REVIEW

Economic Evaluations of Child Nutrition Interventions in Low- and Middle-Income Countries: Systematic Review and Quality Appraisal

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ABSTRACT

Economic evaluation is crucial for cost-effective resource allocation to improve child nutrition in low and middle-income countries (LMICs). However, the quality of published economic evaluations in these settings is not well understood. This systematic review aimed to assess the quality of existing economic evaluations of child nutrition interventions in LMICs and synthesize the study characteristics and economic evidence. We searched 9 electronic databases, including MEDLINE, with the following concepts: economic evaluation, children, nutrition, and LMICs. All types of interventions addressing malnutrition, including stunting, wasting, micronutrient deficiency, and overweight, were identified. We included economic evaluations that examined both costs and effects published in English peer-reviewed journals and used the Drummond checklist for quality appraisal. We present findings through a narrative synthesis. Sixty-nine studies with diverse settings, perspectives, time horizons, and outcome measures were included. Most studies used data from sub-Saharan Africa and South Asia and addressed undernutrition. The mortality rate, intervention effect, intervention coverage, cost, and discount rate were reported as predictors among studies that performed sensitivity analyses. Despite the heterogeneity of included studies and the possibility of publication bias, 81% of included studies concluded that nutrition interventions were cost-effective or cost-beneficial, mostly based on a country's cost-effectiveness thresholds. Regarding quality assessment, the studies published after 2016 met more criteria than studies published before 2016. Most studies had well-stated research questions, forms of economic evaluation, interventions, and conclusions. However, reporting the perspective of the analyses, justification of discount rates, and describing the role of funders and ethics approval were identified as areas needing improvement. The gaps in the quality of reporting could be improved by consolidated guidance on the publication of economic evaluations and the use of appropriate quality appraisal checklists. Strengthening the evidence base for child malnutrition across different regions is necessary to inform cost-effective investment in LMICs.Trial registration: PROSPERO CRD42020194445. *Adv Nutr* 2022;13:282–317.

Statement of Significance: There was a 111% increase in the number of published economic evaluations of child nutrition interventions in low- and middle-income countries between the 2000s and 2010s. However, gaps in the quality of these publications suggest a need for more robust methodological and reporting guidance to enhance quality and promote confidence in the evidence base. Although the studies published after 2016 met more criteria than studies published before, there is a need for consolidated and commonly agreed quality appraisal checklists. Because most research focused on undernutrition from South Asia and sub-Saharan Africa, more empirical data from different regions and various types of nutrition interventions to address all forms of child malnutrition are needed. Despite the heterogeneity of included studies and possible publication bias, 81% of included studies concluded that nutrition interventions were cost-effective or cost-beneficial.

Keywords: systematic review, quality assessment, economic evaluation, cost-effectiveness, child nutrition, malnutrition, low-and middle-income countries

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Introduction

Children need good nutrition to survive, grow, learn, and play. It is fundamental to human health and for achieving sustainable development both nationally and globally (1, 2). Ending all forms of malnutrition, including stunting, wasting, and overweight, in children aged <5 y by 2030 is among the Sustainable Development Goals adopted by all UN Member States (3). Nevertheless, in 2019, 144 million children were stunted (too short for their ages), 47 million children were wasted (too thin for their height), and 38 million children were overweight (too heavy for their height) globally (1). Most malnourished children were from low- and middle-income countries (LMICs), with 99% of stunted children, 99% of wasted children, and 86% of overweight children from LMICs (1). This highlights that many LMICs suffer the double burden of malnutrition, which is the coexistence of undernutrition and overnutrition (4, 5). Tackling malnutrition is crucial because it can have lifelong consequences for health, human capital, economic development, and equity (6). Several studies have reported the economic losses due to child malnutrition, including inadequate breastfeeding, undernutrition, and overnutrition (7–10), and potential economic benefits over the productive lives of women and children conferred by scaling-up of a set of nutrition interventions (11). Quality economic evaluations are important to assess economic impacts of interventions to inform decision-making.

Limited resource availability also requires decision-makers consider the impact on the use of health care resources, costs associated with the use of those resources, and their value (12). Methods for the economic evaluation of health care interventions have existed for several years, but these are mainly limited to health care technologies, such as drugs, devices, and medical procedures (13, 14). Economic evaluations of broader public health interventions are not widely available and the methods are not well established (14). Evidence-based decisions are highly dependent on the quality of data. A small number of systematic reviews of economic evaluations of child nutrition interventions in LMICs have been conducted (15–18), but only 1 study has focused on quality assessment (18). The study findings indicated that nutrition interventions in LMICs were rarely evaluated using appropriate evaluation methods (15), there was a paucity of evidence on early childhood nutrition and development interventions from LMICs (16), and only half the items of guidelines were partially or fully met by >60% of the included studies (18). In 2019, a systematic review of systematic reviews of health economic evaluations found that 77% of systematic reviews were conducted to provide an overview of existing economic evaluations, whereas 37% of systematic reviews aimed to appraise existing economic evaluations (19). Key evidence gaps lie in the quality of existing economic evaluations in the area of child nutrition in LMICs. Quality assessment is a prerequisite for understanding economic evidence to make evidence-based decisions considering value for money to improve child nutrition. Therefore, this review aimed to assess the quality of existing economic evaluations of nutrition interventions for children aged <5 y in LMICs and synthesize the study characteristics and economic evidence.

Methods

Search strategy

A research librarian with expertise in literature searching (LR) developed the search strategy with input from other reviewers. A combination of subject headings such as MeSH and free-text terms were used to cover the following concepts: *1*) economic evaluation, *2*) children under five, *3*) nutrition/malnutrition, and *4*) LMICs. We searched MEDLINE (Ovid), Embase (Ovid), EconLit (Ebsco), CINAHL Plus (Ebsco), Web of Science, Scopus, NHS Economic Evaluation Database, Global Health, and Maternity & Infant Care (Ovid) to identify studies for this review. In addition, hand searching and citation checking were undertaken to supplement database searching. The search strategy for MEDLINE can be found in **Supplemental Table 1**. The study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (20), and the protocol was prospectively registered in PROSPERO (CRD42020194445).

Eligibility criteria

We included studies based on the following criteria:

- Population: We included studies examining children aged <5 y from LMICs. We included studies with different age groups if disaggregated data on children <5 y were available. LMICs were identified based on the World Bank classification (21) as per the year of publication. For 2020, low-income economies were defined as those with per capita gross national income (GNI) ≤US $1035; lower middle-income economies were those with per capita GNI between US $1036 and US $4045; and upper middle-income economies were those with per capita GNI between US $4046 and US $12,535 (21).
- Intervention: All types of child nutrition interventions addressing malnutrition were included. Malnutrition referred to undernutrition (childhood stunting and wasting, micronutrient deficiencies, and underweight), overweight, obesity, and diet-related noncommunicable diseases (5). We included multisectoral interventions if improving child nutrition was one of the main objectives.

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Abbreviations used: CHEC, Consensus on Health Economic Criteria; CHEERS, Consolidated Health Economic Evaluation Reporting Standards; CMAM, community-based management of acute malnutrition; CSB, corn-soy blend; DALY, disability-adjusted life year; GNI, gross national income; LMICs, low- and middle-income countries; RUSF, ready-to-use supplementary food.

- Comparison: There were no restrictions on comparison. For instance, it could be standard care or no intervention.
- Outcome: There were no restrictions on outcome measures. For instance, they could be mortality avoided, cases averted, or disability-adjusted life years (DALYs) averted.
- Type of study: We included full economic evaluations comparing both the costs and the outcomes of ≥1 intervention and an alternative, such as cost-effectiveness analysis and cost-benefit analysis (12). Review papers, commentaries, and conference proceedings were excluded from this systematic review.
- Other: We included original scientific literature published in English peer-reviewed journals. There were no restrictions on the publication period.

Study selection

Reviewers 1 (YB) and 2 (SP) independently screened titles and abstracts based on the eligibility criteria to reduce bias and errors. The full text of selected articles was assessed independently by Reviewers 1 and 2 for final inclusion. Any disagreements were resolved through discussion at each stage. Other reviewers (ZA, JF, TT, AO) were involved when a consensus could not be reached.

Quality assessment

Reviewers 1 (YB) and 2 (SP) independently assessed the quality of the included studies to mitigate bias and reduce errors. Any disagreements were resolved through discussion, and other reviewers (ZA, JF, TT, AO) were involved when an agreement could not be reached.

We used the Drummond checklist for quality assessment (22). The checklist contains 35 items with 3 sections: study design, data collection, and analysis and interpretation of results (22). The use of this checklist has been recommended (23) and it has been widely used in other systematic reviews to conduct critical appraisal of health economic studies (19, 24). We added questions regarding funding sources, role of funder, conflict of interest, ethical approval, and generalizability of findings, to supplement the checklist.

Data extraction and synthesis

We used a standardized form to extract general characteristics and economic data of included studies. The data extraction form was finalized after pilot testing. To reduce errors, Reviewer 1 (YB) extracted data and Reviewer 2 (SP) verified it. Any disagreements were resolved through discussion, and other reviewers (ZA, JF, TT, AO) were involved when an agreement could not be reached. The following data were extracted, which was in line with other systematic reviews of economic evaluations in health (14, 17, 25–28). Reviewers did not contact authors to obtain missing or additional data because the aim of this review was to assess the existing publications.

- General characteristics: authors, publication year, title, objective, country, study year, target population, sample size, intervention, comparator, study design, type of economic evaluation, funding source, conflict of interest, and ethical approval.
- Economic evaluation methods and results: outcome measures, cost, study perspective, time horizon, discount rate, analysis of uncertainty, results, and use of checklist.

We presented findings through a narrative synthesis due to study heterogeneity. The findings included the characteristics, the summary of economic evidence, and the quality of included studies. We used Excel, Covidence, and Endnote software for data management.

Results

Overview of included studies

The literature search was conducted on July 6, 2020 and identified 4689 studies after removing duplicates. After screening titles and abstracts based on eligibility criteria, 215 studies remained for full-text screening as shown in **Figure 1**. A total of 69 studies met criteria for inclusion, including 3 additional studies identified through backward citation searching. The common reasons for exclusion were that they were not peer-reviewed articles or not full economic evaluations.

Figure 2 presents general characteristics of included studies. There was an increasing trend in the publication of studies in the area of economic evaluations of child nutrition in LMICs starting in 1970. One study was published per decade between 1970 and 1989. The number of studies published between 2000 and 2009 and between 2010 and 2019 increased to 18 and 38, respectively. The majority of studies were conducted using data from sub-Saharan Africa (n = 35), followed by South Asia (n = 26), East Asia and Pacific (n = 14), Latin America and the Caribbean (n = 10), Middle East and North Africa (n = 3), and Central Asia (n = 1), including 12 studies using multicountry data. The most common study design was a modeling study using multiple or single data sources (n = 53), and 16 studies conducted economic evaluations alongside randomized controlled trials or cohort studies. The included studies covered various nutrition interventions, but there was only 1 study targeting overweight (29) and the rest addressed undernutrition. The most common type of economic evaluation was cost-effectiveness analyses (n = 62). Most studies measured outcomes as DALYs averted (n = 32) or death averted/life saved or life years gained (n = 23), and 16 studies used other health outcomes such as stunting averted. The majority of studies considered the health care provider, government, or program perspectives (n = 48). This includes implementation cost such as human resource, supplies, and monitoring and evaluation. Only 16 studies considered the societal perspective. A number of studies did not explicitly state the perspective of economic evaluations, so some assumptions were made for this classification based

