BMJ Global Health

Characteristics and effects of integrated nutrition and stimulation interventions to improve the nutritional status and development of children under 5 years of age: a systematic review and meta-analysis

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To cite: Dulal S, Prost A, Karki S, *et al*. Characteristics and effects of integrated nutrition and stimulation interventions to improve the nutritional status and development of children under 5 years of age: a systematic review and meta-analysis. *BMJ Global Health* 2021;**6**:e003872. doi:10.1136/bmjgh-2020-003872

Handling editor Kerry Scott

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/bmjgh-2020-003872).

Received 2 September 2020
Accepted 29 June 2021

Check for updates

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ABSTRACT

Introduction Around 250 million children in low-income and middle-income countries are at risk of not fulfilling their developmental potential. There is a need to update syntheses investigating the effects of combined nutrition and stimulation interventions on children's growth and development and identify intervention characteristics associated with positive effects.

Methods We did a systematic review to: (1) understand the effects of integrated nutrition and stimulation interventions versus (i) usual care and (ii) standalone nutrition or stimulation interventions, on the growth and development of children under five; (2) explore intervention characteristics (delivery strategies, behaviour change techniques, intensity and personnel) associated with positive effects. We searched eight databases for studies published from inception to 16 November 2020. Eligible studies were randomised and non-randomised controlled trials of integrated nutrition and stimulation interventions examining growth and developmental outcomes. We performed meta-analyses for length-for-age/height-for-age, weight-for-age and weight-for-length/weight-for-height Z scores and cognitive, motor and language development scores, and subgroup analyses by intervention characteristics. We conducted random-effects metaregression to assess potential subgroup differences in outcomes by intervention characteristics.

Results Twenty trials were included in the meta-analysis. Pooled effect sizes showed significant benefits of integrated interventions on developmental outcomes compared with usual care and standalone nutrition interventions (I^2 >75%) but not on growth outcomes. Moreover, integrated interventions have non-significant effects on developmental outcomes compared with standalone stimulation interventions. Integrated interventions showed greater effects on cognitive (p=0.039) and language (p=0.040) outcomes for undernourished children compared with adequately nourished children. The effects of integrated interventions on developmental outcomes did not differ by intervention characteristics.

Conclusion Integrated interventions have greater benefits for children's development than usual care or standalone nutrition interventions, especially in settings with high levels of undernutrition. Future studies should use standardised reporting of implementation processes to identify intervention characteristics linked to positive effects.

Key questions

What is already known?

- Around 250 million children in low-income and middle-income countries are at risk of not meeting their full developmental potential.
- Previous systematic reviews have found strong evidence that benefits from stimulation interventions are maintained when given in combination with nutrition interventions.

What are the new findings?

- Integrated nutrition and stimulation interventions do not have positive effects on growth outcomes when compared with usual care or standalone nutrition interventions.
- Integrated interventions have non-significant effects on developmental outcomes compared with standalone stimulation interventions.
- Compared with usual care, integrated interventions have more positive effects on developmental outcomes for undernourished children than on adequately nourished children.
- We were unable to determine which characteristics of integrated interventions are associated with benefits for developmental outcomes.

What do the new findings imply?

- Implementation of integrated nutrition and stimulation interventions should be considered to benefit children's development, especially in settings with high levels of child undernutrition.
- Future research should map the characteristics of integrated nutrition and stimulation interventions following standardised guidelines to enable comparisons and understand which intervention characteristics influence effects.

BACKGROUND

An estimated 250 million children under 5 years of age in low/middle-income countries (LMICs) are at risk of poor development due to poverty, undernutrition and inadequate stimulation.[1] These have adverse physical and psychosocial consequences that persist beyond childhood, perpetuating the intergenerational cycle of poverty.[2] However, early exposure to nurturing care, including optimal nutrition and adequate stimulation (defined as 'sensory information received from interactions with people and environmental variability that engages a young child's attention and provides information'[3]) strongly influences children's development, protects them from the negative effects of adversities, and increases their opportunity to thrive.[1]

Past research has primarily focused on understanding the effects of nutrition and stimulation interventions on children's growth and development when implemented separately. In a 2017 systematic review, Vaivada and colleagues investigated various nutrition-based approaches designed to improve child growth and developmental outcomes, including promotion of breastfeeding, iron supplementation, multiple micronutrient supplementation, complementary feeding education, supplementary feeding and therapeutic foods for acute malnutrition.[4] These interventions were found to significantly improve growth, but their benefits for developmental outcomes were limited.[4] Another systematic review reported a small effect of prenatal (d=0.042) and postnatal (d=0.076) nutrition interventions on children's cognitive development.[5] In contrast, stimulation interventions (n=21) were found to be more beneficial for cognitive (d=0.43) and language (d=0.47) development than nutrition interventions (n=18, d=0.09) in children younger than 2 years.[6] Furthermore, a recent review by Jeong *et al*[7] found that stimulation-based interventions have considerably larger effects on cognitive (standardised mean difference [SMD]=0.41), motor (SMD=0.26), language (SMD=0.35) and socioemotional (SMD=0.24) development of children under 3 years in LMICs.

Recently, emphasis has been placed on implementing integrated nutrition and stimulation interventions as a more holistic approach to improving child growth and development and a more efficient use of resources.[8 9] In 2014, a systematic review by Grantham-McGregor *et al*[10] concluded that there was no significant loss of effect on nutrition or developmental outcomes in children aged under 5 years when combining stimulation and nutrition interventions compared with single interventions, but little evidence of a synergistic interaction for child development. Meanwhile, two more recent systematic reviews and meta-analyses concluded that integrated interventions produce greater effects on developmental outcomes than nutrition intervention alone.[3 11] Several reviews have highlighted the need to identify characteristics of integrated interventions linked to positive effects.[12–14] Understanding the characteristics of integrated interventions linked to benefits for child development is crucial to assist in the development of context-specific interventions, maximise their quality and support scale up.[6 7 12–14] Aboud and Yousafzai examined the association between three intervention characteristics (delivery strategy, contact hours, behaviour change techniques [BCTs]) and children's developmental outcomes for 21 stimulation interventions.[6] However, existing reviews have not quantified the effects of intervention characteristics for integrated nutrition and stimulation interventions on both growth and developmental outcomes.

To address this research gap, we aimed to (1) systematically identify integrated community-based nutrition and stimulation interventions to improve growth and development among children under 5 years, and assess their quality; (2) describe the characteristics of these interventions using the Consolidated Advice on Reporting Early Childhood Development implementation research (CARE) framework[15]; (3) estimate, using meta-analyses, the effects of such integrated interventions on both growth and developmental outcomes among children under 5 years versus (i) usual care (referring to standard care or placebo) and (ii) standalone nutrition or stimulation interventions; (4) discuss any variations in effect and how these might relate to intervention characteristics.

METHODS

We conducted this systematic review following the 2009 Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement (online supplemental table 1).[16] The review protocol was preregistered in PROSPERO (CRD42019131739).

Search strategy

We first conducted a top-up search, adding to the search conducted by Grantham-McGregor *et al*[10] for studies published between January 2013 and September 2019 in Medline, PsycINFO, Cumulative Index of Nursing and Allied Health Literature (CINAHL), Embase, Global Health CABI Direct, The Cochrane Library, Academic Search Complete and Web of Science (online supplemental figure 1). We then re-ran the search for studies published from inception until 16 November 2020. Online supplemental table 2 shows key terms used in the search strategy. We searched the reference list of studies selected for full-text review.

