

Effectiveness of nutrition interventions in low- and middle-income countries: A meta-review

Authors

Ritu Rana¹, Kavitha Menon^{1,2}, Shuby Puthussery³, Anal Ravalia¹, Pooja Panchal^{1,2}, Gauri Vaze¹, Pei-Ching Tseng³, Dileep V. Mavalankar¹

Affiliations

¹Indian Institute of Public Health Gandhinagar, Gandhinagar, Gujarat, 382042, India

²Symbiosis School of Biological Sciences, Symbiosis International (Deemed University), India

³Institute for Health Research, University of Bedfordshire, Luton, Bedfordshire, LU2 8LE, UK

Correspondence

rrana@iiphg.org

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Ethics approval

Not applicable as this study does not include any primary data.

Conflict of Interest

None declared

ABSTRACT

Background: Undernutrition remains an unfinished agenda for a majority of low- and middle-income countries (LMICs). Numerous nutrition interventions have been implemented in LMICs and various indicators have been used to measure the impact of these interventions. The aim of this meta-review was to summarise the findings on the effectiveness of various nutrition interventions that have been implemented in LMICs on the WHO global nutrition targets-related outcomes. The six outcomes are- reducing stunting, wasting, anemia among women of reproductive age, low birthweight, childhood overweight, and improving exclusive breastfeeding. This study presents the results for one of the outcomes (stunting).

Methods: We conducted a comprehensive search on 21 electronic databases, including six regional and four systematic reviews (SRs) specific databases. Two researchers independently screened identified records against the inclusion criteria. Quality of included SRs were assessed using the AMSTAR tool. Extracted data were narratively synthesised examining the direction of impact. The review protocol was registered with the EPPI-Centre.

Results: Of 6,597 SRs initially identified, 28 SRs that assessed outcomes of WHO global nutrition targets-related outcomes were eligible for inclusion. We found 12 SRs that assessed stunting outcomes, these SRs synthesised 68 quantitative primary studies, from 29 LMICs. All included SRs were of high quality. Eight nutrition interventions were reported in the included SRs- five nutrition-specific ($n=9$) and three nutrition-sensitive ($n=3$). Among all interventions, two nutrition-specific (complementary feeding: $n=1$; dietary supplementation: $n=2$) interventions showed a positive effect.

Conclusion: This meta-review identified, two interventions, complementary feeding and dietary supplementation, with most frequently reported evidence of positive impact on stunting. In LMICs, public health policymakers should consider these two interventions for scaling-up.

Keywords: systematic-review, evidence-based, malnutrition, growth and development, child, meta-review

INTRODUCTION

Maternal and child undernutrition are the world's most serious economic, health and human development challenges [1]. Annually, undernutrition, that encompasses- stunting, wasting, underweight and/or micronutrient deficiencies contribute to an estimated 3.1 million (45%) child deaths worldwide [2]. Maternal and child undernutrition have adverse consequences for pregnancy outcomes, child morbidity and mortality, children's mental and motor development, and chronic diseases in later life [2, 3]. The impact of undernutrition is not limited to health-related outcomes, but can also affect educational performance, economic productivity, and human wellbeing [1, 3].

Globally, in 2011, an estimated 165 million children were stunted (height-for-age below -2sd) and 52 million were wasted (weight-for-height below -2sd) [4]. Recognising that accelerated action is needed to address the problem of undernutrition, the World Health Organisation (WHO), in 2012, specified six global nutrition targets to be achieved by 2025 [5]. The targets included- reducing childhood stunting, childhood wasting, anaemia among women of reproductive age, low birthweight (LBW), childhood overweight, and improving exclusive breastfeeding (EBF) rates in the first six months of life. Undernutrition remains an unfinished agenda for the majority of low- and middle-income countries (LMICs). In 2014, the global nutrition report revealed, a majority of LMICs were off-track to meet the global nutrition targets [6]. Furthermore, globally, in 2018, an estimated 149 million children were stunted and 49 million were wasted- reflecting slow reduction since 2011 [7].

Over the past several years, our understating of interventions for maternal and child undernutrition has improved. The 2008 Lancet maternal and child undernutrition series identified the crucial period (the first 1000 days- conception to a child's second birthday) during which adequate nutrition and healthy growth have benefits throughout life [8]. Further, building on previous evidence, 2013 series provided a new framework with nutrition-specific (address the immediate causes) and nutrition-sensitive (address the underlying determinants) interventions to achieve optimal fetal and child nutrition and development outcomes [1]. However, it is estimated that implementing ten nutrition-specific interventions in LMICs, at 90% coverage could reduce stunting prevalence by only 20% [9]. This is indicative of the need to identify other potential interventions that could accelerate reductions in undernutrition.

To accelerate progress on global nutrition targets in LMICs, there is a need to identify high impact interventions that have the potential for scaling-up. Numerous nutrition interventions, including nutrition-specific [10, 11] and nutrition-sensitive [12, 13] have been tested on maternal and childhood outcomes and numerous systematic reviews (SRs) have synthesised the evidence on the effectiveness of these interventions [14-20].

To bring all the existing evidence together, the UK Department for International Development (DFID) through the Systematic Review Programme for South Asia (SARH) commissioned a nutrition evidence summary project from 2016-2018. The project aimed at synthesising the evidence on the effectiveness of various nutrition interventions on WHO global nutrition targets-related outcomes in LMICs by systematically reviewing the existing reviews. This paper presents evidence syntheses on one of the outcomes (stunting).

METHODS

Protocol and eligibility criteria

We developed and followed a systematic meta-review protocol [21] in accordance with the Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) statement [22]. We framed the review question using Population, Intervention, Comparison, Outcome, Context and Study design (PICOCS) framework. The population included newborns, infants, children, adolescents, women, adults and elderly. The interventions included all nutrition-specific and nutrition-sensitive interventions as mentioned in Lancet 2013 maternal and child nutrition series framework [9]. The outcome measures were the global nutrition targets-stunting, wasting, anaemia, low-birthweight and breastfeeding [5]. SRs were included if they met the following criteria: searched at least two electronic databases, included a method of describing how the studies were included and/or excluded; synthesised findings from individual primary studies from LMICs on the effectiveness of nutrition-specific and/or nutrition-sensitive interventions; and have performed meta-analyses on at least one of the global nutrition targets.