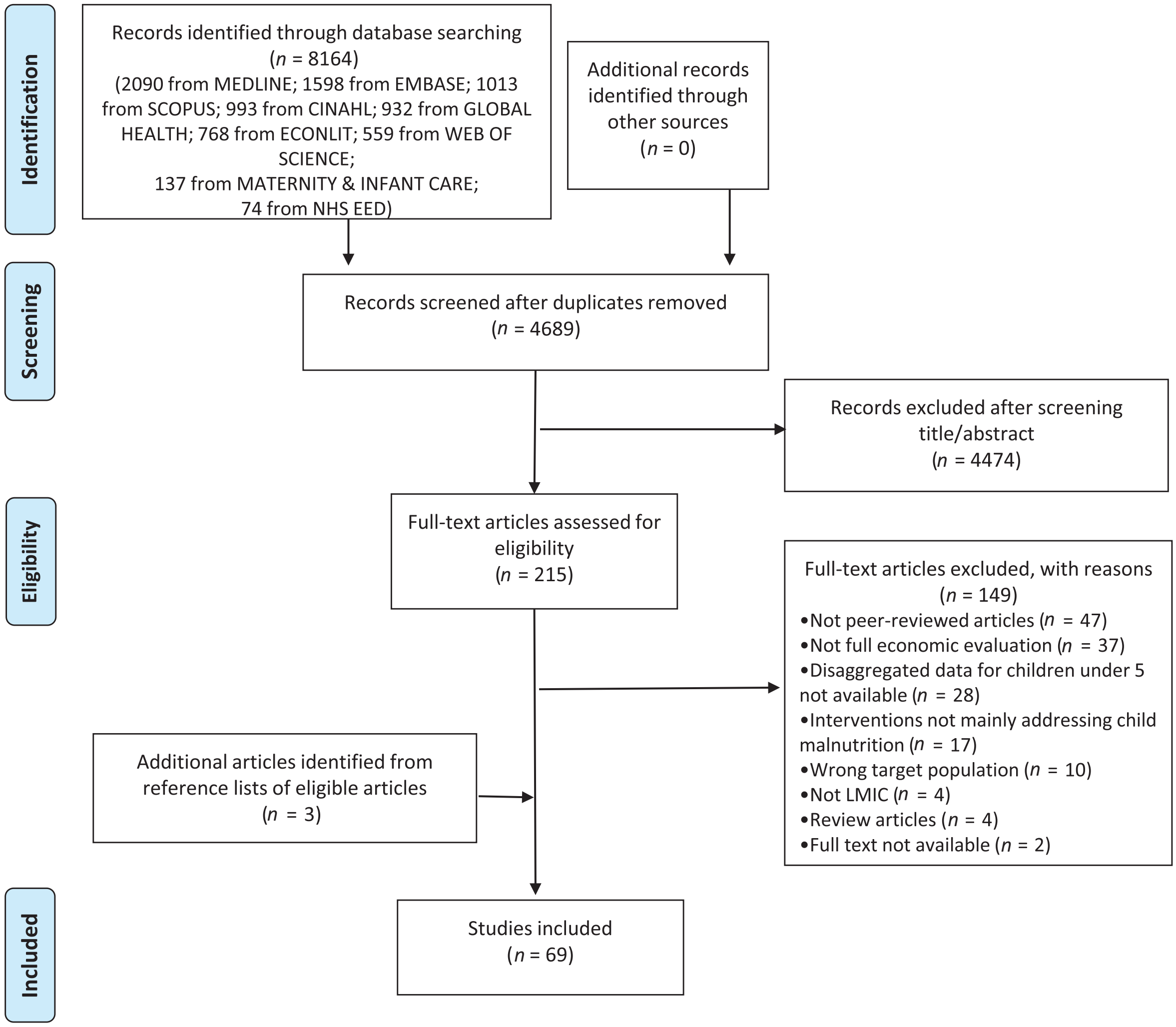

FIGURE 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram showing study selection. LMIC, low- and middle-income countries.

on cost categories. To quantify costs and outcomes, 29 studies used both primary and secondary data. There was only 1 study indicating the use of a checklist as a reporting guideline. The common funding sources were government agencies ($n = 27$), foundations ($n = 21$), and international organizations ($n = 15$).

Quality assessment

Quality assessment findings by each item of the Drummond checklist (22) are shown in **Table 1**. The percentages of "Yes," "No," and "Not Clear" were calculated without the studies that fell into "Not Applicable." We presented the findings by publication periods, 1996–2015 ($n = 43$) and 2016–2020 ($n = 23$) to reflect improved methods for economic evaluations and reporting guidance over time.

All 69 included studies stated the research question and the form of economic evaluation. More than 90% of included studies stated the economic importance of the research question and the alternative intervention; however, 46.4% of included studies did not clearly state and justify the viewpoint of the analyses. Regarding data collection, all included studies stated the sources of effectiveness estimates and the primary outcome measures. However, quantities of resources were reported separately from their unit costs in only 23.2% of studies, and methods for the estimation of quantities and unit costs were described in 47.8% of included studies. The studies published between 2016 and 2020 better articulated details of models used than studies published between 1996 and 2015. Time horizon and the discount rates were stated in 82.6% and 60.9% of studies, respectively, whereas 47.2% of included studies justified their choice of discount rates. More studies published between 2016 and 2020 conducted sensitivity analyses (73.9%) than those published between 1996 and 2015 (67.4%). Most studies stated the choice of variables and their ranges for the analyses. Incremental analyses were reported in 72.1% of included studies. All included studies provided the answer to the study question

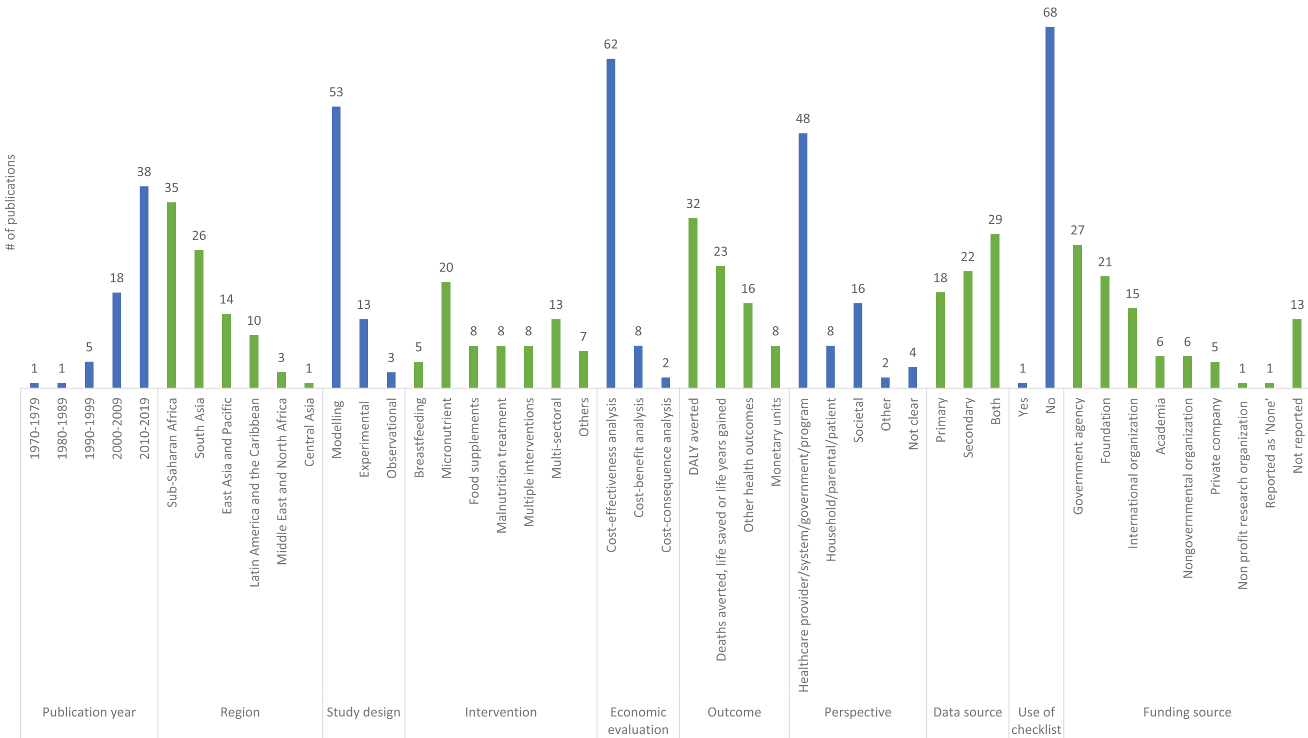

FIGURE 2 General characteristics of included studies (n = 69). Publication year did not include 2020 because the literature search did not cover whole year. Multiple counts for region, economic evaluation, outcome, perspective, and funding source. DALY, disability-adjusted life year.

and their conclusions followed from the data reported with appropriate caveats. Among the included studies, 38.9% of studies described the role of funder, 60.9% described any potential conflict of interest of study, and 54.5% stated ethics approval. The source of funding, the role of funder, conflict of interest, and ethics approval were better stated in more recent publications. Generalizability of the findings was discussed in 76.8% of included studies.

Description of included studies

Intervention types.

Breastfeeding intervention. **Table 2** shows a summary of included studies by intervention types. Four cost-effectiveness studies and 1 cost-benefit analysis study assessed breastfeeding interventions mostly from the provider perspective with a 1-y time horizon (30–34). The breastfeeding promotion program in hospitals in Brazil, Honduras, and Mexico (30) and the use of donor human breast milk from South Africa (34) were found to be cost-effective compared with control hospitals and formula milk, respectively. Another cost-effectiveness study from South Africa explored breastfeeding support programs by differing the intensity of clinic- or home-based interventions and indicated that the simplified version (less frequent pre- and postnatal visits, and more clinic-based as opposed to home-based visits) was the most efficient one (31). A cost-benefit analysis from Vietnam concluded that investing in a national breastfeeding promotion strategy would generate monetary benefits of US $2.39 for every US $1, or a 139% return on investment compared with inadequate breastfeeding (33). Chola et al. (32) found that a community-based peer counseling program for breastfeeding support in Uganda was unlikely to be cost-effective compared with standard care at public health facilities.

Micronutrient intervention. Twenty studies assessed micronutrient interventions that aimed to reduce vitamin and mineral deficiencies in children. The interventions targeted vitamin A ($n = 6$), zinc ($n = 11$), and multiple micronutrients ($n = 3$).

Vitamin A. Two studies from the provider perspective with a 1-y time horizon and 1 study with a 30-y time horizon assessed vitamin A supplementation (35–37). A study from the Philippines reported that universal distribution of vitamin A was more cost-effective than targeting malnourished children (35) and the National Vitamin A Program in Nepal was found to be cost-effective compared with doing nothing (36). The cost per death averted for vitamin A supplementation ranged from ~US $20 in Zambia to US $397 in Nepal compared with no intervention (36, 37). Fiedler et al. (38) explored vitamin A fortification of wheat flour in the Philippines and concluded that fortification could be twice as efficient as the national supplementation program (38). Yet

TABLE 1 Quality assessment of included studies[1]

	Total ($n = 69$)							1996–2015 ($n = 43$)							2016–2020 ($n = 23$)						
	Yes		No		Not clear		NA	Yes		No		Not clear		NA	Yes		No		Not clear		NA
Item	*n*	%	*n*	%	*n*	%	*n*	*n*	%	*n*	%	*n*	%	*n*	*n*	%	*n*	%	*n*	%	*n*
Study design																					
(1) The research question is stated	69	100.0	0	0.0	0	0.0	0	43	100.0	0	0.0	0	0.0	0	23	100.0	0	0.0	0	0.0	0
(2) The economic importance of the research question is stated	67	97.1	2	2.9	0	0.0	0	42	97.7	1	2.3	0	0.0	0	22	95.7	1	4.3	0	0.0	0
(3) The viewpoint(s) of the analysis are clearly stated and justified	37	53.6	32	46.4	0	0.0	0	23	53.5	20	46.5	0	0.0	0	13	50.0	10	50.0	0	0.0	0
(4) The rationale for choosing the alternative programs or interventions compared is stated	60	87.0	8	11.6	1	1.4	0	37	86.0	5	11.6	1	2.3	0	21	91.3	2	8.7	0	0.0	0
(5) The alternatives being compared are clearly described	64	92.8	3	4.3	2	2.9	0	38	88.4	3	7.0	2	4.7	0	23	100.0	0	0.0	0	0.0	0
(6) The form of economic evaluation used is stated	69	100.0	0	0.0	0	0.0	0	43	100.0	0	0.0	0	0.0	0	23	100.0	0	0.0	0	0.0	0
(7) The choice of form of economic evaluation is justified in relation to the questions addressed	63	91.3	6	8.7	0	0.0	0	39	90.7	4	9.3	0	0.0	0	21	91.3	2	8.7	0	0.0	0
Data collection																					
(8) The source(s) of effectiveness estimates used are stated	69	100.0	0	0.0	0	0.0	0	43	100.0	0	0.0	0	0.0	0	23	100.0	0	0.0	0	0.0	0
(9) Details of the design and results of effectiveness study are given (if based on a single study)	19	95.0	0	0.0	1	5.0	49	9	90.0	0	0.0	1	10.0	33	7	100.0	0	0.0	0	0.0	16
(10) Details of the method of synthesis or meta-analysis of estimates are given (if based on an overview of a number of effectiveness studies)	47	95.9	1	2.0	1	2.0	20	31	93.9	1	3.0	1	3.0	10	16	100.0	0	0.0	0	0.0	7
(11) The primary outcome measure(s) for the economic evaluation are clearly stated	69	100.0	0	0.0	0	0.0	0	43	100.0	0	0.0	0	0.0	0	23	100.0	0	0.0	0	0.0	0
(12) Methods to value health states and other benefits are stated	10	90.9	0	0.0	1	9.1	58	6	85.7	0	0.0	1	14.3	36	4	100.0	0	0.0	0	0.0	19
(13) Details of the subjects from whom valuations were obtained are given	9	81.8	1	9.1	1	9.1	58	5	71.4	1	14.3	1	14.3	36	4	100.0	0	0.0	0	0.0	19
(14) Productivity changes (if included) are reported separately	9	90.0	0	0.0	1	10.0	59	4	80.0	0	0.0	1	20.0	38	5	100.0	0	0.0	0	0.0	18
(15) The relevance of productivity changes to the study question is discussed	9	90.0	0	0.0	1	10.0	59	4	80.0-	0	0.0	1	20.0	38	5	100.0	0	0.0	0	0.0	18