Inclusion and exclusion criteria

We included studies carried out with children under 5 years and/or pregnant women. We included interventions that had both nutrition (micronutrient, macronutrient, food supplementation, or nutrition education) and stimulation (parent education, individual parent counselling, responsive care, or play) interventions versus any comparison arm/s (usual care, standalone nutrition or stimulation interventions). To assess the effects of integrated interventions on both growth and developmental outcomes, we included only studies reporting both anthropometric measures (Z scores for either length-for-age/height-for-age [LAZ/HAZ], weight-for-age [WAZ] or weight-for-length/weight-for-height [WLZ/WHZ]) and child development (either cognitive, motor or language development) outcomes. We included randomised controlled trials (RCTs) and non-randomised trials published in peer-reviewed journals and in English (see online supplemental table 3 for details).

Study selection and data extraction

Screening process

All citations were imported into EndNote V.X9 for screening. Titles and abstracts were screened independently by one reviewer (SD). Studies that did not meet the inclusion criteria were excluded. Two reviewers (SD and DM) retrieved and independently assessed the full text of potentially eligible studies. We resolved any disagreements over eligibility through discussion. Reasons for exclusions are reported using a PRISMA flow diagram.[16]

Data extraction

We used a standardised, prepiloted form to extract data on study characteristics. In addition, we extracted data related to intervention characteristics using the CARE guidelines to capture context, implementation strategy, intervention content, intensity, personnel, training and supervision, fidelity and compliance.[15]

Quality appraisal

We assessed the methodological quality of trials using the revised Cochrane for Risk of Bias 2 tool for RCTs and the Risk Of Bias in non-randomised studies of interventions tool for non-randomised trials.[17 18] Four reviewers (SD, AP, NS and DM) assessed the quality of included studies in pairs and resolved any disagreements through discussion.

Data synthesis and meta-analysis

Two reviewers (SD and SK) independently extracted data for the meta-analysis. In studies with more than one outcome measurement time-point, we selected the measurement closest to the intervention's completion date. One study had two control groups; we combined data from these groups to enable a single pairwise comparison.[19] One study reported fine and gross motor scores separately.[20] We first calculated the means and standard deviations for fine and gross motor scores in each arm, then calculated a pooled ES for fine and gross motor scores for each arm. We sought additional information from the authors of nine studies where raw scores of growth or developmental outcomes were reported and received a response from three authors.

As studies used various measures of effect, we calculated Hedge's g as the SMD between two groups of independent observations using the formula described by Higgins *et al* (2019).[21] The ESs 0.2, 0.5 and 0.8 were considered 'small', 'moderate', and 'large' effects, respectively. We then synthesised quantitative data using pooled estimates and forest plots for each intervention type using random-effect models. We used random-effect models to adjust the study weights as heterogeneity was anticipated in the treatment effects due to variations in intervention context, content and intensity. Quantitative data were pooled and analysed together when at least two studies referred to similar interventions and outcomes.

We conducted two broad types of subgroup analyses. In the first, we examined the effects of integrated interventions vs usual care on outcomes according to the baseline nutritional status of children (undernourished and adequately nourished) and the components of nutrition interventions. In the second, we examined effects by delivery strategies (individual, group or both), the number of BCTs used to deliver the intervention (categorised as <3 or ≥3), intervention intensity (duration of the entire intervention and the average number of interactions per month) and personnel (professionals, paraprofessionals, community volunteers, or volunteers and paraprofessionals together). All of these characteristics were prespecified in the review protocol. The proportion of variation in ESs due to heterogeneity was assessed by using the I^2 statistic, and values over 75% indicated a substantial level of heterogeneity.[21] As an additional analysis not prespecified in the review protocol, we used random-effect metaregression to investigate subgroup differences in ESs.[21] We did not test for subgroup differences if the overall ES was not significant. Publication bias was estimated using a funnel plot and the Egger test.[21] All analyses were conducted in STATA V.16.1.

Patient and public involvement

Patients and the public were not involved in the design and conduct of this study.

RESULTS

Search results

The database search for studies published from inception to 16 November 2020 identified 28 554 records. After removing duplicates, 20 615 records were screened for titles and abstracts, which resulted in the exclusion of 20 506 records. We reviewed full texts for the remaining 109 studies. Of those, 25 studies met the inclusion criteria (figure 1 and online supplemental table 4). Four additional studies that met the inclusion criteria were also identified by a forward/backward reference search. Out of 29 studies, four were follow-up studies of controlled trials,[22–25] and one was a process evaluation of the same intervention,[26] resulting in 24 unique studies.

Risk-of-bias assessment

Online supplemental figure 2 is the visual presentation of the review authors' judgement about the risk of bias domains for 24 unique trials: three trials were scored as low risk of bias,[27–29] 16 had some concerns,[19 20 30–43] and five were scored as being at high risk of bias.[44–48]

Study characteristics

Study characteristics are presented in table 1. Fifteen studies were cluster RCTs,[20 27–29 31 33 36 38–43 46 47] eight were individual RCTs,[19 30 32 35 37 44 45 48] and one was a non-randomised trial.[34] Trials were conducted between 1978 and 2020 in 11 countries: Bangladesh (7), Jamaica (3),

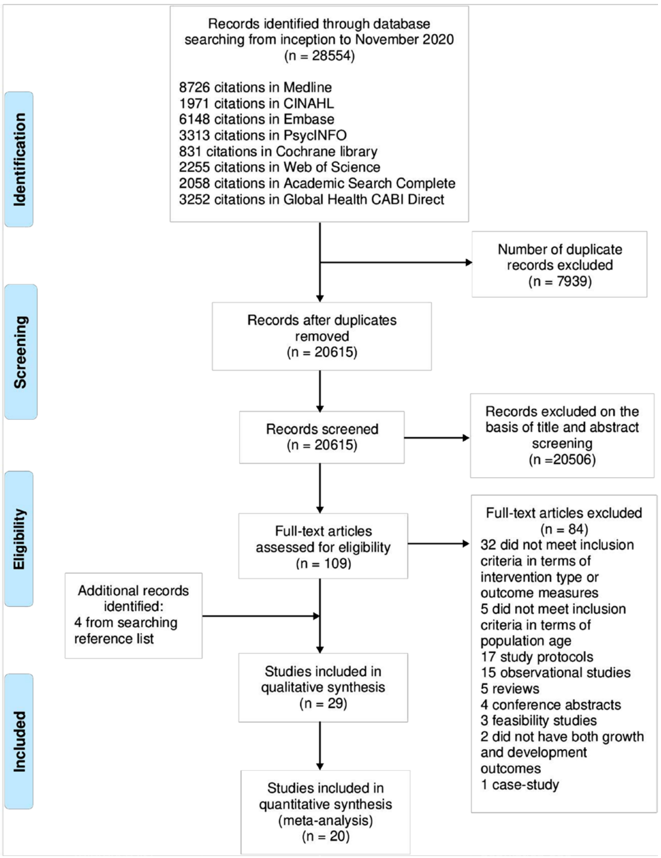

Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram describing the process of articles selection

Colombia (3), Uganda (2), Indonesia (2), Zambia, South Africa, Pakistan, Chile, India (2) and Madagascar. Sample sizes ranged from 110 to 3738 children, and all children were enrolled before 3 years of age, except in two studies where children up to 5 years were enrolled.[37 48] Eleven of 24 trials tested interventions for children with poor nutritional status[19 28 30–35 37 45 46] and four targeted children from the poorest population.[20 36 42 44] The remaining trials were conducted in resource-limited rural[27 29 38–41 43 47] or urban[48] settings.

