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

Sophiya Dulal, Audrey Prost, Surendra Karki, Naomi Saville, Dafna Merom

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

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 metagression 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. These have adverse physical and psychosocial consequences that persist beyond childhood, perpetuating the intergenerational cycle of poverty. 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’) strongly influences children’s development, protects them from the negative effects of adversities, and increases their opportunity to thrive.

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. These interventions were found to significantly improve growth, but their benefits for developmental outcomes were limited. Another systematic review reported a small effect of prenatal ($d=0.042$) and postnatal ($d=0.076$) nutrition interventions on children’s cognitive development. 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. Furthermore, a recent review by Jeong et al 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. In 2014, a systematic review by Grantham-McGregor et al 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. Several reviews have highlighted the need to identify characteristics of integrated interventions linked to positive effects. 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. 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. 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; (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). 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 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 VX9 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 \textit{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 \(\geq 3\)), 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),...
The components of nutrition interventions included nutrition education (n=24), 27–29 31 32 38 39 41–44 48 single or multiple micronutrient supplementation (with/without education) (n=6), 19 33 42 44 45 48 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 29 30 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, 46 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. 57 In addition to childcare, messages on maternal well-being, hygiene and sanitation were also imparted in three trials. 39 41 44. 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 44

In 12 trials, the comparison group received existing standard care, 19 20 29 30 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 32 45 46 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 29 30 33–35 37 45 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), the Weschler Preschool and Primary Scale of Intelligence -IV, 48 the Kaufman’s Assessment Battery for Children II 57 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 31 33 35–36 38–43 43 47 while only eight trials used one or two BCTs. 29 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 30 33 36 39 40–41 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. 29 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                                                                 |
|------------------|--------------|--------|-----------------------------|----------------|----------------------------------------------------------------------------------------------------------------------------------|------------|---------------------------------------------------------------------------------|
| Mckay et al.     | RCT          | Four arms: 1a, 1b, 2, 3 and 4 based on treatment periods | Colombia, Undernourished children (WAZ <-2 SD) Age 9–30 months | February 1971 to August 1974 | Macronutrient and micronutrient supplementation | Detail not available | HAZ, WAZ Language usage, memory, motor control, manual, dexterity, information and vocabulary, quantitative reasoning, logic, verbal and non-verbal production |
| Graff et al.     | 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 | Colombia, Age 6–36 months | Detail not available | Macronutrient supplementation: Food distribution from local store sufficient for the entire family. | 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. | RCT         | Four arms: Nutrition only, Stimulation only, Nutrition+Stimulation and Control | Jamaica, Stunted children with LAZ <-2 SD Age 9–24 months | June 2009 to March 2012 | Macronutrient supplementation: 1kg milk-based formula and 20g 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. | Detail not available | Weekly health visit and free medical care 1. Griffiths mental development scale: locomotor, eye-hand coordination, language, performance developmental quotient 2. Corman-Escalona Einstein Scale: cognitive competence |
| Powell et al.    | Cluster RCT (18 clusters) | Two arms | 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. | Placebo and routine care | LAZ, WAZ, WHZ Griffiths mental development scale: locomotor, eye-hand coordination, language, performance developmental quotient |
| Gardner et al.   | RCT          | Four arms: Nutrition only, Stimulation only, Nutrition+Stimulation and Control | Jamaica, Undernourished children (WAZ<1.5 SD) Age 9–30 months | February 2010 to December 2011 | Micronutrient supplementation: 10mg 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, WHZ Griffiths mental development scale: locomotor, eye-hand coordination, language, performance developmental quotient |
| Hamadani et al.  | Cluster RCT (20 clusters) | Two arms | Bangladesh, Undernourished children (WAZ < -2 SD or WHZ < -1.5 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. Wolfe’s behaviour rating |
| Nahar et al.     | Time-lagged controlled study | Two arms | 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, WHZ BSID II: mental development index and motor development index |
Table 1 Continued

