# Effect of integrated responsive stimulation and nutrition interventions in the Lady Health Worker programme in Pakistan on child development, growth, and health outcomes: a cluster-randomised factorial effectiveness trial

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## Summary

**Background** Stimulation and nutrition delivered through health programmes at a large scale could potentially benefit more than 200 million young children worldwide who are not meeting their developmental potential. We investigated the feasibility and effectiveness of the integration of interventions to enhance child development and growth outcomes in the Lady Health Worker (LHW) programme in Sindh, Pakistan.

**Methods** We implemented a community-based cluster-randomised effectiveness trial through the LHW programme in rural Sindh, Pakistan, with a 2×2 factorial design. We randomly allocated 80 clusters (LHW catchments) of children to receive routine health and nutrition services (controls; n=368), nutrition education and multiple micronutrient powders (enhanced nutrition; n=364), responsive stimulation (responsive stimulation; n=383), or a combination of both enriched interventions (n=374). The allocation ratio was 1:20 (ie, 20 clusters per intervention group). The data collection team were masked to the allocated intervention. All children born in the study area between April, 2009, and March, 2010, were eligible for enrolment if they were up to 2·5 months old without signs of severe impairments. Interventions were delivered by LHWs to families with children up to 24 months of age in routine monthly group sessions and home visits. The primary endpoints were child development at 12 and 24 months of age (assessed with the Bayley Scales of Infant and Toddler Development, Third Edition) and growth at 24 months of age. Analysis was by intention to treat. This trial is registered with ClinicalTrials.gov, number NCT007159636.

**Findings** 1489 mother–infant dyads were enrolled into the study, of whom 1411 (93%) were followed up until the children were 24 months old. Children who received responsive stimulation had significantly higher development scores on the cognitive, language, and motor scales at 12 and 24 months of age, and on the social–emotional scale at 12 months of age, than did those who did not receive the intervention. Children who received enhanced nutrition had significantly higher development scores on the cognitive, language, and social-emotional scales at 12 months of age than those who did not receive this intervention, but at 24 months of age only the language scores remained significantly higher. We did not record any additive benefits when responsive stimulation was combined with nutrition interventions. Responsive stimulation effect sizes (Cohen's d) were 0·6 for cognition, 0·7 for language, and 0·5 for motor development at 24 months of age; these effect sizes were slightly smaller for the combined intervention group and were low to moderate for the enhanced nutrition intervention alone. Children exposed to enhanced nutrition had significantly better height-for-age $Z$ scores at 6 months ($p<0\cdot0001$) and 18 months ($p=0\cdot02$) than did children not exposed to enhanced nutrition. Longitudinal analysis showed a small benefit to linear growth from enrolment to 24 months ($p=0\cdot026$) in the children who received the enhanced nutrition intervention.

**Interpretation** The responsive stimulation intervention can be delivered effectively by LHWs and positively affects development outcomes. The absence of a major effect of the enhanced nutrition intervention on growth shows the need for further analysis of mediating variables (eg, household food security status) that will help to optimise future nutrition implementation design.

**Funding** UNICEF.

## Introduction

More than 200 million children in developing countries are at risk of not meeting their developmental potential by 5 years of age.[1] Risk factors including poverty, malnutrition, and inadequate stimulation are likely to co-occur and accumulate over time, increasing the risk of early childhood mortality, morbidity, poor development, and growth.[2–4] Children who are unable to fulfil their developmental and growth potential are likely to perform poorly in school and earn lower incomes as adults, thus perpetuating social inequalities and contributing to the intergenerational transmission of poverty, poor health, and development.[5,6] The first 2 years of life is an important window of opportunity to implement interventions to promote children's physical growth and development.

Early child stimulation interventions that guide parents to be sensitive (understand their child's signals) and responsive (respond in a contingent and developmentally appropriate way to these signals)[7] through developmentally suitable play with their child have shown consistent benefits to children's development.[8–11] The enhancement of these basic caregiving skills, which are learned during play interactions, can also protect children's health by helping families to recognise and respond to the early signs of illness.[7] Nutritional intervention is needed to promote healthy growth and development; however, few studies have assessed the additive benefits of combined stimulation and nutrition on child outcomes. Studies from Jamaica showed additive developmental benefits when stimulation was combined with macronutrient supplementation[10] and synergistic benefits when it was combined with zinc supplementation.[8]

Early child development programmes in developing countries are likely to be more effective if they are comprehensive (ie, they include health, nutrition, and stimulation), run for longer, have greater intensity (ie, higher frequency and longer duration of contacts), use a structured curriculum, and enable parents and children to participate together to practise stimulation activities and receive feedback.[12,13] Knowledge gaps remain about how best to combine stimulation and nutrition interventions within existing health services to expand programmes to a large scale.[13] To the best of our knowledge, the delivery of integrated early child development interventions with community health workers in public sector effectiveness settings has not been assessed so far.

Pakistan has a high burden of both child undernutrition[14] and poor development.[1] The National Programme for Family Planning and Primary Healthcare (often referred to as the Lady Health Worker [LHW] programme) provides an opportunity to integrate early child development services at scale (panel 1).[15] The LHW programme, started in 1994, is a government-supported community health service providing care to families in rural, remote, and disadvantaged communities across Pakistan. The focus areas for health services are family planning and maternal and child health, which are delivered by LHWs. The programme does not encompass early stimulation at present, and recent assessments have emphasised the need to strengthen nutrition services.[16] The aim of this study was to measure the effects of a responsive stimulation intervention delivered by LHWs to families with infants and young children from birth to 24 months of age living in rural Sindh, Pakistan, either alone or in combination with an enhanced care for nutrition intervention. The primary endpoint was child development and growth and the secondary endpoint was child morbidity; all outcomes were assessed at 24 months of age. The hypothesis to test was that, compared with either a responsive stimulation or an enhanced care for nutrition intervention delivered alone, a combined approach would have independent and additive or synergistic effects on child development, growth, and morbidity outcomes at 24 months.