The components of nutrition intervention included nutrition education (n=8),[27–29 31 38 39 41 43] macronutrient supplementation (with/without education) (n=6),[19 33 42 44 45 48] single or multiple micronutrient supplementation (with/without education) (n=8)[20 32 34–36 40 46 47] and both macronutrient and micronutrient supplementation (n=2).[30 37] In seven trials, stimulation was a new component integrated into existing nutritional services.[20 28 31 33 34 40 47] In two trials, the existing nutrition services were strengthened by adding new components such as micronutrient supplementation, new educational messages, enhancing health workers' counselling skills[40] or intensive nutritional counselling services.[20]

Most stimulation interventions aimed to improve mother–child interactions by sharing information or teaching mothers/caregivers to communicate and play with their child. In 10 trials, the stimulation content was based on the Jamaican Reach up Programme,[45] adapted to fit the local context.[19 20 28 29 31–33 45–47] Two trials adapted the Care for Child Development curriculum by the World Health Organization and the United Nations Children's Fund,[49] which included play and communication activities between a mother and a child.[27 40] Other trials focused on responsive parenting, including feeding and play activities[30 34–36 38 39 41–44 48] and pre-school education.[37] In addition to childcare, messages on maternal well-being, hygiene and sanitation were also imparted in three trials.[39 41 43] Only four trials explicitly mentioned their intervention/manual being guided by a theory of change or social learning theory/social cognitive learning theory.[20 39 41 43]

In 12 trials, the comparison group received existing standard care,[19 20 28 29 31 33 34 36 38–40 43] three trials provided placebo[32 37 48] and six trials employed diverse activities including monitoring growth, health and feeding practices,[27 35 46] medical visits,[45 47] and pre-school construction.[41] Three trials did not provide details about the comparison group.[30 42 44]

All trials used standard scales to measure developmental outcomes: 15 used the Bayley Scales of Infant Development (II and III),[19 28 29 33–36 38–43 46 47] four used the Griffiths Mental Development Scale.[31 32 44 45] Others used the INTERGROWTH-21st Neurodevelopment assessment tool,[27] the Ages and Stages Questionnaire-3 (ASQ-3) and the Weschler Preschool and Primary Scale of Intelligence -IV,[48] the Kaufman's Assessment Battery for Children II[37] or the ASQ-1.[20] When obtained, measurements for height and weight were reported as Z scores, except in five trials which reported raw height and weight.[31 38 44 47 48]

Implementation characteristics of integrated interventions

We summarised the implementation characteristics of interventions in table 2 (see online supplemental table 5 for details).

Delivery strategy: In 13 of 24 trials, interventions were delivered individually to participants, either at home[20 31 32 35 38 44–47] or at a community centre or health clinic or preschool.[19 30 37 48] Three trials tested group sessions in the community[36 42] or a clinic,[28] and seven trials combined both individual (home visit) and group sessions.[27 33 34 39–41 43] One trial used both home visits and group sessions in two separate trial arms.[29]

BCTs: Three or more BCTs were used in 16 trials,[19 28 29 31 33–36 38–43 45 47] while only eight trials used one or two BCTs.[20 27 30 32 37 44 46 48] The most widely used BCTs in all trials were information sharing and demonstration of play and communication activities to caregivers. Problem-solving strategies were employed in eight trials; these included identifying parenting issues, barriers to change, or problems with feeding and discussion of solutions.[20 31 35 36 39–41 43] Materials such as low-cost local or homemade toys and picture books were used in all but nine trials to facilitate caregivers practising play activities with their children.[20 27 30 35–37 39 41 44] Social support was

Table 1 Characteristics of the studies meeting the inclusion criteria

Source	Study design Sample	Population age at enrolment	Study duration	Components of integrated nutrition and stimulation interventions	Comparison	Outcome measures Growth outcomes	Outcome measures Developmental outcomes
Mckay *et al*[30]	RCT Five treatment arms: 1a, 1b, 2, 3 and 4 based on treatment periods n=449	Colombia, Undernourished children Age 36 months	February 1971 to August 1974	**Macronutrient and micronutrient supplementation and nutrition education:** Protein and calories and vitamin A thiamine, riboflavin, niacin and iron provided to children in three meals daily. **Education programme:** Provided education to mothers to support language development, social abilities, and psychomotor skills.	Detail not available	HAZ WAZ	Language usage, memory, motor control, manual, dexterity, information and vocabulary, quantitative reasoning, logic, verbal and non-verbal production
Waber *et al*[44]	RCT Six arms: Nutrition (third trimester to 36 months age), Nutrition (age 6 to 36 months), Nutrition (third trimester to 6 months age), Stimulation, Nutrition+Stimulation and Control n=433	Colombia, Age 6–36 months	Detail not available	**Macronutrient supplementation:** Food distribution from local store sufficient for the entire family. **Education programme:** Offered mothers education about developmental processes to improve their responsiveness towards children.	Detail not available	Length Weight	1. Griffiths mental development scale: locomotor, eye-hand coordination, language, performance developmental quotient 2. Corman–Escalona Einstein Scale: cognitive competence
Grantham-McGregor *et al*[45]	RCT Four arms: Nutrition only, Stimulation only, Nutrition+Stimulation and Control n=129	Jamaica, Stunted children with LAZ <-2 SD Age 9–24 months	Detail not available	**Macronutrient supplementation:** 1 kg milk-based formula and 20 g protein/d to all children. **Psychosocial stimulation:** Taught mothers to play with their children in structured play sessions. Lent homemade toys and simple picture books.	Weekly health visit and free medical care	WLZ	Griffiths mental development scale: locomotor, eye-hand coordination, language, performance developmental quotient
Powell *et al*[31]	Cluster RCT (18 clusters) Two arms n=139	Jamaica, Undernourished children Age 9–30 months	June 2009 to March 2012	**Nutrition education**: Gave nutrition education to mothers through existing health services. **Psychosocial stimulation:** Demonstrated play activities, used homemade toys and books/materials and discussed parenting issues.	Provide health and nutrition education to mothers and monitor the growth of children.	Height Weight	Griffiths mental development scale: locomotor, eye-hand coordination, hearing and speech, performance developmental quotient
Gardner *et al*[32]	RCT Four arms: Nutrition only, Stimulation only, Nutrition+Stimulation and Control n=126	Jamaica, Undernourished children (WAZ≤1.5 SD) Age 9–30 months	February 2010 to December 2011	**Micronutrient supplementation:** 10 mg elemental zinc in a flavoured syrup in 7 vials, each containing one dose, was given daily to all children. **Psychosocial stimulation:** Encouraged play and mother-child interaction, lent homemade toys and exchanged new toys in the next visit.	Placebo and routine care	LAZ WAZ WLZ	Griffiths mental development scale: locomotor, eye-hand coordination, hearing and speech, performance developmental quotient
Hamadani *et al*[33]	Cluster RCT (20 clusters) Two arms n=206	Bangladesh, Undernourished children (WAZ <-2 SD) Age 6–24 months	2000 to 2002	**Macronutrient supplementation:** Referred undernourished children to community nutrition centres, where they received food packets. **Psychosocial stimulation:** Discussed child development and the importance of play, then demonstrated play activities to the mothers using low-cost toys.	They provided food packets to severely undernourished children at Community Nutrition Centres.	HAZ WAZ WHZ	1. Bayley Scales of Infant Development (BSID) II: mental development index and motor development index 2. Wolke's behaviour rating
Nahar *et al*[34]	Time-lagged controlled study Two arms n=110	Bangladesh, Undernourished children (<50% WAZ or <70% WLZ or oedema) Age 6 to 24 months	October 2002 to June 2004	**Nutrition education and micronutrient supplementation** at Hospital Nutritional follow-up unit (HNFU) to all enrolled children for 6 months. **Psychosocial stimulation:** Demonstrated play activities to mothers, encouraged them to play and chat with their children, give positive feedback and continue to play between sessions.	Health and nutrition education at HNFU, growth monitoring and micronutrient supplementation	LAZ WAZ WLZ	1)BSID II: mental development index and motor development index