| Source            | Study design          | Sample | Population age at enrolment | Study duration | Components of integrated nutrition and stimulation interventions | Comparison                                           | Outcome measures                          | Study site       |
|-------------------|-----------------------|--------|----------------------------|----------------|---------------------------------------------------------------|-----------------------------------------------------------|--------------------------------------------|------------------|
| Lozoff et al.10    | 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: 15mg ferrous sulphate for 6 months infants | Surveillance: Record iron intake, feeding and health information. | LAZ, WAZ          | 1. BSID II: cognitive and motor development  |
|                   |                       |        |                            |                | Support mother–child relationship: Modelled positive feedback, provided play activities and information about child development. | 2. Behaviour rating scale: object orientation, motor quality, negative affect, and positive social responsiveness |                             |                  |
|                   |                       |        |                            |                | Studied: Provided messages and skills on responsive feeding and developmental stimulation messages. |                             |                             |                  |
|                   |                       |        |                            |                |                    |                             |                             |                  |
| Aboud et al.13     | Cluster RCT (45 clusters) Two arms: Nutrition only, Nutrition+Stimulation and Control | n=302  | Bangladesh, Very poor population Age 8–20 months | – | Multiple micronutrient supplementation (Sprinkles) | Regular health, nutrition, and child development programme. | LAZ, WAZ          | 1. BSID II: receptive and expressive language skills  |
|                   |                       |        |                            |                | 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. |                             |                             |                  |
|                   |                       |        |                            |                |                    |                             |                             |                  |
| Ogungbade et al.17 | RCT, Two arms | n=151  | South Africa, Children with Hb<12.5g/dL Age 36–79 months | September to November 2008 | Macro- and micronutrient supplementation: Enrolled children received stiff maize-meal porridge with added micronutrient powder (<8g). | Received soft maize-meal porridge with added placebo powder (<8g) containing only maize maltodextrin. | HAZ, WAZ          | KABC-II: learning scale, sequential scale, simultaneous scale, mental processing index, nonverbal index.  |
|                   |                       |        |                            |                | Psychosocial stimulation: All children attended preschool for 52 days. |                             |                             |                  |
|                   |                       |        |                            |                |                    |                             |                             |                  |
| Nahar et al.14     | 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. | 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  |
|                   |                       |        |                            |                | Play sessions and education: Offered play sessions and parental education using a semistructured curriculum. |                             |                             |                  |
|                   |                       |        |                            |                |                    |                             |                             |                  |
| Vazir et al.15     | 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. | Standard care: received ICDS services programme | Height Weight | BSID II: mental and motor development index  |
|                   |                       |        |                            |                | Playgroup educational session: Provided messages and skills on responsive feeding and developmental stimulation messages. |                             |                             |                  |
|                   |                       |        |                            |                |                    |                             |                             |                  |
| Aboud et al.19     | 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. | Standard care: Sharing messages about feeding and hygiene. | LAZ | BSID III: cognitive, receptive language and expressive language, fine motor  |
|                   |                       |        |                            |                | Parenting programme: Discussed parenting practices related to communication, play and nutrition. |                             |                             |                  |
|                   |                       |        |                            |                |                    |                             |                             |                  |
| Tofail et al.16    | 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 35mL ferrous sulphate syrup to children with IDA, parent, fed their child 5mL syrup daily for first 6 months (seven doses). | 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  |
|                   |                       |        |                            |                | Psychosocial stimulation: Provided mothers with demonstrations of how to play with toys and interact with their children. | 2. Modified version of scale developed by Wolke et al.: behaviour |                             |                  |
|                   |                       |        |                            |                |                    |                             |                             |                  |

Continued
| Source          | Study design Sample | Population age at enrolment | Study duration | Components of integrated nutrition and stimulation interventions | Comparison | Outcome measures         |
|-----------------|---------------------|-----------------------------|----------------|------------------------------------------------------------------|------------|--------------------------|
| Yousafzai et al | 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 | 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 | 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 | 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 and 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 | 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 | 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 | LAY WAZ WLZ BSID III: cognitive, language and motor development |
| Source            | Study design | Sample | Population age at enrolment                      | Study duration | Components of integrated nutrition and stimulation interventions                                                                 | Comparison | Outcome measures                                                                 |
|-------------------|--------------|--------|-------------------------------------------------|----------------|-----------------------------------------------------------------------------------------------------------------------------------|------------|----------------------------------------------------------------------------------|
| Schneider et al   | 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    | 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 BSID III: cognitive, language and motor development |
| Galasso et al     | 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 |
| Grantham-McGregor et al | 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 BSID III: cognitive, language and motor development Strengths and difficulties Questionnaire |

