<span id="page-0-2"></span><span id="page-0-1"></span>

# **Can Improved Legume Varieties Optimize Iron Status in Low- and Middle-Income Countries? A Systematic Review**

**Linet N Mutwiri,[1,](#page-0-0)[2](#page-0-1) Florence Kyallo[,1](#page-0-0) Beatrice Kiage[,1](#page-0-0) Bart Van der Schueren,[2,](#page-0-1)[3](#page-0-2) and Christophe Matthy[s2,](#page-0-1)[3](#page-0-2)**

<span id="page-0-0"></span><sup>1</sup> School of Food and Nutrition Sciences, Jomo Kenyatta University of Agriculture and Technology, Nairobi, Kenya; <sup>2</sup>Nutrition & Obesity Unit, Clinical and Experimental Endocrinology, Department of Chronic Diseases, Metabolism and Aging, KU Leuven, Leuven, Belgium; and <sup>3</sup>Department of Endocrinology, University Hospitals Leuven, Leuven, Belgium

#### **ABSTRACT**

Iron and zinc deficiencies are some of the most widespread micronutrient deficiencies in low- and middle-income countries (LMIC). Dietary diversification, food fortification, nutrition education, and supplementation can be used to control micronutrient deficiencies. Legumes are important staple foods in most households in LMIC. Legumes are highly nutritious (good sources of essential minerals, fiber, and low glycemic index) and offer potential benefits in addressing nutrition insecurity in LMIC. Several efforts have been made to increase micronutrient intake by use of improved legumes. Improved legumes have a higher nutrient bioavailability, lower phytate, or reduced hard-to-cook (HTC) defect. We hypothesize that consumption of improved legumes leads to optimization of zinc and iron status and associated health outcomes. Therefore, the objective of this review is to examine the evidence on the efficacy of interventions using improved legumes. Nine relevant studies are included in the review. Consumption of improved legumes resulted in a ≥1.5-fold increase in iron intake. Several studies noted modest improvements in biomarkers of iron status [hemoglobin (Hb), serum ferritin (SF), and transferrin receptor] associated with consumption of improved legumes. Currently, no efficacy studies assessing the relation between consumption of improved legumes and zinc status are available in the literature. Evidence shows that, in addition to repletion of biomarkers of iron status, consumption of improved legumes is associated with both clinical and functional outcomes. The prevalence of iron deficiency (ID) decreases with consumption of improved legumes, with increases of ≤3.0 g/L in Hb concentrations. Improvement in cognition and brain function in women has been reported as well. However, further research is necessary in more at-risk groups and also to show if the reported improvements in status markers translate to improved health outcomes. Evidence from the included studies shows potential from consumption of improved legumes suggesting them to be a sustainable solution to improve iron status. Adv Nutr 2020;11:1315–1324.

Keywords: low- and middle-income countries, micronutrients, iron, legumes, common bean, nutritional status

## **Introduction**

Global data indicate widespread prevalence of chronic micronutrient deficiencies in many low- and middle-income countries (LMIC). Co-occurrence of multiple micronutrient deficiencies in the same population is not uncommon [\(1\)](#page-8-0).

Supplemental Methods and Supplemental Tables 1 and 2 are available from the

"Supplementary data" link in the online posting of the article and from the same link in the online table of contents at [https://academic.oup.com/advances/.](https://academic.oup.com/advances/)

Micronutrient deficiency increases morbidity and mortality rates and has long-lasting effects on physical and mental growth and consequently on the development of populations. Iron and zinc deficiencies are some of the main deficiencies of public health concern in LMIC [\(2,](#page-8-1) [3\)](#page-8-2). Iron deficiency results in microcytic anemia, reduced work capacity, and impaired immune and endocrine function [\(4\)](#page-8-3). Zinc is essential for several aspects of metabolism and cellular growth, with deficiency decreasing resistance to infections and limiting growth  $(5)$ .

Dietary diversification, food fortification, and supplementation are the main strategies that have been used to prevent and combat micronutrient deficiencies [\(3\)](#page-8-2). Tackling iron and zinc deficiencies in LMIC could include combining dietary diversification and optimizing the bioavailability of specific nutrients, preferably by use of a highly consumed and

VLIR-UoS, Belgium, provided the funding for this study.

Author disclosures: The authors report no conflicts of interest.

This is a review article and as such does not require ethical approval.

Address correspondence to CM (e-mail: [christophe.matthys@uzleuven.be\)](mailto:christophe.matthys@uzleuven.be).