Continued

Table 1 Continued

Source	Study design Sample	Population age at enrolment	Study duration	Components of integrated nutrition and stimulation interventions	Comparison	Outcome measures Growth outcomes	Outcome measures Developmental outcomes
Lozoff *et al*[35]	RCT Two arms (infants were stratified by iron-deficient anaemia status) n=277	Chile, Children with (Iron Deficiency Anaemia) IDA and without IDA Age 6–12 months	–	**Micronutrient supplementation:** 15 mg ferrous sulphate for 6 months infants and 30 mg of ferrous sulphate for 12 months old infant on a weekly basis. **Support mother–child relationship:** Modelled positive feedback, provided play activities and information about child development.	Surveillance: Record iron intake, feeding and health information.	LAZ WAZ	1. BSID II: cognitive and motor development 2. Behaviour rating scale: object orientation, motor quality, negative affect, and positive social responsiveness
Aboud *et al*[36]	Cluster RCT (45 clusters) Three arms: Nutrition only, Nutrition+Stimulation and Control n=302	Bangladesh, Very poor population Age 8–20 months	–	**Multiple micronutrient supplementation** (Sprinkles) provided to all enrolled children, one sachet daily with a meal. **Responsive Feeding and Stimulation (RFS):** Demonstrated responsive stimulation and responsive feeding and coaching as the mothers practiced with their children.	Regular health, nutrition, and child development programme.	LAZ WAZ	1. BSID II: receptive and expressive language skills 2. Home inventory: Home environment, 3) Mother–child picture talk task: mother-child responsive talk
Ogunlade *et al*[37]	RCT, Two arms n=151	South Africa, Children with Hb≤12.5 g/dL Age 36–79 months	September to November 2008.	**Macro- and micronutrient supplementation:** Enrolled children received stiff maize-meal porridge with added micronutrient powder (<8 g). **Psychosocial stimulation:** All children attended preschool for 52 days.	Received soft maize-meal porridge with added placebo powder (<8 g) containing only maize maltodextrin.	HAZ WAZ	KABC-II: learning scale, sequential scale, simultaneous scale, mental processing index, nonverbal index.
Nahar *et al*[19]	RCT Five arms: Nutrition only, Stimulation only, Nutrition+Stimulation and Control n=507	Bangladesh, Severely malnourished children (WAZ <-3 SD) Age 6–24 months	–	**Macronutrient supplementation:** Supplied food packets (Pushti Packet) during clinic visits for the first 3 months. **Play sessions and education:** Offered play sessions and parental education using a semistructured curriculum.	Routine clinical management: growth monitoring and promotion, health education, micronutrient supplementation and immunisations.	LAZ WAZ WLZ	BSID II: mental development index and psychomotor development index
Vazir *et al*[38]	Cluster RCT (60 clusters) Three arms: Nutrition only, Nutrition+Stimulation and Control n=600	India Age 3 months	–	**Nutrition education:** Provided nutrition education on breastfeeding and complementary feeding using PAHO/WHO guidelines. **Playgroup and educational session:** Provided messages and skills on responsive feeding and developmental stimulation messages.	Standard of care: received ICDS services programme	Height Weight	BSID II: mental and motor development index
Aboud *et al*[39]	Cluster RCT (47 clusters) Two arms n=463	Bangladesh Age 6–12 months and 12–24 months	November 2010 to February 2012	**Nutrition education:** Provided 10 min of counselling on feeding and child development. **Parenting programme:** Discussed parenting practices related to communication, play and nutrition.	Standard care: Sharing messages about feeding and hygiene.	LAZ	BSID III: cognitive, receptive language and expressive language, fine motor
Tofail *et al*[46]	Cluster RCT (30 clusters) Two arms (infants in each group stratified by their iron status) n=434	Bangladesh, Children with mild to moderate IDA. Age 6–24 months	–	**Micronutrient supplementation:** One bottle of 35 mL ferrous sulphate syrup to children with IDA, parent, fed their child 5 mL syrup daily for first 6 months (seven doses). **Psychosocial stimulation:** Provided mothers with demonstrations of how to play with toys and interact with their children.	Weekly visit in a control group to ask the mother about the health status of their child.	HAZ WAZ WHZ	1. BSID II: mental development Index and Psychomotor Development Index 2. Modified version of scale developed by Wolke al.: behaviour

Continued

Table 1 Continued

Source	Study design Sample	Population age at enrolment	Study duration	Components of integrated nutrition and stimulation interventions	Comparison	Outcome measures Growth outcomes	Outcome measures Developmental outcomes
Yousafzai *et al*[40]	Cluster RCT (80 clusters) Four arms: Nutrition only, Stimulation only, Nutrition+Stimulation and Control n=1489	Pakistan Age birth to 24 months	June 2009 to March 2012	**Multiple micronutrient supplementation** (Sprinkles) daily for 33 months for all children **and nutrition education** (strengthened existing nutrition education services) **Responsive stimulation:** Illustrated play and communication activities, encouraged parents to practice activities with their child through play and communication counselling, provided coaching and feedback.	Standard-of-care services: health, hygiene, and basic nutrition education and immunisation through a monthly home visit and occasional group meetings.	HAZ WAZ WHZ	BSID III: cognitive, language, motor and socioemotional development
Attanasio *et al*[47]	Cluster RCT (96 clusters) Four arms: Nutrition only, Stimulation only, Nutrition+Stimulation and Control n=1429	Colombia Age 12–24 months	February 2010 to December 2011	**Multiple micronutrient supplementation** (Sprinkles) for all children for 18 months. **Psychosocial stimulation:** Demonstrated play activities using low-cost or homemade toys, picture books and form boards to improve maternal-child interactions, changing play materials weekly.	Cash payments for complying with regular health check-ups for children<6 years age and regular school attendance for children>5 years age	Height Weight	BSID III: cognition, receptive language, expressive language, fine motor and gross motor
Singla *et al*[41]	Cluster RCT (25 clusters) Two arms n=319	Uganda Age 12–36 months	December 2012 to November 2013	**Nutrition education:** Reviewed messages on a diverse diet. **Parent education sessions:** Focused on five messages on childcare, including play, talking, diet, hygiene, love and respect and maternal well-being.	Preschools were created for older children with support from Plan Uganda and received nutritional information.	HAZ	BSID III: cognitive and receptive language
Rockers *et al*[27]	Cluster RCT (30 clusters) Two arms n=526	Zambia Age 6–12 months	August 2014 to October 2015	**Educational sessions and nutrition education:** Discussed parenting skills, child nutrition and cooking demonstration, forms of play, cognitive stimulation and language development activities.	Baseline end line evaluations of health and developmental status of children.	HAZ WAZ	1. Savings brains Early Child development Scale: gross motor function and cognition 2. INTERGROWTH-21st Neurodevelopment assessment tool: cognitive and socioemotional development
Helmizar *et al*[42]	Cluster RCT (40 clusters) Four arms: Nutrition only, Stimulation only, Nutrition+Stimulation and Control n=355	Indonesia Age 6–9 months	January to December 2013	**Macronutrient supplementation:** Formula food packets of formula adjusted for age groups (6–8 months, 9–11 months and >12 months) for children. **Psychosocial stimulation:** Delivered play sessions, encouraged mother–child interaction and taught mothers or caregivers about responsive stimulation, provided toys and picture books.	Detail not available	HAZ WAZ WHZ	BSID III: cognitive, language and motor development
Muhoozi *et al*[43]	Cluster RCT (82 clusters) Two arms n=511	South-western Uganda, Age 6–8 months	October 2013 to May 2015	**Nutrition and stimulation education with routine healthcare:** Provided knowledge on nutrition and stimulation, demonstrated cooking and making toys using local resources, provided play activities and counselling.	Routine healthcare	LAZ WAZ WLZ	BSID III: cognitive, language and motor development

