). Relative Si bioaccessibility and bioavailability among different vegetables were different for biofortified and standard crops. Si bioavailability was higher in supplements than any vegetable. Biofortification treatment did not affect bioavailable Si in purslane, tatsoi or mizuna, but had a positive effect on chicory and a negative effect on Swiss chard.
Hohman et al. (2011)	Animal model	Both D2 enriched bread and D3 supplements increased plasma 25(OH)D levels in a dose-dependent manner, but the increase was greater in the D3 supplement group.
Howe, Maziya-Dixon, and Tanumihardjo (2009)	Animal model	Biofortified cassava feed including 4.3 nmol PVA/g effectively maintained vitamin A status, with no difference between varieties, and was as efficacious as β-carotene supplementation.
Itkonen et al. (2016)	Human feeding trial	D2-bread did not affect total S-25(OH)D or S-25(OH)D3, suggesting that D2 in this form is not bioavailable in humans. Both D2 and D3 supplements increased total S-25(OH)D compared with placebo, D3 supplementation resulting in higher S-25(OH)D3.
Jou et al. (2012)	*In vitro* + animal model	Zn bioavailability in biofortified rice was significantly higher than in non-biofortified rice both *in vitro* (2.1-fold) and in the rat model (2.0-fold).
Kirby, Lyons, and Karkkainen (2008)	Human feeding trial	Plasma Se in the biofortified group increased throughout the trial period (122 μg L^{-1} at 0 months to 194 μg L^{-1} at 6 months) more than in the fortified group (122 μg L^{-1} at 0 months to 140 μg L^{-1} at 4 to 6 months).
La Frano et al. (2013)	Human feeding trial	Biofortified cassava porridge increased β-carotene and retinyl palmitate TAG-rich lipoprotein plasma concentrations. The vitamin A equivalency of porridge with and without added oil was not significantly different (4.2 (SD 3.1) and 4.5 (SD 3.1) μg β-carotene:1 μg retinol, respectively).
Li et al. (2010)	Human feeding trial	β-carotene had good bioavailability in biofortified maize. On average, 6.48 ± 3.51 μg (mean ± SD) of the β-carotene in biofortified maize porridge and 2.34 ± 1.61 μg of the β-carotene in the reference dose were each equivalent to 1 μg retinol.
Schmaelzle et al. (2014)	*In vitro* + animal model	Total liver retinol differed among groups fed different biofortified maize varieties. Meal matrix influenced PVA absorption from biofortified carrot, liver retinol being highest in the potato and banana diet groups, while in the maize group it did not differ from baseline. *In vitro* bioaccessibility did not predict bioefficacy.
Tako, Blair, and Glahn (2011)	*In vitro*	Both *in vitro* and *in vivo* tests suggest that biofortified colored beans contain more bioavailable Fe than standard colored beans.
Tang et al. (2009)	Human feeding trial	β-carotene in 'Golden Rice' was effectively converted to vitamin A, with a conversion factor of β-carotene to retinol 3.8 ± 1.7 to 1 by weight (range: 1.9-6.4 to 1).
Zhu et al. (2015)	Human feeding trial	Both fortified and biofortified gari increased area under the curve for α-carotene, β-carotene, and retinyl palmitate, but the increase in retinyl palmitate was greater in the fortified treatment. Vitamin A conversion for fortified and biofortified gari was 2.4 ± 0.3 and 4.2 ± 1.5 μg PVA / 1 μg retinol, respectively.

Table 3. Key findings of studies assessing functionality ($n = 9$).

Author(s) & year	Study type	Key findings
Baldassano et al. (2022)	Human feeding trial	Fe homeostasis improved via increased non-binding hemoglobin Fe (by 37%) and transferrin saturation (by 42%) upon consumption of Mo lettuce. There was no effect on proteins of Fe metabolism, blood parameters, liver function, or lipid metabolism.
Bryszewska et al. (2007)	Human feeding trial	Platelet GPx1 activity was not different between the standard and Se bread groups.
D'Imperio et al. (2017)	*In vitro*	The bioavailable fraction of Si in biofortified purslane and Swiss chard improved osteoblast marker expression more effectively than the Si supplement and other vegetables.
Hohman et al. (2011)	Animal model	Both D2 enriched bread and D3 supplements improved bone quality parameters in a dose-dependent manner, with no significant difference between groups.
Oancea et al. (2015)	*In vitro*	Se biofortified and biostimulant-treated cabbage seedlings had enhanced antitumoral activity compared to water-treated seedlings.
Ravn-Haren et al. (2008)	Human feeding trial	All treatments increased serum Se after 1 week. The effects of Se yeast and milk did not differ from each other, and both increased serum Se more than selenate. As Se milk contained nearly 50% more Se than Se yeast, this suggests that Se in milk is less absorbable than in yeast. Thrombocyte glutathione peroxidase activity increased upon selenate supplementation but not during Se yeast or Se milk consumption. No treatment affected blood lipid markers or enzyme and a transcription factor expression or activity involved in glutathione-mediated detoxification and antioxidation.
Vasto et al. (2022)	Human feeding trial	Consumption of Mo lettuce did not affect beta cell function but reduced fasting glucose, insulin and insulin resistance, and increased insulin sensitivity in healthy adults.
Vasto et al. (2023)	Human feeding trial	Mo supplements did not affect bone remodeling or metabolism. Mo lettuce consumption reduced bone resorption and improved bone metabolism in both middle-aged and older adults.
Wu et al. (2009)	Human feeding trial	Consumption of Se-biofortified wheat biscuits increased plasma Se (from a baseline of 122 μg/L to 192 μg/L), but did not substantially modify the biomarkers of degenerative disease risk and health status studied.

Table 4. Key findings of studies assessing nutrient stability ($n = 11$).