Information sources

We conducted a comprehensive systematic search on the following databases: 1) *Global databases*- Annual Reviews Biomedical, CINAHL, Global Health, the International Bibliography of the Social Sciences (IBSS), Medline, PsycINFO, PubMed, and Web of Science; 2) *Regional* - African Journals Online (AJOL), Bangladesh Journals Online (BanglaJOL), Indian Citation Index (ICI), Latin American and Caribbean Health Sciences Literature (LILACS), Nepal Journals Online (NepJOL), and PakMediNet; 3) *SR databases*- the International Initiative for Impact Evaluation (3ie), Campbell Collaboration of SRs, the Department for International Development (DFID), and Joanna Briggs Institute; and 4) *Digital library*-Bioline International.

Search strategy

The key search terms used included [Intervention* OR initiative* OR process* OR program* OR policy OR policies OR effect* OR "delivery mode" OR implication* OR scheme* OR strategy* OR outcome* OR impact OR evaluat* OR delivery OR implement*] AND [Nutrition* OR "maternal and child health" OR "maternal and child nutrition" OR "MNCH" OR "fortification" OR "single nutrient fortification" OR "folic acid supplementation" OR "iron supplementation" OR "multiple micronutrient powder" OR "early childhood development" OR "micronutrient supplementation" OR "micronutrient powders" OR "micronutrient sprinklers" OR "calcium supplementation" OR "iodine supplementation" OR "iodine fortification" OR "energy protein supplementation" OR "delayed cord clamping" OR "neonatal vitamin K administration" OR "neonatal vitamin A supplementation" OR "kangaroo mother care" OR "early initiation of breastfeeding" OR "promotion of breastfeeding" OR "responsive feeding" OR "promotion of dietary diversity" OR "complementary feeding" or "complementation" OR "vitamin A supplementation" OR "multiple micronutrient supplementation" OR "preventive zinc supplementation" OR "SAM" OR "facility based management" OR "community based management" OR "staple foods fortification" OR "home based fortification" OR "specific foods fortification" OR "cash transfer programs" OR "community based platforms" OR "nutrition education" OR "nutrition promotion" OR "IMNCT" OR "integrated management childhood illness" OR "school based programs" OR "LNS" OR "lipid based nutrient supplements" OR "ready-to-eat foods" OR "RUTF" OR "ready-to-eat therapeutic foods" OR "ready-to-eat supplementary foods" OR "RUSF" OR "vitamin D supplementation" OR "Omega-3 fatty acid supplementation" OR

"nutrition sensitive" OR "home gardens" OR "home gardening" OR "kitchen garden" OR "vegetable garden" OR "household garden" OR "household gardening" OR "garden based nutrition program" OR "kitchen garden" OR "kitchen gardening" OR "project garden" OR "homestead plot" OR "homestead horticulture and gardening" OR "food garden" OR "food gardening" OR "home based food garden" OR "homestead food production" OR "homestead food production systems" OR "fortification" OR "bio-fortification" OR "social safety nets" OR "family allowance program" OR "child grant" OR "child support grant" OR "microfinance" OR "social transfer" OR "social assistance" OR "cash transfer" OR "conditional cash transfers" OR "monetary incentives" OR "unconditional transfers" OR "in-kind household food distribution" OR "transfer programs emergencies" OR "feeding" OR "school feeding" OR "meals" OR "snacks" OR "breakfast" OR "mid-day meal" OR "mid day meal" OR "feeding services" OR "lunch" OR "school feeding programs" OR "motor development" OR "food security" OR "food supply" OR "food distribution" OR "food production" OR "food aid" OR "sustainable agriculture" OR "WASH" OR "water or sanitation and hygiene"]. We used similar keywords with other selected databases and database specific search terms are reported elsewhere [23]. We limited the evidence to abstracts published in the English language from 1 January 2000 to 30 June 2016.

Study selection

Identified SRs were screened by two researchers using a two-stage process. The first stage involved the screening of all titles and abstracts based on the inclusion and exclusion criteria. Full-text articles of all the included SRs in stage one were retrieved and screened for eligibility in stage two.

Quality assessment

We assessed included SRs for methodological quality using the Assessing the Methodological Quality of Systematic Reviews (AMSTAR) tool [24]. Two researchers independently scored and graded the methodological quality of all the SRs. Any discrepancies in scores were examined by a third researcher. SRs were assessed on eleven items on AMSTAR with the scores for individual items summed up. A total score of 11 represented an SR of the highest quality. The scores were grouped into three categories to grade the SR quality: 8-11 represented 'high', 4-7 represented 'medium', and 0-3 represented 'low' quality.

Data extraction

Two researchers independently extracted data from individual SRs using a pre-designed review specific tool. The tool included details on population characteristics, intervention details, the numerical summary findings on outcomes and the success factors/challenges.

Analysis

The extracted data were narratively synthesised in line with the review objective. This involved a detailed examination of the summary findings and conclusions with respect to the effectiveness on outcomes and the categorisation of effectiveness as 'positive', 'no impact' and/or 'inconclusive', taking into account, wherever possible, the magnitude of the effect and the strength of association. Meta-analyses was deemed inappropriate for this review as this was a review of SRs and meta-analyses was already conducted in the included SRs. We used EppiReviewer software (EPPI-Centre, University of London, UK) for managing references [17].

RESULTS

Study selection

Figure 1 presents the search results and SR selection process. The search identified 6,597 records, of which 5,764 were excluded due to either duplication from multiple databases or discordance with the inclusion criteria. Full-texts of the remaining 833 SRs were retrieved. These SRs were screened against the inclusion criteria. Finally, 28 SRs were eligible for inclusion in the meta-review. Of these, 12, 10, 8, 5 and 4 SRs assessed stunting, wasting, anaemia, LBW and EBF outcomes respectively. This review presents the findings for those 12 SRs that assessed stunting outcomes.