## Methods

### Study design and participants

We did a pragmatic, community-based, cluster-randomised effectiveness trial in the Naushero Feroze district of Sindh, Pakistan, between June 1, 2009, and March 31, 2012. The trial had a 2×2 factorial design,[17] and we used the cluster-randomised design to reduce the risk of contamination by ensuring that all members of each cluster received the same intervention. Each cluster was defined as an LHW catchment, and we allocated the same number of clusters to each intervention group On average, each cluster

*Panel 1:* **Lady Health Worker programme**

**Selection criteria for Lady Health Workers**
- 18–45 years of age.
- Live locally.
- Preferably married.
- At least 8 years of education.
- Community acceptance.

**Training and supervision**
- 15 months training (3 months classroom-based training and 12 months field-based training).
- 15 days allocated to refresher training each year.
- Training provided through traditional training cascade.
- Supervision provided by Lady Health Supervisor (1:25 ratio). Supervisors are assigned a vehicle. Supportive supervision is promoted, including use of checklists and problem solving.

**22 core tasks**
- Maintain register of all married couples, pregnant women, births, and deaths in the community.
- Family planning: distribution of condoms, oral contraceptive pills, and injectable contraceptives.
- Care for pregnant women, including health and nutrition education, and provision of iron and folic acid tablets.
- Health and hygiene education.
- Nutrition education for care of infants and young children, including appropriate breastfeeding and complementary feeding practices, and monitoring of child growth.
- Promotion of iodised salt.
- Provision of basic medicines for common ailments.
- Awareness of malaria, HIV/AIDS, and tuberculosis.
- Support for tuberculosis DOTS and immunisation programmes.
- Make referrals to primary health care facilities.

**Catchment**
- Serve 1000 population (about 120–150 households).
- Monthly home visits (expected to visit 5–7 households per day).
- Monthly community meetings.

**Financing**
- The average cost of each Lady Health Worker is 44 000 Pakistani rupees per year (US$570). The main cost is her monthly stipend, which was increased in 2010.

contained 44 children younger than 24 months of age. The four intervention groups were control (no intervention; n=368), enhanced nutrition (n=364), responsive stimulation (n=383), and a combination of responsive stimulation and enhanced nutrition (n=374). All four groups continued to receive the standard health-care services provided by the LHW programme. The comparisons of interest were the effectiveness between interventions in the factorial design of the trial (responsive stimulation and enhanced nutrition) on child development, growth, and morbidity outcomes.

The LHWs delivered interventions to every child younger than 24 months of age in their catchments, which encompassed a total of 3550 children across all clusters. All families were free to participate in the interventions delivered in their communities. To ensure that we were assessing change in child outcomes in children of the same age, we recruited a birth cohort with their mothers (or other primary caregiver) from the study clusters. Births were identified by an independent surveillance team. Every infant born in the study area between April 1, 2009, and March 31, 2010, was eligible for enrolment. Inclusion criteria for enrolment were infants up to 2·5 months of age without signs of severe impairments who were born and living in the study cluster. We followed up enrolled mother–infant dyads until the infant reached 24 months of age. All mothers provided written informed consent (or a thumb print for consent) and could refuse an interview or child assessment at any time. Ethics approval was obtained from the ethical review committee of the Aga Khan University in Pakistan. Permission for the trial was granted by the technical steering committee of the LHW programme.