Abbreviations used: BI, body iron; CRP, C-reactive protein; Hb, hemoglobin; HTC, hard-to-cook; ID, iron deficiency; IDA, iron deficiency anemia; LMIC, low- and middle-income countries; lpa, low phytic acid; NaFeEDTA, ferric sodium ethylenediaminetetraacetic acid; PF, plasma ferritin; PHA-L, phytohemagglutinin; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; SF, serum ferritin; sTFR, soluble transferrin receptor; WRA, women of reproductive age.

culturally well-accepted food category, such as legumes. Legumes form a major part of the traditional diet in LMIC [\(6\)](#page-8-5). They are characterized as a good source of protein, fiber, resistant starch, polyphenols, and a variety of micronutrients and thus have a huge potential to meet nutrition-related health goals [\(7\)](#page-8-6). In several cultures, the positive characteristics of legumes have been ignored because legumes are associated with prolonged cooking time leading to loss of nutrients [\(8\)](#page-8-7) and high demand for charcoal, firewood, or gas. Phytic acid and polyphenols inhibit iron and zinc absorption from legumes in the gut [\(9\)](#page-8-8). These negative characteristics have stimulated researchers to develop improved varieties with a focus on increased micronutrient content  $(10, 11)$  $(10, 11)$  $(10, 11)$ , reduced hard-to-cook (HTC) defect [\(8\)](#page-8-7), or low phytic acid content [\(9,](#page-8-8) [12\)](#page-8-11). The average concentrations of iron, zinc, and phytic acid in nonimproved beans are 5.5 mg/100 g, 3.5 mg/100 g [\(13\)](#page-8-12), and 1000 mg/100 g [\(14\)](#page-8-13), respectively. The HTC defect is a hardening phenomenon that occurs in the cotyledon. Adverse conditions during storage, such as high temperatures ( $\geq$ 25°C) and high relative humidity ( $\geq$ 65%), predispose beans to the HTC phenomenon. Beans with the HTC defect are characterized by extended cooking times [\(3\)](#page-8-2), loss of flavor and color, and lower nutritive value (due to leaching of soluble solids and electrolytes) [\(4,](#page-8-3) [5\)](#page-8-4).

Promoting and incorporating (improved and nonimproved) legumes in the traditional diet is part of the diversification strategy to tackle micronutrient deficiencies. For instance, various efforts to promote legume consumption have been made in various regions in Asia [\(15\)](#page-8-14), Africa [\(14,](#page-8-13) [15\)](#page-8-14), and Latin America [\(16,](#page-8-15) [17\)](#page-8-16). The incorporation of improved legumes in the daily diet should result in improved nutrition status and associated health outcomes. Use of randomized controlled efficacy trials to demonstrate the effect of improved foods on status and health indicators is a first step to inform and support the continuation of research to examine effectiveness of programs in noncontrolled conditions. Such information is important for evaluation of interventions aimed at promoting legumes for mitigating micronutrient malnutrition and associated health outcomes. Currently, there is a lack of integration of available evidence on the impact of consumption of improved legume varieties in LMIC. This article aims to evaluate the efficacy of improved legume interventions on iron and zinc status and associated health outcomes.

## **Methods**

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were used to report this systematic review. An internal protocol for the review process was developed.

#### **Search methods**

A database search was first conducted in PubMed, Embase, and the Cochrane Library (**Supplemental Methods**). The general search strategy was developed following the Population, Intervention, Comparison, and Outcome model:

population (people living in LMIC), intervention (consumption of improved legumes), comparator (not applicable), and outcome (improvement in zinc and iron status based on established indicators of body stores and clinical/health outcomes). The search string was developed for use in the different databases (Supplemental Methods). References from the identified publications were then screened for additional relevant studies. Google Scholar was also used to search for pertinent documents based on key words. The last search was performed on February 22, 2019.

#### **Eligibility criteria**

The review included only papers published in English. There were no restrictions imposed on date of publication. Randomized controlled trials in humans living in LMIC were included. Studies assessing the efficacy of improved legumes on intake, status, and health outcomes were included. Studies conducted in populations with specific clinical diagnoses related to severe zinc- and iron-related deficiencies or severe illnesses were excluded. The primary outcomes considered in this review are biomarkers of zinc and iron status, and clinical/health outcomes (**[Table 1](#page-2-0)**). Measurement of iron status was preferably through combination of different biomarkers—hemoglobin (Hb), serum transferrin receptor (sTFR), serum ferritin (SF), and body iron (BI)—to increase specificity and sensitivity  $(18)$ . The search for a reliable biomarker of zinc has been challenging because there is no functional reserve or body store of available zinc, and also because zinc homeostasis is complex [\(19\)](#page-8-18). Additionally, zinc deficiency is characterized by very general signs and symptoms such as lowered immunity and growth impairment, which can also have many other causes and thus might not specifically point to zinc deficiency [\(20\)](#page-8-19). For zinc status, serum, plasma, hair, or urinary zinc can be used. Plasma zinc is, however, the most useful biomarker because it responds to increases and decreases in zinc intake  $(21)$ . Some limitations in the use of plasma zinc concentration include lack of sensitivity to detect marginal zinc deficiency, diurnal variations, fluctuations influenced by recent meal consumption, confounding by inflammation, and contamination from skin and collection materials during sample collection [\(18,](#page-8-17) [19\)](#page-8-18). Health outcomes associated with iron and zinc intakes are as described in the intervention studies, and from public health and nutrition reports [\(Table 1\)](#page-2-0). Adverse side effects (if any) were considered to be secondary outcomes.

#### **Identification of studies**

Identified studies were screened according to the inclusion criteria to select relevant ones (LM and CM). Prior to this, duplicates were removed. One reviewer (LM) screened the titles. Abstracts of selected studies were then reviewed independently by LM, FK, and CM. If insufficient information was provided in the title and abstract, the full text was read by 1 reviewer (LM) to determine whether the article met the inclusion criteria. Reasons for the exclusion of studies were described using the PRISMA flowchart (**[Figure 1](#page-2-1)**).