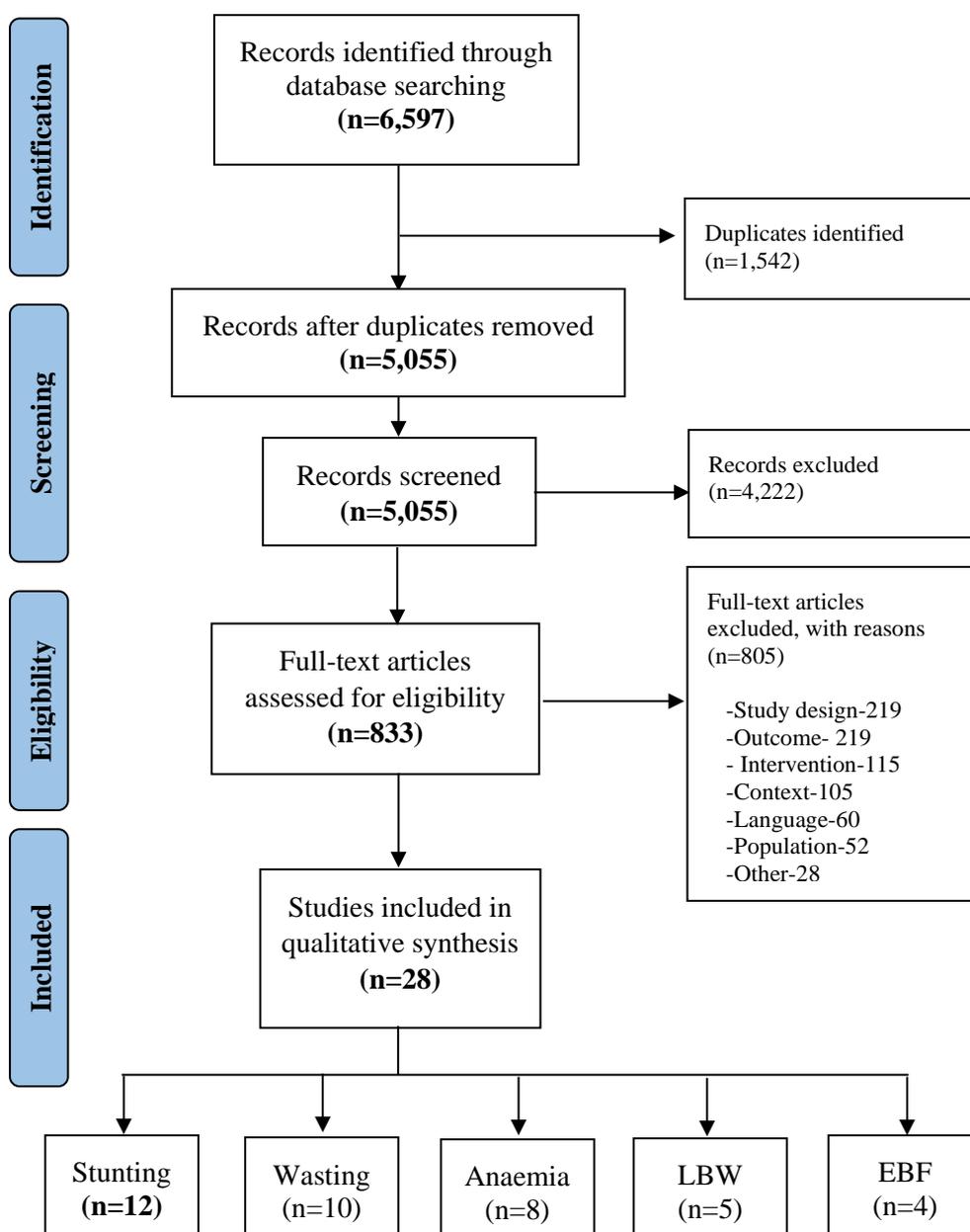


Figure 1: Flowchart of the SR selection process

Characteristics of the included systematic reviews

A total of 12 SRs synthesised 68 primary studies from LMICs (table 1). Nine primary studies were conducted in Bangladesh; five in Malawi; four each in Indonesia and South Africa; three each in Brazil, Cambodia, China, Ghana, Mexico, Nepal, Pakistan, and Vietnam; two each in Burkina Faso, Columbia, Ecuador, India, and Nicaragua; and one each in Bolivia, Ethiopia, Haiti, Honduras, Kenya, Mali, Mozambique, Niger, Peru, Sri Lanka, and Zambia.

Majority SRs included RCTs, while two included other types of studies [25, 26]. However, all SRs included meta-analyses. Included SRs were critically appraised for methodological quality and the result is presented in table 2. The methodological quality assessment showed all SRs with high quality. The included SRs had a mean AMSTAR of 10. All the SRs met the AMSTAR criteria 3, 5, 6, 7, 9 and 11. SRs that fulfilled all criteria were Cochrane Collaboration reviews conducted using set guidelines [27-33].

Participants

The participants included children ($n=7$), pregnant women ($n=2$) and households ($n=3$). Of seven SRs that included children, four SRs included children <5 years [29-32], two included children <2 years [34, 35] and one included children <12 years [27]. These SRs had both intervention and outcomes measured on the same participants, while the remaining five SRs included different participants for interventions, and outcomes were measured on a different group. In two SRs, interventions were targeted on pregnant women, while outcomes were measured on children [35, 36]. Similarly, three SRs targeted households for interventions and assessed outcomes on women and/or children [25, 26, 33].

Interventions

Eight nutrition interventions were reported in the included SRs. The interventions identified in the SRs, included both nutrition-specific ($n=9$) and nutrition-sensitive ($n=3$) interventions. The nutrition-specific interventions included- complementary feeding [34], iron supplementation [27], multiple micronutrient supplementation/fortification [28, 35, 36], prevention and treatment of acute malnutrition [29, 30], and supplementary feeding [31, 32]. Similarly, nutrition-sensitive interventions included- agriculture [25], social safety net [26], and water, sanitation and hygiene (WASH) [33].

Effectiveness of interventions on stunting and/or height-for-age outcomes

Table 3 presents the effectiveness of various nutrition interventions on stunting outcomes- stunting rate (Relative Risk-RR) and height-for-age z score (Standard Mean Difference-SMD).