See Online for appendix

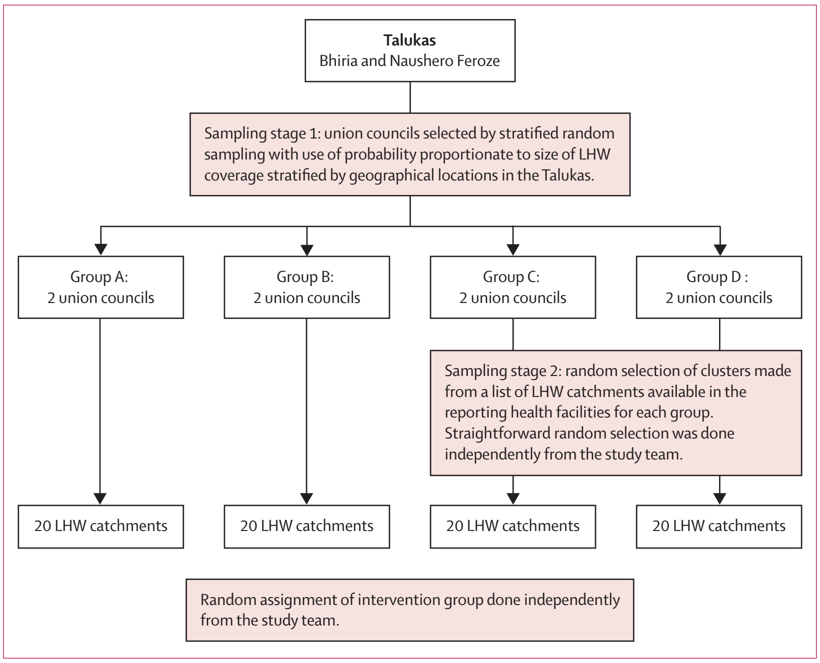


***Figure 1:*** **Cluster sampling strategy**
LHW=Lady Health Worker.

## Randomisation and masking

In Pakistan, districts are administratively organised into talukas (subdistricts), which in turn are subdivided into union councils and then divided further into villages. The catchment of an LHW can include more than one village. Before the start of the study, we arbitrarily chose two talukas (Bhiria and Naushero Feroze) to take samples from, taking transport costs and travel time into consideration so that we could make timely visits to the households for data collection and to ensure that data collectors could visit households and return to the field office within appropriate hours of the day. To minimise the risk of contamination of interventions across groups, we used a two-stage stratified random sampling strategy (figure 1). In the first stage, we selected union councils with probability proportionate to size of LHW coverage stratified by locations in the talukas. In the second stage, we identified LHW catchments (clusters) from a list available in the reporting health facilities within each intervention group. From this list, straightforward random selection of these clusters was undertaken independently from the study team until the necessary sample size was reached. Random assignment of the intervention group was done independently from the study team. The allocation ratio was 1:20 (ie, 20 LHW catchments per intervention group). Figure 2 shows the geographical locations of the clusters for each intervention group.

The data collection team were masked to the intervention. The team comprised 16 data collectors and eight community-based child development assessors who did not work with the LHWs and received no information about the interventions delivered in the community. To help with masking, the data collection team were rotated every 3 months to reduce familiarity with families and villages; families were asked to remove any materials that could have indicated the intervention assignment (eg, micronutrient packets); the data collection team were trained to not ask families about the interventions they were receiving; and the data collection and intervention delivery teams were trained in separate areas. Quality assurance in data collection strategies to ensure precision in data collection included refresher training sessions every 6 months and monthly supervised field observations and meetings.

## Procedures

Full details of the interventions are available in the appendix.[8–13,18–21] All interventions were delivered by LHWs and were integrated within existing services through home visits and group meetings, and agreed upon during stakeholder consultations (panel 1). The control group received the standard-of-care services provided by LHWs, including health, hygiene, and basic nutrition education. The enhanced nutrition group received nutrition education, and all children aged 6–24 months in this group were given a multiple micronutrient powder

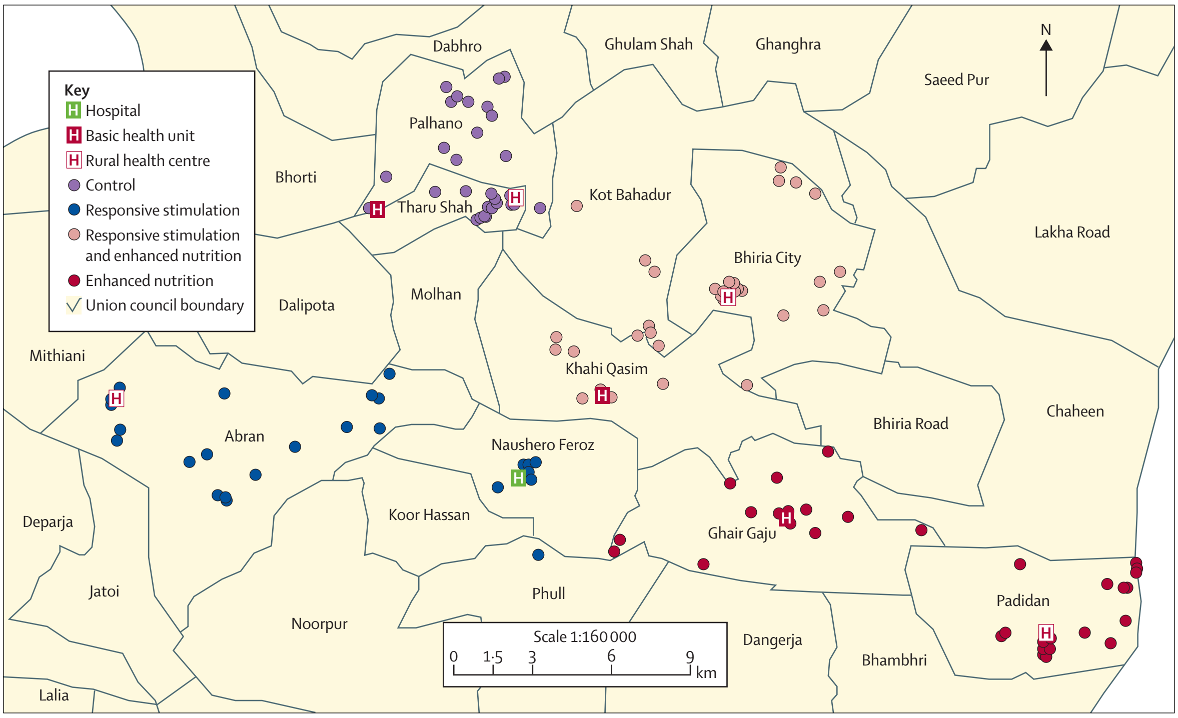


*Figure 2:* **Map of Lady Health Worker catchments (clusters) for each intervention group in Naushero Feroze district, Pakistan**