<span id="page-2-0"></span>**TABLE 1** Summary of intake, status, and health indicators for zinc and iron

<b>Nutrient</b>	<b>Intake indicators</b>	<b>Status markers</b>	<b>Health outcomes</b>
$\text{Iron}^1$	Intake from legumes (improved and nonimproved)	Hemoglobin (Hb) Serum ferritin (SF) Soluble transferrin receptor (sTFR) Body iron (BI): gives a guantitative estimate of the size of the body iron store and is estimated as the ratio of sTFR and SF using Cook equation <sup>2</sup>	Iron deficiency anemia Impaired brain function Reduced cognitive function Reduced learning and work capacity Increased risk of mortality
Zinc <sup>3</sup>	Intake from legumes (improved and nonimproved)	Serum/plasma zinc Urinary zinc Hair zinc	Delayed growth; stunting Delayed sexual maturation Impaired immunity; recurrent infections Diarrhea Dermatitis Dementia

<span id="page-2-2"></span><sup>1</sup> Source: Lynch et al. [\(4\)](#page-8-3). <sup>2</sup>Source: Cook et al. [\(22\)](#page-8-21).

<span id="page-2-4"></span><span id="page-2-3"></span><sup>3</sup> Source: King et al. [\(21\)](#page-8-20).

## **Data collection**

First, a standardized form was developed and piloted on 3 papers to assess usability in the included studies (LM, CM). Information extracted from the included studies comprised of: study information [author(s), title, journal, year of publication]; study location; sample size; study design; participant description (age, gender, characteristics of participants); intervention (description of legume food– based intervention); study duration; status and/or clinical/health outcomes. Extraction was done by 1 reviewer (LM) (**[Tables 2](#page-3-0)** and **[3](#page-5-0)**). Extracted data were then scrutinized by 2 reviewers (FK and CM).

<span id="page-2-1"></span>

**FIGURE 1** Flowchart of literature search.



(Continued)

(Continued)

<span id="page-3-0"></span>TABLE 2 Summary of the legume food-based iron intervention studies conducted in low- and middle-income countries<sup>1</sup> **TABLE 2** Summary of the legume food–based iron intervention studies conducted in low- and middle-income countrie[s1](#page-4-0)



**TABLE 2** (Continued)

**TABLE 2** (Continued)

## **Risk of bias**

Domain-based risk of bias was assessed using a standardized quality assessment tool by 2 authors (CM and LM) as described in the Cochrane Handbook for Systematic Reviews of Interventions (**Supplemental Tables 1** and **2**). The final manuscript was read by all the authors.

## **Results**

CIAT, International Center for Tropical Agriculture; Hb, hemoglobin; PF, plasma ferritin; SF, serum ferritin; SMC, code used to identify a CIAT bean line [colored drought tolerant bean with high zinc and iron content (not

CIAT, International Center for Tropical Agriculture; Hb, hemoglobin; PF, plasma ferritin; SF, serum ferritin; SMC, code used to identify a CIAT bean line [colored drought tolerant bean with high zinc and iron content (not

of reproductive age.

<span id="page-4-0"></span>of reproductive age

[Figure 1](#page-2-1) shows the flowchart of the literature search and study selection. Nine studies were included in the final review. The studies were from rural communities in countries in sub-Saharan Africa ( $n = 6$ ) and Latin America ( $n = 3$ ). All studies used improved legume varieties based on the following strategies: fortification  $[n = 2]$ , fortified with either ferric sodium ethylenediaminetetraacetic acid (NaFeEDTA) or ferrous sulphate, FeSO<sub>4</sub>], biofortification ( $n = 4$ , focus on iron), modification ( $n = 1$ , low phytate content), and 1 study combining different strategies [\(Table 2\)](#page-3-0).

In all trials, iron intake (grams per day) was higher in participants who consumed meals prepared using the improved legumes compared with those in the control group. Consumption of improved legumes resulted in a  $\geq$ 1.5fold increase in daily iron intake [\(Table 2\)](#page-3-0). The higher iron concentration in the improved bean groups resulted in significant differences in iron intake [\(27\)](#page-8-26), fractional iron absorption [\(9\)](#page-8-8), and total amount of iron absorbed [\(9,](#page-8-8) [31\)](#page-8-30) when compared with nonimproved beans. Difference in iron concentration in meals made from improved beans and nonimproved beans was nonsignificant in the study by Pachón et al. [\(25\)](#page-8-24).

Different markers (or a combination thereof) were used to measure iron status: Hb  $(n = 6)$ ; SF  $(n = 5)$ ; plasma ferritin (PF;  $n = 1$ ); BI ( $n = 4$ ); and sTFR ( $n = 4$ ). Improvements in iron status outcomes by use of improved legumes were reported as increases in Hb [\(19,](#page-8-18) [32\)](#page-8-31), SF [\(19,](#page-8-18) [27,](#page-8-26) [32\)](#page-8-31), PF [\(9\)](#page-8-8), BI [\(19,](#page-8-18) [27,](#page-8-26) [32\)](#page-8-31), and sTFR [\(23\)](#page-8-22) concentrations (**Table 4**). **[Figure 2](#page-6-0)** [shows the change in Hb, SF, sTFR, and BI from](#page-5-1) 4 studies [\(20,](#page-8-19) [26,](#page-8-25) [27,](#page-8-26) [32\)](#page-8-31). In each of the 4 studies, participants consumed varied amounts of iron from both improved and nonimproved legumes during the study period [\(Figure 2,](#page-6-0) [Table 4\)](#page-5-1). Some studies reported on clinical and functional outcomes associated with the reported improvement in iron biomarker status: for instance, reduction in the prevalence of iron deficiency (ID), and iron deficiency anemia (IDA) [\(23\)](#page-8-22); improvement in cognitive performance [\(28\)](#page-8-27); and changes in brain activity [\(29\)](#page-8-28) [\(Table 3\)](#page-5-0).

