Effects of responsive stimulation and nutrition interventions on children’s development and growth at age 4 years in a disadvantaged population in Pakistan: a longitudinal follow-up of a cluster-randomised factorial effectiveness trial

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Summary
Background A previous study in Pakistan assessed the effectiveness of delivering responsive stimulation and enhanced nutrition interventions to young children. Responsive stimulation significantly improved children’s cognitive, language, and motor development at 2 years of age. Both interventions significantly improved parenting skills, with responsive stimulation showing larger effects. In this follow-up study, we investigated whether interventions had benefits on children’s healthy development and care at 4 years of age.

Methods We implemented a follow-up study of the initial, community-based cluster-randomised effectiveness trial, which was conducted through the Lady Health Worker programme in Sindh, Pakistan. We re-enrolled 1302 mother–child dyads (87% of the 1489 dyads in the original enrolment) for assessment when the child was 4 years of age. The children were originally randomised in the following groups: nutrition education and multiple micronutrient powders (enhanced nutrition; n=331), responsive stimulation (n=345), combined responsive stimulation and enhanced nutrition (n=315), and routine health and nutrition services (control; n=331). The data collection team were masked to the allocated intervention. The original enrolment period included children born in the study area between April 1, 2009, and March 31, 2010, if they were up to 2·5 months old without signs of severe impairments. The primary endpoints for children were development and growth at 4 years of age. Interventions were given in monthly group sessions and in home visits. The primary endpoint for mothers was wellbeing and caregiving knowledge, practices, and skills when the child was 4 years of age. Analysis was by intention to treat. The original trial is registered with ClinicalTrials.gov, number NCT00715936.

Findings 1302 mother–child dyads were re-enrolled between Jan 1, 2013, and March 31, 2013, all of whom were followed up at 4 years of age. Children who received responsive stimulation (with or without enhanced nutrition) had significantly higher cognition, language, and motor skills at 4 years of age than children who did not receive responsive stimulation. For children who received responsive stimulation plus enhanced nutrition, effect sizes (Cohen’s d) were 0·1 for IQ (mean difference from control 1·2, 95% CI –0·3 to 2·7), 0·3 for executive functioning (0·18, –0·07 to 0·29), 0·5 for pre-academic skills (7·53, 5·14 to 9·92) and 0·2 for pro-social behaviours (0·08, 0·03 to 0·13). For children who received responsive stimulation alone, effect sizes were 0·1 for IQ (mean difference with controls 1·7, –0·3 to 3·7), 0·3 for executive functioning (0·17, 0·07 to 0·27), 0·2 for pre-academic skills (3·86, 1·41 to 6·31), and 0·2 for pro-social behaviours (0·07, 0·02 to 0·12). Enhanced nutrition improved child motor development, with effect size of 0·2 for responsive stimulation plus enhanced nutrition (0·56, –0·03 to 1·15), and for enhanced nutrition alone (0·82, 0·18 to 1·46). Mothers who received responsive stimulation (with or without enhanced nutrition) had significantly better responsive caregiving behaviours at 4 years of child age than those who did not receive intervention. Effect size was 0·3 for responsive stimulation plus enhanced nutrition (1·95, 0·75 to 3·15) and 0·2 for responsive stimulation (2·01, 0·74 to 3·28). The caregiving environment had a medium effect size of 0·3 for all interventions (responsive stimulation plus enhanced nutrition 2·99, 1·50 to 4·48; responsive stimulation alone 2·82, 1·21 to 4·43; enhanced nutrition 3·52, 1·70 to 5·34).

Interpretation Responsive stimulation delivered in a community health service can improve child development and care, 2 years after the end of intervention. Future analyses of these data are needed to identify which children and families benefit more or less over time.