Author(s) & year	Study type	Key findings
Budke et al. (2021)	Storage assessment	The I content of apples and pears decreased by 14% after washing with deionized water. Three months of cold storage decreased the I content of apples by 20% but had no significant effect in pears.
Burt et al. (2010)	Storage assessment	Carotenoid profiles in biofortified maize remained stable during storage after room temp. drying. Carotenoid levels decreased after 3–6 months, but then remained stable for a year. Carotenoid levels were sensitive to storage and handling conditions. Freeze-drying resulted in better nutrient retention than either high or low heat drying, which did not differ from each other.
Cerretani et al. (2014)	Cooking assessment	In focaccia, no significant I losses were detected. In dumplings and pies, significant I losses occurred (27.5% and 55.3%), but all dishes maintained a good final I content (33.3–52.7% of daily recommended intake per serving).
Comandini et al. (2013)	Processing + cooking assessment	Boiling did not affect I content in biofortified potatoes but decreased I in biofortified carrots (by over 50%). The effect of baking on biofortified potatoes varied with variety (no effect or reduction by 21.27–36.17%). Pasteurization had varying effects on tomato I content. Iodized salt was not absorbed by non-biofortified potatoes or carrots during boiling, but mashed potatoes baked with iodized salt retained pre-cooking I levels.
Hart et al. (2011)	Processing + cooking assessment	There was minimal loss of Se during wheat processing. The application of Se at 10 g/ha increased total Se in white and wholemeal bread by 155 and 185 ng/g, respectively, equivalent to 6.4 and 7.1 μg Se per slice of bread.
Ortiz, Rocheford, and Ferruzzi (2016)	Storage assessment	Carotenoid losses from biofortified maize during traditional drying were low (<9%). Carotenoid stability during storage was dependent on temperature and humidity (slower degradation at lower temp. & humidity) and varied among genotypes. Different carotenoids had different degradation rates.
Poblaciones, Rodrigo, et al. (2014)	Processing + cooking	Milling caused a 27% loss of Se from biofortified grains due to the removal of Se in the bran and germ. Loss of Se during pasta making and cooking was around 7%.
Poblaciones, Rodrigo, et al. (2014)	Processing assessment	There was a 28% loss of Se during milling, but biofortified flour still had increased Se content. Dough properties were unaffected or slightly improved in biofortified flour, but grain protein was slightly negatively affected in the dry year of the study.
Puccinelli et al. (2020)	Storage assessment	Se biofortification improved antioxidant capacity and phenol and rosmarinic acid contents. After 5 days of storage, ethylene production decreased in plants treated with 4 mg Se L^{-1}, suggesting that it could prolong shelf-life.
Rodrigo et al. (2015)	Processing assessment	Beer contained around 10% of the added Se initially present in wheat, most Se losses (54%) occurring during the mashing stage of the brewing process.
Sowa et al. (2017)	Storage + cooking assessment	Carotenoid loss from biofortified maize flour was accelerated by increasing storage temperature, degrading rapidly at room temperature or above. PVA carotenoids were well retained in biofortified maize and eggs after cooking, except in maize puffs. Boiling whole grain maize flour into porridge had the highest (112%), deep-fried maize and scrambled eggs the lowest carotenoid retention rates (67–78 and 84–86%, respectively).

found that β-carotene was effectively absorbed from biofortified cassava porridge, and a similar cross-over feeding trial in women ($N = 8$) by Zhu et al. (2015), which found that both gari (a traditional West African food) made from biofortified cassava and gari fortified with red palm oil were effective at improving vitamin A status, although the vitamin A equivalency of carotenoids in red palm oil was higher. Similarly, a cross-over feeding trial in women ($N = 6$) (Li et al. 2010) found that β-carotene in biofortified maize porridge had a good bioavailability,

Table 5. Key findings of studies assessing opinions and attitudes ($n=9$).

Author(s) & year	Study type	Key findings
Colson, Huffman, and Rousu (2011)	Experimental auction; willingness to pay	Consumers showed high willingness to pay for vegetables labeled as having enhanced antioxidant and vitamin C levels produced by moving genes within species, but not for transgenic produce. The premium participants were willing to pay for GM free vs transgenic GM produce was considerably affected by information treatments (objective, pro-biotech or anti-biotech).
Cox and Bastiaans (2007)	Questionnaire survey; acceptance, willingness to buy	For meat, dairy and wheat products, Se enrichment during manufacturing was rated less favorably than agronomic biofortification or supplements. Se biofortification was preferred over supplements for wheat, and among older respondents. Respondents reported lower confidence to consume Brazil nuts and supplements compared to foods enriched with Se.
Foti et al. (2021)	Questionnaire survey + interviews; understanding, acceptance, willingness to buy, willingness to pay	Tomato choice was determined by taste, origin, certification and price. Over 60% of consumers equated the term "biofortified" with "organic", which they associated with health benefits. Most respondents disapproved of the use of genetic modification and did not see this as a possible biofortification method. 64% of respondents were willing to pay more for biofortified tomatoes, only 28% were willing to buy them regularly.
Kleine-Kalmer et al. (2021)	Questionnaire survey; acceptance, willingness to buy	Apple choice was mainly influenced by price, health claims, and plastic-free packaging. Respondents had a preference for I biofortified apples. Se on its own did not affect apple choice, but apples with both Se and I were preferred over those with I only.
Marshall et al. (1994)	Questionnaire survey; acceptance, willingness to buy	The majority (65%) of consumers were willing to purchase omega-3 eggs, 71% of whom were willing to pay an additional $0.50 per dozen eggs.
Timpanaro et al. (2020)	Questionnaire survey; understanding, acceptance, willingness to buy	Four groups of consumers with differing attitudes toward biofortified products were identified (aware, uninformed, health-conscious, non health-conscious). Consumers showed an interest in biofortified products, associating them with health benefits, but attributing these to organic growing, not to improved micronutrient content, and rejected genetic engineering as a production method.
Welk et al. (2021)	Questionnaire survey; acceptance, willingness to buy, willingness to pay	I enriched fruits and vegetables were most attractive to those who tended to shop at farmers' markets, organic shops or farm stores, 39% of whom rated these "very appealing". This group attached importance to naturally I-rich food, preferred domestic produce, and focused on sustainability and naturalness, unlike typical users of supplements, who were more concerned with health benefits. Overall, 85% of respondents preferred biofortified fruits and vegetables over supplements. The greatest market potential for I biofortified produce may be supermarkets, the preferred food shopping location of most consumers, 28% of whom rated these "very appealing".
Welk et al. (2023)	Questionnaire survey; understanding, willingness to pay	Most respondents were interested in Fe vegetables, bell pepper having the highest acceptance (79%), followed by spinach (76%), broccoli (74%), kohlrabi (62%) and arugula (54%). Acceptance was higher among females and urban residents. Preferences were linked to enjoyment, sustainability and naturalness. 77% of respondents preferred "naturally Fe rich" (i.e., biofortified) vegetables over fortified products or supplements, and were willing to pay EUR 0.10–0.20 more for biofortified vegetables. Only 20% of respondents could match the term "biofortified" with its correct definition, many respondents associating it with organic production. Consumers found the claims "rich in iron" (71%) and "rich in iron and vitamin C" (78%) most appealing, while the label "biofortified with iron" scored the lowest (28%).
Wortmann, Enneking, and Daum (2018)	Interviews + focus groups + questionnaire survey; acceptance	There was a moderate acceptance of Se apples, with 46.6% of respondents reacting positively to the idea. Acceptance was positively associated with increasing age, a preference for the most appealing Se-related nutrition ("rich in Se") and health claim ("Se contributes to a normal function of the immune system"), usually shopping for apples in supermarkets, belief in the health benefits of Se, preference for Se-rich apples over supplements, and provision of positive health information. Those who consumed convenience food more than once a week had a higher acceptance than those who ate apples more than once a week.