Specific nutrient-related health outcomes were assessed in 4 studies. Consumption of cowpea flour with a high iron content (11.5 mg Fe/100 g) resulted in a 30% and 47% significant decrease in prevalence of ID and IDA, respectively, in children aged  $5-12$  y  $(23)$ . One study used an array of tests to assess cognitive outcomes in women of reproductive age [\(28\)](#page-8-27). Changes in status outcomes (Hb, SF, sTFR, and BI) were used to predict changes in cognitive performance. The study results showed cognitive improvement with increases in SF concentrations after consumption of improved beans. SF concentrations increased by a mean of 2.4  $\mu$ g/L and

<span id="page-5-0"></span>**TABLE 3** Summary of study results of the legume food–based iron intervention studies conducted in low- and middle-income countries[1](#page-5-2)



<span id="page-5-2"></span><sup>1</sup>+P < 0.1; <sup>∗</sup>P < 0.05; ∗∗P < 0.01; ∗∗∗P < 0.001. AGP, α1-acid glycoprotein; BI, body iron; CRP, C-reactive protein; CRT, cued recognition task; EEG, electroencephalography; Hb, hemoglobin; ID, iron deficiency; IDA, iron deficiency anemia; PF, plasma ferritin; SF, serum ferritin; SMS, Sternberg memory search; sTFR, soluble transferrin receptor.

5.3 μg/L in participants consuming nonimproved and improved beans, respectively. The increase in SF in the women consuming improved beans was associated with a >2-fold increase in both speed and efficiency of memory relative to those consuming nonimproved beans. Another study assessed iron bioavailability from meals cooked with differing phytate content [\(26\)](#page-8-25). Iron bioavailability from meals cooked with low phytic acid (lpa) beans, ironbiofortified beans, and conventional beans was compared. The observed iron absorption from both the improved beans

<span id="page-5-1"></span>**TABLE 4** Relative difference in Hb, SF, sTFR, and BI status from 4 legume food–based iron intervention studies conducted in low- and middle-income countries[1](#page-5-3)



<span id="page-5-3"></span><sup>1</sup>Difference (Diff.) in iron biomarker status is obtained by (endline reading minus baseline reading/baseline reading) × 100. n/a indicates that a particular biomarker was not assessed. Effect of legume food–based interventions on iron biomarker status (Hb, SF, sTFR, and BI): +P < 0.1; \*P < 0.05; \*\*P < 0.01; \*\*\*P < 0.001 shows significance of differences in baseline and endline measurements between the improved and nonimproved legume groups. BI, body iron; Hb, hemoglobin; SF, serum ferritin; sTFR, soluble transferrin receptor.

<span id="page-6-0"></span>

**FIGURE 2** Change in iron biomarker status from consumption of improved and nonimproved legumes. The graphs illustrate the change in iron biomarker status: (A) Hb; (B) SF; (C) sTFR, and (D) BI, from baseline and endline assessments associated with consumption of improved and nonimproved legumes from 4 studies: Haas et al., 2016 [\(27\)](#page-8-26); Abizari et al., 2012 [\(23\)](#page-8-22); Finkelstein et al., 2019 [\(30\)](#page-8-29); and Schümann et al., 2005 [\(24\)](#page-8-23). The number of intervention days for each study was 128 [\(27\)](#page-8-26), 210 [\(23\)](#page-8-22), 180 [\(30\)](#page-8-29), and 70 [\(24\)](#page-8-23) d. Total iron intake from improved legumes was 1856 mg [\(27\)](#page-8-26); 3622.5 mg [\(23\)](#page-8-22); 3420 mg [\(30\)](#page-8-29); and 2450 mg [\(24\)](#page-8-23). Total iron intake from nonimproved legumes was 1040 mg [\(27\)](#page-8-26); 2173.5 mg [\(23\)](#page-8-22); 1980 mg [\(30\)](#page-8-29); and 259 mg [\(24\)](#page-8-23). BI, body iron; Hb, hemoglobin; SF, serum ferritin; sTFR, soluble transferrin receptor.

[i.e., lpa beans (8.6%; 421  $\mu$ g)] and iron-biofortified beans (7.3%; 431 µg) was ∼1.5 times higher than that from the conventional beans (8.0%; 278  $\mu$ g). The same study also reported gastrointestinal disturbances (vomiting, loose stool, nausea, stomach discomfort, and flatulence) in ∼95% of the participants consuming meals made from the lpa beans. Food analysis revealed the presence of phytohemagglutinin (PHA-L) in the cooked lpa beans, which was associated with the observed side effects. The iron-biofortified beans and control beans were not associated with these adverse effects.