Complementary feeding

Lassi et al. assessed the impact of complementary feeding on stunting/height-for-age z score in children <2 years [34]. The intervention component included education on complementary feeding and provision of complementary feeding (fortified/unfortified, but no micronutrients alone, with or without education). This review excluded studies that included supplementary/therapeutic interventions.

Table 1: Characteristics of the included reviews (n=12)

Authors and year	Title of the study	Aim	Included databases	Total included studies	Studies assessing stunting		
					Number	Design	Countries
Lassi et al., 2013[29, 34]	Impact of education and provision of complementary feeding on growth and morbidity in children less than two years of age in developing countries: a systematic review	To assess the impact of education on CF and provision of CF with or without education on growth and morbidity among children under 2 years of age in LMICs.	PubMed, Cochrane Library, Google Scholar and WHO global database	16	12	RCTs	Bangladesh, Brazil, China, Ghana (2), India, Nigeria, Pakistan, Peru, South Africa, Vietnam, Zambia
De-Regil et al., 2014 [27]	Intermittent iron supplementation for improving nutrition and development in children under 12 years of age	To assess the effects of intermittent iron supplementation, alone or in combination with other vitamins and minerals, on nutritional and developmental outcomes in children from birth to 12 years of age compared with a placebo, no intervention or daily supplementation.	CENTRAL, MEDLINE, EMBASE, CINAHL, POPLINE and WHO International Clinical Trials Registry Platform, SCIELO, LILACS, IBECs and IMBIOMED	33	5	RCTs	Bolivia, Brazil, Indonesia (2), Vietnam
Devakumar et al., 2016 [35]	Maternal antenatal multiple micronutrient supplementation for	To review the evidence from long-term follow-up reports of multiple	PubMed, Web of Science and the Global Health Library	9	6	RCTs	Bangladesh, Burkina Faso, China, Mexico,

Authors and year	Title of the study	Aim	Included databases	Total included studies	Studies assessing stunting		
					Number	Design	Countries
	long-term health benefits in children: a systematic review and meta-analysis	micronutrient supplementation beginning in the later first or second trimester					Nepal (2)
Lu et al., 2014 [36]	Effects of multi-micronutrient supplementation during pregnancy on postnatal growth of children under five years of age: a meta-analysis of randomized controlled trials	To evaluate the effect of maternal multi-micronutrient supplementation on postnatal growth of children under 5 years of age.	PubMed, EMBASE, CENTRAL (OVID platform), Web of Science, BIOSIS Previews, Chinese Science Citation Database, Scopus, ProQuest, ClinicalTrials.gov, Chinese Biomedical Database, and WANFANG database	9	4	RCTs	Bangladesh (2), Indonesia, Nepal
De-Regil et al., 2013 [28]	Home fortification of foods with multiple micronutrient powders for health and nutrition in children under two years of age	To assess the effects and safety of home (point-of-use) fortification of foods with multiple micronutrient powders on nutritional, health and developmental outcomes in children under two years of age.	Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library), MEDLINE, EMBASE, CINAHL, CPCI-S, Science Citation Index, African Index Medicus, POPLINE, ClinicalTrials.gov, mRCT and World Health Organization International Clinical Trials Registry Platform	8	2	RCTs	Ghana, Cambodia
Schoonees et al., 2013 [29]	Ready-to-use therapeutic food for home-based	To assess the effects of home-based RUTF on recovery, relapse and	Cochrane Central Register of Clinical Trials (CENTRAL), MEDLINE, EMBASE,	4	1	RCTs	Malawi

Authors and year	Title of the study	Aim	Included databases	Total included studies	Studies assessing stunting		
					Number	Design	Countries
	treatment of severe acute malnutrition in children from six months to five years of age	mortality in children with severe acute malnutrition.	CINAHL, Science Citation Index, African Index Medicus, LILACS, ZETOC				
Lazzerini et al., 2013 [30]	Specially formulated foods for treating children with moderate acute malnutrition in low- and middle-income countries	To evaluate the safety and effectiveness of different types of specially formulated foods for children with moderate acute malnutrition in low- and middle-income countries, and to assess whether foods complying or not complying with specific nutritional compositions, such as the WHO technical specifications, are safe and effective.	CENTRAL, MEDLINE, LILACS, CINAHL, BIBLIOMAP, POPLINE, ZETOC, ICTRP, mRCT, and ClinicalTrials.gov., EMBASE	8	4	RCTs	Bangladesh, Burkina Faso, Malawi, Mali
Kristjansson et al., 2015 [31]	Food supplementation for improving the physical and psychosocial health of socio-	To assess the effectiveness of supplementary feeding interventions, alone or with co-intervention, for improving the physical and psychosocial health	Cochrane Central Register of Controlled Studies, MEDLINE, Cochrane Database of Systematic Reviews, DARE, SSCI, Web of Science, CPCI-S, CPCI-SSH, ERIC, Proquest, PsycINFO, Clinicaltrials.gov,	32	9	RCTs	Columbia, Haiti, Indonesia, Malawi (3), Mexico, Niger, South Africa

Authors and year	Title of the study	Aim	Included databases	Total included studies	Studies assessing stunting		
					Number	Design	Countries
	economically disadvantaged children aged three months to five years	of disadvantaged children aged three months to five years.	EMBASE, CINAHL, Healthstar, LILACS, OpenGrey, WHOLIS, WHO nutrition databases				
Sguassero et al., 2012 [32]	Community-based supplementary feeding for promoting the growth of children under five years of age in low- and middle-income countries	To evaluate the effectiveness of community-based supplementary feeding for promoting the physical growth of children under five years of age in LMICs.	CENTRAL (The Cochrane Library), MEDLINE, EMBASE, CINAHL, LILACS, WorldCat and ClinicalTrials.gov	8	1	RCTs	China
Girard et al., 2012 [25]	The effects of household food production strategies on the health and nutrition outcomes of women and young children: a systematic review	To assess the effects of agricultural interventions to increase household food production on the nutrition and health outcomes of women and young children.	PubMed, Popline, Web of Science, CINAHL and EMBASE	32	4	QETs and observational studies	Cambodia, Ethiopia, Mozambique, Vietnam
Manley et al., 2012 [26]	How effective are cash transfer programmes at improving nutritional status?	To assess the effectiveness of cash transfer programmes, both conditional and unconditional, at	EconLit, PsycInfo, PubMed, Google Scholar, Eldis, Inter-Science, Science Direct, MEDLINE, IDEAS, the Cochrane Central Register of	24	15	QETs and observational studies	Bangladesh (4), Brazil, Columbia, Ecuador (2),