Table 6. Key findings of studies assessing sensory properties ($n=2$).

Author(s) & year	Study type	Key findings
Grabez et al. (2022)	Sensory assessment	Biofortification of lamb meat by inclusion of I- and Se-rich seaweed in the finishing diet had no effect on the taste profile of dry-cured lamb leg.
Khan et al. (2017)	Sensory assessment	Omega-3 eggs produced by adding flaxseed to hen feed were more acceptable and palatable than those produced using fish oil, which had a fishy aftertaste and odor.

Table 7. Key findings of studies assessing safety ($n=1$).

Author(s) & year	Study type	Key findings
Oliva et al. (2020)	Animal model	No adverse effects associated with the presence of transgenically introduced proteins were found in the PVA biofortified rice.

although its retinol equivalence was lower than that of the β-carotene added to porridge during preparation. Lastly, a 3-month feeding trial in adults ($N=5$) confirmed that β-carotene in Golden rice can be effectively converted to vitamin A in humans (Tang et al. 2009). Moreover, animal models (Mongolian gerbils) suggest that β-carotene in biofortified maize, while it may be less effective than vitamin A supplements, can improve vitamin A status as effectively (Davis et al. 2008), or more effectively than β-carotene supplementation (Howe, Maziya-Dixon, and Tanumihardjo 2009), although the nutritional efficacy of different biofortified maize genotypes may vary (Schmaelzle

Table 8. Key findings of modeling studies ($n=1$).

Author(s) & year	Study type	Key findings
Neill et al. (2021)	Dietary modeling	Increasing pork vit D content by 50, 100, 150, and 200% could increase population vit D intake by 4.9, 10.1, 15.0, and 19.8%, respectively. A greater relative change is expected in males than females (22.6% and 17.8%, respectively, in the last scenario), and in those aged 11–18 years (25.2%).

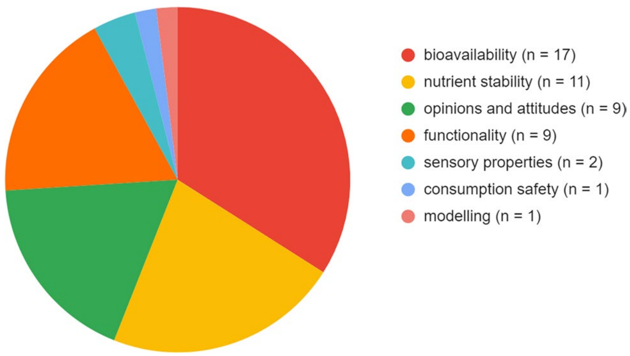

Figure 2. Number of included articles ($N=46$) representing each identified research domain.

et al. 2014). Schmaelzle et al. (2014) also provide evidence that meal matrix can influence the bioefficacy of carotenoids in biofortified carrots. Overall, both animal and human studies suggest that PVA has a good bioavailability in certain biofortified foods.

Silicon (Si) leafy vegetables. Two *in vitro* studies by Italian researchers assessed the bioaccessibility (using chemical digestion) and bioavailability (in a Caco-2 cell system) of Si in various biofortified leafy vegetables (tatsoi, mizuna, purslane, basil, Swiss chard, chicory), finding that biofortified varieties had more bioaccessible Si than their non-biofortified equivalents (D'Imperio et al. 2016; 2017), however, Si bioavailability in biofortified vegetables was not always higher than in their standard counterparts and, in all cases, was lower compared to Si supplements (D'Imperio et al. 2017).

Molybdenum (Mo) lettuce. A 12-day feeding trial in Italian adults ($N=24$) (Baldassano et al. 2022) found that supplementing diets with Mo-biofortified lettuce could increase serum Mo levels, and in turn could contribute to healthy Fe homeostasis.

Selenium (Se) wheat and rye. The nutritional efficacy of Se-enriched grains was asserted by two human studies. A 6-month feeding trial in Australian men ($N=75$) (Kirby, Lyons, and Karkkainen 2008) found that Se-biofortified biscuits were more effective at improving Se status than biscuits made from wheat fortified with Se. A 4-week feeding trial in Polish women ($N=24$) (Bryszewska et al. 2007) found that daily consumption of bread made with Se-biofortified rye seedling powder improved Se status.