## **Discussion**

The review summarizes the available evidence for the efficacy of improved legumes with regard to iron and zinc intake, hematological indicators, and health outcomes. No studies assessing the efficacy of zinc were found, emphasizing the high need for randomized controlled trials to evaluate the effect of improved legumes on zinc status and related health outcomes. Biofortified bean varieties rich in zinc were released in Colombia in 2016 [\(33\)](#page-8-32) and Tanzania in 2018 [\(34\)](#page-9-0).

Most of the available information is for the ironbiofortified beans in women of reproductive age (WRA) from sub-Saharan Africa. These studies focusing on WRA were conducted in Rwanda [\(19,](#page-8-18) [24,](#page-8-23) [27,](#page-8-26) [31,](#page-8-30) [35\)](#page-9-1). Their findings suggest that the use of improved legumes as a food-based intervention results in improved iron status. Incorporation of improved beans in the daily diet met ≤75% of daily iron requirements in WRA. If embraced, the improved beans show potential to address ID and IDA in vulnerable population groups in LMIC. ID, and specifically IDA, remains one of the most important and severe deficiencies of public health concern in LMIC. All age groups are vulnerable [\(36\)](#page-9-2). The most vulnerable population groups for ID and IDA are children aged <5 y, pregnant women, and WRA. The increased risk is attributed to increased iron needs during growth, pregnancy, and childbirth and iron losses during menstruation [\(37,](#page-9-3) [38\)](#page-9-4). Findings from the Rwandan bean studies were consistent with a study using iron-biofortified pearl millet in iron-deficient Indian children to resolve deficiency [\(38\)](#page-9-4).

Improvements in cognitive performance and brain activity have been linked to improvements in iron status after consuming improved beans with additional iron [\(24,](#page-8-23) [27\)](#page-8-26). Based on past research, ID leads to delayed brain development in children, with possibilities of affected neural functioning beyond childhood [\(39\)](#page-9-5). Changes in functional (cognitive or affective) outcomes associated with changes in systemic iron result from changes in neural function. Various irondependent mechanisms have been linked with changes in neural function. Hemoglobin and ferritin concentrations influence the magnitude of cognitive demand and subsequently performance behavior [\(29\)](#page-8-28). Ferritin has been linked with the integrity of neurotransmitter systems, and hemoglobin associated with energy provision for expressing information processing results [\(29\)](#page-8-28). The findings on improvements in cognitive performance and brain activity [\(24,](#page-8-23) [27\)](#page-8-26) are in line with evidence on the effects of ID on different learning domains and mediation of changes in the brain reported elsewhere [\(40\)](#page-9-6).

An absorption study assessing the potential of beans as a vehicle of iron biofortification reported higher absorption rates in nonimproved beans [\(12\)](#page-8-11). Fractional iron absorption for improved beans and nonimproved beans was reported to be 7.3% and 9.2%, respectively. Higher phytic acid concentration in the improved beans was suggested to be responsible. Phytic acid is a major inhibitor of zinc and iron absorption from beans [\(12\)](#page-8-11). Positive correlations between phytic acid and iron concentrations have been found in improved beans [\(12,](#page-8-11) [21,](#page-8-20) [41\)](#page-9-7). Phytic acid concentrations increase with increase in iron concentrations in improved (biofortified) beans. Absorption rates in improved beans (7.3%) and nonimproved beans (9.2%) were used to estimate iron absorption rates in other studies that used similar beans [\(19,](#page-8-18) [21,](#page-8-20) [24,](#page-8-23) [27,](#page-8-26) [31\)](#page-8-30). Consumption of these improved beans resulted in higher iron intake (14.5 mg/d compared with 8.6 mg/d from nonimproved beans) and higher total absorption (1.06 mg/d compared with 0.79 mg/d from nonimproved beans) [\(19,](#page-8-18) [21,](#page-8-20) [27\)](#page-8-26).

In an effort to further improve iron bioavailability from improved beans, the efficacy of improved beans with varied iron and phytic acid concentrations was assessed. Studies have reported on the proportion of additional iron (as influenced by phytate concentration) absorbed from improved bean meals compared with nonimproved bean meals [\(21,](#page-8-20) [31\)](#page-8-30). In 1 study, the high phytic acid concentration associated with improved beans limited their effectiveness [\(41\)](#page-9-7). Dephytinization resulted in higher quantities of iron absorbed from the improved beans compared with the

nonimproved beans. The negative influence of phytic acid on iron bioavailability informed development of improved beans' lpa content [\(42\)](#page-9-8). The reduction in phytic acid content in these improved (lpa) beans by ∼90% improved iron bioavailability. A study using the improved (lpa) beans showed lower than expected iron bioavailability [\(26\)](#page-8-25). The low fractional iron absorption was hypothesized to be due to the incomplete hydrolysis (during cooking) of PHA-L resulting in residues in the cooked beans. Hemagglutinins have been associated with irritation in the digestive tract [\(43\)](#page-9-9) and reduction in iron bioavailability [\(44\)](#page-9-10). Following this, to conclusively report on the efficacy of lpa beans used for the study, the HTC defect and cooking times that affect hydrolysis of PHA-L need to be studied.