(*Continued*)

TABLE 1 (*Continued*)

Item	Total (n = 69)							1996–2015 (n = 43)							2016–2020 (n = 23)						
	Yes		No		Not clear		NA	Yes		No		Not clear		NA	Yes		No		Not clear		NA
	n	%	*n*	%	*n*	%	*n*	*n*	%	*n*	%	*n*	%	*n*	*n*	%	*n*	%	*n*	%	*n*
(16) Quantities of resources are reported separately from their unit costs	16	23.2	53	76.8	0	0.0	0	13	30.2	30	69.8	0	0.0	0	2	8.7	21	91.3	0	0.0	0
(17) Methods for the estimation of quantities and unit costs are described	33	47.8	3	4.3	33	47.8	0	22	51.2	2	4.7	19	44.2	0	10	43.5	1	4.3	12	52.2	0
(18) Currency and price data are recorded	51	73.9	2	2.9	16	23.2	0	33	76.7	2	4.7	8	18.6	0	18	78.3	0	0.0	5	21.7	0
(19) Details of currency of price adjustments for inflation or currency conversion are given	46	66.7	23	33.3	0	0.0	0	29	67.4	14	32.6	0	0.0	0	15	65.2	8	34.8	0	0.0	0
(20) Details of any model used are given	55	90.2	1	1.6	5	8.2	8	33	86.8	1	2.6	4	10.5	5	21	95.5	0	0.0	1	4.5	1
(21) The choice of model used and the key parameters on which it is based are justified	53	86.9	2	3.3	6	9.8	8	31	81.6	2	5.3	5	13.2	5	21	95.5	0	0.0	1	4.5	1
Analysis and interpretation of results																					
(22) Time horizon of costs and benefits is stated	57	82.6	6	8.7	6	8.7	0	34	79.1	5	11.6	4	9.3	0	21	91.3	1	4.3	1	4.3	0
(23) The discount rate(s) is stated	42	60.9	25	36.2	2	2.9	0	27	62.8	15	34.9	1	2.3	0	15	65.2	7	30.4	1	4.3	0
(24) The choice of rate(s) is justified	17	47.2	19	52.8	0	0.0	33	13	56.5	10	43.5	0	0.0	20	4	30.8	9	69.2	0	0.0	10
(25) An explanation is given if costs or benefits are not discounted	7	77.8	2	22.2	0	0.0	60	4	100.0	0	0.0	0	0.0	39	3	60.0	2	40.0	0	0.0	18
(26) Details of statistical tests and CIs are given for stochastic data	6	30.0	14	70.0	0	0.0	49	3	30.0	7	70.0	0	0.0	33	3	42.9	4	57.1	0	0.0	16
(27) The approach to sensitivity analysis is given	46	66.7	23	33.3	0	0.0	0	29	67.4	14	32.6	0	0.0	0	17	73.9	6	26.1	0	0.0	0
(28) The choice of variables for sensitivity analysis is justified	43	95.6	0	0.0	2	4.4	24	26	92.9	0	0.0	2	7.1	15	17	100.0	0	0.0	0	0.0	6
(29) The ranges over which the variables are varied are stated	43	95.6	2	4.4	0	0.0	24	26	92.9	2	7.1	0	0.0	15	17	100.0	0	0.0	0	0.0	6
(30) Relevant alternatives are compared	68	98.6	0	0.0	1	1.4	0	42	97.7	0	0.0	1	2.3	0	23	100.0	0	0.0	0	0.0	0
(31) Incremental analysis is reported	44	72.1	17	27.9	0	0.0	8	29	74.4	10	25.6	0	0.0	4	15	78.9	4	21.1	0	0.0	4
(32) Major outcomes are presented in a disaggregated as well as aggregated form	54	78.3	15	21.7	0	0.0	0	33	76.7	10	23.3	0	0.0	0	20	87.0	3	13.0	0	0.0	0
(33) The answer to the study question is given	69	100.0	0	0.0	0	0.0	0	43	100.0	0	0.0	0	0.0	0	23	100.0	0	0.0	0	0.0	0
(34) Conclusions follow from the data reported	69	100.0	0	0.0	0	0.0	0	43	100.0	0	0.0	0	0.0	0	23	100.0	0	0.0	0	0.0	0
(35) Conclusions are accompanied by the appropriate caveats	69	100.0	0	0.0	0	0.0	0	43	100.0	0	0.0	0	0.0	0	23	100.0	0	0.0	0	0.0	0

(*Continued*)

TABLE 1 (*Continued*)

Item	Total (*n* = 69)							1996–2015 (*n* = 43)							2016–2020 (*n* = 23)						
	Yes		No		Not clear		NA	Yes		No		Not clear		NA	Yes		No		Not clear		NA
	n	%	*n*	%	*n*	%	*n*	*n*	%	*n*	%	*n*	%	*n*	*n*	%	*n*	%	*n*	%	*n*
Supplementary																					
S1. The source of funding is described	54	78.3	15	21.7	0	0.0	0	31	72.1	12	27.9	0	0.0	0	21	91.3	2	8.7	0	0.0	0
S2. The role of the funder is described	21	38.9	33	61.1	0	0.0	15	9	29.0	22	71.0	0	0.0	12	12	57.1	9	42.9	0	0.0	2
S3. Any potential conflict of interest of study is described	42	60.9	27	39.1	0	0.0	0	23	53.5	20	46.5	0	0.0	0	19	82.6	4	17.4	0	0.0	0
S4. Ethics approval is stated	24	54.5	20	45.5	0	0.0	25	11	45.8	13	54.2	0	0.0	19	13	76.5	4	23.5	0	0.0	6
S5. Generalizability of the findings is discussed	53	76.8	16	23.2	0	0.0	0	34	79.1	9	20.9	0	0.0	0	18	78.3	5	21.7	0	0.0	0

[1]Used the Drummond checklist; % calculated without NA. The studies published before 1996 were not included ($n = 3$) for comparison of studies published 1996–2015 and studies published 2016–2020. NA, not applicable.

the authors mentioned that fortification alone would not be enough, so recommended a combination of fortification and targeted supplementation interventions. Two studies from Cameroon employed an economic optimization modeling approach to assess cost-effectiveness of vitamin A programs with a 10-y time horizon and found that the models could identify cost-effective interventions compared with existing strategy (39, 40).

Zinc. Eleven studies assessed cost-effectiveness of zinc-related interventions (41–51). Three of these studies addressed zinc supplementation as a treatment for acute diarrhea with various outcome measures, including death, DALYs, and diarrhea averted (41, 45, 49). Robberstad et al. (41) found that zinc as adjunct therapy improved acute diarrhea management and that it was cost-effective in Tanzania compared with no treatment. Similarly, a study from Colombia showed that zinc supplementation was more cost-effective than standard treatment without zinc (49). However, zinc supplementation compared with placebo was not shown to be cost-effective in India (45).

Seven studies examined zinc interventions for disease prevention (42–44, 46, 47, 50, 51). Two modeling studies from India and 2 modeling studies from China examined the biofortification of wheat or rice with zinc compared with status quo, and found it to be cost-effective with a 1–30-y time horizon (42, 43, 50, 51). A study looking at strategies for delivering zinc supplements from sub-Saharan Africa found that weekly or intermittent preventive zinc supplementation interventions were cost-effective compared with daily preventive or therapeutic zinc supplementation (44). Chhagan et al. (46) reported that universal zinc distribution in addition to vitamin A supplementation in South Africa could be cost-effective compared with the standard of care when the prevalence of stunting was ∼20%. One modeling study based on data from 77 countries concluded that preventive zinc supplementation would be a highly cost-effective intervention compared with no intervention in the developing country setting (47). Lastly, a study from Myanmar explored the cost-effectiveness of social franchising as a platform to promote zinc and oral rehydration salt from the societal and medical perspectives, and concluded that the franchised approach was cost-effective compared with standard practices (48).

Multiple micronutrients. Two studies assessed the effects of a home fortification program in Pakistan using Sprinkles that contained zinc, iron, and other micronutrients (52, 53). The studies reported economic benefit as gain in earnings per dollar spent was US \$37 from the provider perspective (52), and US \$106 from the societal perspective, with a 55-y time horizon compared with placebo (53). A modeling study looking at the cost-effectiveness of multiple micronutrient powders for children in 78 countries found various health benefits across countries compared with no intervention (54).

TABLE 2 Description of included studies[1]

Author, year	Country	Intervention vs. comparator	Study design	Type/ perspective	Time horizon/ discount	Cost and outcome: Intervention	Cost and outcome: Comparator	Results
Breastfeeding								
Horton et al., 1996 (30)	Brazil, Honduras, Mexico	Hospital-based breastfeeding promotion vs. control hospitals and other health interventions from published literature	Modeling /observational study	CEA NS (assumed provider)	1 y / 3%	US $2.70–11.47/birth Per 1000 births: 255–561 diarrheal cases averted; 0.83–1.59 acute respiratory infection and 1.47–3.66 diarrheal deaths averted; 75–171 DALYs gained	US $0.09–8.74/birth Data from control hospital used as baseline to measure reduction in mortality and morbidity	Concluded as cost-effective compared with other health intervention from published literature
Desmond et al., 2008 (31)	South Africa	*1)* Full scenario (group education, home visits, postnatal visits, clinic visits); *2)* Simplified scenario (less frequent pre- and postnatal visits, and more clinic-based as opposed to home-based visits); *3)* Basic scenario (entirely clinic-based) vs. doing nothing	Modeling/quasi-experimental study	CEA Provider	7 mo / NS	*1)* US $13.6 million; *2)* US $6.7 million; *3)* US $1.9 million Months of EBF: *1)* 330,220, *2)* 275,223; *3)* 69,771	US $0 48,273 mo of EBF	ICERs of Nothing to Basic: $88; Basic to Simplified: $23; and Simplified to Full: $126 per increased month of EBF
Chola et al., 2015 (32)	Uganda	Community-based peer counseling in addition to standard care to promote EBF for 6 mo vs. standard care provided at public health facilities	Modeling/cluster randomized trial A decision tree, Markov model	CEA Provider	24 wk / 3%	US $250/child 3.5 mo of EBF; 5.78 DALYs averted	US $113/child 1.5 mo of EBF; 5.76 DALYs averted	ICERs were US $68 per month of EBF and US $11,353 per DALY averted. Less likely cost-effective

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TABLE 2 (*Continued*)