Vitamin D bread. Two studies focused on vitamin D enriched bread. In a rodent model, Hohman et al. (2011) reported that vitamin D2 in bread made with D2-biofortified yeast was effective at improving vitamin D status, although this was less effective than vitamin D3 supplements. In an 8-week randomized-controlled trial in Finnish women ($N=33$) (Itkonen et al. 2016), it was concluded that vitamin D2 in this form has limited bioavailability in humans.

Iron (Fe) beans. Two studies explored bioavailability of Fe in beans. Fe was more bioavailable in biofortified beans compared to their non-biofortified counterparts, both *in vitro* and in a chicken model in an American study (Tako, Blair, and Glahn 2011). An Italian study (Campion et al. 2013) found that *in vitro* bioavailability of Fe in genetically biofortified (low phytic acid and lectin free) bean lines was linked to seed color, being no different between biofortified and non-biofortified varieties of brown and black beans, but being twelve times higher in the biofortified line of white beans compared to white non-biofortified beans.

Zinc (Zn) rice. Zn bioavailability in biofortified rice was assessed in one study in the USA (Jou et al. 2012). This study showed that the bioavailability of Zn in biofortified rice was around twice as high compared to non-biofortified rice, *in vitro* and in a rodent model.

Functionality

The functionality of nutrients in biofortified foods in terms of nutrition-related health outcomes, including biomarkers of disease risk and indicators of health status, was assessed in nine articles, including six human feeding trials, one animal model, and two *in vitro* studies (Table 3).

Molybdenum (Mo) lettuce. Three human studies from Italy, all involving 12-day controlled feeding trials, suggest that consuming Mo-biofortified lettuce (100 g per day) could have multiple benefits, including improved iron homeostasis (Baldassano et al. 2022) and reduced fasting glucose, insulin, and insulin resistance, and increased insulin sensitivity (Vasto et al. 2022) in healthy adults ($N=24$ in both studies), as well as a potential role in preventing osteoporosis in middle-aged ($n=42$) and older adults ($n=42$), which was not associated with taking Mo supplements (Vasto et al. 2023).

Silicon (Si) leafy vegetables. An *in vitro* study conducted in Italy (D'Imperio et al. 2017) indicates that Si biofortified

Swiss chard and purslane (but not tatsoi, mizuna, or chicory) could support bone mineralization based on their ability to increase the expression of osteoblast (cells responsible for bone formation) markers more effectively than Si supplements.

Vitamin D bread. In an American study using a rodent model, Hohman et al. (2011) provides preliminary evidence that vitamin D2-rich bread made using D2 biofortified yeast could be a good source of vitamin D for humans, as it was as effective in improving bone quality as D3 supplementation.

Selenium (Se) yeast, wheat, rye and cabbage. Multiple human studies on Se biofortified foods suggest that, despite being bioavailable, Se in these foods may have limited physiological functionality (Bryszewska et al. 2007; Ravn-Haren et al. 2008; Wu et al. 2009). For example, a randomized cross-over feeding trial in healthy Danish men ($N = 20$) (Ravn-Haren et al. 2008) found that both yeast and milk biofortified with Se were more effective at increasing serum Se than selenate supplementation (an inorganic form of Se), however, neither improved markers of antioxidant defense or cardiovascular disease risk. Similarly, in a 24-week placebo-controlled feeding trial in Se-replete healthy older Australian men ($N = 62$) (Wu et al. 2009), consuming Se-biofortified wheat biscuits increased plasma Se levels but did not substantially modify biomarkers of degenerative disease risk or health status. A 4-week feeding trial in Polish women ($N = 24$) found that consuming bread made with Se-biofortified rye seedling powder, despite effectively increasing plasma Se levels, did not increase antioxidant enzyme activity (Bryszewska et al. 2007). A Romanian *in vitro* study (Oancea et al. 2015) suggests that Se biofortified biostimulant treated cabbage seedlings may have cancer-fighting properties, as indicated by their enhanced antitumoral activity compared to water-treated seedlings.

Nutrient stability

The stability of target micronutrients upon storage, processing or cooking of biofortified foods was evaluated in eleven studies, most of which were conducted in the USA and Italy (Table 4).

Provitamin A (PVA) maize and eggs. Research on PVA biofortified foods suggests that, while affected by storage conditions and cooking methods, PVA can be generally well retained in these foods. This was demonstrated in an American study (Ortiz, Rocheford, and Ferruzzi 2016), which found that carotenoid losses from biofortified maize kernels during traditional drying were low (<9%), and that degradation rates over 12 months were dependent on storage temperature and humidity and varied among genotypes. Similarly, Canadian research (Burt et al. 2010) found that carotenoid levels in biofortified maize kernels were sensitive to storage and handling conditions, with freeze-drying resulting in better nutrient retention than either high or low heat drying, which did not differ from each other. Likewise, another American study (Sowa et al. 2017) found that β-cryptoxanthin (a PVA carotenoid) loss from biofortified maize flour was accelerated by increasing storage temperature. In addition, Sowa et al. (2017) assessed the effects of cooking on β-cryptoxanthin biofortified maize and eggs, finding that boiling of whole grain maize into porridge resulted in the highest (112%) carotenoid retention among the cooking methods studied (making muffins, tortillas, porridge, and fried puffs from maize flour; frying, scrambling, boiling, and microwaving eggs), while deep-fried maize puffs and scrambled eggs had the lowest retention rates (67–78 and 84–86%, respectively).