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Articles

Research in context

Evidence before this study
We conducted a review of recent systematic reviews for stimulation or nutrition interventions published since the last Lancet series on child development in developing countries in 2011 (Jan 1, 2011, to Nov 30, 2015). We searched for reviews on PubMed and PsycINFO. Key terms used were psychosocial stimulation, stimulation, parenting, responsive care, nutrition, supplementation, micronutrients, growth, child development, early, interventions, longitudinal, follow up. Inclusion criteria included studies conducted in low- and middle-income countries, stimulation or nutrition interventions for children younger than 2 years, and outcomes that included a measure of children's development. We identified three reviews with meta-analyses of intervention effect on children’s development or growth. We found consistent medium-size effects on child development as a result of stimulation and small-size effects as a result of nutrition interventions. Nutrition interventions also improved growth and nutrition status. In the review that specifically analysed integrated stimulation and nutrition interventions, little evidence was available to determine additive or synergistic effects on child outcomes. Only four studies from Jamaica and Colombia were identified that had followed up cohorts after the intervention had ended. The earliest age of follow-up began at 6 years. The two Colombian studies had high attrition rates (>25%). The Jamaican cohort showed stimulation intervention showed sustained benefits in to adulthood, while the effects of nutrition supplement were not observed after 7 years of age. In summary, there is limited information on the long-term effects of early stimulation (with or without nutrition intervention) on later child and adult outcomes.

Added value of this study
Our results show sustained improvement during the preschool period as a result of early responsive stimulation (with or without enhanced nutrition) on child IQ, executive functions, pre-academic skills, and pro-social behaviours, while children who received early enhanced nutrition sustained significant benefits to motor development. Our study also contributes to the evidence by investigating sustained benefits to caregiving. Mothers who were exposed to early responsive stimulation (with or without enhanced nutrition) showed significant continued improvement in responsive caregiving behaviours and in the quality of the caregiving environment, while the enhanced nutrition exposure showed significant continued benefit to the quality of the caregiving environment. This longitudinal follow-up demonstrated that responsive stimulation delivered in a programme setting in a rural highly disadvantaged low-income and middle-income population can sustain benefits on children's development 2 years after the end of intervention. However, compared with the short-term effects at the end of the original intervention, the effect sizes are reduced.

Implications of all the available evidence
More studies are needed to investigate the independent and combined effects of early stimulation and nutrition interventions. These studies should be designed not only to provide insights into the effectiveness of these interventions, but also how to optimise integrated implementation. Further, in contexts such as Pakistan, in which access, retention, and attainment in future primary education remains extremely poor, the extent of development protection that early responsive stimulation might provide in the long term is likely to be small. Risks that threaten children's development will continue to accumulate; therefore strategies to bolster development along the life course should be explored.

reported that responsive stimulation had a medium effect (n=21 studies, Cohen's d=0·42; 95% CI 0·36–0·48) and nutrition supplementation with or without nutrition education had a small effect (n=18, 0·09; 0·04–0·14) on cognitive development at 2 years of age. A systematic review of combined stimulation and nutrition interventions reported that stimulation consistently benefited child development, while nutrition usually improved nutritional status and growth, and sometimes improved child development. The review found little evidence for additive benefits on children’s development, although no significant loss of independent intervention benefits was reported. Increased attention to combining interventions is warranted in order to determine potential additive benefits to outcomes, evaluate cost-effectiveness, and identify optimal early childhood intervention bundles to affect many outcomes in children.

Evidence of the enduring effects of interventions that promote early child development on later life outcomes and the potential cost-benefits to society from low-income and middle-income countries is scarce. Only four cohorts (from Colombia and Jamaica) have been followed up after the original stimulation interventions were implemented between 1978 and 2004. The Jamaica cohort is the most prominent example of a cohort tracked into adulthood following exposure to early stimulation and nutrition interventions. In the efficacy randomised controlled trial, undernourished infants from poor neighbourhoods of Kingston, Jamaica, were randomly assigned into four groups to receive stimulation, nutritional supplementation, combined interventions, or control (standard health care). After 24 months of intervention exposure, both interventions had independent and additive benefits on child development and the nutrition intervention improved early growth. The effects of the stimulation intervention on cognitive capacity and behaviour were sustained into adulthood, whereas the nutrition intervention sustained small cognitive benefits only up to 7 years of age. Neither intervention had long-term benefits on growth.
Although these data support integration of stimulation interventions in child nutrition and health services, a knowledge gap remains in understanding how similar interventions affect outcomes along the life course for children growing up in different settings, with varying risks from physical environments, sociocultural contexts, political systems, and access to health, nutrition, and learning. Evidence from longitudinal evaluations of large-scale programmes in high-income countries suggest that early gains can be threatened if children do not transition from an early intervention programme to high quality educational services.