Continued

Table 1 Continued

Source	Study design Sample	Population age at enrolment	Study duration	Components of integrated nutrition and stimulation interventions	Comparison	Outcome measures Growth outcomes	Developmental outcomes
Schneider *et al*[48]	RCT Two arms n=192	Indonesia Age between 3 and 5 years	2014	**Macronutrient supplementation:** Two servings per day of a fortified milk powder for children for six months. **Psychosocial stimulation:** Children performed cognitive stimulation task with the assistance of the parent/caregiver. Parent/caregiver was provided standardised learning activities to perform with the child at home.	1. Did not visit the community centre and did not receive any Psychosocial stimulation. 2. Consumed at home two servings of an unfortified milk powder (placebo).	Height Weight	1. ASQ-3 & parental report: cognitive development 2. WPPSI-IV, adapted: cognitive abilities including verbal comprehension, visual-spatial processing, working memory, fluid reasoning and processing speed 3. CBCL 1.5–5: behaviour
Hamadani *et al*[28]	Cluster RCT (90 clusters) Two arms n=2423	Bangladesh, Undernourished children (WAZ <-2 SD) Age 5–24 months	November 2014 to April 2015	**Nutrition education:** Provided nutrition-related messages during play sessions and provided nutrition cards with a recipe for diets for underweight children. **Psychosocial stimulation:** Mothers were shown how to support their children's development through play and interaction.	No extra attention, they used the clinic for treatment as usual, some were immunised.	LAZ WAZ WLZ	BSID III: cognitive, language and motor development
Galasso *et al*[20]	Cluster RCT (125 clusters) Five arms: Intensive nutrition counselling (1), 1+supplementation (0–5 months age), 1+supplementation (6–11 months age), 1+stimulation and Control n=3738	Madagascar Age: pregnant women, women with children 0–5 months and 6–11 months	June 2014 to November 2016	**Intensive nutrition counselling and micronutrient supplementation:** Lipid-based nutrient supplementation to children 6–18 months and pregnant and lactating mothers. **Early stimulation counselling:** Stimulation messages were provided to parents.	Standard-of-care programme: community-based health and nutrition services with growth monitoring and education.	LAZ WAZ WLZ	ASQ-I: gross motor, fine motor, problem-solving, socioemotional development, communication skills
Grantham-McGregor *et al*[29]	Cluster RCT (192 clusters) Four arms: Nutrition only, Nutrition+Stimulation (Home visits), Nutrition+Stimulation (Group sessions), Control n=1449	India Age 7–16 months	August 2015 to November 2017	**Health and Nutrition Service Link** **Nutrition education:** Education provided to improve feeding and hygiene practices in the household through games, stories and cooking demonstration. **Psychosocial stimulation:** Demonstrated play activities and encouraged mothers to play with their child using locally available toys.	**Health and Nutrition Service Link**: Discussed the availability of services such as growth monitoring and food supplementation in the community.	HAZ WAZ	BSID III: cognitive, language and motor development Strengths and difficulties Questionnaire

ASQ, ages and stages questionnaire; CBCL, child behaviour checklist; ICDS, integrated child development services programme; IDA, iron deficiency anemia; KABC II, Kaufman assessment battery for children-second edition; LAZ/HAZ, length-for-age/height-for-age z score; PAHO, Pan American Health Organization; RCT, randomised control trial; WAZ, weight-for-age z score; WLZ/WHZ, weight-for-length weight-for-height z score; WPPSI, weschler preschool and primary scale of intelligence.

Table 2 Summary implementation characteristics of the included studies

Study	Delivery mode	Behaviour change techniques used in nutrition and/or stimulation interventions						Average sessions per month§	Duration (months)	Personnel¶	Compliance¶	Effect on child growth**	Effect on child development**
		Information	Performance*	Problem solving	Social support	Materials†	Media‡						
Mckay *et al*[30]	Centre-based visit	+	+					22	9	Teachers and childcare workers	>95% attended		C +
Waber *et al*[44]	HV	+											
Grantham-McGregor *et al*[45]	HV	+	+			+		4	12	Community health aides		WLZ –	C +, M +, L +
Powell *et al*[31]	HV		+	+		+		4	12	Community health aides	Median of 32.5 visits conducted	Height – Weight –	C +, M –, L +
Gardner *et al*[32]	HV		+			+		4	12	Community health worker	62% children received 3-4 visits per month		C +, M +, L +
Hamadani *et al*[33]	HV and GS	+	+			+		7	12	Play leaders	60% of mothers attended>=20 meetings	HAZ – WAZ – WHZ –	C +, M –
Nahar *et al*[34]	HV and GS	+	+			+		3	6	Female health workers	–	LAZ – WAZ + WLZ –	C +, M +
Lozoff *et al*[35]	HV	+	+	+			+	4	12	Professional educators	-		C+, M +, L +
Aboud *et al*[36]	GS	+	+	+			+	3	2	Peer educators	S>85%, N 80%	LAZ – WAZ +	L +
Ogunlade *et al*[37]	Pre-school	+							3	Front line assistant	n=81.3%	HAZ – WAZ –	C +
Nahar *et al*[19]	Clinic visit	+	+			+		2	6	Female health workers		LAZ – WAZ + WLZ –	C +, M –
Vazir *et al*[38]	HV	+	+			+		3	12	Trained mothers		Height – Weight –	C +, M –
Aboud *et al*[39]	HV and GS	+	+	+			+		10	Community facilitators+Family welfare assistants	GS 85%	LAZ –	C +, L +
Tofail *et al*[46]	HV		+			+			9	Play leaders	99%	HAZ + WAZ – WHZ –	C +, M –
Yousafzai *et al*[40]	HV and GS	+	+	+	+	+		2	33	Female Health workers	S>55% n>75%		C +, M +, L +
Attanasio *et al*[47]	HV		+			+	+	4	18	Mother leaders	S 83%, N 73%	Height – Weight –	C +, M +, L +
Singla *et al*[41]	HV and GS	+	+	+	+		+	3	7	Community volunteers	GS 75%	HAZ –	C +, L +
Rockers *et al*[27]	HV and GS	+	+					4	12	Community development agents and head mothers	GS 89%, HV 68%	HAZ + WAZ –	C +, M +