Iodine (I) potatoes, carrots, tomatoes, apples and pears. Studies on various iodine biofortified foods show that I can be well retained after processing and cooking, but its levels are dependent on the crop and methods used (Comandini et al. 2013; Cerretani et al. 2014; Budke et al. 2021). In Italy, Comandini et al. (2013) found that boiling decreased the I content of biofortified carrots, but in biofortified potatoes I content was not affected by boiling and the effect of baking varied depending on variety. In biofortified tomatoes, pasteurization had varying effects on I content, depending on variety and processing method. Similarly, Cerretani et al. (2014) found that I showed good stability in different Italian dishes made with biofortified potatoes, especially in focaccia bread, where no significant losses were detected. During boiling of dumplings and baking of vegetable pies, significant losses of I occurred (27.5% and 55.3%, respectively), but all dishes maintained a good final I content, equivalent to 33.3% to 52.7% of the daily recommended intake for adults in an individual serving. Research in Germany (Budke et al. 2021) found that washing decreased the I content of biofortified apples and pears by 14%, while three months of cold storage decreased the I content of apples by 20% but had no significant effect in pears.

Selenium (Se) wheat and basil. Evidence suggests that the Se retention in biofortified wheat products depends on the processing method. Two studies looked at this in the UK. Rodrigo et al. (2015) found that, in beer, only around 10% of the Se supplied to the grain from which it was made was retained, while Hart et al. (2011) found that milling and bread making was associated with minimal loss of Se, with biofortification increasing total Se in white and wholemeal bread by 155 and 185 ng/g, respectively, equivalent to 6.4 and 7.1 µg Se per average slice (around 10% of the daily Recommended Nutrient Intake). Moreover, research in Spain found that milling caused a 27% loss of Se from biofortified durum wheat, while Se loss during pasta making and cooking was only around 7% (Poblaciones, Rodrigo, et al. 2014). They observed a similar 28% loss of Se during the milling of biofortified bread wheat, with dough properties being unaffected or slightly improved compared to standard flour (Poblaciones, Santamaría et al. 2014). In addition, Italian researchers (Puccinelli et al. 2020) found that biofortifying basil with a Se solution can prolong shelf life by reducing ethylene production by the plants, as well increasing their Se content and antioxidant capacity of the herb.

Opinions and attitudes

Consumer understanding, attitudes toward, including general acceptance of and willingness to buy or willingness to pay for biofortified foods were explored in nine studies (Table 5), four of which were conducted in Germany (Wortmann, Enneking, and Daum 2018; Kleine-Kalmer et al. 2021; Welk et al. 2021; 2023).

Selenium (Se) and iodine (I) fruits and vegetables; Se meat, dairy and wheat products. Three studies in Germany suggest that fruits and vegetables biofortified with I and/or Se are positively perceived by consumers (Wortmann, Enneking, and Daum 2018; Kleine-Kalmer et al. 2021; Welk et al. 2021). For example, Welk et al. (2021) found that I biofortified fruits and vegetables were preferred over supplements by 85% of survey respondents ($N = 1016$) and were particularly attractive to those who tended to shop at farmers' markets, organic food shops, or farm stores, who focused on sustainability, naturalness and domestic produce in their food choices. Among those who regularly shopped at supermarkets (the majority of those surveyed), 28% rated I enriched fruit and vegetables as "very appealing". Likewise, a high willingness to purchase I biofortified apples among German consumers ($N = 1042$) was revealed in a discrete choice experiment (Kleine-Kalmer et al. 2021), which also found that apples biofortified with both Se and I were preferred over those with I only. Wortmann, Enneking, and Daum (2018) also studied German consumers' acceptance of Se biofortified apples, finding that 46.6% of respondents ($N = 356$) reacted positively to the product idea. Acceptance was positively associated with increasing age, a preference for certain nutrition and health claims (such as "rich in Se" and "Se contributes to a normal function of the immune system"), usually shopping for apples in supermarkets, a belief in the health benefits of Se, a preference for Se-rich apples over Se supplements, and being provided with positive health information on the effects of Se. Participants who consumed convenience food more than once a week also had a higher acceptance of Se biofortified apples than those who ate apples more than once a week. In addition, Australian residents ($N = 274$), especially older survey respondents, rated Se enrichment during food manufacturing less favorably than agronomic biofortification or supplements for meat, dairy and wheat products, and for wheat, preferred biofortification over supplements (Cox and Bastiaans 2007).

Iron (Fe) vegetables. German consumers, particularly females and urban residents, showed a high acceptance of Fe biofortified vegetables in a survey by Welk et al. (2023), where 77% of respondents ($N = 1000$) preferred "naturally Fe rich" (i.e., biofortified) vegetables over conventionally fortified products and supplements, with food preferences linked to enjoyment, sustainability, and naturalness. Among the biofortified vegetables studied, bell pepper had the highest acceptance (79%), followed by spinach (76%), broccoli (74%), kohlrabi (62%) and arugula (54%). On average, respondents also stated their willingness to pay €0.10–0.20 more for biofortified versions of vegetables. However, only a fifth of respondents could match the term "biofortified" with its correct definition, which the majority associated with organic production. Consumers found the labels "rich in iron" (71%) and "rich in iron and vitamin C" (78%) the most appealing, while "biofortified with iron" scored lowest (28%).

Lycopene tomatoes. Two Italian studies by the same group of researchers (Timpanaro et al. 2020; Foti et al. 2021) found that, while consumers showed an interest in lycopene biofortified tomatoes, which they associated with health benefits, most (>60%) attributed these benefits to organic growing methods rather than improved micronutrient content, and rejected genetic engineering as a production method. Further, Foti et al. (2021) found that 64% of respondents ($N = 500$) were willing to pay more for biofortified tomatoes, although only 28% were willing to buy these regularly. Using data from the same sample, Timpanaro et al. (2020) identified four consumer groups with differing attitudes toward biofortified food (uninformed, aware, health-conscious and non-health-conscious).

Omega-3 eggs. One study (Marshall et al. 1994) suggests a high acceptance of omega-3 enriched eggs in the USA, with nearly two thirds of Texan consumers ($N = 500$) surveyed stating their willingness to purchase these products, 71% of whom indicated that they were willing to pay an additional $0.50 per dozen eggs.

"Antioxidant and vitamin C" vegetables. Consumers in Pennsylvania and Iowa ($N = 190$) stated a high willingness to pay for broccoli, tomatoes and potatoes labeled as having enhanced antioxidant and vitamin C levels, if this was achieved by moving genes within species, but not if produce was transgenic (Colson, Huffman, and Rousu 2011). Willingness to pay for vegetables biofortified using different genetic methods was also affected by whether objective, pro-biotech or anti-biotech information had been presented to participants.