Overall, the evidence shown in the current review warrants the continuation of research to assess efficacy of both improved legumes and legume-based meals. Consumption of iron-biofortified beans has been shown to result in positive changes in iron status and consequently ID. Findings also show the potential of improved beans to increase cognitive performance, though further studies in different subgroups of the population are needed to provide more conclusive evidence. Evidence also suggests that to optimize iron bioavailability from beans, agriculturalists should target phytic acid in the improved varieties as an additional trait. Food processing technologies have been reported to improve the bioavailability of iron and zinc by reducing phytate concentrations through soaking, sprouting, phytase enzymatic treatment, and fermentation [\(37,](#page-9-3) [38\)](#page-9-4). Iron absorption from meals has also been shown to be enhanced by mineral chelating peptides [\(45\)](#page-9-11), vitamins A and C, and saccharides [\(46\)](#page-9-12). Nevertheless, the majority of the improved legumes in this review are based on agricultural breeding techniques. Additionally considering use of food processing technologies to augment research on legumes improved through agricultural techniques would be an innovative approach. All in all, use of improved legumes could be a promising long-term approach to improve iron (and possibly even other micronutrients) status and remedy deficiencyrelated health outcomes. More specifically, comparison of improved beans alongside other improved grains (e.g., pearl millet and rice) suggests strong evidence on the efficacy of improved beans in repletion and maintenance of iron status and some functional outcomes [\(47\)](#page-9-13).

The strengths of this review lie in the included studies, which are randomized controlled studies conducted over sufficient duration to assess changes in iron status indicators. We acknowledge the paucity of randomized controlled trials in the literature. We recommend further research aimed at conducting efficacy trials of zinc-biofortified legume foods to assess if they support the present findings and exhibit intakestatus-health relations in target populations. Additionally the findings of this review cannot be generalized because of the heterogeneity of methodology in the different trials. The findings suggest improved legumes to be a viable intervention to improve iron biomarker status thus addressing IDA. Further research is needed in diverse age groups and regions. Additional health outcomes such as physical activity related to improved legume consumption should also be studied. This will allow evidence-based recommendations to enable large-scale adoption of improved legumes to address micronutrient deficiencies.

#### **Acknowledgments**

The authors thank VLIR-UoS, Belgium, through the Legumes Centre of Excellence in Food and Nutrition Security (LCEFoNS), for their financial assistance.

The authors' responsibilities were as follows—conception: LM, FK, and CM; analysis: LM, FK, and CM; original draft preparation: LM, FK, and CM; manuscript review and editing: LM, FK, BK, BVS, and CM; supervision: FK, BK, BVS, and CM; and all authors: read and approved the final manuscript.