Authors and year	Title of the study	Aim	Included databases	Total included studies	Studies assessing stunting		
					Number	Design	Countries
		improving child nutritional status.	Controlled Trials, the Database of Abstracts of Reviews of Effectiveness, JOLIS, POPLINE, CAB Direct, Ovid.com, WHOLIS, British Library for Development Studies, JSTOR, LILACS, MEDCARIB, ADOLEC, PAHO, SSRN, Social Sciences Citation Index plus Conference Proceedings Citation Index, ProQuest Dissertations, Theses Database, SIGLE, the ntis.gov search engine of U.S. Government documents, and the Effective Practice and Organization of Care Group Register				Honduras, India, Mexico, Nicaragua (2), South Africa, Sri Lanka
Dangour et al., 2013 [33]	Interventions to improve water quality and supply, sanitation and hygiene practices, and their effects on the nutritional Status of children	To evaluate the effect of interventions to improve water quality and supply (adequate quantity to maintain hygiene practices), provide adequate sanitation and promote handwashing with soap, on the nutritional status of	Cochrane, MEDLINE, Web of Science, SCI-EXPANDED, SSCI, CPCI-S, CPCI-SSH, EMBASE, Econlit, Global Health, Greenfile, CAB Abstracts, CENTRAL, metaRegister of Controlled Trials, Grey literature, CBM, China National Knowledge Infrastructure, VIP	14	5	RCTs	Cambodia, Kenya, Pakistan, South Africa

Authors and year	Title of the study	Aim	Included databases	Total included studies	Studies assessing stunting		
					Number	Design	Countries
		children under the age of 18 years.	information/Chinese Scientific Journals database				

RCTs: randomized control trials; QET: quasi-experimental trials

Table 2: Quality assessment of the reviews using AMSTAR

Study	1	2	3	4	5	6	7	8	9	10	11	Total	Grading
Lassi et al., 2013 [34]	0	0	1	1	1	1	1	1	1	0	1	8	High
De-Regil et al., 2011 [27]	1	1	1	1	1	1	1	1	1	1	1	11	High
Devakumar et al., 2016 [35]	0	1	1	1	1	1	1	1	1	1	1	10	High
Lu et al., 2014 [36]	0	0	1	0	1	1	1	1	1	1	1	8	High
De-Regil et al., 2013 [28]	1	1	1	1	1	1	1	1	1	1	1	11	High
Schoonees et al., 2013 [29]	1	1	1	1	1	1	1	1	1	1	1	11	High
Lazzerini et al., 2013 [30]	1	1	1	1	1	1	1	1	1	1	1	11	High
Kristjansson et al., 2015 [31]	1	1	1	1	1	1	1	1	1	1	1	11	High
Sguassero et al., 2012 [32]	1	1	1	0	1	1	1	1	1	1	1	10	High
Girard et al., 2012 [25]	0	1	1	1	1	1	1	1	1	0	1	9	High
Manley et al., 2012 [26]	1	1	1	0	1	1	1	0	1	1	1	9	High
Dangour et al., 2013 [33]	1	1	1	1	1	1	1	1	1	1	1	11	High

AMSTAR TOOL Key: 1 = Yes, 0 = No/Unclear/Not applicable. Areas assessed are numbered 1 to 11 on horizontal axis; 1-Priori design provided, 2-Duplicate selection/extraction, 3-Comprehensive literature search conducted, 4-Status of publication (i.e, grey literature) used as an inclusion criterion, 5-List of included & excluded studies provided, 6-Characteristics of included studies provided, 7-Quality of included studies assessed and documented, 8-Use of the scientific quality of the studies in formulating conclusions, 9-Use of appropriate methods to combine the findings of studies, 10-Assessment of publication bias, 11- Conflict of interest included

The population included both food secure and food insecure children. The education interventions included- counselling, nutrition messages on food preparation and messages on prioritising food security and health-seeking behaviour. These interventions were delivered for at least six months through health facility/community-based platforms. The provision of complementary feeding included Nutributter, maize and cowpea diet, fortified milk-based cereals, enriched bread, powdered skim milk, and micronutrient fortified complementary food. The duration of intervention ranged from 6-14 months.

Overall, education on complementary feeding significantly improved height-for-age z score (SMD: 0.23; 95% CI: 0.09, 0.36; n=1,981, 5 trials) and significantly reduced stunting rates (RR: 0.71; 95% CI: 0.56, 0.91; n=1,940, 5 trials). Subgroup analysis showed, studies from food secure population indicated education had a significant impact on height-for-age z score (SMD: 0.22; 95% CI: 0.01, 0.43; n=1,409, 4 trials), however stunting reduced non-significantly (RR: 0.70; 95% CI: 0.49, 1.01, n=1,368, 4 trials). Among food insecure population, education alone significantly improved height-for-age z score (SMD: 0.25; 95% CI: 0.09, 0.42, n=572, 1 trial) and significantly reduced stunting rates (RR: 0.68; 95% CI: 0.60, 0.76, n=572, 1 trial); while provision of complementary food improved height-for-age z score significantly (SMD: 0.39; 95% CI: 0.05, 0.73, n=1,652, 7 trials) with non-significant effect on stunting rates.

Micronutrient supplementation/fortification: Iron supplementation

De-Regil et al. assessed the impact of intermittent iron supplementation for improving nutrition and development in children <12 years [27]. This review had two comparison groups- 'intermittent iron supplementation versus no supplementation or placebo', and 'intermittent iron supplementation versus daily iron supplementation'. The primary outcomes included- anaemia, iron deficiency, all-cause mortality, while height-for-age z score was a secondary outcome.