ASQ, ages and stages questionnaire; CBQL, child behaviour checklist; ICDS, integrated child development services programme; IDA, iron deficiency anaemia; 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** |
|----------------------|---------------|--------------------------------------------------------------------------------|------------------------------|-------------------|------------|--------------|---------------------------|-------------------------------|
| Mckay et al.⁵⁰       | 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.⁴⁴      | HV            | +                                                                               | 4                            | 12                | Community health aides         | Median of 32.5 visits conducted | C +, M –, L +       |
| Gardner et al.⁴²      | HV            | +                                                                               | 4                            | 12                | Community health worker         | 62% children received 3-4 visits per month | C +, M +, L +       |
| Hamadani et al.²³     | HV and GS     | +                                                                               | 7                            | 12                | Play leaders                    | 60% of mothers attended>=20 meetings | HAZ – WAZ – WHZ –       |
| Nahar et al.²⁴       | HV and GS     | +                                                                               | 3                            | 6                 | Female health workers           | –                           | C +, M –                  |
| Lozoff et al.²⁶      | HV            | +                                                                               | 4                            | 12                | Professional educators          | –                           | C+, M +, L +             |
| Aboud et al.³⁸       | GS            | +                                                                               | 3                            | 2                 | Peer educators                  | S>85%, N 80%               | LAZ – WAZ +               |
| Ogunlade et al.²⁷     | Pre-school    | +                                                                               | 3                            |                   | Front line assistant            | n=81.3%                    | C +                        |
| Nahar et al.³⁹       | Clinic visit  | +                                                                               | 2                            | 6                 | Female health workers           | LAZ – WAZ + WHZ –          | C +, M –                  |
| Vazir et al.³⁸       | HV            | +                                                                               | 3                            | 12                | Trained mothers                 | Height – Weight –          | C +, M –                  |
| Aboud et al.⁴⁰       | HV and GS     | +                                                                               | 3                            |                   | 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.⁴⁶   | HV and GS     | +                                                                               | 2                            | 33                | Female Health workers           | S>55%, n=75%              | C +, M +, L +            |
| Attanasio et al.²⁶   | HV            | +                                                                               | 4                            | 18                | Mother leaders                  | S 83%, N 73%              | C +, M +, L +            |
| Singla et al.⁴⁸      | HV and GS     | +                                                                               | 3                            |                   | 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
| Study               | Delivery mode      | Information | Performance* | Problem solving | Social support | Materials† | Media‡ | Average sessions per month§ | Duration (months) | Personnel¶ | Compliance¶ | Effect on child growth** | Effect on child development*** |
|---------------------|--------------------|-------------|--------------|-----------------|----------------|------------|--------|----------------------------|------------------|------------|-------------|--------------------------|-----------------------------|
| Helmizar et al⁴²     | GS                 | +           | +            |                 | +              |            |        | 4                          | 6                | Community health workers | -            | HAZ + WAZ + WHZ +         | C +, M +, L +             |
| Muhoovi et al⁴³      | HV and GS          | +           | +            |                 | +              |            |        | 3                          | 6                | Village health team leaders | GS 84%        | LAZ – WAZ – WLZ –         | C +, M +, L –            |
| Schneider et al⁴⁸     | Community centre   | +           |             |                 | +              |            |        | 13–22                      | 6                | Psychologists             | S 93.7%, N 91.7    | Height – Weight –         | C +                      |
| Hamadani et al⁴⁸     | GS at Clinic       | +           | +            |                 | +              |            |        | 2                          | 12               | Community health workers and health assistants | 46%           | LAZ – WAZ – WLZ –         | C +, M +, L +            |
| Galasso et al⁴⁹      | HV                 | +           | +            |                 |                |            |        | 3                          | 24               | Community health workers | >80%          | LAZ – WAZ – WLZ –         | C –, M –, L –            |
| Grantham-McGregor et al⁵⁰ | HV and GS separately | +          | +            |                 | +              |            |        | 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, informative 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.\textsuperscript{29} \textsuperscript{40} \textsuperscript{41} Eight trials used media such as written instructions, illustrative cards, activity booklets with prompts, and behaviour change cues.\textsuperscript{29} \textsuperscript{29} \textsuperscript{33} \textsuperscript{36} \textsuperscript{39} \textsuperscript{41} \textsuperscript{42} \textsuperscript{44} \textsuperscript{47}