(Sprinkles, Genera Pharmaceuticals, Pakistan), which contains iron, folic acid, vitamin A, and vitamin C. The LHW was expected to deliver a 1-month supply of the powder during her home visit, and, if it had been consumed, again in the next month. During the study, no government provider was distributing multiple micronutrient powder routinely in the district. The basic nutrition education curriculum of the LHW programme was strengthened by the provision of knowledge about the associations between good nutrition and health, additional advice on responsive feeding, and development of counselling skills and problem solving about feeding. The LHWs received 2 days of basic training, and delivery was integrated into existing routine home visits, thus enriching the basic nutrition service. LHWs in the responsive stimulation group delivered an adaptation of the UNICEF and WHO Care for Child Development package.[22] This package promotes caregivers' sensitivity and responsiveness by using the context of developmentally appropriate play activities. In this approach, caregivers try an activity with their child while the LHW observes, coaches, and provides feedback to enhance the quality of the interactions. The Care for Child Development package was contextualised with a set of messages about care for development and problem solving. The LHWs received 3 days of basic training and delivery was integrated into existing routine home visits. Additionally, this new curriculum was delivered in monthly community group sessions since existing group sessions were not running optimally because of an absence of programme objectives.

The combined intervention group received a combination of both enriched interventions with 5 days of basic training for the LHWs. The health workers providing the enriched interventions each received one refresher training day every 6 months, and training was supported by on-the-job coaching every month. A six-member team of early child development facilitators supported the training and supervision of the LHWs following the expected number of training and supervision contacts permitted by the routine programme.

All questionnaires and child assessments were administered in Sindhi. We followed language adaptation protocols to ensure that the conceptual integrity of the original items was retained in translation.[23] Data were collected at home visits, and a window period of 7 days beforehand or afterwards for all follow-ups was established to ensure that data for age-based assessments were collected when the infants were the correct age. Development was assessed at 12 and 24 months of age on the Bayley Scales of Infant and Toddler Development, Third Edition[24] (BSID III). We used four scales: cognitive, language, motor, and social-emotional. We did comparisons between intervention groups; therefore, any cultural bias was expected to be distributed equally. BSID III data gathered in the same district in a separate study showed good internal consistency reliability estimates (data not shown). These data were gathered by the community-based child development assessors, all of whom had an undergraduate degree and were trained for 3 months before the rollout of the trial. Four refresher training sessions of 5 days each were provided for the BSID III administration beforehand, and at the halfway points of the 12-month and 24-month follow-ups. Permission was obtained from families to allow the data collection team privacy to reduce distractions for young children during developmental assessments (therefore, only the child and the mother or other primary caregiver were present for the direct child assessments). The supervisor observed one child development assessor each week in random unannounced visits. Interobserver agreement between the supervisor and the child development assessors, measured with the Bland Altman test, was high (cognition: n=84, R=0·99, p<0·0001; receptive communication: n=83, R=0·97, p=0·01; expressive communication: n=84, R=0·97, p=0·001; fine motor: n=83, R=0·97, p<0·0001; gross motor: n=83, R=0·95, p<0·0001; social-emotional: n=81, R=0·99, p<0·0001).

Trained data collectors assessed growth at enrolment and at 6, 12, 18, and 24 months of age by length and weight according to standard protocols.[25] Length or height (Length Boards, Life Care, Karachi, Pakistan) was measured to the nearest 0·1 cm. Weight was measured to the nearest 0·1 kg, and the electronic weighing scales (LAICA Baby Scale, LAICA S.P.A, Ponte di Barbarano Viceza, Italy) were calibrated each morning before data collection with standard weights. A 10% sample of enrolled children, chosen randomly, were visited each month by the supervisor to ensure interobserver reliability of anthropometric measurements. The relative technical error of measurement (TEM)[26] was good for anthropometric measures in 645 children (length/height TEM 0·7%, R=0·9; weight TEM 1·3%, R=0·9; mid-upper arm circumference TEM 2·9%, R=0·9; head circumference TEM 0·8%, R=0·9).

To assess anaemia status in the infants, blood haemoglobin was measured at 24 months of age by a finger prick assay with HemoCue machines (HemoCue B-Haemoglobin System, HemoCue AB, Sweden), which were calibrated daily before data collection visits. Morbidity data were gathered every month by maternal report with standard protocols.[27] Household demographic and socioeconomic status data were collected at enrolment with validated protocols that have been used previously in this region.[27] The socioeconomic status score was created by assignment of scores to individual variables, including ownership of property, access to water and electricity, and ownership of livestock. Next, a factor score was generated with a principal component analysis, in which a lower socioeconomic status score is denoted by a negative score and a higher status by a positive score.[28] The community had experienced two summers of floods; therefore, we also collected these data and data for household food security[29] at the end of the study. Measures of treatment compliance were collected at the cluster level by health workers' records of women participating in group sessions and an independent monitoring team who gathered information about services received from LHWs from 10% of randomly selected households every month. For enrolled families, maternal reports were collected on services received from LHWs at enrolment, and at 6, 12, 18, and 24 months of follow-up.

## Statistical analyses

We used ACluster software to establish the sample size.[30] The required sample size was based on an improved child development quotient, which was based on published studies reported with BSID II and Griffiths Mental Development Scales because no published studies were available that used the BSID III. Previous studies report an average difference in child development quotient of about five points (ranging from 0·3 to 0·5 of a standard score) between the intervention and control groups;[8,17,21] however, because we expected a lower intensity of intervention delivery because the routine LHW programme requires a monthly home visit (ie, less than is typically reported for early childhood development home visiting studies), a more conservative change in child development quotient was judged realistic. A sample of 333 children per group was estimated at 80% power and α of 0·05 to detect differences of at least three points with SD of 7·9.[31] We estimated intracluster correlation as 0·15 for maternal education,[32] which was used as a proxy indicator for child development. The required sample size was calculated to be 20 clusters of 20 new births during the enrolment period (a realistic average number of births from each LHW's catchment for the enrolment period). With the assumption of a 10% attrition rate, the required sample size was 366 per group across 20 clusters.