Sensory properties

Two studies involved sensory analysis of biofortified animal products (Table 6). Norwegian research (Grabez et al. 2022) found that I- and Se-enriched lamb, consumed as dry-cured legs, had a taste profile no different from that of non-biofortified meat. However, in assessing the sensory properties of eggs enriched with omega-3 fatty acids among Saudi consumers, Khan et al. (2017) found that, unlike eggs produced by adding flaxseed to laying hen diets, eggs biofortified through the addition of fish oil to hen feed had limited acceptability due to their fishy odor and aftertaste.

Safety

One American study (Oliva et al. 2020) assessed the consumption safety of a newly developed transgenic PVA biofortified rice in an acute oral toxicity test in mice, which showed no adverse effects, suggesting that the new rice is safe to consume (Table 7).

Modeling

One modeling study (Neill et al. 2021) estimates that biofortifying pork and pork products in the UK with vitamin D could increase population vitamin D intakes by up to 19.8% (assuming a doubling of pork vitamin D content), with the greatest increase expected to occur among those aged 11–18 years (25.2%) and in males (22.6% compared to 17.8% in females) (Table 8).

Discussion

The objectives of this review were: to determine the extent, range and nature of existing research on biofortified foods in relation to human consumption in HICs, and to summarize current knowledge on different aspects of biofortification in a HIC context. Forty-six studies met the inclusion criteria. Identified studies were conducted in 13 different HICs, predominantly in Europe and North America. By country, most studies were conducted in the USA, Italy and Germany. The included papers were synthesized under seven research domains, which were determined after identifying relevant literature. Most research focused on nutrient bioavailability, nutrient stability, consumer opinions and attitudes and the physiological functionality of these foods, with a relatively small number of articles on the sensory properties of biofortified products, consumption safety of new biofortified foods, and modeling of the potential impact of interventions. The majority of studies involved *in vitro* methods, human feeding trials or surveys, followed by animal models, sensory analyses, and modeling. The most studied food types were cereals and non-leguminous vegetables, followed by animal products, starchy tubers, fruits, legumes and other foods. The use of micronutrient fertilizers was the most common biofortification method in the literature, followed by selective breeding, while animal feed supplementation, genetic engineering, and UV-irradiation were less studied. Eleven micronutrients were considered in the literature, with selenium and provitamin A receiving the most attention.

Bioavailability and functionality

The bioavailability of micronutrients in biofortified foods was assessed in seventeen studies in HICs (Table 2), many of which had promising results. Although over half of these used either *in vitro* or animal models, and so the findings of these might be considered somewhat limited in their relevance to humans, these studies are extremely useful and directly related to human consumption, because if efficacy is indicated, this provides a good basis to investigate bioavailability in humans. As regards human feeding trials focusing on bioavailability included in this review, it should be noted that the results of some of these studies (e.g., Li et al. 2010; La Frano et al. 2013; Zhu et al. 2015) may have limited relevance to HICs, as these involved foods that are likely unfamiliar (e.g., cassava gari or porridge) and may therefore have low cultural acceptability in HIC contexts (Prescott 1998). A recent systematic review, which identified 18 and 58 studies, respectively, on the bioaccessibility and bioavailability of micronutrients in crops biofortified through conventional breeding, concluded that these crops generally provide more absorbed micronutrients compared to their non-biofortified counterparts, the magnitude of this difference depending on the exact cultivar, processing method, food matrix and experimental method used (Huey, Konieczynski et al. 2023). Nonetheless, research on the bioavailability of nutrients in biofortified staples that are widely consumed in HICs, such as bread, pasta or potatoes, are still relatively limited. Regarding studies on the effectiveness of biofortified foods at improving health outcomes identified in this scoping review (Table 3), some research had promising results. For example, D'Imperio et al. (2017) found Si biofortified purslane and Swiss chard to be more effective than Si supplements at enhancing osteoblast expression *in vitro*, Hohman et al. (2011) showed that D2 enriched bread was as effective at improving bone quality as D3 supplements in an animal model, and Vasto et al. (2022) found that Mo-enriched lettuce reduced fasting glucose, insulin and insulin resistance in healthy adults. However, other studies had mixed results, some showing no positive physiological effect despite apparently good nutrient bioavailability (e.g., Bryszewska et al. 2007; Ravn-Haren et al. 2008; Wu et al. 2009). In addition, it is worth noting that none of the human studies looking at the bioavailability of micronutrients in biofortified foods or the physiological effects of consuming these were conducted with participants deficient in the target micronutrients, with only one study selecting participants with somewhat lower nutrient (Se) status (Wu et al. 2009). Therefore, while there is strong evidence for the effectiveness of biofortification interventions at improving diet-related health outcomes in LMICs (e.g., Bouis and Saltzman 2017; Garg et al. 2018), more longer-term studies are needed to investigate the impacts of consuming biofortified foods on health in HIC contexts.