Continued

Table 2 Continued

Study	Delivery mode	Behaviour change techniques used in nutrition and/or stimulation interventions						Average sessions per month§	Duration (months)	Personnel¶	Compliance¶	Effect on child growth**	Effect on child development**
		Information	Performance*	Problem solving	Social support	Materials†	Media‡						
Helmizar *et al*[42]	GS	+	+			+	+	4	6	Community health workers	-	HAZ + WAZ + WHZ +	C +, M +, L +
Muhoozi *et al*[43]	HV and GS	+	+	+		+		3	6	Village health team leaders	GS 84%	LAZ – WAZ – WLZ –	C +, M +, L –
Schneider *et al*[48]	Community centre		+			+		13–22	6	Psychologists	S 93.7%, N 91.7	Height – Weight –	C +
Hamadani *et al*[28]	GS at Clinic	+	+			+	+	2	12	Community health workers and health assistants	46%	LAZ – WAZ – WLZ –	C +, M +, L +
Galasso *et al*[20]	HV	+		+				3	24	Community health workers	>80%	LAZ – WAZ – WLZ –	C –, M –, L –
Grantham- McGregor *et al*[29]	HV and GS separately	+	+		+	+	+	HV: 4 GS: 4	24	Female facilitators	GS 51% HV 75% N 84%	LAZ – WAZ –	C +, M –, L +

*Performance includes demonstration and practice of play and communication activities.
†Materials included toys and picture books provided to facilitate play activities between mother and child.
‡Media refers to interactive media such as leaflets, illustrative cards, activity booklets with prompts and cues for behaviour change as a part of a BCT.
§Number of encounters per month over the trial period.
¶As reported by the author.
Effect of integrated nutrition and stimulation interventions on growth and developmental outcomes: +positive effect, **– no significant effect.
C, cognitive; GS, group sessions; HV, home visit; L, language; LAZ/HAZ, length-for-age/height-for-age z score; M, motor; N, nutrition; S, stimulation; WAZ, weight-for-age z score; WLZ/WHZ, weight-for-length/weight-for-height z score.

provided to mothers in only three trials so they could replicate play activities with their spouses and peers.[29 40 41] Eight trials used media such as written instructions, illustrative cards, activity booklets with prompts, and behaviour change cues.[28 29 35 36 39 41 42 47]

Intensity: In 11 trials, the duration of intervention was less than 12 months.[19 30 34 36 37 39 41–43 46 48] Twelve trials tested interventions that lasted for 12 months or more.[20 27–29 31–33 35 38 40 45 47] We calculated the average number of intended contact sessions (individual, group or both) per month (table 2). Out of 24 trials, the least intensive interventions involved monthly group sessions lasting 1 hour and 20 min, along with 30 min individual sessions at participants' homes for 33 months.[40] The most intensive intervention involved individual sessions at a community centre for 5 days per week, lasting for 6 hours a day over 9 months.[30]

Delivery personnel: Most interventions (n=10) were delivered by paraprofessionals who were specially trained to provide health services, had 8–12 years of education and were paid.[19 20 29 31 32 34 37 40 42 45] Seven trials tested interventions delivered by trained community volunteers (women from local communities).[33 36 38 41 43 46 47] In four trials, interventions were delivered by professionals with relevant degrees, including psychologists,[48] teachers,[30] professional educators,[35] and health assistants.[28] Two trials included both volunteers and paraprofessionals.[27 39]

Pooled ESS on growth and developmental outcomes

A total of 24 trials met the review's inclusion criteria. Of these, 20 trials with 16 568 participants were included in the meta-analysis.[19 20 27–34 36 38–43 45–47] We were unable to calculate ES for both growth and developmental outcomes for the four remaining trials due to insufficient/incompatible information such as reporting raw scores.[35 37 44 48] Seventeen trials tested integrated interventions vs usual care.[19 20 27–30 32 36 38–43 45–47] One trial had two arms with integrated interventions delivered using two different modes.[29] Thirteen and eight trials, respectively, compared integrated versus standalone nutrition[19 20 29 31–34 38 40 42 45–47] and stimulation interventions.[19 32 36 40 42 45–47] Five trials examined synergistic interactions between nutrition and stimulation interventions.[19 32 40 45 47]

Integrated interventions versus usual care

Compared with usual care, integrated nutrition and stimulation interventions had a moderate positive effect on children's cognitive (n=17, ES 0.53, 95% CI 0.30, 0.75, I^2=96%, p<0.001), motor (n=14, ES 0.30,95% CI0.08, 0.51,I^2=94%,p<0.001) and language (n=13, ES 0.42, 95% CI 0.16, 0.68, I^2=96%, p<0.001) outcomes (online supplemental figure 3). We found non-significant effects of integrated interventions on growth outcomes. We conducted a sensitivity analysis excluding three trials with a high risk of bias, and found similar ESs, with high heterogeneity.

In order to explore possible reasons for the heterogeneity of intervention effects on developmental outcomes, we performed subgroup analyses by (1) baseline nutritional status of children and (2) components of nutrition intervention (online supplemental figure 4). In the subgroup analyses stratifying studies by nutritional status, heterogeneity within each subgroup remained high and significant (I^2 >75%, p<0.001). The ESs for cognitive (mean ES diff=0.49, 95% CI 0.03, 0.96, p=0.039) and language (mean ES diff=0.63, 95% CI 0.03, 1.23, p=0.040) outcomes were significantly greater among undernourished children compared with adequately nourished children. The effect on motor outcome was non-significant for the undernourished group. When disaggregating by three components of nutrition intervention, ES for macronutrient supplementation (with/without education) and stimulation interventions had a positive effect on cognitive (n=3, ES 0.77, 95% CI 0.24, 1.30, I^2=83%, p=0.003) and motor (n=3, ES 0.32, 95% CI 0.01, 0.63, I^2=53%, p=0.119) but not on language outcomes. Single or multiple micronutrient supplementation (with/without education) and stimulation interventions had a moderate effect on cognitive (n=5, ES 0.24, 95% CI 0.04, 0.44, I^2=83%, p<0.001) and language (n=5, ES 0.26, 95% CI 0.004, 0.51, I^2=90%, p<0.001) but not on motor outcomes. Nutrition education and stimulation interventions showed positive effects on all developmental outcomes (6–8 studies; ES range: 0.40 to 0.59, I^2 >75%). The subgroup differences in any developmental outcomes by nutrition components were not significant.

Funnel plots (online supplemental figure 5) suggest that publication bias is unlikely for both growth and developmental outcomes, as ESs from the published studies were roughly equally distributed around the mean, indicating a low risk of bias towards the larger ES. The Egger test provided no evidence of any publication bias on cognitive (p=0.205), motor (p=0.907), language (p=0.949), LAZ/HAZ (p=0.635), and WLZ/WHZ (p=0.128) scores. However, there was a slight indication of publication bias in reporting of WAZ (p=0.024) score.

Integrated interventions versus single interventions

Figures 2 and 3 include forest plots describing the effects of integrated interventions versus standalone nutrition and stimulation interventions on growth and developmental outcomes. Compared with the nutrition intervention only group, the pooled effect for the integrated interventions group indicated moderate effects for cognitive (n=14, ES 0.31, 95% CI 0.19 to 0.42, I^2=72%, p<0.001) and language (n=9, ES 0.24, 95% CI 0.09 to 0.40, I^2=82%, p=<0.001) outcomes, small effects for motor outcome (n=14, ES 0.07, 95% CI 0.008 to 0.14, I^2=20%, p=0.240); non-significant effects on WAZ (n=6, ES 0.09, 95% CI −0.06 to 0.23, I^2=58%, p=0.037), WLZ/WHZ (n=6, ES 0.03, 95% CI −0.05 to 0.10, I^2=0, p=0.669) scores and no effect on LAZ/HAZ score.