We did statistical analyses with SPSS version 15.0. All analyses reported are adjusted for clustering effects, accounting for both levels of sampling, using generalised estimating equations. Significance has been defined as p<0·05 unless stated otherwise. First we assessed, by intention-to-treat analysis, whether primary and secondary child outcomes differed between the two interventions of our factorial design (responsive stimulation *vs* no responsive stimulation, and enhanced nutrition *vs* no enhanced nutrition) at each timepoint with generalised estimating equations controlling for specified confounding factors (socioeconomic status, household food security, number of siblings, the sex of each child, maternal education, and, when appropriate, differences between the intervention groups at baseline). We then tested for interactions between the two interventions. Second, we adopted a longitudinal approach in which we used linear mixed models and generalised estimating equations to assess the effect of intervention over time compared with the control group, controlling for the specified confounding factors. Finally, effect sizes for the treatment groups are reported for significant outcomes at 24 months of age. Effect sizes, denoted by Cohen's d, were calculated as the difference in adjusted means between the intervention and control group over the pooled SD.

This trial is registered at ClinicalTrials.gov, number NCT007159636.

### Role of the funding source

The funder had no role in study design, data collection, data analysis, data interpretation, or writing of the report. However, the funder did make two site visits during the trial. The authors of this report had full access to all the data in the study. AKY and ZAB had primary responsibility for the decision to submit for publication.

## Results

1489 mother–infant dyads were enrolled in the study for the in-depth assessment, which represents 42% of all young children receiving LHW services in the study area. 368 infants were enrolled into the control group, 364 into the enhanced nutrition group, 383 into the responsive stimulation group, and 374 into the combined enhanced nutrition and responsive stimulation group. 1391 of 1489 (93%) of the enrolled mother–infant dyads were followed up until the infants reached 24 months of age (figure 3). During the trial, 11 children were discovered to have mild-to-moderate impairments (eg, cerebral palsy, hydrocephalus, and developmental delays) and were therefore excluded from the outcomes analysis. Table 1 shows the characteristics of the study population at enrolment. Analysis of these variables shows that randomisation was quite successful. The mean household socioeconomic status scores, the nutritional status of infants at the time of enrolment as measured by available low birthweight records, and the proportions of infants who were moderately to severely underweight or had moderate to severe stunting or wasting did not differ significantly between the groups. A similar proportion of girls and boys were enrolled in each group, and on average the enrolled infant was the third or fourth child in the family. However, significant differences between intervention groups were noted in maternal education between the groups that received enhanced nutrition (average grade 3 completed maternal education) versus those that had no enhanced nutrition (average grade 2). Additionally, infants in the responsive stimulation and enhanced nutrition groups were significantly older at enrolment than were those in the comparative groups that did not receive these interventions (table 1). Comparisons with endpoint data collection showed that mean household socioeconomic status did not differ significantly to that at enrolment; however, the average number of siblings increased by one by the end of the study (data not shown). The assessment of food-insecure households at the end of the study showed slightly higher food security in the responsive stimulation and enhanced nutrition groups than in the respective groups that did not receive these interventions.

Intervention monitoring at the cluster level suggested that group meetings occurred as expected (one meeting per month), and 533/1720 (31%) of all female caregivers participated each month. On average, meetings lasted for 1 h, 20 min. 2446/3248 (75%) of all households received monthly home visits. A home visit lasted for an average of 30 min in the responsive stimulation and combined intervention groups, 11 min in the enhanced nutrition group, and 7 min in the control group. In enrolled household reports of the most recent home visit, 227/364 (62%) reported receiving care for child development advice in the responsive stimulation group, and 189/344 (55%) reported receiving this advice in the combined enhanced nutrition and responsive stimulation intervention group. Enrolled household reports indicated that 43/347 (12%) in the control group, 251/335 (75%) in the enhanced nutrition group, 271/364 (75%) in the responsive stimulation group, and 264/344 (77%) in the combined intervention group received nutrition advice