Between 2009 and 2012, a pragmatic, community-based, cluster-randomised effectiveness trial was done in an impoverished rural district of Sindh, Pakistan. The trial was conducted in partnership with the National Programme for Family Planning and Primary Healthcare (often referred to as the Lady Health Worker [LHW] programme). The LHWs delivered either responsive stimulation or enhanced nutrition interventions to young children younger than 2 years and their caregivers via monthly home visits and parenting groups. The results showed that responsive stimulation significantly improved children’s cognitive, language, and motor development at 2 years of age, and enhanced nutrition showed modest benefits on linear growth at 6 and 18 months. With respect to maternal outcomes, responsive stimulation had larger effect sizes on mother–child interactions, caregiving environment, and parenting knowledge and practices compared with enhanced nutrition, and the combined intervention had a modest effect on decreasing maternal depressive symptoms over time.

We aimed to measure the effects of the responsive stimulation and enhanced nutrition intervention delivered in Sindh in children now 4 years old. Although we intend to follow this cohort through schooling years, the assessment of children’s development and growth at 4 years offers valuable insights. First, it is important to document longitudinal attenuation in the intervention effects before children are exposed to variable education opportunities. Second, the period between 3 and 5 years of age captures accelerated maturation and function of the prefrontal cortex, a brain region that supports regulation of emotions, attention, and behaviour, and emergent reasoning skills, which are modifiable through environment and experience. These skills are important markers of school readiness, and are crucial for successful transition to preschool. Third, competencies assessed in this age group have been shown to predict school engagement and longer term academic attainment. Therefore, this longitudinal follow-up comprised assessments of verbal and non-verbal intelligence, executive functions, and pre-academic learning skills in addition to measures of growth, physical health, and motor development. For mothers, the most proximal influence on children’s healthy growth and development, intervention effects on sustained parenting practices were investigated.

**Methods**

**Study design and participants**

The original pragmatic, community-based, cluster-randomised effectiveness trial with a 2 × 2 factorial design tested the effectiveness and feasibility of integrating new interventions with routine services in the LHW programme to improve child development and growth outcomes. The LHWs delivered responsive stimulation interventions, enhanced nutrition interventions, or both in combination to children younger than 2 years or their caregivers residing in their health catchments (clusters) through monthly home visits and community group sessions. The control group received routine health and nutrition services. The responsive stimulation intervention was a local adaptation of the Care for Child Development approach developed by UNICEF and WHO. This intervention had two goals, to help caregivers provide a variety of play and communication activities using everyday household items or homemade toys to stimulate children’s cognitive, language, motor, and affective skills, and to use the context of play and communication activities to strengthen responsive care by guiding caregivers to observe and respond to their child’s cues, thereby promoting the quality of the caregiver–child interactions that support healthy development. The method of play and communication counselling encouraged the caregivers to try out an activity with their child, and receive coaching and feedback from the LHW. The enhanced nutrition intervention enriched the existing nutrition education curriculum of the LHW programme through the addition of responsive feeding messages (recognising and responding to early cues of hunger, communication, encouragement, and patience during feeding, and independent feeding); distribution of a multiple micronutrient supplementation (Sprinkles, Genra Pharmaceuticals, Pakistan) for children aged 6–24 months; guiding LHWs to link nutrition and health messages; and training LHWs to move away from a didactic delivery approach to nutrition education to a counselling approach involving listening, asking questions, and problem solving.