Author, year	Country	Intervention vs. comparator	Study design	Type/ perspective	Time horizon/ discount	Cost and outcome: Intervention	Cost and outcome: Comparator	Results
Walters et al., 2016 (33)	Vietnam	Comprehensive breastfeeding promotion strategy at national-scale vs. inadequate breastfeeding	Modeling	CBA Government and societal	1 y for cost; effect from breastfeeding ≤2 y of age / NS	US $30.13 million/y The monetary benefits based on cognitive losses averted and reduced health system treatment costs: US $72.14 million	— Cognitive losses US $70.4 million; health expenditure costs US $23.36 million	It could result in preventing 200 child deaths per year and generate monetary benefits of US $2.39 for every US $1, or a 139% return on investment
Taylor et al., 2018 (34)	South Africa	Donor milk (various scenarios by birthweight and days of feeding) vs. formula milk	Modeling Markov decision model	CEA Health services	14 or 28 d of feeding; <98 d in care / No discounting	Incremental costs: 1,249,641 to 298,823 86–229 lives saved per 10,000 very-low-birthweight infants	—	Very cost-effective in South Africa based on the WHO threshold of 1 GDP per capita per DALY averted
Micronutrient: vitamin A								
Loevinsohn et al., 1997 (35)	Philippines	Universal distribution of vitamin A supplementation vs. *1*) broad targeting (mild, moderate, or severe malnutrition), *2*) narrow targeting (moderate and severe malnutrition)	Modeling	CEA Provider	1 y for cost / NS	US $992,894/y 14,773 deaths averted	US $/y *1*) 1,034,510; *2*) 888,659 *1*) 7178 deaths averted; *2*) 3455 deaths averted	Concluded that universal distribution of vitamin A to all preschoolers is the most effective method for preventing deaths
Fiedler, 2000 (36)	Nepal	Nepal National Vitamin A Supplementation Program vs. assumed doing nothing	Modeling	CEA NS (assumed provider)	1 y / NS	US $1.7 million/y; $1.25 to deliver 2 vitamin A capsules/participant Startup phase: 4200 lives saved; long-term: 7500 lives saved/y	—	The cost per death averted ranged from US $289 to US $397. Concluded as cost-effective compared with other primary care interventions

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TABLE 2 (*Continued*)

Author, year	Country	Intervention vs. comparator	Study design	Type/ perspective	Time horizon/ discount	Cost and outcome		Results
						Intervention	Comparator	
Fiedler et al., 2000 (38)	Philippines	Vitamin A fortification of wheat flour with different vitamin A contents; supplementation; combination of fortification and supplementation vs. Philippines National Vitamin A Supplementation Program	Modeling	CEA NS (assumed government)	1 y / NS	Fortification 149–270 million pesos; supplementation 830–834 million pesos; combined 819 million pesos Person years of vitamin A gap reduction: fortification 982,000 to 1.8 million; supplementation 2.4–2.8 million; combined 2.2 million	Nationwide 834 million pesos; targeted rural areas 481 million pesos .Nationwide 1.3 million; targeted rural areas 555,000 person-years of vitamin A gap eliminated	ICERs of fortifications ranged from 104 to 240 pesos/person year of vitamin A gap reduction in comparison with other fortification scenarios
Fiedler and Lividini, 2014 (37)	Zambia	Vitamin A capsule through Child Health Week vs. assumed no intervention	Modeling	CEA NS	30 y / 3%	—	—	<$20 per DALY saved This analysis was part of multiple vitamin A program portfolio so data on individual intervention not shown
Vosti et al., 2015 (39)	Cameroon	Combination of vitamin A interventions suggested by the economic optimization model vs. a constructed business-as-usual scenario—vitamin A supplementation, deworming tablets, edible oil fortification	Modeling Economic optimization model	CEA NS (assumed provider)	10 y / 3%	US $21.0 million nationwide for 10 y 12.9 million children covered	US $37.7 million nationwide for 10 y 12.9 million children covered	Programs based on the optimization model are 44% less expensive, with no change in the total number of children effectively covered nationwide

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TABLE 2 (*Continued*)

Author, year	Country	Intervention vs. comparator	Study design	Type/ perspective	Time horizon/ discount	Cost and outcome: Intervention	Cost and outcome: Comparator	Results
Vosti et al., 2020 (40)	Cameroon	New vitamin A strategy by Micronutrient Intervention Modeling tool vs. current business-as-usual vitamin A strategy (national vitamin A–fortified edible oil and vitamin A supplementation)	Modeling Lives Saved Tool, optimization model	CEA NS (assumed provider)	10 y / No discounting	US $9.5 million 13.1 million child-years	US $30.1 million 12.8 million child-years	The tool identifies the national economically optimal strategy
Micronutrient: zinc								
Robberstad et al., 2004 (41)	Tanzania	(I) Current standard treatment with ORS; (II) zinc as adjunct therapy to current standard treatment for children with nondysenteric diarrhea; (III) zinc as adjunct therapy to current standard treatment for all children with acute diarrhea, including those with dysentery vs. no treatment	Modeling A decision tree model	CEA Societal perspective	NS / 3%	Incremental cost US $0.47/treatment; US $0.0194/tablet Cost/effect: (I) US $113/DALY, US $3213/death averted; (II) NS; (III) US $73/DALY, US $2098/death averted	US $1.92/treatment	ICER of (II) vs. (I): US $40 per DALY averted; US $1176 per death averted. ICER of (III) vs. (II): US$11 per DALY averted; US $307 per death averted. Cost-effective as they cost less than the Tanzanian GDP per capita of US $270 per DALY averted
Stein et al., 2007 (42)	India	Zinc biofortification of *1*) wheat; *2*) rice; *3*) wheat and rice vs. status quo	Modeling	CEA NS (assumed provider)	30 y / 3%	*1*) US $1.3–2.4 million/y; *2*) US $1.4–2.6 million/y DALYs gained *1*) 60,000; *2*) 0.5 million; *3*) 0.56 million (pessimistic); *1*) 0.33 million; *2*) 1.16 million; *3*) 1.45 million (optimistic)	— 2.83 million DALYs lost/y	Cost for DALY saved (US $) *1*) 39.45; *2*) 3.90; *3*) 7.31 (pessimistic); *1*) 1.98; *2*) 0.40; *3*) 0.73 (optimistic) Cost for life saved (US $) *1*) 1194.03; *2*) 119.37; *3*) 115.04 (pessimistic); *1*) 59.70; *2*) 12.03; *3*) 11.62 (optimistic) Cost-effective by the World Development

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TABLE 2 (*Continued*)

Author, year	Country	Intervention vs. comparator	Study design	Type/ perspective	Time horizon/ discount	Cost and outcome		Results
						Intervention	Comparator	
								Report (saving 1 DALY <$US150), the WHO (<3 times per capita income)
De Steur et al., 2012 (43)	China	Zinc biofortification of rice for children under 5 vs. status quo	Modeling	CEA NS (assumed provider)	30 y / 3%	US $16.9 million for 30 y DALYs saved/y: 0.4 million (pessimistic); 1.6 million (optimistic)	2.6 million DALYs lost/y	Cost for saving 1 DALY (US $): 4.8 (pessimistic); 1.2 (optimistic) Highly cost-effective as per the World Bank cut-off levels: cost per DALY saved <US $258
Brown et al., 2013 (44)	Sub-Saharan Africa	Zinc supplementation *1)* daily preventive; *2)* weekly preventive; *3)* intermittent short-term preventive; *4)* therapeutic as adjunctive treatment for episodes of diarrhea vs. among interventions	Modeling	CEA NS (assumed provider)	Per year / NS	US $ *1)* 7.8–10.1; *2)* 1.6–3.9; *3)* 1.0–4.4; *4)* 1.3–2.1 per child/y *1)* and *2)* 0.15–0.29 million deaths averted; 7.4–13.6 million YLL gained; *3)* 0.1–0.19 million deaths averted; 4.9–9.0 million YLL gained; *4)* 27,000–110,000 deaths averted; 1.3–5.2 million YLL gained	—	The most cost-effective interventions were weekly or intermittent preventive zinc supplementation
Patel et al., 2013 (45)	India	*1)* Zinc only; *2)* zinc and copper together vs. placebo	Modeling/ randomized controlled trial	CEA Provider (government) and patient	NS	*1)* US $1495/treatment; *2)* US $1657/treatment Duration of diarrhea (hours): *1)* 64.4; *2)* 64.4	US $952.6/treatment Duration of diarrhea (hours): 62.2	Increased cost for averting an hour of diarrhea *1)* Rs 74.3; *2)* Rs 169.2 as compared with placebo. Both cost and duration of diarrhea were more in interventions
Chhagan et al., 2014 (46)	South Africa	Universal zinc plus vitamin A supplementation vs. standard of care (Universal vitamin A supplementation)	Modeling	CEA Societal	Over 1 y / No discounting	Int $85,905 2256 diarrhea cases prevented compared with comparator	Int $83,141	ICER of Int $1.23 per additional case of diarrhea prevented. It had low incremental costs or became cost-saving when the

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TABLE 2 (*Continued*)

Author, year	Country	Intervention vs. comparator	Study design	Type/ perspective	Time horizon/ discount	Cost and outcome		Results
						Intervention	Comparator	
								prevalence of stunting was close to 20%
Fink and Heitner, 2014 (47)	77 countries classified as least developed	Zinc distribution through *1)* direct pills; *2)* micronutrient biscuits; *3)* deployment of home-based water filtration systems vs. no intervention at all	Modeling Health impact model	CEA External financing agency	1 y / 3%	US $/child/y *1)* 14.6; *2)* 29.2; *3)* 12.5 1.4. DALYs per 100 households (health effect parameters were modeled to be equal across zinc delivery modes)	—	ICER per DALY saved: *1)* US $606 (pessimistic 151; optimistic 908); *2)* US$ 1211 (pessimistic 454; optimistic 1211); *3)* US $879 (pessimistic 527; optimistic 1230) . Cost-effective by WHO's standard if costs per DALY <US $1500
Bishai et al., 2015 (48)	Myanmar	Adding ORS-Z as an additional product line in an existing social franchise program vs. continue making ORS and zinc available in government clinics, and to do nothing to promote their sale in private retail outlets	Modeling/quasi-experimental community randomized trial The Lives Saved Tool model, decision tree	CEA Societal; medical	1 y / 3%	US $104,486 77.28 DALYs averted; 2.85 deaths averted compared with comparator	US $88,522	ICER from the societal perspective: US $5955 per death averted; US $214 per DALY averted; from the medical perspective: US $8980 per death averted; US $339 per DALY averted Highly cost-effective by the Commission for Macroeconomics and Health, the cost per DALY less than the Myanmar 2010 GDP per capita (US $876.2)
Mejía et al., 2015 (49)	Colombia	The standard treatment with the addition of zinc vs. the standard treatment without zinc	ModelingA decision model	CEA Health system	1 mo / No discounting	US $34.36/acute diarrhea treatment 0.0000243 deaths	US $42.5/acute diarrhea treatment 0.0000562 deaths	Zinc supplementation is less costly and more effective than standard treatment without zinc (reduction of US $8.14 per child)

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TABLE 2 (*Continued*)

Author, year	Country	Intervention vs. comparator	Study design	Type/ perspective	Time horizon/ discount	Cost and outcome		Results
						Intervention	Comparator	
Wang et al., 2016 (50)	China	Biofortification of wheat *1*) combined foliar application of Zn fertilizer plus pesticide; *2*) the foliar Zn fertilization alone vs. status quo	Modeling	CEA NS (assumed provider)	10 y / NS	*1*) US $16.6–93.0 million (pessimistic); 49.7–278.9 million (optimistic); *2*) US $91.0–510.6 million (pessimistic); US $273.1–1531.8 million (optimistic); DALYs saved 27,990–96,329 (pessimistic); 120,622–437,987 (optimistic)	—	*1*) Cost for DALY saved (US $): 79.0–108.2 (pessimistic); 41.2–87.9 (optimistic); *2*) cost for DALY saved (US$) 434.1–594.3 (pessimistic); 226.4–482.6 (optimistic) *1*) highly cost-effective according to the World Bank: <US $258
Tewari et al., 2017 (51)	India	Biofortified wheat vs. status quo	Modeling	CEA NS	Per year / 3%	6 (pessimistic) to 10 (optimistic) million rupee/y DALYs saved/y: 16,891 to 101,349 depending on adoption rate	913,055 DALYs lost	The cost per DALY saved: Rs 79 (optimistic) to 177 (pessimistic) Very cost-effective as per the WHO: less than national per capita income
Multiple micronutrients								
Sharieff et al., 2006 (52)	Pakistan	Home fortification with Sprinkles that contain zinc, iron, iodine, vitamins C, D, and A, and folic acid vs. control	Modeling	CEA; CBA Provider	Over 4 mo of intervention for >5 y CBA: ≤55 y of age CBA: 3%	US$1.20/child Probability of death: 1.64% for 6–12-mo-old; 0.164% 12–24-mo-old Cumulative difference in earnings: US$54	Probability of death: 2% for 6–12-mo-old; 0.2% 12–24-mo-old	Cost per death averted: US $406; cost per DALY saved: US $12.2 . For each dollar spent, the return was US $37 . Cost-effective compared with primary health care prevention programs from published literature

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TABLE 2 (*Continued*)