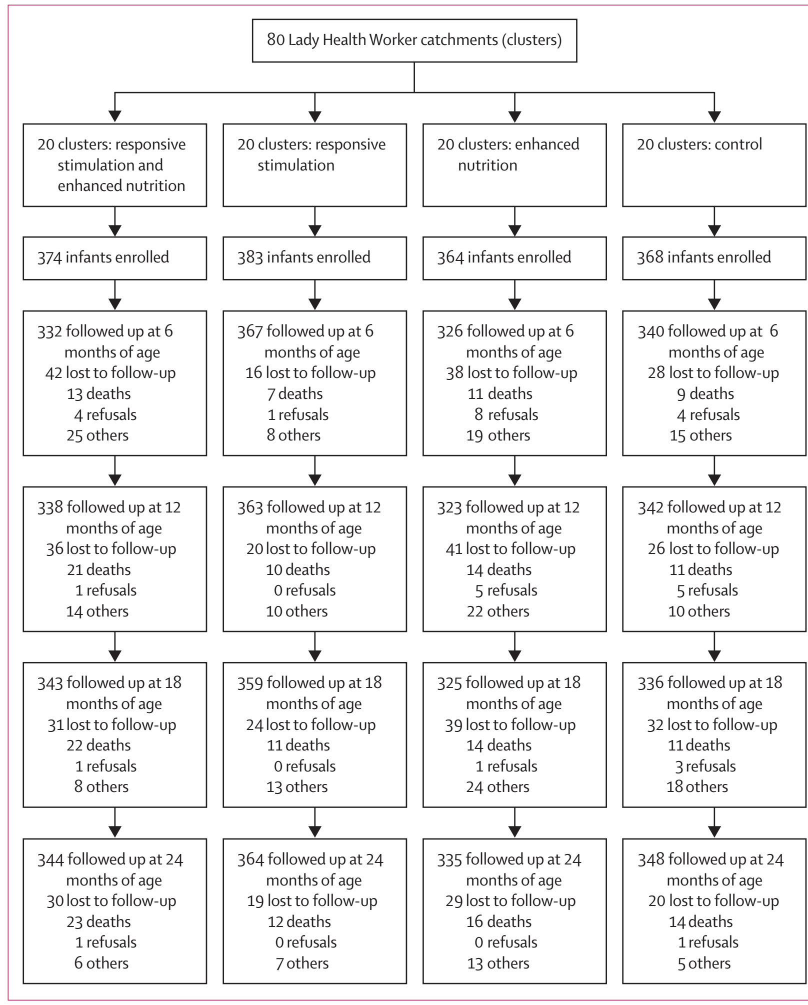


***Figure 3:* Trial profile**

Loss to follow-up described as "others" includes non-availability of child for data collection following repeat visits and reported cases of family migration. It was possible for families to not be available at one timepoint and have availability in the second timepoint; therefore, the "others" category is not incremental. During the trial, 11 children were identified to have mild-to-moderate impairments (1 in the responsive stimulation and enhanced nutrition group, 5 in the responsive stimulation group, 2 in the enhanced nutrition group, and 3 in the control group) and were therefore excluded from the outcomes analysis.

in the most recent home visit. At the cluster level, multiple micronutrient powder was received by 60% of all households with a young child. Of the enrolled households, mothers reported that a 30-day dose was delivered to 226/301 (75%) children in the enhanced nutrition group and to 192/261 (74%) children in the combined intervention group, and a 60-day dose was delivered to 58/301 (19%) of children in the enhanced nutrition group and 36/261 (14%) of those in the combined intervention group in the last LHW home visit. Of these households, 71/301 (24%) mothers in the enhanced nutrition group and 29/261 (11%) in the combined intervention group did not give the micronutrient powder delivered by the LHW to the enrolled child, 27% (27/100) of whom said that the reason was the belief that the powder would make the child sick. During the trial, 16 LHWs stopped working for a prolonged period of time. Four LHWs left their posts officially, all of whom were in the combined responsive stimulation and enhanced nutrition group.

The development outcomes show that compared with children who received no responsive stimulation, the children exposed to responsive stimulation had significantly higher mean cognitive, language, motor, and social-emotional scores at 12 months of age and, with the exception of social-emotional development, also

| | Responsive stimulation intervention | | | Enhanced nutrition intervention | | |
|---|---|---|---|---|---|---|
| | Yes (n=757) | No (n=732) | p value | Yes (n=738) | No (n=751) | p value |
| **Household characteristics** | | | | | | |
| Socioeconomic status | 0·0 (1·0; –0·2 to 2·3) | –0·0 (0·9; –0·2 to 0·1) | 0·82 | –0·0 (0·9; –0·2 to 0·2) | 0·0 (1·0; –0·2 to 0·2) | 0·13 |
| **Parent characteristics** | | | | | | |
| Mother's education, grades | 2 (3·8; 1·6 to 2·8) | 2 (3·7; 1·9 to 2·7) | 0·64 | 3 (4·0; 2·1 to 3·2) | 2 (3·4; 1·4 to 2·3) | <0·0001 |
| **Child characteristics** | | | | | | |
| Recruitment age, months | 0·6 (0·6; 0·5 to 0·7) | 0·8 (0·6; 0·7 to 0·8) | <0·0001 | 0·6 (0·6; 0·5 to 0·7) | 0·7 (0·7; 0·6 to 0·8) | 0·008 |
| Girls | 348 (46%) | 344 (47%) | 0·51 | 347 (47%) | 338 (45%) | 0·43 |
| Mean birth order | 4 | 3 | 0·23 | 3 | 4 | 0·43 |
| Moderately to severely underweight* | 212 (28%) | 227 (31%) | 0·43 | 214 (29%) | 225 (30%) | 0·55 |
| Moderate to severe stunting* | 151 (20%) | 183 (25%) | 0·33 | 177 (24%) | 150 (20%) | 0·12 |
| Moderate to severe wasting* | 151 (20%) | 161 (22%) | 0·33 | 140 (19%) | 172 (23%) | 0·03 |
| Low birthweight† | 46 (34%) | 26 (33%) | 0·86 | 37 (34%) | 34 (32%) | 0·78 |
| Food-secure households‡ | 537 (71%) | 468 (64%) | 0·04 | 546 (74%) | 458 (61%) | <0·0001 |

Data are mean (SD; 95% CI) or %, unless otherwise indicated. *Moderate to severe defined as less than –2 SD *Z* scores. †Low birthweight data includes only cases in which weight was measured in the first 3 days of life (responsive stimulation n=134, no responsive stimulation n=80, enhanced nutrition n=108, no enhanced nutrition n=106). ‡Data for food-secure households were gathered only at the end of the study to assess where there was any significant effect after severe flooding in the district. The analysis is adjusted for clustering by generalised estimating equations.