Intensity: In 11 trials, the duration of intervention was less than 12 months.\textsuperscript{19} \textsuperscript{20} \textsuperscript{30} \textsuperscript{34} \textsuperscript{36} \textsuperscript{37} \textsuperscript{39} \textsuperscript{41} \textsuperscript{45} \textsuperscript{46} \textsuperscript{48} Twelve trials tested interventions that lasted for 12 months or more.\textsuperscript{20} \textsuperscript{27} \textsuperscript{29} \textsuperscript{31} \textsuperscript{33} \textsuperscript{35} \textsuperscript{38} \textsuperscript{40} \textsuperscript{42} \textsuperscript{45} \textsuperscript{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.\textsuperscript{30} 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.\textsuperscript{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.\textsuperscript{19} \textsuperscript{20} \textsuperscript{29} \textsuperscript{31} \textsuperscript{32} \textsuperscript{34} \textsuperscript{37} \textsuperscript{40} \textsuperscript{42} \textsuperscript{45} Seven trials tested interventions delivered by trained community volunteers (women from local communities).\textsuperscript{33} \textsuperscript{36} \textsuperscript{38} \textsuperscript{41} \textsuperscript{43} \textsuperscript{45} \textsuperscript{46} \textsuperscript{47} In four trials, interventions were delivered by professionals with relevant degrees, including psychologists,\textsuperscript{35} teachers,\textsuperscript{30} professional educators,\textsuperscript{35} and health assistants.\textsuperscript{28} Two trials included both volunteers and paraprofessionals.\textsuperscript{27} \textsuperscript{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.\textsuperscript{19} \textsuperscript{20} \textsuperscript{27} \textsuperscript{29} \textsuperscript{31} \textsuperscript{34} \textsuperscript{36} \textsuperscript{38} \textsuperscript{43} \textsuperscript{45} \textsuperscript{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.\textsuperscript{33} \textsuperscript{37} \textsuperscript{44} \textsuperscript{48} Seventeen trials tested integrated interventions vs usual care.\textsuperscript{19} \textsuperscript{20} \textsuperscript{27} \textsuperscript{30} \textsuperscript{32} \textsuperscript{36} \textsuperscript{38} \textsuperscript{43} \textsuperscript{45} \textsuperscript{47} One trial had two arms with integrated interventions delivered using two different modes.\textsuperscript{29} Thirteen and eight trials, respectively, compared integrated versus standalone nutrition,\textsuperscript{19} \textsuperscript{20} \textsuperscript{29} \textsuperscript{31} \textsuperscript{34} \textsuperscript{38} \textsuperscript{40} \textsuperscript{42} \textsuperscript{45} \textsuperscript{47} and stimulation interventions.\textsuperscript{19} \textsuperscript{32} \textsuperscript{36} \textsuperscript{40} \textsuperscript{42} \textsuperscript{45} \textsuperscript{47} Five trials examined synergistic interactions between nutrition and stimulation interventions.\textsuperscript{19} \textsuperscript{32} \textsuperscript{40} \textsuperscript{45} \textsuperscript{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% CI 0.08, 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 ($F>75\%$, 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, $F=83\%$, p=0.003) and motor (n=3, ES 0.32, 95% CI 0.01, 0.63, $F=53\%$, 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, $F=83\%$, p<0.001) and language (n=5, ES 0.26, 95% CI 0.004, 0.51, $F=90\%$, 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, $F>75\%$). 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, $F=72\%$, p<0.001) and language (n=9, ES 0.24, 95% CI 0.09 to 0.40, $F=82\%$, p<0.001) outcomes, small effects for motor outcome (n=14, ES 0.07, 95% CI 0.008 to 0.14, $F=20\%$, p=0.240); non-significant effects on WAZ (n=6, ES 0.09, 95% CI -0.06 to 0.23, $F=58\%$, p=0.037), WLZ/WHZ (n=6, ES 0.03, 95% CI -0.05 to 0.10, $F=0$, p=0.609) scores and no effect on LAZ/HAZ score.

In contrast, in comparison to the stimulation intervention only group, the integrated interventions group
showed non-significant effects on cognitive (n=7, ES 0.18, 95% CI −0.09 to 0.45, I²=86%, p<0.001), motor (n=7, ES 0.19, 95% CI −0.03 to 0.42, I²=79%, p<0.001), language (n=6, ES 0.06, 95% CI −0.33 to 0.45, I²=92%, p<0.001), WAZ (n=4, ES 0.02, 95% CI −0.09 to 0.14, I²=0, p=0.780) and WLZ/WHZ (n=4, ES 0.06, 95% CI −0.06 to 0.19, I²=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.

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.

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 0.54). 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

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.

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.
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,\(^31\) 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.\(^5\) 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
The high heterogeneity found among trials emphasises on their own within the limited timescale of most trials. 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. We did not report effects on socioemotional development, a critical aspect of child development, as only three studies reported socioemotional outcomes.

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, 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.