In contrast, in comparison to the stimulation intervention only group, the integrated interventions group

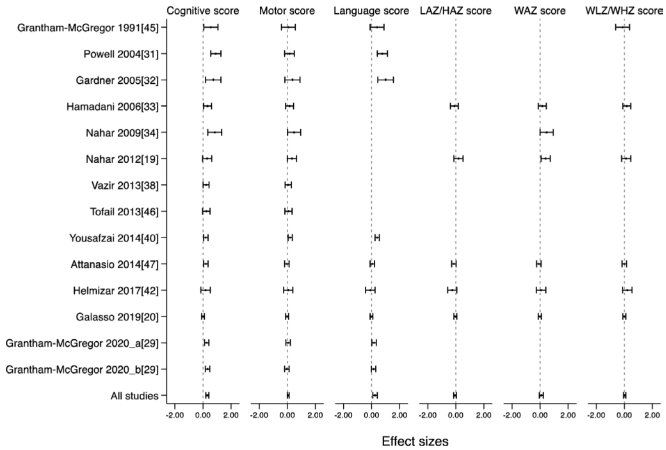

Figure 2 Effects of integrated nutrition and stimulation interventions versus standalone nutrition interventions on each outcome. Note: the size of squares is proportional to the analytical weights.

showed non-significant effects on cognitive (n=7, ES 0.18, 95% CI −0.09 to 0.45, I^2=86%, p<0.001), motor (n=7, ES 0.19, 95% CI −0.03 to 0.42, I^2=79%, p=<0.001), language (n=6, ES 0.06, 95% CI −0.33 to 0.45, I^2=92%, p<0.001), WAZ (n=4, ES 0.02, 95% CI −0.09 to 0.14, I^2=0, p=0.780) and WLZ/WHZ (n=4, ES 0.06, 95% CI −0.06 to 0.19, I^2=0, p=0.911) scores and no effect on LAZ/HAZ score.

Subgroup analyses of pooled ESs by intervention characteristics

Online supplemental table 6 describes the results of subgroup analyses of integrated interventions versus usual care, by four intervention characteristics: delivery strategy, number of BCTs, intervention intensity and personnel delivering the intervention. Online supplemental table 6 also includes p values corresponding to the test of subgroup differences for developmental outcomes. We did not conduct a test of subgroup differences for any growth outcomes because overall ESs were not significant.

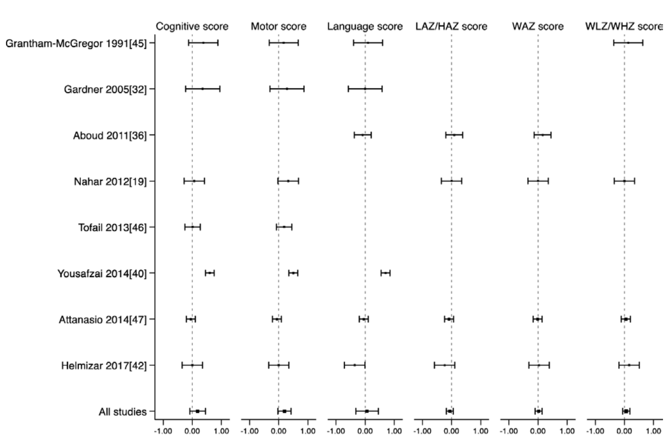

Figure 3 Effects of integrated nutrition and stimulation interventions versus standalone stimulation interventions on each outcome. Note: the size of squares is proportional to the analytical weights.

Delivery strategy: Integrated interventions that included both home visits and group sessions had a positive effect on all developmental outcomes (3–5 studies; ES range: 0.35 to 0.48). Similarly, integrated interventions with individual visits were found to have a significant positive effect on cognitive (n=9, ES 0.40, 95% CI 0.21 to 0.59) and language (n=5, ES 0.20, 95% CI 0.03 to 0.37) but not motor outcomes. Group sessions alone had non-significant effects on developmental outcomes (3 to 4 studies; ES range: 0.55 to 0.92). There were no subgroup differences in any developmental outcomes. Heterogeneity remained high and significant.

BCTs: Interventions incorporating three or more BCTs had a positive effect on all three developmental outcomes (10–12 studies; ES range: 0.38 to 0.62). The pooled effect of interventions using less than three BCTs was moderate for cognitive outcome (n=5, ES 0.27, 95% CI 0.03 to 0.50) and not significant for motor and language outcomes. The subgroup differences in ESs were not significant. Heterogeneity was high and significant for all developmental outcomes.

Intensity:The interventions with a duration of ≥12 months and ≥4 average sessions per month had a positive effect on all developmental outcomes (7–10 studies; ES range: 0.15 to 0.53). Similarly, interventions with a duration of <12 months had a significant positive effect on cognitive and motor (7 and 4 studies; ESs 0.52 and 0.35, respectively) but not on language outcomes. Interventions with <4 average sessions per month had a significant positive effect on cognitive outcomes only (n=7, ES 0.58, 95% CI 0.12, 1.05). There were no significant subgroup differences in ESs. Heterogeneity was observed for all developmental outcomes and was significant.

Personnel: Interventions delivered by paraprofessionals had positive effects for all developmental outcomes (7–8 studies; ES range: 0.18 to 0.44). Similarly, interventions delivered by community volunteers had positive effects for all three developmental outcomes (4–5; ES range: 0.13 to 0.34). The pooled effect for the cognitive outcome was positive for interventions delivered by professionals only and was not significant when delivered by both volunteers and paraprofessionals together. The ES was significantly greater for interventions delivered by professionals for cognitive outcome (mean ES diff=0.99, 95% CI 0.38 to 1.59, p=0.004) compared with paraprofessionals. Significant heterogeneity was observed.

DISCUSSION

This systematic review and meta-analysis assessed the effects of integrated nutrition and stimulation interventions on both growth and developmental outcomes in children under 5 years, first overall, and then considering four intervention characteristics, including delivery strategy, BCTs, intensity and personnel. Our findings suggest that, in LMICs, integrated interventions tested to date produced better results in cognitive, motor, and language outcomes than usual care or standalone nutrition interventions, but they had no effects on growth outcomes. The effects of integrated interventions on developmental outcomes were non-significant compared with standalone stimulation interventions. These findings are consistent with previous systematic reviews that have highlighted that the effect of integrated nutrition and stimulation interventions on developmental outcomes is greater than those of standalone nutrition interventions.[3 10 11] We observed considerable heterogeneity in effects on developmental outcomes, which could not be fully elucidated through subgroup analyses. The greatest benefits of integrated interventions accrue to undernourished children, which echoes findings from a study in Bangladesh that showed significant benefits of stimulation intervention among undernourished children.[33] Lastly, there were no negative consequences of integrated interventions on children's nutritional or developmental outcomes.