Three trials (Bolivia, Indonesia, Vietnam; n=366) compared 'intermittent iron supplementation versus no supplementation or placebo' and reported height-for-age z score for school-aged children. Meta-analyses showed no statistically significant effect. Similarly, three trials (Brazil, Indonesia, Vietnam; n=279) compared 'intermittent iron supplementation versus daily iron supplementation' and reported a non-significant effect on height-for-age z score.

Micronutrient supplementation/fortification: Multiple micronutrients

Three reviews evaluated the impact of multiple micronutrient supplementation/fortification on height-for-age z score. Devkumar et al. and Lu et al. assessed the effect of multiple micronutrient supplementation during pregnancy on the growth of children [35, 36]. Devkumar et al. review included a follow-up of children born in the 2015 Cochrane review [37]. De-Regil et al. assessed home fortification of foods with multiple micronutrient powders (MNP) on nutrition, health and development outcomes of young children [28]. Devkumar et al. and Lu et al. review reported height-for-age z score as primary outcomes, while De-Regil et al. review reported height-for-age z score as a secondary outcome.

Table 3: Effectiveness of nutrition interventions on stunting

Review	Population	Intervention component	Outcomes	Evidence of impact
Complementary feeding				
Lassi et al., 2013 [34]	Children <2 years	Education on CF, Provision of CF with/ without education, Both	<p>Type: Primary</p> <ul style="list-style-type: none"> • <i>Overall impact</i> <ul style="list-style-type: none"> <u>Education on CF</u> HAZ: SMD: 0.23 (0.09, 0.36, n=1,981) Stunting rates: RR: 0.71 (0.56, 0.91, n=1,940) [5 studies: China, Peru, Brazil, Pakistan, Bangladesh] <u>Provision of CF with or without education</u> HAZ: Not applicable Stunting rates: Not applicable • <i>Food secure population</i> <ul style="list-style-type: none"> <u>Education on CF</u> HAZ: SMD 0.22 (0.01, 0.43, n=1,409) Stunting rates: RR 0.70 (0.49 1.01, n=1,368) [4 studies: China, Peru, Brazil, Pakistan] • <i>Food insecure population</i> <ul style="list-style-type: none"> <u>Education on CF</u> HAZ: SMD 0.25 (0.09, 0.42, n=572) Stunting rates: RR 0.68 (0.60, 0.76, n=572) [1 study: Bangladesh] <u>Provision of CF with or without education</u> HAZ: SMD 0.39 (0.05, 0.73, n=1,652) Stunting rates: RR 0.33 (0.11, 1.00, n=not given) 	Positive

			[7 studies: Ghana (2), India, SA, Nigeria, Zambia, Vietnam]	
Micronutrient supplementation/fortification: Iron supplementation				
De-Regil et al., 2011 [27]	Children <12 years	Intermittent iron supplementation alone or with other V & M vs placebo, no intervention or daily supplementation	<p>Type: Secondary <u>Intermittent iron supplementation versus no supplementation or placebo</u> HAZ: SMD 0.03 (-0.04, 0.10, n=366) [3 studies: Bolivia, Indonesia, Vietnam]</p> <p><u>Intermittent iron supplementation versus daily iron supplementation</u> HAZ: SMD -0.26 (-0.80, 0.28, n=279) [3 studies: Brazil, Indonesia, Vietnam]</p>	No impact
Micronutrient supplementation/fortification: Multiple Micronutrients				
Devakumar et al., 2016 [35]	<p>I: Pregnant women (9-23 weeks)</p> <p>O: Children (2-9 years)</p>	3 or more micronutrients vs IFA	<p>Type: Primary HAZ: SMD 0.01 (-0.04, 0.06, n=not given) [6 studies: Mexico, China, Burkina Faso, Bangladesh, Nepal (2)]</p>	No impact
Lu et al., 2014 [36]	<p>I: Pregnant women</p> <p>O: Children <5 years</p>	MMN supplements with 3 or more MN vs placebo/no supplements/2 or less MN	<p>Type: Primary HAZ: SMD 0.01 (-0.07, 0.10, n=2,096) [4 studies: Indonesia, Bangladesh (2), Nepal]</p>	No impact
De-Regil et al., 2013 [28]	Children 6 to 23 months	Fortification of foods (point-of-use) with MMN powders (at least iron, zinc and vitamin A) vs placebo/nothing/iron supplements	<p>Type: Secondary <u>Home (point-of-use) fortification of foods with MNP versus no intervention or placebo</u> HAZ: SMD 0.04 (-0.15, 0.23, n=304) [2 studies: Ghana, Cambodia]</p> <p><u>Home (point-of-use) fortification of foods with MNP versus iron supplements</u> Not applicable</p> <p><u>Home (point-of-use) fortification of foods with MNP versus iron and folic acid supplements</u> Not applicable</p>	No impact

			<p><u>Home (point-of-use) fortification of foods with MNP versus same multiple micronutrients as supplements</u> Not applicable</p>	
Treatment of acute malnutrition				
Schoonees et al., 2013 [29]	Children 6-60 months of age with SAM	Home-based RUTF vs standard diet/different formulations of RUTF	<p>Type: Secondary <u>RUTF meeting total daily requirements versus standard diet (flour porridge)</u> Not applicable <u>RUTF supplement versus RUTF meeting total daily requirements</u> Not applicable <u>RUTF containing less milk powder versus standard RUTF</u> HAZ: SMD -0.10 (-0.24, 0.04, n=1,874) [1 study: Malawi]</p>	No impact
Lazzerini et al., 2013 [30]	Children 6-60 months of age with MAM	Specially formulated foods (\pm counselling and medical care) vs counselling and standard medical care without food provision	<p>Type: Secondary <u>Specially formulated foods vs Standard care</u> HAZ: SMD 0.23 (-0.07, 0.54, n=1,546) [2 studies: Bangladesh, Burkina Faso] <u>Lipid-based nutrient supplements vs any Blended foods</u> HAZ: SMD 0.00 (-0.12, 0.13, n=3,631) [3 studies: Mali, Malawi, Burkina Faso] <u>Lipid-based nutrient supplements versus specific types of blended foods</u> HAZ: SMD 0.20 (-0.37, 0.77, n=1,018) [1 study: Burkina Faso]</p>	No impact
Dietary supplementation for children				
Kristjansson et al., 2015 [31]	Children 3-60 months of age	Supplementary food (with or without co-intervention) vs no treatment	<p>Type: Primary HAZ: SMD 0.15 (0.06, 0.24, n=4,544)</p>	Positive