Nutrient stability

Eleven articles were identified focusing on micronutrient stability in biofortified foods (Table 4). These studies offer useful insight regarding the ways in which biofortified foods should be stored and prepared to maximize micronutrient retention and potential nutritional benefit, which is important to consider because storage conditions, milling and cooking methods, and the food matrix are known to affect the bioavailability of several micronutrients in food (Maiani et al. 2009; Suri and Tanumihardjo 2016; Bechoff and Dhuique-Mayer 2017). Studies identified in this review demonstrated that, while affected by storage and cooking, PVA is generally well retained in maize (Burt et al. 2010; Ortiz, Rocheford, and Ferruzzi 2016, Sowa et al. 2017) and eggs (Sowa et al. 2017). These findings align with global research on micronutrient retention in conventionally bred biofortified crops upon post-harvest handling. For instance, a recent systematic review, which identified 67 articles on seven crops (maize, orange sweet potato, cassava, pearl millet, rice, beans and wheat), reported that provitamin A crops maintained high amounts of PVA compared with their non-biofortified counterparts (Huey, Konieczynski, et al. 2023). The authors also reported that micronutrient retention in iron and zinc enriched crops was more variable, dependent on processing method. Nutrient stability in iron and zinc crops was not assessed in the literature identified in HICs, but studies on selenium enriched wheat (Hart et al. 2011; Poblaciones, Rodrigo, et al. 2014; Poblaciones, Santamaría, et al. 2014; Rodrigo et al. 2015), and iodine enriched apples and pears (Budke et al. 2021), potatoes (Comandini et al. 2013; Cerretani et al. 2014) and carrots and tomatoes (Comandini et al. 2013) had similar results regarding variable nutrient retention between crop types and processing and cooking methods. Therefore, it is important that nutrient stability in biofortified foods is assessed on a case-by-case basis, focusing on effects of the most relevant, culturally appropriate preparation methods and locally relevant storage conditions in different contexts.

Opinions and attitudes

Exploring consumer perceptions of target foods is important because negative attitudes could preclude the successful uptake of new products, limiting any potential public health benefit. In terms of consumer attitudes toward biofortified foods, some studies identified in this scoping review suggest a positive perception of, and good market potential for, these foods in HICs (Marshall et al. 1994; Cox and Bastiaans 2007; Wortmann, Enneking, and Daum 2018; Kleine-Kalmer et al. 2021; Welk et al. 2021; 2023). However, the quality of evidence for consumer acceptance is diminished due to apparent misconceptions of the term "biofortified", which in some cases was understood as a synonym for "organic" (Timpanaro et al. 2020; Foti et al. 2021), while in another study the term was rated considerably less favorably than other synonyms for nutrient enrichment (Welk et al. 2023). In addition to using interviews, focus groups and questionnaires exploring consumer attitudes, willingness to pay studies yield another important indication of consumer acceptability (Voelckner 2006). A systematic review and meta-analysis by De Steur et al. (2017) reported that worldwide, consumers stated that they would be willing to pay an average 23.9% more for genetically modified (GM) biofortified crops (not yet available on the market), especially when provided with positive information on the benefits of these foods. However, few studies exist on consumers' purchase intentions or willingness to pay for biofortified (GM or otherwise) foods in HICs. Our review identified four studies assessing willingness to pay for biofortified foods in HICs (Marshall et al. 1994; Colson, Huffman, and Rousu 2011; Foti et al. 2021; Welk et al. 2023). These articles all found that consumers would be willing to pay a premium for biofortified foods, but they also provide evidence that the way in which products are labeled and what information consumers are exposed to can considerably affect willingness to pay. Thus, these factors must be taken into consideration before the market launch of any new product, as labeling and the provision of clear and accurate information could considerably affect consumer choices. In addition, none of the studies on consumer opinions identified in this review specifically recruited participants with, or at increased risk of, micronutrient deficiencies, which could be a potentially important factor affecting attitudes toward biofortified foods. Moreover, it is important to note that the majority of studies in this domain identified in our scoping review did not use a representative sample, which limits the generalizability of their findings. Also important to note is that, while farmers' acceptance and adoption of biofortified crops was addressed in 24 studies in LMICs in a systematic review on the topic (Samuel et al. 2023), neither that study nor our scoping review could locate any research exploring this in HICs. To ensure that biofortified foods can be successfully integrated into food systems in HICs, we need to develop a better understanding of various food system stakeholders' perspectives and identify potential challenges, as well as ways in which these could be overcome. One particularly salient question in this area is regarding the use of the term "biofortified" on food packaging, which may not necessarily be appropriate or even legal in some cases given the current lack of an official definition and the likelihood of confusion among consumers around its meaning.

Sensory properties

The sensory acceptability of biofortified foods is a key determinant of the success of potential interventions, as people may be reluctant to consume these foods in sufficient amounts if they find them unpalatable or dislike some of their other properties, such as smell or appearance. Yet, sensory acceptability of biofortified foods was only explored in two studies in HICs, both looking at animal products. These two articles found that the sensory properties of I- and Se-enriched lamb were not different from those of standard lamb meat (Grabez et al. 2022), while the sensory acceptance of omega-3 eggs depended on what diets the laying hens were fed, with eggs produced using fish oil in hen feed having limited acceptability due to their fishy odor and aftertaste (Khan et al. 2017). By contrast, the sensory acceptance and adoption of biofortified crops among consumers and producers in LMICs is well-researched, already addressed in 72 studies according to a 2017 systematic review (Talsma, Melse-Boonstra, and Brouwer 2017). These studies in LMICs (mostly on sweet potato and maize) suggest that biofortified crops generally have a good sensory acceptance despite being different from their traditional counterparts in color or other attributes, and that the availability of these crops and information on their health benefits are important determinants of acceptance and adoption. Another, more recent, systematic review identified 49 studies assessing the acceptability of 10 selected biofortified crops, and similarly found that, despite some differences between crop varieties, foods biofortified with provitamin A or minerals are generally acceptable to both adults and children in rural, low-income settings across Africa, Latin America, and India (although the evidence for mineral-biofortified foods is weaker due to the relatively limited amount of research on these) (Huey, Bhargava, et al. 2023). However, the authors did not locate any studies in HICs. Thus, the extent to which findings of research on the acceptability of biofortified foods in LMICs will hold true in different settings is yet to be determined. In particular, controlled studies, including ones involving blind sensory testing of biofortified products, would be valuable, as well as further research on how the sensory and processing attributes of biofortified varieties of foods may differ from those of their non-biofortified counterparts when subjected to different preparation and cooking methods.