Existing evidence suggests that interventions providing both macronutrients and micronutrients supplementation have the largest effects on LAZ/HAZ score,[11] but interventions providing only single or multiple micronutrient or nutrition education alone tend to have only small or no effects.[50 51] In our review, only two integrated interventions provided children with a known effective strategy, that is, both macronutrients and micronutrients supplementation,[30 37] which might explain the lack of significant effects on LAZ/HAZ score. Further, nine out of 20 trials in the meta-analysis were conducted in food insecure settings with high baseline levels of child undernutrition, and in which supplementation, health service strengthening and nutrition-sensitive actions would be required for any substantial gains in any growth outcomes.[51 52]

We observed large heterogeneity of effects on all three developmental outcomes, as well as, in the intervention context, nutrition components and their characteristics, which makes the interpretation of the findings challenging. This substantial heterogeneity was highlighted by the authors of a previous review[10] and a recent meta-analysis,[7] emphasising the diversity in the field of early childhood interventions in general. In our review, heterogeneity remained significant in all subgroup analyses except in one analysis by nutrition components, which only included three studies. Participant characteristics may be a potential source of heterogeneity. We did not conduct subgroup analyses by child's age because the age at enrolment and assessment varied greatly, and the latter was not reported in all studies. While three trials were deemed to have a low risk of bias, most trials did not adequately report allocation concealment, blinding, and there were concerns about selective outcome reporting. Removal of the three trials included in the meta-analysis with the highest risk of bias[45–47] did not reduce the heterogeneity, suggesting ESs may not have been influenced by trials' quality.

We sought to understand how four key intervention characteristics (delivery strategy, BCTs, intensity and personnel) might be associated with effects. There were no marked differences in ESs by delivery strategy. In 2015, a systematic review found that stimulation delivered through group sessions with some home visits by dedicated paraprofessionals had a moderate effect (n=7, ES 0.59, 95% CI 0.50 to 0.68) on children's cognitive score.[6] The advantages of using combined home visits and group session strategies compared with home visiting alone are that interventions are less labour intensive, may reduce contact hours, encourage peer support and have a potential to modify the norms for caregiving practices.[6] However, the feasibility of combining home visiting and group-based strategies to deliver integrated interventions requires further investigation.

When considering BCTs, Aboud and Yousafzai suggested that interventions with more than two BCTs, particularly media for information sharing (posters, cards or brochures), problem-solving strategies and performances (demonstration and practice of play and communication), are effective in improving developmental outcomes.[6] However, most studies included did not report whether or how they used theory in the development of interventions and the selection of BCTs. Theoretical foundations encourage rigorous intervention design, elucidating the proposed mechanisms through which an intervention is hypothesised to change behaviour.[53] Further prioritisation of theory-informed BCTs could facilitate efforts to enhance and scale-up effective integrated interventions.[54]

We did not find subgroup differences in ESs by intervention intensity, which resonates with findings from Aboud and Yousafzai, who did not find any association between developmental outcomes and contact hours.[6] Other studies suggest that high-intensity interventions are likely to have positive effects on developmental outcomes. For example, Powell and Grantham-McGregor found that children who received stimulation through weekly visits had better outcomes than those who had fortnightly visits.[55] Similarly, in Bolivia and Philippines, effects on child development were stronger for children exposed to the interventions for longer (seven or more and at least 17 months, respectively).[56 57] The robustness of these findings concerning intervention characteristics should be explored in future studies using alternative cut-off points.

We found little evidence of differences in cognitive outcome by the type of personnel delivering the interventions. However, as only two interventions were delivered by professionals, this finding is inconclusive. The existing evidence highlights that delivery of maternal and child health interventions by paraprofessionals such as Community Health Workers (CHWs) is often effective in LMICs.[58] Two trials that tested integrating stimulation interventions into existing nutrition services reported promising results.[28 40] However, CHWs' existing work burden must be considered when integrating interventions within existing services. For instance, a study in Brazil found that turnover was higher among CHWs in a parenting programme due to increased workload.[59] Alternative strategies, such as increasing the number of existing CHWs or creating a new cadre of staff, can be considered. Moreover, the knowledge and skills of personnel, supervision support and their relationships with caregivers and children are critical for a successful intervention, yet these aspects are often inadequately reported.[13 60 61] Further efforts are needed to assess competency gaps among personnel delivering integrated interventions and map the adequacy and continuity of their training and supervision.

Our review has several limitations. We included studies published in peer-reviewed journals and in English only. Therefore, our search might not have captured all potentially relevant studies with negative results. Similarly, we could not use all studies with growth outcomes because they were not extractable (11 studies); this reduced the power of our analyses. However, we did not observe any indication of publication bias in funnel plots and Egger tests for any outcome except WAZ. Given the effect on the WAZ score was not significant, the risk of reporting bias appears to be low. To further reduce potential reporting bias, we contacted nine authors where data were not extractable and received data from three authors. We did not include studies that reported only growth or developmental outcomes, but only two studies were excluded based on this criterion.[62 63] We did not report effects on socioemotional development, a critical aspect of child development, as only three studies reported socioemotional outcome and did so differently.[20 29 43] Although we explored possible sources of heterogeneity by study-level characteristics, there were still notable differences that could not be accounted for, such as participants' age at enrolment/assessment, intervention characteristics (curriculum components, training and supervision of personnel, and participants' adherence to the intervention). Moreover, we conducted many subtests (n=30) with a small number of studies in each subgroup to explore intervention characteristics related to the outcome effects, which increased the risk of Type I error. It is also possible that some of our analyses were underpowered and with insufficient precision to guide decision-making. While the integrated interventions had a greater effect on cognitive and language outcomes in undernourished children than in adequately nourished children, there was significant unexplained heterogeneity within these groups. Therefore, these findings should be interpreted cautiously as individual trial results are inconsistent. Finally, none of the trials included in the review reported characteristics of integrated interventions using standard guidelines uniformly, except one,[26 40] making it challenging to map the intervention components accurately.

Integrated interventions can be considered as part of a comprehensive set of actions to improve nurturing care, even if they do not yield improvements in growth on their own within the limited timescale of most trials. The high heterogeneity found among trials emphasises the need for additional studies to assess the effectiveness of integrated interventions, such as follow-up studies of trials to examine the sustainability of effects, as well as process evaluations and implementation research to investigate barriers and enablers to implementation and positive effects. Moreover, there is a need for cost-effectiveness evaluations to identify the most effective integrated intervention strategies for scale up. Finally, few studies have reported intervention characteristics in a standardised manner; this needs to be improved to strengthen the evidence base.

CONCLUSIONS

Our findings confirm that integrated nutrition and stimulation interventions have positive but not synergistic effects on developmental outcomes when compared with standalone nutrition and stimulation interventions. We were unable to determine which component of the integrated interventions was associated with significant positive ES for developmental outcomes. Our findings suggest that programme developers and policy-makers should consider integrated interventions and support implementation research to better understand which interventions characteristics lead to positive outcomes and inform scale up.

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Acknowledgements We thank Ms Katrina Chaudhary (Librarian at Western Sydney University) to support the development of our search strategy and for conducting the database search and Mr Paul Fahey (Statistician at Western Sydney University) for his guidance and inputs in the meta-analysis. We also thank the authors who responded to our emails and provided data.

Contributors SD, AP and DM conceived the original idea. SD designed the study protocol with inputs from DM, AP, NS, and SK. SD conducted the database search. SD and DM finalised the choice of articles included in the review. SD, AP, NS and DM assessed the risk of bias. SD adn SK extracted data for the meta-analysis and conducted the analyses. SD wrote the first draft. All authors contributed to the interpretation and critical revision of the manuscript. All authors read and approved the final manuscript for submission.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement No additional data are available.

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