Author, year	Country	Intervention vs. comparator	Study design	Type/ perspective	Time horizon/ discount	Cost and outcome: Intervention	Cost and outcome: Comparator	Results
Sharieff et al., 2008 (53)	Pakistan	Home fortification with Sprinkles that contain zinc, iron, iodine, vitamins C, D, and A, and folic acid vs. placebo	Modeling Markov model	CBA Societal	55 y / 3%	US $2.4–108/child Incremental benefit: US $106/child	US $0.3–117/child	The present value of incremental benefit of intervening with Sprinkles in childhood was US $106 per child, and varied from US $21 (low-risk scenario) to US $367 (high-risk scenario)
Pasricha et al., 2020 (54)	78 countries	Program of daily multiple micronutrient powders vs. no program	Modeling Microsimulation model	CEA NS (assumed provider)	6-mo course, follow-up after additional 6 mo / No discounting	Powders: US $0.03/dose; non-drug program: US $4.50/child The median net effect across all 78 countries: 22.7 DALYs averted per 10,000 children compared with no intervention	—	The median cost-effectiveness in countries where multiple micronutrient powders were beneficial: US $3576 per DALY averted (US $3897 in Africa, US $3136 in Asia and the Middle East, and US $3216 in Latin America)
Food supplements								
Parker et al., 1978 (55)	India	*1)* Nutrition supplementation; *2)* supplementation in addition to medical care; *3)* medical care vs. control village	Cohort	CEA NS (assumed provider)	36 mo / NS	Per child/y: *1)* Rs 176; *2)* Rs 160; *3)* Rs 68 Infant mortality: *1)* 97; *2)* 81; *3)* 70; child mortality: *1)* 11; *2)* 13; *3)* 11 per 1000 live births	Per child/y: Rs 58 Infant mortality: 128; child mortality: 18 per 1000 live births	*3)* Had the lowest child service costs per death averted. Using "cost/effect of *3)*" as an index of 1.0, *1)* 1.5; *2)* 1.6 for infant deaths averted; *1)* 21.2; *2)* 27.9 for child deaths averted
Glewwe et al., 2001 (56)	Philippines	Supplementary child feeding vs. not explicitly reported	Modeling	CBA NS (assumed program)	2-y program, working life of 45 y / 3–5%	US $100/child Wage increase: US $310–1840	—	A labor market return of US $3–18 for every dollar spent from the gain in academic achievement

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TABLE 2 (*Continued*)

Author, year	Country	Intervention vs. comparator	Study design	Type/ perspective	Time horizon/ discount	Cost and outcome		Results
						Intervention	Comparator	
Puett et al., 2013 (57)	Chad	Staple rations plus a ready-to-use supplementary food vs. Food Assistance rations consisting of staple foods	Cluster-randomized controlled trial	CEA Societal	5 mo / 25% for sites; 3% for capital items	Incremental cost €374/child Diarrhea per child-month: 0.81 Anemia prevalence: 56.5%	728 EUR/child Diarrhea per child-month: 1.17 Anemia prevalence: 66.8%	Incremental cost per episode of diarrhea averted: 1083 EUR; per case of anemia averted: 3627 EUR . Less cost-effective than other standard interventions
Yang et al., 2013 (58)	Democratic Republic of Congo	Allocates either RUTF, some supplementary food, or no food to each child based on the child's sex, age, HAZ, and WHZ vs. currently recommended policies, which do not use HAZ information	Modeling Mathematical optimization model	CEA NS (assumed provider)	3 mo of intervention throughout 5 y / 3%	Per intervention per child: US $3.30 for RUTF; US $17.10 for RUSF Estimated mortality rate: logit (−0.414HAZ −0.236WHZ − 0.059t − 4.989) for boys and logit(−0.403HAZ −0.431WHZ − 0.054t − 5.144) for girls	Per intervention per child: US$33.30 for RUTF; US $17.10 for RUSF	The proposed policy achieves either a 9% reduction in expected DALYs at the same expected cost, or a 61% reduction in expected cost at the same expected DALYs
Rogers et al., 2017 (59)	Malawi	*1*) 2.6 L oil, 8 kg CSB provided either in bulk, or *2*) four 2-kg packages with printed messages, and enhanced social and behavior change communication emphasizing the target oil:CSB ratio vs. monthly rations of 1 L oil, 8 kg CSB in bulk, and social and behavior change communication	Quasi-experimental	CEA NS (assumed societal)	4 mo / NS	US $ per beneficiary: *1*) 143.38; *2*) 157.97 Mean added oil per 100 g CSB compared with the control group: *1*) 18 g; *2*) 13 g	US$ per beneficiary: 83.29	The marginal cost-effectiveness in US $: *1*) 188; *2*)300. Both interventions were more cost-effective

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TABLE 2 (*Continued*)

Author, year	Country	Intervention vs. comparator	Study design	Type/ perspective	Time horizon/ discount	Cost and outcome: Intervention	Cost and outcome: Comparator	Results
Isanaka et al., 2019 (60)	Mali	Moderate acute malnutrition treatment with *1)* Ready-to-use supplementary foods; *2)* a specially formulated CSB (Super Cereal Plus); *3)* Misola, a locally produced, micronutrient-fortified, cereal-legume blend; *4)* locally milled flour vs. no treatment. Severe acute malnutrition only	Modeling/cluster-randomized trial Decision tree model	CEA Health care provider	1 y / 0–5%	US $ per child: *1)* 89.01; *2)* 90.43; *3)* 90.86; *4)* 99.91 Probability of death (%): *1)* 2.89; *2)* 2.99; *3)* 3.01; *4)* 3.06	US $ per child: 36.96 Probability of death (%): 3.42	ICERs per death averted (US $): *1)* 9821, *2)* 12,435, *3)* 13,146, *4)* 17,486; per DALY averted: *1)* 347, *2)* 446, *3)* 490, *4)* 630 compared with comparator . Very cost-effective as per WHO: <1 time per capita GDP per DALY averted (US $732)
Cliffer et al., 2020 (61)	Burkina Faso	*1)* Corn-Soy-Whey Blend (a new formulation) with oil, *2)* SuperCereal Plus, *3)* ready-to-use supplementary food vs. CSB Plus program with separate fortified vegetable oil	A geographically randomized trial	CEA Program	18 mo / NS	Cost per child in US $: *1)* 140; *2)* 226; *3)* 245 Stunting (%): *1)* 27.5; *2)* 21.9; *3)* 20.3 Wasting (%): *1)* 3.1; *2)* 2.4; *3)* 2.3	Cost per child in US $: 122 Stunting (%): 20.1 Wasting (%): 2.4	CSB with oil (standard of care) was the most cost-effective ration in the prevention of wasting and stunting (least expensive and similar in effectiveness)
Shen et al., 2020 (62)	Burkina Faso	*1)* Corn Soy Whey Blend with fortified vegetable oil, *2)* Super Cereal Plus, *3)* Ready-to-Use Supplementary Food vs. standard of care: CSB Plus with fortified vegetable oil	A geographically randomized trial	CEA Multiple: program; program and caregiver	18 mo / NS	Cost per child in US $: *1)* 350; *2)* 434; *3)* 387 Stunting (%): *1)* 27.5; *2)* 21.9; *3)* 20.3 Wasting (%): *1)* 3.1; *2)* 2.4; *3)* 2.3	Cost per child in US $: 317 Stunting (%): 20.1 Wasting (%): 2.4	The current standard-of-care, CSB with oil, was found to be the most cost-effective of the 4 arms

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TABLE 2 (*Continued*)

Author, year	Country	Intervention vs. comparator	Study design	Type/ perspective	Time horizon/ discount	Cost and outcome: Intervention	Cost and outcome: Comparator	Results
Malnutrition treatment								
Khanum et al., 1994 (63)	Bangladesh	*1)* Inpatients, *2)* day-care, *3)* care at home after 1 wk of day-care vs. compared among interventions	Controlled trial	CEA Institutional; parental	<42 d / NS	*1)* 6363, *2)* 2517, *3)* 1552 taka Days to achieve 80% weight for height: *1)* 18, *2)* 23, *3)* 35	-	*3)* Care at-home management of severely malnourished children after 1 wk of inpatient care is the most cost-effective strategy
Ashworth et al., 1997 (64)	Bangladesh	*1)* In-patient management, *2)* day-care, *3)* domiciliary care vs. compared among interventions	Controlled trial	CEA Institutional; parental	Until children's weight for height reached 80% / NS	Institutional (US $): *1)* 155.9; *2)* 59.3; *3)* 29.4; Parental (US $): *1)* 3.1; *2)* 4.5; *3)* 9.4 ; Days to achieve 80% weight for height: *1)* 18, *2)* 23, *3)* 35	-	When the institutional and parental costs were combined, *3)* domiciliary care was 1.6 times more cost-effective than day-care, and 4.1 times more cost-effective than inpatient care
Bachmann, 2009 (65)	Zambia	Community-based therapeutic care vs. do nothing (no treatment)	Modeling Decision tree model	CEA Health services	1 y / No discounting	Int $203/child Death rate: 9.2%	— Death rate: 20.8%	Int$1760 per life saved and 53 per DALY gained. Highly cost-effective as per WHO, if the cost per DALY gained less than country's GDP per capita ($1000)
Wilford et al., 2012 (66)	Malawi	Existing health services with community-based management of acute malnutrition vs. without intervention	Modeling Decision tree model	CEA Health services	1 y / 3%	US $494,097 342 fewer deaths; 10,883 DALYs averted than comparator	US $39,714	The ICER of US $42 per DALY averted; US $1365 per life saved . Highly cost-effective as per WHO, the cost per DALY <2007 GNI per capita of US $250

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TABLE 2 (*Continued*)

Author, year	Country	Intervention vs. comparator	Study design	Type/ perspective	Time horizon/ discount	Cost and outcome: Intervention	Cost and outcome: Comparator	Results
Puett et al., 2013 (67)	Bangladesh	Community-based management of severe acute malnutrition vs. standard of care (inpatient treatment) compared with no treatment alternative	Modeling	CEA Societal	1 y / 3%	US $119,697 (US $165/child treated) 138 deaths averted; 4683 DALYs averted	US $82,324 (US $1344/child treated) 2 deaths averted; 67 DALYs averted	US $26 per DALY; US $869 per death averted for community-based management; US $1344 per DALY; US $45,688 per death averted for standard of care compared with no treatment. Highly cost-effective according to the WHO's GDP per capita threshold for cost per DALY averted
Goudet et al., 2018 (68)	India	Adding a community-based prevention and treatment for acute malnutrition intervention to Integrated Child Development Services standard care vs. standard care	Modeling Decision tree model	CEA NS (assumed program, household)	1-y period extended by the 3 following months / No discounting	US $335,126 (US $27/child) 15,016 DALYs averted	—	The ICER of US $23 per DALY averted . Highly cost-effective according to the WHO's classification, cost per DALY averted less than per capita GNI (US $1570)
Rogers et al., 2018 (69)	Mali	Community health workers-delivered care for severe acute malnutrition treatment vs. outpatient facility-based care compared with "Do nothing" alternative	Cohort study	CEA Societal	Over 12 mo / NS	US $244/child treated Recovery rate: 94.17%	US $442/child treated Recovery rate: 88.21%	Cost per child recovered was US $259 for community-based care; US $501 for outpatient facility-based care compared with "Do nothing"

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TABLE 2 (*Continued*)

Author, year	Country	Intervention vs. comparator	Study design	Type/ perspective	Time horizon/ discount	Cost and outcome		Results
						Intervention	Comparator	
Rogers et al., 2019 (70)	Pakistan	Lady Health Workers delivered care complemented by outpatient facility-based care vs. existing outpatient health facilities operated by an NGO compared with "Do nothing" alternative	Modeling/cluster randomized controlled trial Using TreeAge	CEA Societal	1 y / 3% for capital item	US $291/child treated Recovery rate: 76.00%	US $301/child treated Recovery rate: 82.95%	Cost per child recovered was US $382 for community-based care; US $363 for outpatient facility-based care compared with "Do nothing"
Multiple interventions								
Jha et al., 1998 (71)	Guinea	Nutrition related among 40 interventions. *1)* Mild malnutrition treatment; *2)* severe malnutrition treatment; *3)* monitor growth, counsel mothers on nutrition and pneumonia vs. assumed doing nothing	Modeling	CEA NS (assumed health provider)	1 y / 3%	US $/person: *1)* 16; *2)* 71; *3)* 17 Life years saved/person: *1)* 0.021; *2)* 1.687; *3)* 0.029	-	Per life saved: *1)* US $779; *2)* US $42; *3)* US $600
Adam et al., 2005 (72)	Sub-Saharan Africa, Southeast Asia	*1)* Support for breastfeeding mothers; *2)* support for low-birthweight babies; *3)* community-based management of neonatal pneumonia vs. no intervention	Modeling Population model PopMod	CEA NS	Annual / Not clear	*1–3)*: Int $58 million in sub-Saharan Africa; *1)* Int $49–98 million in Southeast Asia DALYs averted *1–3)*: 9 million in sub-Saharan Africa; *1)* 8–16 million in Southeast Asia (presented various combinations)	-	ICERs per DALY averted of *1)* and *2)*: Int $57 in sub-Saharan Africa; *1)* Int$6–7 in Southeast Asia