#### **References**

- <span id="page-8-0"></span>1. Global Nutrition Report. Global nutrition report 2018 – executive summary [Internet]. [cited 2019 Jul 2]. Available from: https:// [globalnutritionreport.org/reports/global-nutrition-report-2018/.](https://globalnutritionreport.org/reports/global-nutrition-report-2018/)
- <span id="page-8-1"></span>2. World Bank Group. World Bank country and lending groups [Internet]. [cited 2019 Jul 2]. Available from: https://datahelpdesk.worldbank.org/ [knowledgebase/articles/906519-world-bank-country-and-lending](https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups)groups.
- <span id="page-8-2"></span>3. Bhutta ZA, Salam RA, Das JK. Meeting the challenges of micronutrient malnutrition in the developing world. Br Med Bull 2013;106:7–17.
- <span id="page-8-3"></span>4. Lynch S, Pfeiffer CM, Georgieff MK, Brittenham G, Fairweather-Tait S, Hurrell RF, Mcardle HJ, Raiten DJ. Biomarkers of Nutrition for Development (BOND)—iron review. J Nutr 2018;148:1001–67.
- <span id="page-8-4"></span>5. FAO and CAB International. Combating micronutrient deficiencies: food-based approaches. Rome: FAO, CAB International; 2011.
- <span id="page-8-5"></span>6. Nedumaran S, Abinaya P, Jyosthnaa P, Shraavya B, Rao P, Bantilan C. Grain legumes production, consumption and trade trends in developing countries. Working Paper Series No 60. ICRISAT Research Program, Markets, Institutions and Policies. International Crops Research Institute for the Semi-Arid Tropics, Telangana (India), 2015.
- <span id="page-8-6"></span>7. Akibode S, Maredia M. Global and regional trends in production, trade and consumption of food legume crops. Report submitted to Standing Panel on Impact Assessment (SPIA), CGIAR; 2011.
- <span id="page-8-7"></span>8. Kamau VW, Wafula EN, Sila DN, Makokha AN, Njoroge DM, Kinyanjui PK. The hard to cook defect in common beans: understanding the effect of storage conditions on physical, cooking and nutritional properties. Department of Food Science and Technology, Jomo Kenyatta University of Agriculture & Technology, Nairobi, Kenya; 2013. pp. 969–75.
- <span id="page-8-8"></span>9. Petry N, Egli I, Gahutu JB, Tugirimana PL, Boy E, Hurrell R. Phytic acid concentration influences iron bioavailability from biofortified beans in Rwandese women with low iron status. J Nutr 2014;144(11):1681–7.
- <span id="page-8-9"></span>10. Garcia-Casal MN, Peña-Rosas JP, Giyose B, Bechoff A, Blancquaert D, Birol E, Bouis H, Boukerdenna H, Boy E, Brunoro N, et al. Staple crops biofortified with increased vitamins and minerals: considerations for a public health strategy. Ann N Y Acad Sci 2017;1390(1):3–13.
- <span id="page-8-10"></span>11. Bouis H, Saltzman A, Low J, Ball A, Covic N. An overview of the landscape and approach for biofortification in Africa. Afr J Food Agric Nutr Dev 2017;17(2):11848–64.
- <span id="page-8-11"></span>12. Petry N, Egli I, Gahutu JB, Tugirimana PL, Boy E, Hurrell R. Stable iron isotope studies in Rwandese women indicate that the common bean has limited potential as a vehicle for iron biofortification. J Nutr 2012;142(3):492–7.
- <span id="page-8-12"></span>13. Beebe S, Gonzalez AV, Rengifo J. Research on trace minerals in the common bean. Food Nutr Bull 2000;21(4):387–91.
- <span id="page-8-13"></span>14. Barampama Z, Simard RE. Nutrient composition, protein quality and antinutritional factors of some varieties of dry beans (Phaseolus vulgaris) grown in Burundi. Food Chem 1993;47(2):159–67.
- <span id="page-8-14"></span>15. FAO. Future smart food: rediscovering hidden treasures of neglected and underutilized species for zero hunger in Asia. Bangkok: FAO.2018.
- <span id="page-8-15"></span>16. International Food Policy Research Institute, Concern Worldwide, and Welthungerhilfe. Global hunger index: the challenge of hidden hunger. 2014.
- <span id="page-8-16"></span>17. Larochelle C, Alwang J. Impacts of improved bean varieties on food security in Rwanda., Agricultural & Applied Economics Association's 2014 AAEA Annual Meeting, Minneapolis 2014.
- <span id="page-8-17"></span>18. Zimmermann MB. Methods to assess iron and iodine status. Br J Nutr 2008;99(S3):S2–9.
- <span id="page-8-18"></span>19. Zlotkin SH, Cherian MG. Hepatic metallothionein as a source of zinc and cysteine during the first year of life. Pediatr Res 1988;24(3): 326–9.
- <span id="page-8-19"></span>20. Wieringa FT, Dijkhuizen MA, Fiorentino M, Laillou A. Determination of zinc status in humans: which indicator should we use? Nutrients 2015;7(5):3252–63.
- <span id="page-8-20"></span>21. King JC, Brown KH, Gibson RS, Krebs NF, Lowe NM, Siekmann JH, Raiten DJ. Biomarkers of Nutrition for Development (BOND)—zinc review. J Nutr 2016;146(4):858S–85S.
- <span id="page-8-21"></span>22. Cook JD, Flowers CH, Skikne BS. The quantitative assessment of body iron. Blood 2003;101(9):3359–64.
- <span id="page-8-22"></span>23. Abizari AR, Moretti D, Zimmermann MB, Armar-Klemesu M, Brouwer ID. Whole cowpea meal fortified with NaFeEDTA reduces iron deficiency among Ghanaian school children in a malaria endemic area. J Nutr 2012;142:1836–42.
- <span id="page-8-23"></span>24. Schümann K, Romero-Abal M, Mäurer A, Luck T, Beard J, Murray-Kolb L, Bulux J, Mena I, Solomons N. Haematological response to haem iron or ferrous sulphate mixed with refried black beans in moderately anaemic Guatemalan pre-school children. Public Health Nutr 2005;8(6):572–81.
- <span id="page-8-24"></span>25. Pachón H, Ortiz DA, Araujo C, Blair MW, Restrepo J. Iron, zinc, and protein bioavailability proxy measures of meals prepared with nutritionally enhanced beans and maize. J Food Sci 2009;74(5):H147– 54.