1489 mother–infant dyads were enrolled into the original trial, and randomised into one of four groups; control (n=368), responsive stimulation (n=383), enhanced nutrition (n=364), and a combination of responsive stimulation and enhanced nutrition (n=374). The control group received the routine LHW services, delivered in monthly home visits and occasional group meetings, which included health and hygiene advice, infant and young child feeding recommendations (basic nutrition education), child growth monitoring, and immunisations. The responsive stimulation, enhanced nutrition, and combination groups also received these
Inclusion criteria for re-enrolment were children without signs of moderate to severe impairments and those who were resident in Sindh province. We used the Ten Questions Screen\(^a\) to screen for child impairment followed by a physician or an allied health professional’s confirmation. We conducted follow-up assessments on child development and growth, maternal wellbeing, and parenting practices from April 1, 2013, to March 31, 2014, within 1 month of the child’s fourth birthday. All mothers provided written informed consent (or a thumb print for numbers). Following a review of scores, we found the alphabet and numbers with Sindhi alphabet and numbers. We measured pre-academic skills using the Wechsler Preschool and Primary Scales of Intelligence, Third Edition.\(^b\) Sociocultural modifications were made to ensure words, concepts, and pictures were relevant to the study population. We used seven subtests to assess full-scale IQ, which were block design, information, matrix reasoning, vocabulary, picture concepts, symbol search, and word reasoning. Internal consistency was good (Cronbach’s \(\alpha=0.91\)) and inter-observer agreement between the supervisors and child development assessors was high for each subtest (Bland Altman test range \(n=120–125\), \(R=0.94–0.99\); \(p<0.0001\)). We followed a systematic procedure to identify a shortlist of tasks, locally adapt these tasks, and try out assessments of executive functions in children. We created a battery of six executive function tasks, of which fruit Stroop task, knock-tap task, big-little task, and go/no go task captured children’s inhibitory control; forward word span captured working memory; and the Separated Dimensional Change Card Sort captured cognitive flexibility. We determined the child’s comprehension of tasks by performance on practice trials. We created a final executive function composite score by calculating a mean of test scores across six executive function tasks for children who demonstrated comprehension of task rules via performance on the practice trials. Tests were different to those used in the original trial because of the difference in age and developmental stage of the children. In view of findings that a three-task battery provides a reliable measure of overall executive function skills, the final executive function composite includes final scores for children who passed comprehension criteria for three or more tasks.\(^h\) The executive function composite showed acceptable internal consistency (Cronbach’s \(\alpha=0.64\)) and the inter-observer agreement was high for each subtest (Bland Altman test range \(n=115–123\), \(R=0.922–0.966\); \(p<0.0001\)). We measured pre-academic skills using the Bracken School Readiness Assessment, Third Edition,\(^i\) which comprises five subtests for colour recognition, letter recognition, number and counting, sizes and comparisons, and shapes. We made modifications to the assessment, including replacement of the Roman alphabet and numbers with Sindhi alphabet and numbers. Following a review of scores, we found the
distribution of subtests for colour recognition, letter recognition, and numbers and counting were significantly skewed and the majority of individuals scored zero; therefore, we did not analyse these subtests. Mean scores were calculated for the remaining two subtests (sizes and comparisons [Cronbach’s α=0.768, Bland Altman test n=119; R=1.000, p<0.0001], and shapes [0.842, n=119; R=0.00, p<0.0001]) for use in the outcome analysis.

We assessed social-emotional development in the children by use of the results of the maternal Strengths and Difficulties Questionnaire, adapted for the study population. Following analysis of data, we retained 12 items and organised these into subscales with moderate internal consistency and good inter-observer agreement. Behavioural problems comprised five items (0.61, n=123; R=0.976, p<0.0001), and pro-social behaviours comprised seven items (0.60, n=123; R=0.969, p<0.0001).

We assessed child motor development using a composite score of six items identified from the Bruininks-Oseretsky Test for Motor Proficiency, Version 2, Brief Form (BOT-2 BF), which were suitable for assessing fine and gross motor skills in 4-year-olds. The six items included were filling a star, drawing a line through a path, copying overlapping circles, stringing blocks, touching nose with index finger and eyes closed, and walking forward heel-to-toe. The BOT-2 BF composite showed acceptable internal consistency (Cronbach’s α=0.60) and good inter-observer reliability (Bland Altman test n=80–91, R=0.876–1.000; p<0.0001).

We measured child height and weight according to standard protocols.22 Height (ShorrBoard, Weigh and Measure LLC, USA) was measured to the nearest 0.1 cm and weight (Seca 877 Digital Flat Scale, Weigh and Measure LLC, USA) was measured to the nearest 0.1 kg, and the scales were calibrated each morning before data collection visits with standard weights. The relative technical error of measurement (TEM) was good for anthropometric measures assessed in 133 children (height TEM 1.86%, R=0.99; weight TEM 0.71%, R=0.99). To assess anaemia status in children, we assessed haemoglobin by a finger prick assay with HemoCue machines (HemoCue B-Haemoglobin System, HemoCue AB, Sweden), which were calibrated daily before data collection visits.

Parenting knowledge and practices were assessed by maternal report of the case child’s current preschool exposure and learning opportunities in the home using one item from the early child development module of the UNICEF Multiple Cluster Index Surveys (“In the past three days, did you or any household member over 15 years of age engage in any of the following activities with your child: read books or looked at pictures together, told stories, sang songs, took child outside of the home, played with child, named or counted, or drew thing to or with child”).23 The caregiver was asked about each activity separately and a point was given for every positive response; therefore, a caregiver might obtain a score between 0 and 6. Responses were reported separately for mothers, fathers, and other adult caregivers.