(*Continued*)

TABLE 2 (*Continued*)

Author, year	Country	Intervention vs. comparator	Study design	Type/ perspective	Time horizon/ discount	Cost and outcome		Results
						Intervention	Comparator	
Edejer et al., 2005 (73)	Sub-Saharan Africa, Southeast Asia	*1)* Oral rehydration therapy; *2)* case management of pneumonia; *3)* vitamin A supplementation; *4)* zinc supplementation; *5)* vitamin A fortification; *6)* zinc fortification; *7)* provision of supplementary food; *8)* measles immunization vs. doing nothing	Modeling	CEA NS	10 y / 3%	Millions Int $/y: from *6)* $7 to *7)* $7684 DALYs averted/y (millions): *7)* 0.04 to combination of *1–4)*, *7)*, *8)* 15.73 (presented various combinations)	-	*5–6)* ICER per DALY averted: 19 in sub-Saharan Africa; 70 in Southeast Asia . Indicated *5)* or *6)* as the most cost-effective, and *7)* as the least cost-effective
Evans et al., 2005 (74)	Sub-Saharan Africa, Southeast Asia	*1)* Vitamin A fortification; *2)* Zinc fortification; *3)* Vitamin A supplementation; *4)* Zinc supplementation; *5)* Oral rehydration therapy for diarrhea; *6)* improved complementary feeding, growth monitoring, and promotion; *7)* community-based breastfeeding support vs. assumed doing nothing	Modeling	CEA Policy maker	Annual / NS	Incremental cost (millions Int $)/y from *1)* and *2)* 23, to *6)* 4452 Incremental DALYs averted (millions)/y: from *6)* 0.1 to *7)* 8.50 (presented various combinations)	—	ICERs per DALY averted ranged from *1)* and *2)* Int $19 to *6)* Int $12,791 in sub-Saharan Africa; *7)* Int $6 to *6)* Int$44,384 in Southeast Asia . Highly cost-effective except *6)* as cost per DALY averted less than GDP per capita
Fiedler and Tesfaye, 2008 (75)	Ethiopia	Enhanced Outreach Strategy: twice annual, mass mobilizations to provide vitamin A supplementation,	Modeling	CEA NS (assumed provider)	Annual / 3%	US $0.56/beneficiary 20,203 lives saved; 547,769 DALYs averted	—	The average cost per life saved was US $228 and the cost per DALY averted was US $9 . Cost-effective according to WHO criteria, cost

(*Continued*)

TABLE 2 (*Continued*)

Author, year	Country	Intervention vs. comparator	Study design	Type/ perspective	Time horizon/ discount	Cost and outcome		Results
						Intervention	Comparator	
		deworming, nutrition screening vs. doing nothing						per DALY averted less than per capita GDP
Niessen et al., 2009 (76)	40 countries	Nutrition related among 8 interventions: *1)* breastfeeding promotion; *2)* zinc supplementation to reduce pneumonia mortality vs. baseline situation	Modeling	CEA Health care provider	10 y / 3%	Reduction in pneumonia incidence: *1)* 15–23%; *2)* 14–25%	—	Int $ per DALY averted: *1)* 35–407; *2)* 12–137
Chola et al., 2015 (77)	South Africa	*1)* Breastfeeding promotion; *2)* appropriate complementary feeding; *3)* oral rehydration solution; *4)* therapeutic feeding for severe wasting vs. baseline	Modeling Lives Saved Tool (LiST)	CEA NS (assumed health provider)	5 y / NS	Incremental costs in US $: *1)* 227.9 million; *2)* 47 million; *3)* −9 million (negative as the total cost would reduce over time); *4)* 14.7 million Additional lives saved: *1)* 427; *2)* 117; *3)* 1153; *4)* 462	—	Incremental costs for life years gained in US $: *1)* 8896; *2)* 6700; 3) −139; *4)* 531 Highly cost-effective as per WHO criteria if GDP per capita <US $7500; cost-effective if 1–3 times the GDP per capita (US $7500–22,500)
Shekar et al., 2016 (78)	Democratic Republic of the Congo (DRC), Mali, Nigeria, and Togo	*1)* Vitamin A supplementation; *2)* therapeutic zinc supplementation with ORS; *3)* public provision of complementary food for the prevention of moderate acute malnutrition; *4)* community-based management of severe acute malnutrition vs. without intervention	Modeling Lives Saved Tool (LiST)	CEA NS (assumed health provider)	NS / 3%	Cost per DALY averted (US $): *1)* 13 (Mali) to 321 (Togo); *2)* 41 (Mali) to 84 (Nigeria); *3)* 478 (DRC) to 803 (Mali); *4)* 47 (Togo) to 174 (DRC)	—	All except public provision of complementary food estimated to be highly cost-effective according to the WHO criteria as the cost per DALY averted less than GDP per capita

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TABLE 2 (*Continued*)

Author, year	Country	Intervention vs. comparator	Study design	Type/ perspective	Time horizon/ discount	Cost and outcome		Results
						Intervention	Comparator	
Multisectoral interventions								
Solon et al., 1985 (90)	Philippines	*1*) Education on nutrition, health, sanitation; *2*) immunization with *1*); *3*) supplementary food with *1*); *4*) sanitation with *1*) vs. control	Longitudinal study	CEA NS (assumed health provider)	Intervention 1 y, follow-up 1 y / NS	Philippine pesos/person: education 29; immunization 48; food 194; sanitation 10 Presented average standard weight at different times ≤29 mo (%). E.g., 11 mo: *1*) 85.7; *2*) 85.7; *3*) 87.1; *4*) 84.5	Average standard weight 11 mo: 83.7%	*1*) Was the most cost-effective, *3*) was the least Through age 9 mo: *1*) is best; 17–20 mo: immunization alone is best; and 23 and 26 mo: sanitation alone is best
Gonzalez et al., 2000 (91)	Tanzania	*1*) Daily iron supplementation; *2*) weekly malaria chemoprophylaxis with a combination of 3.125 mg pyrimethamine and 25 mg dapsone per 5 mL; *3*) a combination of *1*) and *2*) vs. standard case management	Modeling/ randomized controlled trial	CEA Health provider and sociocultural perspective	1 y for cost / 3% for effect; 2% for cost	(US $) Health care provider: *1*) 26,853; *2*) 22,264; *3*) 22,498; health care provider and households: *1*) 33,175; *2*) 26,670; *3*) 26,315 DALYs saved: *1*) 963; *2*) 1794; *3*) 2054	(US $) Health care provider: 23,600; health care and households: 30,164 Burden of disease: 2999 DALYs	ICER of *3*) compared with *1*): US $14.9; *2*): US $1.2 per DALY averted from health care provider perspectives. *3*) Is the most cost-effective. Highly cost-effective as defined by the World Bank: <US $25 per DALY
Lechtig et al., 2009 (86)	Peru	Good Start in Life Program, including promotion of growth and development, prenatal controls, adequate complementary feeding, early stimulation of the child, breastfeeding, control of iron and vitamin A deficiency, promotion of iodized salt intake,	Before-and-after study	CBA NS (assumed provider)	46 mo during 15-y period / NS	US $116.5/child/y Stunting: 36.9%; iron-deficiency anemia: 52.3%; vitamin A deficiency 5.3% Ratio of investment to benefit: US $1.64/inhabitant during the first year; US $0.86 during each of the subsequent years	Stunting: 54.1%; iron-deficiency anemia: 76.0%; vitamin A deficiency 30.4%	An annual increase of US $1.15 in the GNP for each dollar invested during this 15-y period. This is equivalent to a return of 115%/y year in the GNP, beginning in the first year following the 15-y period

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TABLE 2 (*Continued*)

Author, year	Country	Intervention vs. comparator	Study design	Type/ perspective	Time horizon/ discount	Cost and outcome: Intervention	Cost and outcome: Comparator	Results
		and personal and family hygiene vs. baseline						
Manasyan et al., 2011 (79)	Zambia	The 5-d training course on Essential Newborn Care vs. before training	Before-and-after study	CEA NS (assumed health provider)	1 y / NS	US $20,224 Neonatal mortality: 6.8 per 1000 live births	Neonatal mortality: 11.5 per 1000 live births	US $208 per life saved; US $5.24 per DALY averted Good value for money as per the WHO standards <3 times the GDP per capita (US $1500) per DALY averted
Fottrell et al., 2013 (80)	Bangladesh	Women's groups in identifying and prioritizing maternal and neonatal problems vs. control with traditional birth attendant	Cluster randomized controlled trial	CEA Provider	24 mo / No discounting	NS 21.3 neonatal deaths per 1000 live births	30.1 neonatal deaths per 1000 live births	US $220–393 per year of life lost averted; US $6695–11,974 per neonatal death averted Very cost-effective as per the WHO standards less than GDP per capita of US $775 per year of life lost averted
Fiedler et al., 2014 (81)	Zambia	Child Health Weeks, including vitamin A supplementation, growth monitoring and promotion, vaccinations, deworming and insecticide-treated mosquito nets vs. assumed no intervention	Modeling	CEA Provider	Annual / NS	US $5.7 million; US $0.46/child Saved 1323 deaths; 38,148 DALYs	Loss of 3714 lives; 108,246 DALYs	US $4958–6757 per life saved; US $73–234 per DALY saved Very cost-effective as per WHO, cost per DALY saved less than per capita GDP
Gowani et al., 2014 (88)	Pakistan	*1*) Enhanced nutrition receiving a multiple micronutrient powder and additional nutrition education; *2*) responsive stimulation; *3*) integrated	Cluster randomized trial	CEA NS (assumed health provider)	24 mo / NS	US $ per Lady Health Worker/y: *1*) 1503; *2*) 1591; *3*) 1461 Child development score: cognitive *1*) 74.1; *2*) and *3*) 81.7; language *1*) 79.3; *2*) and *3*) 85.7; motor *1*) 84.8; *2*) and *3*) 92.1	—	*3*) Is the most cost-effective intervention that promotes children's psychosocial and nutritional development

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TABLE 2 (*Continued*)

Author, year	Country	Intervention vs. comparator	Study design	Type/ perspective	Time horizon/ discount	Cost and outcome: Intervention	Cost and outcome: Comparator	Results
		receiving a combination of both *1*) and *2*) vs. standard Lady Health Worker services						
Lopez Boo et al., 2014 (87)	Nicaragua	Integrated nutritional and early childhood development program including micronutrient supplementation vs. without treatment	Modeling/ longitudinal	CBA NS (assumed provider)	5-y intervention; 50 y of labor market / 5%	US $4.2 million/y; US $37/child 3.12% increase in annual earnings, US $25.6/y	—	A cost-benefit ratio of 1.50
Bergmann et al., 2017 (82)	Malawi, Mozambique	Integrated HIV and nutrition service delivery vs. no intervention in Malawi; baseline in Mozambique	Modeling/before-and-after study	CEA NS (assumed provider)	2 y / NS	US $0.7–1.18 million in Malawi; US $2.21 million in Mozambique DALYs averted: 39,938–82,463 in Malawi; 37,558–134,471 in Mozambique	—	US $11–29 per DALY in Malawi; US $16–59/DALY in Mozambique Cost-effective compared with other health interventions in similar contexts
Saha and Varghese, 2017 (83)	India	Institutional maternal and neonatal care through birth companions vs. without intervention	Modeling/quasi-experimental	CEA Provider	2 y during postpartum period / 3%	US $26,350/y or US $0.83/live birth 45 neonatal deaths averted per 100,000 births	—	US $1832 per neonatal death averted; US $29 per life year saved Highly cost-effective as per the WHO benchmark
Wynn et al., 2017 (84)	South Africa	Pre- and postnatal home visits by community health workers (known as Mentor Mothers) vs. standard care	Cluster randomized controlled trial	CEA Health system	24 mo / 6% for equip-ment/furniture	Recurrent US $80,001 (startup US $12,146); US $124/mother-child pair Low birthweight 10%; stunting 9%; optimal breastfeeding 10%	Low birthweight 13%; stunting 14%; optimal breastfeeding 3%	US $2397 per case of low birthweight averted; US $2454 per case of stunting averted; US $1618 per case of suboptimal breastfeeding averted Concluded as cost-saving