- <span id="page-8-25"></span>26. Petry N, Rohner F, Gahutu JB, Campion B, Boy E, Tugirimana PL, Zimmerman MB, Zwahlen C, Wirth JP, Moretti D. In Rwandese women with low iron status, iron absorption from low-phytic acid beans and biofortified beans is comparable, but low-phytic acid beans cause adverse gastrointestinal symptoms. J Nutr 2016;146(5):  $970 - 5.$
- <span id="page-8-26"></span>27. Haas JD, Luna SV, Lung'aho MG, Wenger MJ, Murray-Kolb LE, Beebe S, Gahutu JB, Egli IM. Consuming iron biofortified beans increases iron status in Rwandan women after 128 days in a randomized controlled feeding trial. J Nutr 2016;146(8):1586–92.
- <span id="page-8-27"></span>28. Murray-Kolb LE, Wenger MJ, Scott SP, Rhoten SE, Lung'aho MG, Haas JD. Consumption of iron-biofortified beans positively affects cognitive performance in 18- to 27-year-old Rwandan female college students in an 18-week randomized controlled efficacy trial. J Nutr 2017;147:2109– 17.
- <span id="page-8-28"></span>29. Wenger MJ, Rhoten SE, Murray-Kolb LE, Scott SP, Boy E, Gahutu JB, Haas JD. Changes in iron status are related to changes in brain activity and behavior in Rwandan female university students: results from a randomized controlled efficacy trial involving iron-biofortified beans. J Nutr 2019;149(4):687–97.
- <span id="page-8-29"></span>30. Finkelstein JL, Mehta S, Villalpando S, Mundo-Rosas V, Luna SV, Rahn M, Shamah-Levy T, Beebe SE, Haas JD. A randomized feeding trial of iron-biofortified beans in school children in Mexico. Nutrients 2019;11(2):1–13.
- <span id="page-8-30"></span>31. Pinna K, Woodhouse LR, Sutherland B, Shames DM, King JC. Exchangeable zinc pool masses and turnover are maintained in healthy men with low zinc intakes. J Nutr 2001;131(9):2288–94.
- <span id="page-8-31"></span>32. Krebs NF. Update on zinc deficiency and excess in clinical pediatric practice. Ann Nutr Metab 2013;62(Suppl 1):19–29.
- <span id="page-8-32"></span>33. Beintema JJS, Gallego-Castillo S, Londoño-Hernandez LF, Restrepo-Manjarres J, Talsma EF. Scaling-up biofortified beans high in iron and zinc through the school-feeding program: a sensory acceptance study with schoolchildren from two departments in southwest Colombia. Food Sci Nutr 2018;6(4):1138–45.
- <span id="page-9-0"></span>34. Patricia O. Improved high-iron and zinc bean varieties for better nutrition [Internet]. [cited 2019 Jul 2]. Available from: [http://www.pabra-africa.org/improved-high-iron-and-zinc-bean](http://www.pabra-africa.org/improved-high-iron-and-zinc-bean-varieties-for-better-nutrition/)varieties-for-better-nutrition/.
- <span id="page-9-1"></span>35. Palmer N. High-iron beans: a new 'superfood' for Colombia [Internet]. CIAT website. [cited 2019 Aug 25]. Available: https://blog.ciat.cgiar.org/ [high-iron-beans-a-new-superfood-for-colombia/.](https://blog.ciat.cgiar.org/high-iron-beans-a-new-superfood-for-colombia/)
- <span id="page-9-2"></span>36. WHO. Iron deficiency anaemia. WHO; 2001.
- <span id="page-9-3"></span>37. Kassebaum NJ, Jasrasaria R, Naghavi M, Wulf SK, Johns N, Lozano R, Regan M, Weatherall D, Chou DP, Eisele TP, et al. A systematic analysis of global anemia burden from 1990 to 2010. Blood J 2015;123(5): 615–25.
- <span id="page-9-4"></span>38. Finkelstein JL, Mehta S, Udipi SA, Ghugre PS, Luna SV, Wenger MJ, Murray-Kolb LE, Przybyszewski EM, Haas JD. A randomized trial of iron-biofortified pearl millet in school children in India. J Nutr 2015;145(7):1576–81.
- <span id="page-9-5"></span>39. Pollitt E. Early iron deficiency anemia and later mental retardation. Am J Clin Nutr 1999;69(1):4–5.
- <span id="page-9-6"></span>40. Wenger MJ, DellaValle DM, Murray-Kolb LE, Haas JD. Effect of iron deficiency on simultaneous measures of behavior, brain activity, and energy expenditure in the performance of a cognitive task. Nutr Neurosci 2019;22(3): 196–206.
- <span id="page-9-7"></span>41. Petry N, Egli I, Gahutu JB, Tugirimana PL, Boy E, Hurrell R. Phytic acid concentration influences iron bioavailability from biofortified beans in Rwandese women with low iron status. J Nutr 2014;144(11):1681–7.
- <span id="page-9-8"></span>42. Petry N, Egli I, Campion B, Nielsen E, Hurrell R. Genetic reduction of phytate in common bean (Phaseolus vulgaris L.) seeds increases iron absorption in young women. J Nutr 2013;143(8):1219–24.
- <span id="page-9-9"></span>43. Ramadass B, Dokladny K, Moseley PL, Patel YR, Lin HC. Sucrose coadministration reduces the toxic effect of lectin on gut permeability and intestinal bacterial colonization. Dig Dis Sci 2010;55(10):2778–84.
- <span id="page-9-10"></span>44. Carrasco-Castilla J, Hernández-Álvarez AJ, Jiménez-Martínez C, Jacinto-Hernández C, Alaiz M, Girón-Calle J, Vioque J, Dávila-Ortiz G. Antioxidant and metal chelating activities of peptide fractions from phaseolin and bean protein hydrolysates. Food Chem 2012;135(3):1789–95.
- <span id="page-9-11"></span>45. Guo L, Harnedy PA, Li B, Hou H, Zhang Z, Zhao X, FitzGerald RJ. Food protein-derived chelating peptides: biofunctional ingredients for dietary mineral bioavailability enhancement. Trends Food Sci Technol 2014;37(2):92–105.
- <span id="page-9-12"></span>46. Christides T, Sharp P. Sugars increase non-heme iron bioavailability in human epithelial intestinal and liver cells. PLoS One 2013;8(12):e83031.
- <span id="page-9-13"></span>47. Finkelstein JL, Fothergill A, Hackl LS, Haas JD, Mehta S. Iron biofortification interventions to improve iron status and functional outcomes. Proc Nutr Soc 2019;78(02):197–207.