We assessed maternal and child interactions using the Observation for Mother-Child Interactions (OMCI) measure24–26 with good internal consistency and inter-observer agreement. Behavioural problems comprised five items (0.60, n=123; R=0.974, p<0.0001), and pro-social behaviours comprised seven items (0.60, n=123; R=0.963, p<0.0001).

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observer reliability (Cronbach's α=0·807, Bland Altman test n=126; R=0·752, p<0·0001). The OMCI is a measure of sensitive and responsive behaviours observed during a 5 min structured activity exploring a picture book. The assessor scored the frequency of behaviours live, and 10% of the observations were videotaped for independent scoring by an expert to check for reliability. We assessed the caregiving environment using the Home Observation for the Measurement of the Environment, Early Childhood version (HOME-EC) with good internal consistency and high inter-observer reliability for each subset (Cronbach’s α=0·820, Bland Altman test n=126; ranging per subscale from R=0·751–0·961, p<0·0001). We measured maternal depressive symptoms using the self-reporting questionnaire (SRQ-20) with good internal consistency and high inter-observer reliability (0·873, n=92; R=0·988, p<0·0001). In Pakistan, an SRQ-20 score of 9 or more indicates risk of depression.\(^{21}\)

### Cognitive capacity

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### Social-emotional development (SDQ)

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<td>n=624</td>
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### Motor development (BOT2-BF)

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### Statistical analyses

We adjusted for clustering effects using generalised linear models. We used Gaussian distribution to model continuous coded variables and binomial distribution to model binary coded variables. Significance was defined as a p value lower than 0·05 unless stated otherwise. This was an intention-to-treat analysis. We tested baseline differences between groups to identify potential confounders that would need to be accounted for in the analyses of outcome variables. We then assessed group differences across child and maternal outcomes following the factorial design of the original study, testing differences between exposures to the two interventions (responsive stimulation vs no responsive stimulation and enhanced nutrition vs no enhanced nutrition) with generalised equations. In all models we controlled for the effect of baseline confounding variables (socioeconomic status, household food security, maternal education, number of children, sex of child). We tested interaction effects between the two interventions (responsive stimulation and enhanced nutrition). A significant interaction effect denoted that the effect of a single intervention was different from the effect of the combined interventions. We then interpreted the type of interaction effect by analysing the means of the independent intervention with the combined intervention. Finally, we calculated Cohen’s d effect sizes as differences in adjusted means between the intervention and control group over the pooled SD. We used Stata version 12.1 to conduct all statistical analyses. The original trial is registered with ClinicalTrials.gov, number NCT00715936.

### Role of the funding source

The funder had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The authors of this report had full access to all data in the study. AKY and JO had primary responsibility for the decision to submit the manuscript for publication.

### Results

We identified and re-enrolled 1335 mother–child dyads and 1302 participated in the assessments of development, growth, and care (87% of 1489 subjects enrolled in the original trial [figure 1]). We did not find any significant differences in baseline characteristics between children lost to follow-up and those assessed at 4 years of age, except for in height-for-age Z score, which was poorer in the lost to follow-up sample (appendix). Table 1 shows the baseline characteristics of re-enrolled participants across the four treatment groups (responsive stimulation plus enhanced nutrition, responsive stimulation, enhanced nutrition, control). Analysis of these variables shows that group characteristics were similar, and the only significant difference was seen in the proportion of food-secure households, which was controlled for in subsequent analyses (appendix).
Child development outcomes are reported in table 2. Child cognitive outcomes showed that compared with children who received no responsive stimulation, the children exposed to responsive stimulation had significantly higher mean scores for IQ, executive function, and pre-academic skills. The effect sizes were small for IQ (Cohen’s d = 0.1 for responsive stimulation plus enhanced nutrition and 0.0 for responsive stimulation), medium for executive function (0.3 for responsive stimulation plus enhanced nutrition and 0.3 for responsive stimulation) and large-to-small for pre-academic skills (0.5 for responsive stimulation plus enhanced nutrition and 0.2 for responsive stimulation). No significant differences in cognitive outcomes were observed between children who received enhanced nutrition and those were not exposed to enhanced nutrition. Interaction effects between the two interventions were not significant for IQ, executive function, or pre-academic skills. Children exposed to responsive stimulation had significantly higher mean pro-social behaviour scores with a small effect size than did children who received no responsive stimulation (Cohen’s d = 0.2 for responsive stimulation plus enhanced nutrition and 0.2 for responsive stimulation); and children who did not receive enhanced nutrition had significantly higher mean pro-social behaviour scores than did children who were exposed to enhanced nutrition intervention. A significant interaction effect was observed between the two interventions. Further analyses suggest an additive effect with a higher mean in the combined group compared with either responsive stimulation alone or enhanced nutrition alone (appendix table C). The two interventions did not affect child behavioural problems. Mean motor development scores were significantly higher in children exposed to enhanced nutrition than in children who did not receive enhanced nutrition, with a small effect size (Cohen’s d = 0.1 for enhanced nutrition). A significant interaction effect was observed between the two interventions; however, further analyses suggests a higher mean score in the combined group compared with either responsive stimulation alone or enhanced nutrition alone (appendix).