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TABLE 2 (*Continued*)

Author, year	Country	Intervention vs. comparator	Study design	Type/ perspective	Time horizon/ discount	Cost and outcome		Results
						Intervention	Comparator	
Dragojlovic et al., 2020 (89)	Cambodia	Received enhanced homestead food production vs. no intervention	Modeling	Multiple: cost-consequence analysis; CBA Societal	10 y / 3%	$4.18 million $8.72 million monetary benefit 71.1 DALYs averted	$3.25 million $7.12 million monetary benefit 115.7 DALYs averted	A total benefit estimate of US $1.51 million. A benefit-cost ratio of 1.62
Heckert et al., 2020 (85)	Burundi and Guatemala	Food assisted multisectoral maternal and child health and nutrition: 5 treatment arms that differed in the quantity and composition of the food rations (Guatemala) and 3 that differed in the timing and duration of food assistance (Burundi) vs. control	Cluster-randomized controlled trial	CCA NS (assumed provider)	2 y, 2-y extension / 3%	US $ per beneficiary: Guatemala 854–1090; Burundi 676–766 % points reduction in stunting: Guatemala 6.5, 11.1 from 2 arms (no significant effect in others); Burundi 4.6, 5.7, 7.4	—	Cost per % point reduction in stunting: US $97–166 in Guatemala; US $103–155 in Burundi Lowest cost when delivering larger rations (Guatemala) and rations for the full first 1000 d (Burundi). Extending the programs for 2 y would have saved 11–18% per beneficiary
Others								
Awasthi et al., 2000 (96)	India	600 mg albendazole powder every 6 mo vs. placebo (600 mg calcium powder)	Randomized controlled trial	CEA Family (payer)	2 y / 1%	Annual family expenditure on illness: Rs 743; albendazole Rs 20/dose Proportion of stunted children increased by 2.06%	Annual family expenditure on illness: Rs 625 Proportion of stunted children increased by 11.44%	The ICER was Rs 543 for each case of stunting prevented Concluded as considerably low incremental cost
Waters et al., 2006 (97)	Peru	Health facility-based nutrition education program vs. control health facilities	Modeling/cluster randomized controlled trial	CEA Health provider and household	18 mo / NS	US $749 monthly/health facility Prevented 11.1 cases of stunting per 100 children; 15.2% of mortality prevented	US $417 monthly/health facility	US $55.16 per case of stunting prevented; US $1952 per death averted. Concluded as economically feasible

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TABLE 2 (*Continued*)

Author, year	Country	Intervention vs. comparator	Study design	Type/ perspective	Time horizon/ discount	Cost and outcome		Results
						Intervention	Comparator	
Carrera et al., 2012 (94)	14 countries and 1 province in Pakistan	An equity-focused approach that prioritized operational strategies to reach the most deprived populations vs. current mainstream approach	Modeling Marginal Budgeting for Bottlenecks Toolkit, LiST	CEA NS (assumed societal)	5 y / NS	For each US $1million invested, 81 under-5 deaths and 244 cases of stunting could be averted	For each US $1 million invested, 49 under-5 deaths and 84 cases of stunting could be averted	An equity-focused approach could result in sharper decreases in child mortality and stunting and higher cost-effectiveness than mainstream approaches
Marsh et al., 2016 (29)	Mexico	Lower protein infant formula vs. currently used formula	Modeling Health economic model	CEA; CBA NS	Lifetime / 3.5%	% of population becoming obese: 15.5 Life years: 26.098; QALYs: 24.76; direct health costs: 6715 Mexican pesos/person	% of population becoming obese: 17.1 Life years: 26.097; QALYs: 24.75; direct health costs/person: 6975 Mexican pesos	10.5% reduction in the likelihood of developing obesity; 3.9% reduction in direct health costs. The reduced risk of disease translates into lifetime economic benefits of MXN 984/individual
Plessow et al., 2016 (92)	India	Price subsidies on fortified packaged infant cereals (varying the level of the price subsidy) vs. no intervention	Modeling/before-after experiment	CEA Provider of the subsidy; social	Lifetime cost / 3%	Various by the level of subsidy and target household US $7.7–550.3 million 8462–268,301 DALYs averted by the level of subsidy, target household	Production losses of US $3222 million; 726,000 DALYs	Interventions targeted at the poorest deciles of households save most dollars per DALY. The cost-DALY averted ratio ranged from US $909 to US $3649. Cost-effective as per the WHO criteria, if cost per DALY between 1 and 3 times GDP per capita US $1487

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TABLE 2 (*Continued*)

Author, year	Country	Intervention vs. comparator	Study design	Type/ perspective	Time horizon/ discount	Cost and outcome		Results
						Intervention	Comparator	
Trenouth et al., 2018 (95)	Pakistan	*1)* "Double cash" US $28 monthly cash distribution, *2)* "standard cash" US $14 monthly cash distribution, *3)* "fresh food voucher" US $14 monthly voucher distribution vs. standard care	Modeling/cluster randomized controlled trial Using TreeAge Pro 2016	CEA; cost-efficiency Societal	6 mo for interventions (stunting at 12 mo) / 3%	US$/child: *1)* 203; *2)* 135; *3)* 160 Decrease in prevalence of wasting (%): *1)* 4.17; *2)* and *3)* not effective; stunting (%): *1)* 15.72; *2)* 15.26; *3)* 18.14; DALYs averted: *1)* 136–265; *2)* 144–281; *3)* 127–247	—	The cost per case of stunting averted (US $): *1)* 1290; *2)* 882; *3)* 883; cost per DALY averted: *1)* 641; *2)* 434; *3)* 563 (without discounting or age weighting); *1)* 1252; *2)* 845; *3)* 1096 (discounted, age weighted) Highly cost-effective as per the WHO, country's GDP per capita, $1435
Wieser et al., 2018 (93)	Pakistan	Price subsidies on fortified packaged complementary foods: 20% subsidy, 50% subsidy, 80% subsidy, free vs. without the subsidies	Modeling Health economic model	CEA Societal	Lifetime cost / NS	Various by the level of subsidy and target household US $0.6–38.3 million US $1.9–55.2 million production losses averted; 1648–45,571 DALYs averted	Production losses of US $209 million; 175,000 DALYs	Interventions targeted at poorest household deciles were most cost-effective Net saving of US $65–783 per DALY averted

[1]CBA, cost-benefit analysis; CCA, cost-consequence analysis; CEA, cost-effectiveness analysis; CSB, corn-soy blend; DALY, disability-adjusted life year; EBF, exclusive breastfeeding; GDP, gross domestic product; GNI, gross national income; GNP, gross national product; HAZ, height-for-age *z*-score; ICER, incremental cost-effectiveness ratio; Int$, International dollar; LiST, Lives Saved Tool; NS, not explicitly stated; ORS, oral rehydration solution/salts; ORS-Z, ORS-Zinc; Rs, Rupees; RUSF, ready-to-use supplementary food; RUTF, ready-to-use therapeutic food; WHZ weight-for-height *z*-score; YLL, years of life lost.

Food supplements. Eight articles presented the economic effect of various food supplements such as ready-to-use supplementary food (RUSF) and corn-soy blend (CSB) with different outcome measures, perspectives, and time horizons (55–62). Two articles based on the same trial from Burkina Faso found that CSB with oil as a standard of care was more cost-effective than other supplements, including RUSF, specially formulated CSB called Supercereal Plus, and corn-soy-whey blend with fortified vegetable oil to prevent stunting and wasting from both the program and caregiver perspectives (61, 62). A study from Chad exploring cost-effectiveness of RUSF compared with food assistance in the form of staple rations found that adding RUSF was less cost-effective to avert diarrhea and anemia from the societal perspective (57). However, RUSF was found to be more cost-effective than other supplementary foods, such as Supercereal Plus or local products, to treat moderate acute malnutrition in Mali from the health care provider perspective (60). Rogers et al. (59) reported that programmatic changes for increasing the amount of oil that caregivers add to CSB porridge in Malawi could be cost-effective to reach the target ratio of oil to CSB compared with standard programming. A modeling study examining ready-to-use food allocation policy suggested that the total number of DALYs attributable to childhood undernutrition could be reduced by considering height-for-age *z*-score in addition to weight-for-height score with less cost (58). Parker et al. (55) found that nutrition supplementation in addition to medical care was less cost-effective compared with medical care alone to prevent infant and child death in India. Lastly, a cost-benefit analysis from Philippines found economic benefit of supplementary child feeding (56).

Malnutrition treatment. Eight studies assessed the cost-effectiveness of malnutrition treatment interventions, including 6 articles focusing on community-based management of acute malnutrition (CMAM) from different perspectives (63–70). Seven of these studies indicated that CMAM was cost-effective to treat severe acute malnutrition in children compared with doing nothing or standard of care (65–69). The cost of CMAM per DALY averted ranged from US $23 to Int $53 in Zambia, Malawi, Bangladesh, and India with a 1-y time horizon (65–68). The cost of CMAM per child recovered ranged from US $259 in Pakistan to US $382 in Mali from the societal perspective (69, 70). Two articles based on the same study from Bangladesh found that care at home after 1 wk of day-care was more cost-effective for children with severe malnutrition to achieve 80% weight-for-height than inpatient or day-care interventions (63, 64).

Multiple interventions. Eight modeling studies conducted cost-effectiveness analyses of multiple interventions from various LMICs (71–78). The cost per DALY averted ranged from Int$6 for breastfeeding support to Int $44,384 for complementary feeding, growth monitoring, and promotion mostly from the provider perspective compared with doing nothing (72–76, 78). The data showed that supplementation and fortification with vitamin A and zinc, breastfeeding support, oral rehydration solution, therapeutic feeding, and CMAM were cost-effective compared with doing nothing (72–75, 77, 78). In contrast, complementary feeding, growth monitoring and promotion, and complimentary food provision were not likely to be cost-effective compared with doing nothing (73, 74, 78). Still, Shekar et al. (78) indicated that scaling up a set of nutrition interventions is highly cost-effective when considered as a package.

Multisectoral interventions. Seven studies assessed maternal, newborn, and child health and nutrition interventions mostly from the provider perspective with a 1–2-y time horizon (79–85). The newborn care training from Zambia (79), women's groups from Bangladesh (80), Child Health Week (a package of child health and nutrition services) from Zambia (81), integrated HIV and nutrition service delivery from Malawi and Mozambique (82), and facility-based maternal and newborn care from India (83) were estimated to be cost-effective to prevent deaths compared with no intervention or baseline. The pre- and postnatal home visits by community health workers from South Africa were estimated to be cost-effective to reduce low birthweight and stunting and improve breastfeeding compared with the standard of care (84). Heckert et al. (85) examined food-assisted health interventions by differing quantity, composition, timing, and duration of food assistance and indicated that delivering larger rations and rations for the full first 1000 d (from pregnancy to 2 y) costed least in reducing stunting in Burundi and Guatemala.

Regarding early childhood development, 2 studies from Peru and Nicaragua conducted cost-benefit analyses and found monetary benefits compared with baseline and no treatment (86, 87). Integrated child health and nutrition intervention was more cost-effective to promote child development than nutrition or simulation intervention alone in Pakistan (88). A further 3 studies examined nutrition-sensitive agricultural intervention (89), nutrition with immunization and sanitation intervention (90), and iron supplementation with malaria chemoprophylaxis (91). Dragojlovic et al. (89) found that enhanced homestead food production could improve child health and generate a positive societal net monetary benefit compared with doing nothing due to increased agricultural production in Cambodia. A study from Philippines found that education with immunization, supplementary food, or safe water was less cost-effective than education alone (90). The combination of iron supplementation and malaria chemoprophylaxis was more cost-effective to prevent severe anemia than supplementation or medication alone in Tanzania (91).

Others. Two cost-effectiveness studies from India and Pakistan assessed price subsidies on fortified packaged foods and indicated that interventions, which were targeted at the poorest deciles of households, were most cost-effective (92, 93). A modeling study using data from various countries concluded that an equity-focused approach could result in better health outcomes, including child mortality and stunting, compared with the current mainstream approach (94). A study of cash-based interventions from Pakistan found that US $14 monthly cash distribution was more cost-effective than US $28 monthly cash distribution or fresh food voucher to prevent DALYs (95). Awasthi et al. (96) found that deworming could reduce child stunting risk with low incremental cost in India compared with placebo. A study from Peru indicated that the cost per case of stunting prevented was US $55.16 and the cost per death averted was US $1952 for health facility–based child nutrition education programs compared with control groups (97). Marsh et al. (29) reported that low-protein infant formula compared with currently used formula could generate considerable health and economic benefits in the long term by reducing the risk of becoming obese in Mexico.