***Table 1:*** **Study population characteristics at enrolment**

| | Responsive stimulation intervention | | | Enhanced nutrition intervention | | | p value for interaction |
|---|---|---|---|---|---|---|---|
| | Yes (n=696 at 12 months, n=701 at 24 months) | No (n=661 at 12 months, n=680 at 24 months) | p value | Yes (n=658 at 12 months, n=676 at 24 months) | No (n=699 at 12 months, n= 705 at 24 months) | p value | |
| **Cognitive scale** | | | | | | | |
| 12 months | 97·1 (14·2; 95·6–98·7) | 92·0 (13·0; 90·7–93·3) | <0·0001 | 95·9 (12·7; 94·5–97·4) | 93·4 (14·8; 91·7–95·1) | 0·007 | 0·08 |
| 24 months | 81·7 (14·7; 80·1–83·4) | 74·1 (13·5; 72·3–75·9) | <0·0001 | 78·4 (14·6; 76·5–80·3) | 77·6 (14·7; 75·4–79·9) | 0·881 | <0·0001 |
| **Language scale** | | | | | | | |
| 12 months | 77·1 (14·8; 75·4–78·8) | 72·5 (12·5; 71·2–73·9) | <0·0001 | 76·8 (12·9; 75·3–78·4) | 73·0 (14·7; 71·3–74·7) | <0·0001 | 0·18 |
| 24 months | 85·7 (13·3; 84·3–87·1) | 79·3 (12·8; 77·4–81·3) | <0·0001 | 84·3 (13·7; 82·6–85·9) | 80·9 (12·9; 78·9–82·9) | <0·0001 | <0·0001 |
| **Motor scale** | | | | | | | |
| 12 months | 83·7 (14·3; 82·2–85·2) | 80·8 (12·9; 79·4–82·2) | 0·002 | 83·2 (13·4; 81·9–84·5 | 81·5 (13·9; 79·9–83·1) | 0·10 | 0·13 |
| 24 months | 92·1 (17·3; 90·2–93·9) | 84·8 (16·4; 82·7–86·9) | <0·0001 | 89·4 (16·8; 87·3–91·4) | 87·7 (17·5; 85·2–90·1) | 0·466 | <0·0001 |
| **Social-emotional scale** | | | | | | | |
| 12 months | 80·5 (13·4; 79·2–81·7) | 77·6 (13·8; 76·1–79·0) | <0·0001 | 81·0 (13·7; 79·8–82·2) | 77·2 (13·5; 75·8–78·6) | <0·0001 | 0·05 |
| 24 months | 93·2 (18·4; 91·2–95·2) | 94·9 (39·3; 91·7–98·1) | 0·69 | 94·8 (20·3; 92·6–97·0) | 93·3 (37·8; 90·4–96·3) | 0·06 | 0·66 |

Data are mean (SD; 95% CI). The analysis is adjusted for clustering and controlled for several covariates (socioeconomic status, household food security, maternal education, number of siblings, and sex of the child) by generalised estimating equations. The sex of each child was not a significant covariate for language and social-emotional development outcomes.

***Table 2:*** **Composite scores for the Bayley Scales for Infant and Toddler Development, Third Edition at 12 and 24 months of age**

at 24 months of age (table 2). Compared with children who were not exposed to enhanced nutrition, those who received enhanced nutrition had significantly higher mean cognitive, language, and social-emotional scores at 12 months of age, but at 24 months age only the language scores remained significantly higher (table 2). In all groups, language, motor, and social-emotional scores increased between 12 and 24 months of age; however, cognitive scores decreased during this same period (table 2). The decline in cognitive scores was 15·4 points in the responsive stimulation group, 17·9 in the no responsive stimulation group, 17·5 in the enhanced nutrition group, and 15·8 in the no enhanced nutrition group (table 2). A significant interaction was recorded between the two interventions for cognitive, language, and motor development at 24 months of age (table 2). Repeated measures analyses showing change in cognition, language, and motor development outcomes from 12 to 24 months of age showed a benefit over time in the responsive stimulation intervention. The direction of the interaction (negative coefficient values) suggests that responsive stimulation combined with enhanced nutrition had a smaller treatment effect over time than did responsive stimulation alone (table 3).

Table 4 shows mean height-for-age, weight-for-age, and weight-for-height *Z* scores at each age interval. Mean weight-for-age *Z* score did not differ significantly between the groups at 6, 12, 18, or 24 months. Children exposed to enhanced nutrition had significantly better height-for-age *Z* scores at 6 and 18 months than did

| | Responsive stimulation intervention | | | Enhanced nutrition intervention | | | Interaction | | |
|---|---|---|---|---|---|---|---|---|---|
| | β | SE | 95% CI | β | SE | 95% CI | β | SE | 95% CI |
| Cognition | 8·5 | 1·1 | 6·3–10·8 | 3·4 | 1·1 | 1·1–5·7 | −4·6 | 1·6 | −7·8 to −1·4 |
| Language | 7·8 | 1·1 | 5·7–9·9 | 5·1 | 1·1 | 2·9–7·3 | −4·8 | 1·5 | −7·8 to −1·8 |
| Motor | 5·9 | 1·2 | 3·6–8·3 | 2·9 | 1·2 | 0·5–5·3 | −3·8 | 1·7 | −7·1 to −0·5 |

Linear mixed model, adjusted for clustering and controlled for covariates of socioeconomic status, household food security, maternal education, number of siblings, and the sex of each child. The β coefficient is the standardised coefficient that shows the size effects of the covariates on the outcomes. The negative interaction values of the β coefficient suggest that the intervention of responsive stimulation and enhanced nutrition combined has a smaller treatment effect than does the responsive stimulation intervention alone.