Table 3 shows that mean levels of height-for-age, weight-for-age, and weight-for-height Z scores or proportions of moderate to severe undernutrition did not differ significantly across groups. No significant interaction effects were observed between the two interventions on child growth indicators. Mean haemoglobin value was significantly higher in children who received no responsive stimulation than in children who were exposed to responsive stimulation. Similarly, significantly higher mean haemoglobin concentrations were observed in children who received no enhanced nutrition than in children who were exposed to enhanced nutrition (table 3). A significant interaction effect was observed between the two interventions; however, further analyses suggests a higher mean score in the combined group compared with either responsive stimulation alone or enhanced nutrition alone (appendix).

Table 4 reports outcomes at the level of the caregiver. Children who received responsive stimulation had significantly higher levels of maternal responsive behaviours than did children who received no responsive stimulation, as indicated by the observation of mother–child interactions with small to medium effect sizes (Cohen’s d = 0.0–0.2 for responsive stimulation plus enhanced nutrition and 0.0–0.2 for responsive stimulation) and by the quality of the caregiving environment indexed by the HOME-EC with a medium effect size (0.3 for responsive stimulation plus enhanced nutrition and 0.3 for responsive stimulation). The mean score for the quality of the caregiving environment was significantly higher in children exposed to enhanced nutrition than in children who did not receive enhanced nutrition, also with a medium effect size (0.3 for enhanced nutrition). A significant interaction effect was observed between the two interventions on the quality of the caregiving environment.
Further analyses suggest a lower mean in the combined group compared with either responsive stimulation alone or enhanced nutrition alone (appendix table C). The total number of maternal depressive symptoms did not differ between groups. Figure 2 shows that the proportion of mothers, fathers, and other adult caregivers playing four or more games with their children over 3 days was significantly higher in the no enhanced nutrition group than in those families who received enhanced nutrition (figure 2). Further details on the treatment effect sizes can be found in the appendix.

Discussion

This study analysed whether enriched interventions (responsive stimulation and enhanced nutrition alone or in combination) integrated with routine LHW programme services in the first 2 years of life showed sustained benefits on child development and growth at 4 years of age. A responsive stimulation intervention (with or without enhanced nutrition) benefited children’s cognitive abilities and pro-social behaviours with small to large effects compared with routine services, whereas the enhanced nutrition intervention benefited motor development with a small effect compared with routine services. Early nutrition interventions have generally shown a smaller effect on children’s cognitive development in low-income and middle-income countries than have responsive stimulation interventions, and more work is warranted on associations with motor development. Neither intervention made a difference to preschool enrolment. However, the motivation of families should be explored further in the context of variable access and quality to preschool services. Of the significant interaction effects observed, pro-social behaviour suggests an additive benefit of the combined group compared with either responsive stimulation alone or enhanced nutrition alone. Haemoglobin data suggest neither responsive stimulation alone nor enhanced nutrition alone were beneficial, but a significant interaction effect indicated the combined group mean effect size was higher; however, these data should be interpreted with caution. Trial monitoring data suggested a lower uptake of the micronutrient supplementation; thus these findings could be residual effects of receiving basic infant and young child dietary diversity recommendations delivered as part of the routine LHW programme.

The responsive stimulation intervention had a greater effect on children’s executive functions than on IQ.