Study design.

Modeling based on multiple data sources including clinical trials ($n = 53$) was the most common study design, with diverse types of interventions, study outcomes, and perspectives employed. The time horizon of modeling studies ranged from 1 mo to lifelong. Economic evaluations alongside trials such as randomized trials and cohort studies were less common ($n = 13$). Most were cost-effectiveness studies using 1-mo to 4-y time horizons. The interventions under study were found to be cost-effective in 83% of modeling studies and in 75% of trial-based studies.

Study outcome.

DALYs averted. Among 69 studies, 32 studies reported DALYs with various nutrition interventions and study designs. The cost per DALYs averted ranged from <US $1 for zinc biofortification in India from the provider perspective (42) to Int$44,000 for young child complementary feeding and growth monitoring in Southeast Asia from the perspective of a policy maker (74) compared with doing nothing.

Deaths averted, life saved, or life years gained. Twenty-two studies used deaths averted or life saved to assess nutrition interventions with different study designs. The cost per life years gained was reported as the result of the interventions in 4 studies. The cost per death averted/life saved ranged from US $12 for zinc biofortification in India from the provider perspective using a 30-y time horizon (42) to US $17,500 for food supplements in Mali from the provider perspective using a 1-y time horizon (60), compared with doing nothing.

Other health outcomes. Some studies reported other health outcomes, including stunting or wasting averted/reduced ($n = 10$), diarrhea prevented ($n = 4$), malnutrition treated ($n = 3$), months of exclusive breastfeeding ($n = 2$), improved vitamin A intake ($n = 2$), weight gain ($n = 1$), child development ($n = 1$), and oil:corn soy blend ratio in prepared porridge ($n = 1$). The cost per stunting prevented ranged from Rs 543 for albendazole power compared with placebo in India from the payer perspective with a 2-y time horizon (96) to US $2500 for pre- and postnatal home visits by community health workers compared with the standard care in South Africa from the health system perspective with a 24-mo time horizon (84).

Monetary units. The cost-benefit analyses reported outcomes in monetary units ($n = 8$). The return on investment for each US $1 spent was from US $2 for a national breastfeeding promotion strategy in Vietnam (33) to US $37 for micronutrient fortification intervention in Pakistan (52) compared with no intervention. The lifetime economic benefits were MXN 984 per individual for low-protein infant formula by reducing the risk of becoming obese in Mexico compared with currently used formula (29).

Sensitivity analysis.

Among 46 studies that conducted sensitivity analyses, 17 studies undertook multiple approaches mostly using 1-way and probability analyses. The 1- or 2-way sensitivity analysis was the most common type ($n = 26$), followed by probabilistic analysis ($n = 20$) and scenario analysis ($n = 16$). Some studies indicated that their findings were relatively robust to uncertainties around model parameters or consistent with main model (32, 34, 35, 40, 58, 59, 61, 62, 66, 72, 73, 89, 91). Other studies reported that their findings were sensitive to mortality rate (32, 41, 65–67, 83), effect (45, 49, 57, 60, 70, 83, 91, 96), intervention coverage (46, 48, 65, 69, 91), cost of intervention (46, 65, 70), or discount rate (41). The approach and findings of sensitivity analyses can be found in **Supplemental Table 2**.

Discussion

This systematic review aimed to assess the quality of economic evaluations in child nutrition interventions in LMICs and synthesize the study characteristics and economic evidence. Among the included 69 studies, ∼81% concluded that nutrition interventions were cost-effective or cost-beneficial mostly based on a country's cost-effectiveness thresholds despite the heterogeneity of included studies. The review identified several gaps in the quality of economic evaluation reporting. Reporting the perspective of the analyses, justification of discount rates, and describing the role of funders and ethics approval, were identified as areas needing improvement in quality and consistency of reporting.

There was an increasing trend in number of publications starting in the 1970s, which could reflect growing need for and research interest in economic evaluation. However, there were gaps in regions and types of nutrition interventions assessed. Only 1 study included data from Central Asia and 3 studies included data from the Middle East and North Africa. These are modeling studies using secondary data, highlighting a lack of empirical evidence in these regions. Additionally, we identified only 1 study focusing on overweight whereas the rest of the studies addressed undernutrition alone. In contrast to decreasing prevalence of stunting and wasting, the global data showed that the percentage of overweight children increased from 4.9% in 2000 to 5.6% in 2019, with a significant increase in North Africa from 8.4% to 11.3% (1). Among undernutrition interventions, most studies focused on micronutrients. The economic evidence toward micronutrients is relatively well established according to the Copenhagen Consensus 2008, which ranked the vitamin A and zinc supplements for children first and iron and salt iodization fortification third, based on high benefits compared with costs among 10 global challenges such as conflicts, diseases, education, or global warming (98). Evidence gaps still remain for other interventions such as multisectoral nutrition interventions, supplementary feeding, malnutrition treatment, or overweight prevention.

As for the quality assessment, most included studies stated well the research question, the form of economic evaluation, alternative intervention, the sources of effectiveness, the primary outcome measures, sensitivity analysis methods, and conclusions. We present the findings by publication periods, 1996–2015 and 2016–2020. We considered that studies published after 2016 would reflect advanced guidance given that the Panel on Cost-Effectiveness in Health and Medicine updated their recommendations in 2016 following the first recommendations in 1996 (99, 100). Overall, studies published after 2016 met more checklist criteria than studies published before 2016, which possibly reflects the advanced economic evaluation guidance on methods and reporting over time. However, many studies did not clearly state or justify the perspective of the analyses, quantities of resources, the justification of the discount rate, the role of funder, nor identify those responsible for ethical review and approval. The issue of poor reporting on discount rate or quantities of resources has also been raised by previous reviews (25, 28, 101–103). Discount rates commonly vary between 3% and 6% when the time horizon is >1 y, and the recommendations are to perform a scenario analysis with different discount rates and report the methods (22). Reporting quantities of resources and unit costs separately is recommended to help the reader judge their relevance to their settings (22). Almost half of the included studies did not state and justify the perspective of the analysis. The perspective of the evaluation is critical because it determines cost and outcome measure and eventually influences results. Adopting a broader societal perspective to consider all the costs and benefits accrued would be ideal, but the health sector perspective is commonly used in practice (22, 104). One in 3 articles did not provide any information on uncertainty around input parameters, showing another area for improvement in reporting needed. Quality evidence requires well-described and appropriately collected data to enable judgment about whether drawn findings are robust, and outcomes are sensitive to certain variables. Other areas of improvement would include declaring the role of funder, conflict of interest, and ethics approval because a number of studies failed to report this information. Lastly, in our review, only 1 study stated the use of a checklist as a reporting guideline for economic evaluation (32). Because this has more recently become a requirement of many journals, we would expect to see an improvement in this over time. There are a variety of checklists currently available, including the Drummond checklist (22), Consolidated Health Economic Evaluation Reporting Standards (CHEERS) (105), or Consensus on Health Economic Criteria (CHEC) (106). A review study found that nearly 20 different checklists were used in systematic reviews of health economic evaluations between 2010 and 2018, indicating the variability in the use of checklists (24). Watts and Li (24) concluded that a validated and commonly used checklist would be more consistent to assess quality, and results would be more transparent and comparable over time .

A quantitative synthesis of results was not possible due to the heterogeneity of included studies in study designs, settings, interventions, comparators, characteristics of participants, perspectives, time horizons, outcome measures, and more. For instance, some interventions aimed to treat malnutrition, whereas others aimed to prevent malnutrition, or some interventions were carried out at the community level, whereas others were done at the national level. Several systematic reviews of health economic evaluations addressed similar challenges and indicated that making comparisons of cost-effectiveness was practically impossible and formulating a general conclusion could be problematic (16, 18, 25, 107–109). Overall, ∼81% of the included studies concluded that nutrition interventions were cost-effective or cost-beneficial, 10% concluded that the interventions were not cost-effective, and 9% did not explicitly interpret it. Among studies that concluded the interventions were cost-effective, the comparator was "doing nothing" in ∼45% of studies, which could affect certainty of results. Studies that concluded the interventions were not cost-effective mainly used a short time horizon and primary data sources to measure costs and outcomes. More evidence is necessary to understand whether any of these could have had implications for the findings. It is also possible that the number of studies reporting negative economic outcomes was underestimated. A study examined trials that intended to conduct an economic evaluation and found that economic evaluations were less likely to be published than clinical effectiveness results, and economic output could be more susceptible than effectiveness data to publication bias (110).

This review has some limitations. The quality assessment could be open to interpretation, although 2 reviewers independently assessed the quality and resolved any disagreements. Moreover, the Drummond checklist is commonly used in systematic reviews (19, 24), but application of other checklists such as CHEERS (105) or CHEC (106) in the present study could have produced other findings. A systematic review that used 2 checklists, Drummond and CHEERS, found that each checklist identified different low-quality studies and different weaknesses (102). Because there was no single standardized checklist, we used the Drummond checklist, which focused on reporting, and added additional items to supplement it. Our judgment was based on the published data, so there might be a difference between what was reported and what actually happened (25).

Lastly, the focus on English literature in scientific journals for this review could have limited the number of included studies. Our study's strength is that this review covered all forms of child malnutrition from LMICs without limiting certain nutritional issues, and provided a comprehensive overview of existing economic evidence from nearly 70 studies. Additionally, 2 reviewers independently screened and selected studies, and assessed the quality of included studies, and other reviewers were involved in resolving discrepancies to minimize potential bias and errors.

Conclusions

Quality economic evidence is critical for priority setting, especially in LMICs with limited resources. Overall, child nutrition interventions reported in the literature appeared to be cost-effective or cost-beneficial in a resource-limited setting. Still, insufficient data from Central Asia, the Middle East, and North Africa and the primary focus on micronutrient interventions highlight the need for more economic evidence from diverse regions and interventions to tackle all forms of child malnutrition. Quality assessment findings identified some areas for improvement, including reporting the perspective of the analyses, resource utilization, granular unit costs, and describing the role of funders and ethics approval, although the studies published after 2016 met more criteria than studies published before. Researchers should explicitly state all relevant information to ensure transparency and accountability in generating evidence. Consolidated guidance on the publication of economic evaluation and the use of quality appraisal checklists would improve the quality of economic evidence.

This review identified several gaps indicating suggestions for future research. There is little economic evidence on long-term societal impacts of child nutrition interventions. Future research incorporating all costs and effects including out-of-pocket costs, caregiver time, and long-term societal effects such as productivity gain (111) will better estimate lifelong economic benefits of investing in child nutrition. In addition, this review found only 1 study on economic evaluation of overweight intervention. Obesity has significant economic impacts due to increased mortality and disabilities and reduced productivity though the evidence is limited to high-income countries (9, 10, 112). Continued economic growth in LMICs will exacerbate the burden of obesity (112), requiring more economic evidence on child overweight and obesity in LMIC settings to address the double burden of malnutrition.

Lastly, more guidance on priority setting and optimization analyses will support efficient budgeting, which is crucial in LMICs with constrained resources. There have been some efforts on maximizing the investment through cost-effectiveness threshold, league table and program budgeting and marginal analysis, Lives Saved Tool, optimization model, and Optima Nutrition tool (39, 40, 77, 113–115). Further economic evaluations of packages of child interventions for priority setting would improve budget allocation and maximize impacts of interventions.

The next task would be to ensure that this quality economic evidence is used to improve child nutrition. Translating evidence into practice is challenging, bringing the attention of governments, academia, and implementing institutions to the need for a better understanding of the importance of economic evidence, quality assurance, and evidence application. Another essential feature is equity. Equity could be easily overlooked in economic evaluations while solely focusing on efficiency. In our review, only 1 study assessed the outcome by different socioeconomic groups (97) whereas another study addressed the equity-focused strategy (94). A systematic review on equity effects of health economic evaluations found that broad application of equity analysis is feasible, but further refinement is necessary considering varying levels of complexity and quality in methods (116). Achieving health equity and leaving no one behind is a primary global commitment (3), and incorporating equity in economic evaluations will contribute to it. Governments, nongovernment funders, academia, and implementing institutions need to agree on how to translate data into practice and incorporate equity into economic evaluations to optimize the delivery of interventions to improve child nutrition in LMIC settings.

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