			[9 studies: Indonesia, Haiti, Niger, Malawi (3), Columbia, South Africa, Mexico]	
Sguassero et al., 2012 [32]	Children <5 years	Community-based supplementary feeding vs no intervention/placebo	Type: Primary <u>Yogurt supplementation versus no supplementation</u> HAZ: SMD 0.05 (0.01, 0.08, n=348) [1 study: China]	Positive
Agriculture and food security				
Girard et al., 2012 [25]	I: Households O: Women and children < 5 years	Agricultural strategies to improve household food production	Type: Primary Stunting Rate: RR 0.93 (0.84, 1.04, n=2,066) [4 studies: Vietnam, Ethiopia, Mozambique, Cambodia]	No impact
Social safety nets				
Manley et al., 2012 [26]	I: Households O: Women and children <5 years	Cash transfer programmes	Type: Primary HAZ: SMD 0.04 (-0.02, 0.11) [15 studies: Bangladesh (4), Sri Lanka, Brazil, Nicaragua (2), South Africa, Honduras, Ecuador (2), Colombia, Mexico, India]	No impact
WASH				
Dangour et al., 2013 [33]	I: Households O: Children <5 years	Improve water quality and supply, sanitation and hygiene practices vs usual practice	Type: Primary HAZ: SMD 0.08 (0.00, 0.16, n=4627) [5 studies: Pakistan (2), Kenya, Cambodia, South Africa]	Positive (inconclusive)

Notes: CF: complementary feeding; HAZ: height-for-age z score; IFA: iron and folic acid; MAM: moderate acute malnutrition; MMN: multiple micronutrient; MN: micronutrient; MNP: micronutrient powder; RR: relative risk; RUTF: ready-to-use therapeutic food; SAM: severe acute malnutrition; SMD: standard mean difference; V&M: vitamin and mineral; I: Participant on which intervention was targeted; O: Participant on which outcome was measured

Meta-analyses from Devkumar et al. showed no difference (height-for-age z score of children <9 years, 6 trials) between three or more multiple micronutrient (≥ 3) and 60 mg iron and folic acid groups. Similarly, meta-analyses from Lu et al. showed no difference (height-for-age z score of children <5 years, 4 trials) between three or more multiple micronutrients and two or fewer micronutrients.

De-Regil et al. review had four comparison groups; home (point-of-use) fortification of foods with MNP versus- 1) no intervention or placebo, versus 2) iron supplements, versus 3) iron and folic acid supplements, and versus 4) same multiple micronutrients as supplements. However, height-for-age z score was reported in only two trials, which compared home fortification of foods with MNP versus no intervention or placebo. These trials with 304 children from Ghana and Cambodia, where intervention duration ranged between six to 12 months did not find a significant effect on height-for-age z score among children <2 years.

Treatment of acute malnutrition

Two reviews evaluated the impact of therapeutic and specially formulated foods on height-for-age z score. Schoonees et al. assessed the impact of ready-to-use therapeutic food (RUTF) for home-based treatment of severe acute malnutrition [29], while Lazzerini et al. assessed the impact of specially formulated foods for treating children with moderate acute malnutrition [30]. Both the reviews reported height-for-age z score as secondary outcomes.

Schoonees et al. review had three comparisons; RUTF meeting total daily requirements versus standard diet (porridge), RUTF supplement versus RUTF meeting total daily requirements, and RUTF containing less milk powder versus standard RUTF. The review found only one trial from Malawi reporting height-for-age z score outcome, which compared RUTF containing less milk powder versus standard RUTF. However, the comparison showed no difference between the groups (SMD: -0.10; 95% CI: -0.24, 0.04; n=1,874).

Similarly, the other review also had three comparison categories [30]; specially formulated foods versus standard care; lipid-based nutrient supplements versus any blended foods, lipid-based nutrient supplements versus specific types of blended foods. The review included two trials (Bangladesh and Burkina Faso, n=1,546), where a comparison between specially formulated foods versus standard care showed no significant difference in height-for-age z score at discharge. Similarly, three trials (Mali, Malawi and Burkina Faso, n=3,631) compared lipid-based nutrient supplements versus any blended foods, while one trial (Burkina Faso, n=1,018) compared lipid-based nutrient supplements versus specific types of blended foods. Both of these comparisons showed height-for-age z score gain was not significantly improved in children treated with lipid-based nutrients.

Dietary supplementation for children

Two reviews evaluated the impact of dietary supplementation on height-for-age z score. Kristjansson et al. compared supplementary food (with/without added micronutrients) with no treatment [31], while Sgussero et al. compared community-based supplementary feeding with no intervention/placebo [32].

Meta-analyses from Kristjansson et al. review showed a significant effect of supplementation on height-for-age z score (SMD: 0.15; 95% CI: 0.06, 0.24, n=4,544, 9 trials). The average duration of the study was six months. The supplementation included snacks given in daycare, lipid-based supplements, RUTF, milk/soy-based fortified spread, corn-soy blend, and dry cereal and the population included undernourished children. Similarly, one trial reporting height-for-age z score outcome from Sgussero et al. review also showed a significant effect

of supplementation (SMD: 0.05; 95% CI: 0.01, 0.08; n=348). The trial included yogurt supplementation for nine months in nutritionally at-risk children in China.

Agriculture and food security

Girad et al. review assessed the effects of household food production on stunting [25]. Meta-analyses showed, agriculture strategies aiming to improve household food production were not significantly associated (RR: 0.93; 95% CI: 0.84, 1.04, n=2,066, 4 studies) with stunting.