Table 4: Care and maternal outcomes

<table>
<thead>
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<th>Responsive stimulation intervention</th>
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<tr>
<td>Mother–child interactions (observation)</td>
<td>20·64 (18·33–21·19)</td>
<td>17·70 (18·96)</td>
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<td>Caregiving environment (HOME-EC)</td>
<td>32·68 (31·42–33·29)</td>
<td>30·79 (32·08)</td>
<td>&lt;0·0001</td>
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<td>Maternal depressive symptoms (SRQ-20)</td>
<td>6·60 (4·62; 7·44)</td>
<td>7·04 (6·87)</td>
<td>0·513</td>
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</table>

Data are n (mean; 95%CI) unless otherwise stated. The analysis is adjusted for clustering by generalised linear model and controlled for several baseline covariates (socioeconomic status, household food security, number of children, maternal education, and sex of child). HOME-EC=Home Observation and Measurement of the Environment, Early Childhood Version. SRQ-20=Self Reporting Questionnaire.

Table 4: Care and maternal outcomes

Figure 2: Proportion of family members who engaged in four or more learning activities with the case child over 3 days

(A) Responsive stimulation. (B) Enhanced nutrition. No significant differences were found between responsive stimulation (n=655) compared with no responsive stimulation (n=635) groups for mothers (p=0·201), fathers (p=0·680), and other caregivers (p=0·675). There were significant differences between enhanced nutrition (n=670) compared with no enhanced nutrition (n=619) groups for mothers (p=0·001), fathers (p=0·0001), and other caregivers (p=0·0001). A significant interaction effect was found between interventions for other caregivers (p=0·0001).
Executive functions are a useful measure of cognitive abilities because assessments can be designed to reduce measurement biases resulting from lack of formal education exposure. However, few studies have implemented these tasks in low-income and middle-income countries with the exception of a small number of nutrition intervention studies that assessed child executive functions in middle childhood. Executive function skills are crucial to support children’s school readiness independent of language and general intelligence. Executive functions are a useful measure of cognitive abilities because assessments can be designed to reduce measurement biases resulting from lack of formal education exposure. However, few studies have implemented these tasks in low-income and middle-income countries with the exception of a small number of nutrition intervention studies that assessed child executive functions in middle childhood. Executive function skills are crucial to support children’s school readiness independent of language and general intelligence. Executive functions are a useful measure of cognitive abilities because assessments can be designed to reduce measurement biases resulting from lack of formal education exposure. However, few studies have implemented these tasks in low-income and middle-income countries with the exception of a small number of nutrition intervention studies that assessed child executive functions in middle childhood. Executive function skills are crucial to support children’s school readiness independent of language and general intelligence. Executive functions are a useful measure of cognitive abilities because assessments can be designed to reduce measurement biases resulting from lack of formal education exposure. However, few studies have implemented these tasks in low-income and middle-income countries with the exception of a small number of nutrition intervention studies that assessed child executive functions in middle childhood. Executive function skills are crucial to support children’s school readiness independent of language and general intelligence. Executive functions are a useful measure of cognitive abilities because assessments can be designed to reduce measurement biases resulting from lack of formal education exposure. However, few studies have implemented these tasks in low-income and middle-income countries with the exception of a small number of nutrition intervention studies that assessed child executive functions in middle childhood. Executive function skills are crucial to support children’s school readiness independent of language and general intelligence. Executive functions are a useful measure of cognitive abilities because assessments can be designed to reduce measurement biases resulting from lack of formal education exposure. However, few studies have implemented these tasks in low-income and middle-income countries with the exception of a small number of nutrition intervention studies that assessed child executive functions in middle childhood. Executive function skills are crucial to support children’s school readiness independent of language and general intelligence.

In addition to the sustained intervention effects on the child, both interventions showed significant benefits to maternal care. Responsive stimulation continued to improve maternal responsive behaviours, and both interventions improved the quality of the caregiving environment as indexed by the HOME-EC. The responsive stimulation intervention was designed to focus on the child and caregiver by coaching the caregiver to strengthen responsive caregiving skills in the play and communication context rather than adopting an approach of the LHW directly playing with the child. The findings (both for responsive stimulation and enhanced nutrition) indicate that mothers are likely to adapt learned responsive caregiving skills during infancy and toddlerhood to the needs of preschool-aged children. Current evidence suggests a focus on behaviour modification techniques which support learning-responsive caregiving skills in early childhood are likely to benefit children in later years. Landry and colleagues’ study in a US population showed that mothers were able to adapt responsive caregiving skills learned in one activity to other contexts of care; therefore, in future work it might also be important to examine whether these skills transferred to other care practices in our study population (eg, feeding). Nonetheless, future research needs to examine how various caregiving practices, including feeding, might mediate the effect of early interventions on later child outcomes.