Author affiliations
1 School of Health Sciences, Western Sydney University, Penrith South, New South Wales, Australia
2 Institute for Global Health, University College London, London, UK
3 School of Population Health, University of New South Wales, Sydney, New South Wales, Australia
4 Research and Development, Australian Red Cross Lifeblood New South Wales and Australian Capital Territory, Alexandria, New South Wales, Australia

Twitter Sophiya Dulal @DulalSophiya and Audrey Prost @Audreyprost2

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 and 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.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.
REFERENCES

1. Black MM, Walker SP, Fernald LCH, et al. Early childhood development coming of age: science through the life course. Lancet 2017;389:77–90.
2. Grantham-McGregor S, Cheung YB, Cueto S, et al. Developmental potential in the first 5 years for children in developing countries. Lancet 2007;369:60–70.
3. World Health Organisation. Improving early childhood development: WHO guideline. Licence: CC BY-NC-SA 3.0 IGO. Geneva: World Health Organization, 2020.
4. Vaivada T, Gaffey MF, Bhatta ZA. Promoting early child development with interventions in health and nutrition: a systematic review. Pediatrics 2017;139:1453–61.
5. Larson LM, Yousafzai AK. A meta-analysis of nutrition interventions on mental development of children under-two in low- and middle-income countries. Maternal Child Nutr 2013;13:12229.
6. Aboud FC, Yousafzai AK. Global health and development in early childhood. Annu Rev Psychol 2015;66:433–57.
7. Jeong J, Franchetti EE, Ramos de Oliveira CV, et al. Parenting interventions to promote early child development in the first three years of life: a global systematic review and meta-analysis. PLoS Med 2021;18:e1003602.
8. DiGirolamo AM, Stansbury P, Lung’aho M. Advantages and challenges of integration: opportunities for integrating early childhood development and nutrition programming. Ann N Y Acad Sci 2014;1308:46–53.
9. Hurley KM, Yousafzai AK, Lopez-Boo F. Early child development and nutrition: a review of the benefits and challenges of implementing integrated interventions. Adv Nutr 2016;7:357–63.
10. Grantham-McGregor SM, Fernald LCH, Kagawa RMC, et al. Effects of integrated child development and nutrition interventions on child development and nutritional status. Ann N Y Acad Sci 2014;1308:11–22.
11. Prado EL, Larson LM, Cox K, et al. Do effects of early life interventions on linear growth correspond to effects on neurobehavioural development? A systematic review and meta-analysis. Lancet Glob Health 2019;7:e1388–413.
12. Yousafzai AK, Aboud FE. Review of implementation processes for integrated nutrition and psychosocial stimulation interventions. Ann N Y Acad Sci 2014;1308:33–45.
13. Britto PR, Singh M, Dua T, et al. What implementation evidence matters: scaling-up nurturing interventions that promote early child development. Ann N Y Acad Sci 2018;1419:5–6.
14. Alderman H, Fernald L. The nexus between nutrition and early childhood development. Annu Rev Nutr 2017;37:447–76.
15. Yousafzai AK, Aboud FE, Nores M, et al. Reporting guidelines for implementation research on nurturing care interventions designed to promote early child development. Ann N Y Acad Sci 2018;1419:26–37.
16. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med 2009;6:e1000097.
17. Higgins JPT, Sterne JAC, Savovic J. A revised tool for assessing risk of bias in randomised trials in: Chandler J, McKenzie J, Bouter L, Welch V (editors). Cochrane methods. Cochrane Database of Syst Rev 2018;10.
18. Sterne JAC, Hernán MA, McAlenian A, Chapter 25: Assessing risk of bias in a non-randomised study. In: Higgins JPT, Thomas J, Chandler J, et al. eds. Cochrane Handbook for systematic reviews of interventions version 6.1 (updated September 2020). London: Cochrane, 2020.
19. Nahar B, Hossain MI, Hamadani JD, et al. Effects of a community-based approach of food and psychosocial stimulation on growth and development of severely malnourished children in Bangladesh: a randomised trial. Eur J Clin Nutr 2021;75:701–9.
20. Galasso E, Weber AM, Stewart CP, et al. Effects of nutritional supplementation and home visiting on growth and development in young children in Madagascar: a cluster-randomised controlled trial. Lancet Glob Health 2019;7:e1257–68.
21. Higgins JPT, Thomas J, Chandler J, et al. Cochrane Handbook for systematic reviews of interventions version 6.0. London: Cochrane, 2019. www.training.cochrane.org/handbook.
52 Li Z, Kim R, Vollmer S, et al. Factors associated with child stunting, wasting, and underweight in 35 low- and middle-income countries. JAMA Netw Open 2020;3:e200386.
53 Breuer E, Lee L, De Silva M. Using theory of change to design and evaluate public health interventions: a systematic review. Implement Science 2016;11:1–7.
54 Glanz K, Bishop DB. The role of behavioral science theory in development and implementation of public health interventions. Annu Rev Public Health 2010;31:399–418.
55 Powell C, Grantham-McGregor S. Home visiting of varying frequency and child development. Pediatrics 1989;84:157–64.
56 Behrman JR, Cheng Y, Todd PE. Evaluating preschool programs when length of exposure to the program varies: a nonparametric approach. Rev Econ Stat 2004;86:108–32.
57 Armecin G, Behrman J, Duazo P. Early childhood development through an integrated program: evidence from the Philippines. World Bank Policy Research Working Paper 3992 2006 https://papers.ssrn.com/sol3/papers.cfm?abstract_id=917493
58 Gilmore B, McAuliffe E. Effectiveness of community health workers delivering preventive interventions for maternal and child health in low- and middle-income countries: a systematic review. BMC Public Health 2013;13:847.
59 Smith JA, Baker-Henningham H, Brentani A, et al. Implementation of reach up early childhood parenting program: acceptability, appropriateness, and feasibility in Brazil and Zimbabwe. Ann N Y Acad Sci 2018;1419:120–40.
60 Aboud FE, Prado EL. Measuring the implementation of early childhood development programs. Ann N Y Acad Sci 2018;1419:249–63.
61 Shankar AV, Asirila Z, Kadha JK, et al. Programmatic effects of a large-scale Multiple-Micronutrient supplementation trial in Indonesia: using community facilitators as intermediaries for behavior change. Food Nutr Bull 2009;30:S207–14.
62 Cremer HD, Florez A, de Navarro L, et al. Influence of food supplementation and/or psychological stimulation on mental development. Giessen-Harvard-ICBF project. Nutr Metab 1977;21 Suppl 1:231–4.
63 Super CM, Herrera MG, Mora JO. Long-Term effects of food supplementation and psychosocial intervention on the physical growth of Colombian infants at risk of malnutrition. Child Dev 1990;61:29–49.