Safety

Ascertaining the safety of biofortified foods for human consumption is essential to make sure micronutrient enriched products do not have any unintended negative effects on consumers, and such research should always precede interventions involving new foods. Our review only identified one study exploring this, which confirmed the lack of acute toxic effects of consuming transgenically biofortified rice in an animal model (Oliva et al. 2020). However, this is not to suggest that this question has been overlooked in the literature. Rather, it is likely that most studies assessing the safety of biofortified foods for human consumption were not included in this review because, in many cases, potential toxicity can be determined using chemical analysis, typically as part of developing new biofortified foods, and these kinds of studies were not considered sufficiently relevant to human consumption in this review. With regards to the safety of bioengineered foods, despite widespread concerns, evidence for the safety of using such methods, particularly precision gene editing, for the development of crops with beneficial traits continues to emerge. A recent analysis of the top seven risks of genome-edited crops found the risks associated with these to be comparable to those of accepted breeding methods (Pixley et al. 2022).

Modeling

Modeling enables us to determine potential longer-term effects at a population level of a particular (food-based or other) intervention on various outcomes, such as improvement in health and quality of life, and associated economic costs (Ramponi, Tafesse, and Griffin 2021; Wun et al. 2022; Birol and Bouis 2023). This literature review only identified one modeling study, focusing on the potential effects of increasing the vitamin D content of pork on the nutritional status of the UK population (Neill et al. 2021). In comparison, multiple modeling studies have been conducted in LMICs (Garg et al. 2018; Wun et al. 2022), which generally found that biofortification interventions in these contexts are cost-effective in the long-term and can have substantial positive effects on population nutritional status. There is a need for more similar studies, such as exploring the potential impacts of introducing iron biofortified foods into the UK, as iron deficiency is fairly common in many segments of the UK population (Public Health England 2018). However, as any such modeling study will rely on data on the nutritional efficacy of biofortified foods, more randomized controlled trials assessing this are also required.

Overall, considering the number of studies and the range of foods, nutrients, and research domains in the literature, research on each crop–nutrient combination in each domain in HICs is scarce, or in some cases entirely absent. There is also a notable mismatch between the list of foods tested for nutrient bioavailability (maize, cassava, rice, leafy greens, wheat, beans) or functionality (leafy greens, wheat, cabbage), and those assessed for consumer acceptability (apples, tomatoes, peppers, spinach, broccoli, arugula, potatoes, eggs) in HICs, which limits the potential impact of research in both domains. There also appears to be a misalignment between what micronutrients received most attention in the literature and what deficiencies are most common in HICs. For example, in the UK, suboptimal intakes are most prevalent for vitamin D, folate, Fe, I, and Zn (Public Health England 2018), and across Europe vitamin D is the micronutrient of most concern (Mensink et al. 2013). By contrast, most studies identified in this review focused on Se or PVA, which are arguably less relevant to key nutritional inadequacies in HIC contexts. And while it is important to bear in mind that the findings of certain types of research (e.g., bioavailability tests *in vitro* or using animal models) conducted in LMICs that were not included in the present review may also be relevant in HICs (e.g., Nathani et al. 2023), there are clearly important research gaps in areas sensitive to differences in the socio-economic context, such as the cultural and sensory acceptability of biofortified foods, willingness to pay for products with different attributes, the nutritional efficacy of biofortified foods when prepared in ways that are appealing to HIC consumers, and potential costs and benefits of different dietary interventions.

Strengths and limitations

A key strength of our study is the use of a systematic, transparent and reproducible methodology for identifying available evidence, which enabled us to uncover the types of existing research on the topic and determine gaps in the literature. One challenge we faced during the design of the study is the lack of consistency in the literature regarding the use of the term "biofortification", with these foods often being referred to using different terms. Whilst efforts were made to locate studies using alternative terminology by including a range of search terms describing nutrient enrichment in our query strings, it is possible that some articles not using any of our selected terms were missed. Furthermore, there may be more research on biofortified foods in the private sector that is not publicly available due to the commercial competitiveness of these organizations. Nonetheless, the paucity of research on the topic in HICs evident in some recent global systematic reviews can dispel some concerns regarding the comprehensiveness of our search strategy.

Another related issue is the lack of a universally agreed definition of biofortification (Kellogg et al. 2022). Here, we used a broad definition that includes all types of food and micronutrient enrichment via any method before harvest, in order to encompass the breadth of potentially available evidence. However, it is worth noting that there is an ambiguous area after harvest but before further processing–exemplified by the exposure of freshly picked mushrooms to UV light to trigger vitamin D synthesis (see e.g., Urbain et al. 2011)–that we did not consider to be biofortification according to our definition, but which could be argued to be included in this category. In addition, certain practices used in regenerative agriculture may also contribute to enhanced crop micronutrient content, but these may not necessarily be considered biofortification as the main aim is not nutrient enrichment. Another limitation of our study, intrinsic to scoping reviews, is that while it makes a valuable contribution to the literature by identifying and synthesizing research evidence in a so-far overlooked area, it does not undertake quality assessment and thus cannot speak to the confidence of findings of identified studies. Lastly, we acknowledge that only articles available in English were included in this review, which means that potentially relevant research in languages other than English may have been missed.

Conclusion

While there is a growing body of research focusing on the development of biofortified crops, these efforts must be guided by and complemented with an understanding of how effective these foods could be at improving nutrition-related public health in different real-world contexts. Our results demonstrate that the potential of biofortified foods to address micronutrient shortfalls in HICs merits further study. There is a need to better understand potential barriers to and facilitators of uptake of biofortified foods in HIC contexts, particularly among groups most affected by suboptimal micronutrient intakes. Such work will facilitate the development of strategies for the successful integration of biofortified foods into food systems in ways that their nutritional benefits can reach those who need them most. It is hoped that our study will help guide such efforts.

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Authors contributions

BZG and SJC designed the study, BZG conducted the literature searches and screened titles and abstracts, BZG and SJC assessed full-text articles for eligibility, BZG and BM extracted the data, BZG and SJC interpreted the results, and BZG, SJC, JW and PJ wrote the manuscript.

Disclosure statement

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Data availability statement

The authors confirm that the data supporting the findings of this study are available within the article and its supplementary materials.

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