Social safety nets

Manley et al. review assessed the effect of cash transfer programmes on stunting [26]. Meta-analyses showed a non-significant effect of cash transfer programmes on height-for-age z score (SMD: 0.04; 95% CI: -0.02, 0.11, 15 programme evaluations). The programmes included: RMP-rural maintenance program (Bangladesh), Samrudhi (Sri Lanka), FFA-food for asset creation (Bangladesh), Bolsa Alimentacao (Brazil), Atencion a Crisis (Nicaragua), Old-age pension (South Africa), PRAFII (Honduras), BDH (Ecuador), Familias en Accion (Colombia), RPS (Nicaragua), Progresia (Mexico), Bono Solidario (Ecuador), Primary school stipend (Bangladesh), FSVGD-food security (Bangladesh) and Apni Beti Apna Dhan (India).

Water, sanitation, and hygiene (WASH)

Dangour et al. assessed the effect of improving water quality and supply, sanitation and hygiene practices on stunting [33]. Meta-analyses identified a borderline statistically significant effect of WASH interventions on height-for-age z score (SMD: 0.08; 95% CI: 0.00, 0.16; n=4,627, 5 trials). The interventions tested were solar disinfection of drinking water, promoting washing hands with soap (antibacterial or plain) and point of use water treatment with flocculent-disinfectant.

DISCUSSION

This meta-review appraised and synthesised the evidence from 12 SRs on the effectiveness of nutrition-specific and nutrition-sensitive interventions on stunting. All included SRs were of high methodological quality and these included primary studies (mainly RCTs) from the diverse geographical background, 29 LMICs. We identified 12 SRs assessing eight nutrition interventions, including five nutrition-specific and three nutrition-sensitive interventions.

Among all interventions, two nutrition-specific (complementary feeding: n=1; dietary supplementation: n=2) [31, 32, 34] and one nutrition-sensitive (WASH, n=1) intervention showed a positive effect [33]. The positive impact of complementary feeding intervention review on stunting and linear growth is based on five studies with total 1,981 children. The two reviews on dietary supplementation, both with a positive impact, however, differ on the quality of evidence. The evidence in Kristjansson et al. review is derived from nine studies with 4,544 children, while the Sguassero et al. review is derived from a single study with 348 children. Similarly, the borderline positive impact reported in WASH intervention review is based on inconclusive evidence.

The education on complementary feeding intervention review highlighted the following success factors- the educational messages should lay emphasis on the importance of appropriate home prepared food, particularly affordable animal source products; importance of hygiene and high energy foods; and importance of assessing the recall of these messages [34]. Additionally, the review emphasised, for food insecure population, the educational messages should be combined with the provision of complementary foods. Similarly, dietary supplementation review identified a set of factors that are crucial for impact [16] at scale.

These were age; sex; socioeconomic status and baseline nutrition status; nutritional adequacy of dietary supplement; and mode of delivery, amount of supervision (location of feeding), leakage (supply chain) and substitution (disruption of breastfeeding).

Reviews on nutrition-specific interventions targeted pregnant women and/or children, while those on nutrition-sensitive interventions targeted the household, in general. Considering the life cycle approach, only two reviews targeted pregnant women [35, 36], while six reviews included interventions that were introduced after birth until five years of age [28-32, 34], except one review on iron supplementation- that followed children until 12 years [27]. Although it is well recognised that adolescence, a period of critical growth, is a life stage worthy of nutrition and health investments [38, 39], none of the included reviews targeted interventions specifically on adolescent girls.

Compared to nutrition-specific interventions, reviews on nutrition-sensitive interventions were limited- one review each on agriculture, social safety net, and WASH. Moreover, these reviews highlighted the research gap in the area of nutrition-sensitive interventions. Review author's reported high heterogeneity and low methodological quality of primary studies as limitations [25, 26, 33]. Regarding stunting as an outcome, four included reviews considered these as secondary outcomes and showed either no impact or inconclusive impact [27-30]. These reviewed focused on iron supplementation ($n=1$), multiple micronutrient supplementation ($n=1$), and prevention and treatment of acute malnutrition ($n=2$).

Strengths and limitations of the review

To our knowledge, this is the first meta-review on nutrition interventions from LMICs that followed robust evidence synthesis methodology. We developed and followed the peer-reviewed protocol; searched 21 databases; applied double screening, data extraction, and quality appraisal processes; and involved trained reviewers and external quality check mechanisms through EppiReviewer Software. In addition, evidence generated from our meta-review is based on all high-quality reviews, representing 29 LMICs, signifying high internal and external validity of our review. However, our findings have some limitations. The included reviews varied in the intervention components and quality of the primary studies included in the SRs. In addition, not all included reviews defined stunting or linear growth as a primary outcome. As a meta-review, our findings are limited to the direction of the effect, with indications of significance wherever possible, rather than providing the overall magnitude of the effect itself. We were able to neither assess findings separately by primary study designs nor account for any overlapping effects that might have existed due to the primary studies being included in more than one SR.

Implications for practice and research

Post 2013 Lancet maternal and child nutrition series, many LMICs have adopted the recommendations on scaling up ten proven nutrition-specific interventions to tackle undernutrition [40]. Our review provided updated evidence on the effectiveness of nutrition interventions on stunting in LMICs, post lancet 2013 series. We found evidence of positive impact of complementary feeding and dietary supplementation interventions on childhood stunting. The Lancet series concluded, to achieve higher impact on stunting, nutrition-specific interventions must be supplemented by nutrition-sensitive interventions that address the underlying determinants, such as- poverty, low education level and lack of women's empowerment. However, the evidence from included reviews with nutrition-sensitive interventions showed no effect [25, 26, 33].

As previously mentioned, there are limited reviews on the effectiveness of nutrition-sensitive interventions, particularly from well-conducted trials/evaluations. Hence, future research

should focus on designing good quality studies to assess the effectiveness of nutrition-sensitive interventions. We also identified research gap on nutrition intervention studies/reviews targeting adolescent girls. This population group is especially important as interventions during the adolescent period offer multiple routes that could help break the intergenerational cycle of undernutrition [39].

CONCLUSIONS

This meta-review identified two interventions, complementary feeding, and dietary supplementation, with most frequently reported positive evidence of impact on stunting. In LMICs, public health policymakers should consider these two interventions for scaling-up. Considering intervention specific success factors is key to good implementation.

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