References

43 Muhoozi GKM, Atukunda P, Diep LM, et al. Nutrition, hygiene, and stimulation education to improve growth, cognitive, language, and motor development among infants in Uganda: a cluster-randomized trial. Matern Child Nutr 2016;12:1257.
44 Waber DP, Vuori-Christiansen L, Ortiz N, et al. Nutritional supplementation, maternal education, and cognitive development of infants at risk of malnutrition. Am J Clin Nutr 1981;34:807–13.
45 Grantham-McGregor SM, Powell CA, Walker SP, et al. Nutritional supplementation, psychosocial stimulation, and mental development of stunted children: the Jamaican study. Lancet 1991;338:1–5.
46 Tofail F, Hamadani JD, Mehrin F, et al. Psychosocial stimulation benefits development in nonanemic children but not in anemic, iron-deficient children. J Nutr 2013;143:885–93.
47 Attanasio OP, Fernández C, Fitzsimons EOA, et al. Using the infrastructure of a conditional cash transfer program to deliver a scalable integrated early child development program in Colombia: cluster randomized controlled trial. BMJ 2014;349:g6785.
48 Schneider N, Geiser E, Gosoniu L, et al. A combined dietary and cognitive intervention in 3–5-Year-Old children in Indonesia: a randomized controlled trial. Nutrients 2018;10:1394.
49 World Health Organization and United Nations Children’s Fund. Care for child development: improving the care for young children, 2012. Available: https://www.who.int/maternal_child_adolescent/documents/child-heathy-growh-development/en/
50 Park JH, Harari O, Siden E, et al. Interventions to improve linear growth during complementary feeding period for children aged 6–24 months living in low- and middle-income countries: a systematic review and network meta-analysis. Gates Open Res 2019;3:1660.
51 Dewey KG, Adu-Afarwuah S. Systematic review of the efficacy and effectiveness of complementary feeding interventions in developing countries. Matern Child Nutr 2008;4 Suppl 1:24–85.
52 Li Z, Kim R, Vollmer S, et al. Factors associated with child stunting, wasting, and underweight in 35 low- and middle-income countries. JAMA Netw Open 2020;3:e200386.