With respect to maternal depressive symptoms, neither responsive stimulation nor enhanced nutrition intervention was significant. More research is warranted on the integration of maternal and family mental health interventions with early child development interventions. One previous study of children with disabilities reported that participation in a child development programme increased maternal stress, and authors speculated this might be due to greater knowledge and the responsibility of new practices in child care; however, the complexities of maternal mental health and the influence on daily responsibilities in low-income and middle-income countries are not well explored.

Compared with the short-term effects at the end of the original intervention, the effect sizes were reduced from medium-to-large to small-to-medium on significant child and care outcomes. Although investigations of interventions in high-income countries indicate loss of impact over time in the general population, beneficial effects on the most vulnerable children and families remain. Previous longitudinal follow-up of efficacy studies on early stimulation and nutrition interventions in low-income and middle-income countries have not followed children in the preschool age group, making comparisons with this study difficult. However, evidence from longitudinal evaluations of large-scale programmes in high-income countries suggest that early gains can be threatened if children do not transition from an early intervention programme to high quality educational services. The effect size of the original intervention, the type of study (efficacy or effectiveness), the child’s level of risk, continued positive parenting practices, and the specific health and educational services the child receives are all factors that need to be better understood. Better understanding is particularly important when designing early childhood interventions that are responsive to the needs of the local population and identifying later sensitive windows for boosting early effects and supporting a continuum of healthy development. The Jamaican cohort demonstrated sustained benefits as a result of stimulation intervention into adulthood. Although the effect of early intervention for schooling and early adulthood is yet to be followed in this cohort, a lack of early childhood services might mitigate early intervention benefits, as access, retention, and attainment in future education programmes remains extremely poor. Therefore, strategies to bolster development and build on early interventions must be tested in many delivery platforms in health education and social protection sectors. Previous intervention studies have shown benefits by integrating stimulation and parenting advice in primary health-care services or in visits with a paediatrician. However, in low-income and middle-income countries with weaker primary and secondary health services, other platforms such as reaching children through so-called Child Health Days could also be assessed.

The strengths of this study include a relatively low attrition rate, a comprehensive battery of child development and growth assessments, and good reliability of data collection. However, there are also several limitations. First, changes in caregiving responsibilities within households as children transition from infancy to the preschool age group was not tracked; therefore, while the assessment of the quality of care focused on the mother, in...
households with large extended or joint family structures, the role of elder siblings, grandparents, and other relatives could have a more significant role. Second, an independent assessment of whether the LHWs continued to deliver advice on responsive stimulation and enhanced nutrition was not undertaken, which might moderate outcomes. Finally, child behaviour data were collected by maternal report while other child development measures were performance-based. A direct observation of children’s behaviour (eg, interactions with siblings or peers) might have provided a more objective behavioural measure.

Nevertheless, this longitudinal follow-up demonstrates that responsive stimulation delivered as part of a community health service can have sustained benefits on children’s development 2 years after intervention. These data might be generalisable to similarly impoverished rural populations in low-income and middle-income countries. However, research is needed to investigate what effect these interventions might have on disadvantaged urban populations. Crucially, the interventions were delivered by community health workers that might be comparable with similarly qualified and educated health workers. However, the LHWs are paid community health workers; therefore, these data are not generalisable to the many volunteer-based community health services in low-income and middle-income countries. Importantly, these data showed benefits to child executive functions that are crucial to support school readiness, and showed benefits to care practices that could be adapted to support later development in young children. Future analyses of these data need to identify which children and families benefit more or less young children. Future analyses of these data need to identify which children and families benefit more or less young children. Future analyses of these data need to identify which children and families benefit more or less young children.

**Contributors**

AKY and JO conceptualised the study and planned the analysis. AKY, JO, and MAR developed the data collection materials with inputs from XAP, NT-S, SS, and UM. AKY oversaw the study, data analysis, and interpretation, and drafted the manuscript. MAR, UM, and SS trained the data collection team and oversaw quality assurance. AR was the statistician for the study and participated in the study design, data analysis and interpretation. All authors critically reviewed drafts of the manuscript.

**Declaration of interests**

We declare no competing interests.

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**References**