***Table 3:*** **Repeated measures analyses of change in development outcomes in the Bayley Composite Scores for Infant and Toddler Development, Third Edition, from 12 to 24 months in the intervention groups compared with the control group**

| | Responsive stimulation intervention | | | Enhanced nutrition intervention | | |
|---|---|---|---|---|---|---|
| | Yes | No | p value | Yes | No | p value |
| **Weight-for-height Z score** | | | | | | |
| 6 months | −1·1 (1·3; −1·1 to − 0·8) | −0·8 (1·2; −1·0 to −0·7) | 0·007 | −1·0 (1·2; −1·1 to −0·8) | −0·8 (1·3; −1·0 to −0·7) | 0·001 |
| 12 months | −1·0 (1·2; −1·2 to −0·8) | −1·0 (1·1; −1·1 to −0·9) | 0·75 | −0·9 (1·1; −1·0 to −0·8) | −1·1 (1·3; −1·2 to −0·9) | 0·09 |
| 18 months | −0·8 (1·2; −1·0 to −0·7) | −0·8 (1·5; −1·0 to −0·7) | 0·95 | −0·8 (1·4; −0·9 to −0·6) | −0·9 (1·2; −1·0 to −0·7) | 0·88 |
| 24 months | −0·9 (1·1; −1·1 to −0·8) | −1·0 (1·1; −1·1 to −0·9) | 0·45 | −0·9 (1·0; −1·0 to −0·8) | −1·0 (1·2; −1·2 to −0·9) | 0·16 |
| **Height-for-age Z score** | | | | | | |
| 6 months | −1·2 (1·3; −1·4 to −1·1) | −1·3 (1·3; −1·5 to −1·2) | 0·42 | −1·2 (1·3; −1·3 to −1·0) | −1·4 (1·2; −1·5 to −1·3) | <0·0001 |
| 12 months | −2·0 (1·3; −2·1 to −1·8) | −2·0 (1·2; −2·2 to −1·9) | 0·67 | −1·9 (1·3; −2·1 to −1·8) | −2·1 (1·2; −2·2 to −1·9) | 0·20 |
| 18 months | −2·3 (1·2; −2·5 to −2·2) | −2·3 (1·2; −2·4 to −2·1) | 0·03 | −2·2 (1·2; −2·4 to −2·0) | −2·4 (1·1; −2·5 to −2·3) | 0·02 |
| 24 months | −2·4 (1·2; −2·5 to −2·2) | −2·3 (1·1; −2·5 to −2·2) | 0·03 | −2·3 (1·1; −2·5 to −2·2) | −2·4 (1·1; −2·5 to −2·2) | 0·61 |
| **Weight-for-age Z score** | | | | | | |
| 6 months | −1·6 (1·4; −1·7 to −1·4) | −1·5 (1·4; −1·7 to −1·3) | 0·08 | −1·5 (1·4; −1·7 to −1·4) | −1·5 (1·4; −1·7 to −1·4) | 0·37 |
| 12 months | −1·7 (1·3; −1·9 to −1·6) | −1·8 (1·2; −1·9 to −1·6) | 0·96 | −1·7 (1·2; −1·8 to −1·5) | −1·8 (1·3; −2·0 to −1·7) | 0·20 |
| 18 months | −1·7 (1·2; −1·9 to −1·6) | −1·7 (1·2; −1·9 to −1·6) | 0·29 | −1·7 (1·2; −1·8 to −1·5) | −1·8 (1·2; −1·9 to −1·6) | 0·51 |
| 24 months | −1·9 (1·2; −2·1 to −1·8) | −1·9 (1·1; −2·0 to −1·8) | 0·42 | −1·8 (1·1; −2·0 to −1·7) | −2·0 (1·2; −2·1 to −1·9) | 0·32 |

Data are mean (SD; 95% CI). Number in each group at 6 months of age: responsive stimulation n=748, no responsive stimulation n=725, enhanced nutrition n=732, no enhanced nutrition n=741; at 12 months of age: responsive stimulation n=687, no responsive stimulation n=659, enhanced nutrition n=650, no enhanced nutrition n=696; at 18 months of age: responsive stimulation n=686, no responsive stimulation n=642, enhanced nutrition n=652, no enhanced nutrition n=676; at 24 months of age: responsive stimulation n=687, no responsive stimulation n=667, enhanced nutrition n=661, no enhanced nutrition n=693. Analysis is adjusted for clustering and controlled for covariates of socioeconomic status, household food security, maternal education, number of siblings, and enrolment differences in anthropometry by generalised estimating equations. Interaction is not significant for all indicators. In the repeated measures analysis, with use of the linear mixed model, adjusted for clustering and controlled for covariates (socioeconomic status, household food security, maternal education, number of siblings, child sex, and enrolment differences in age and anthropometry), height-for-age *Z* score was significantly different over time in the groups that received enhanced nutrition intervention compared with those who did not receive enhanced nutrition (p=0·026) (data not shown).

***Table 4: Z*** **scores by age and treatment exposure**

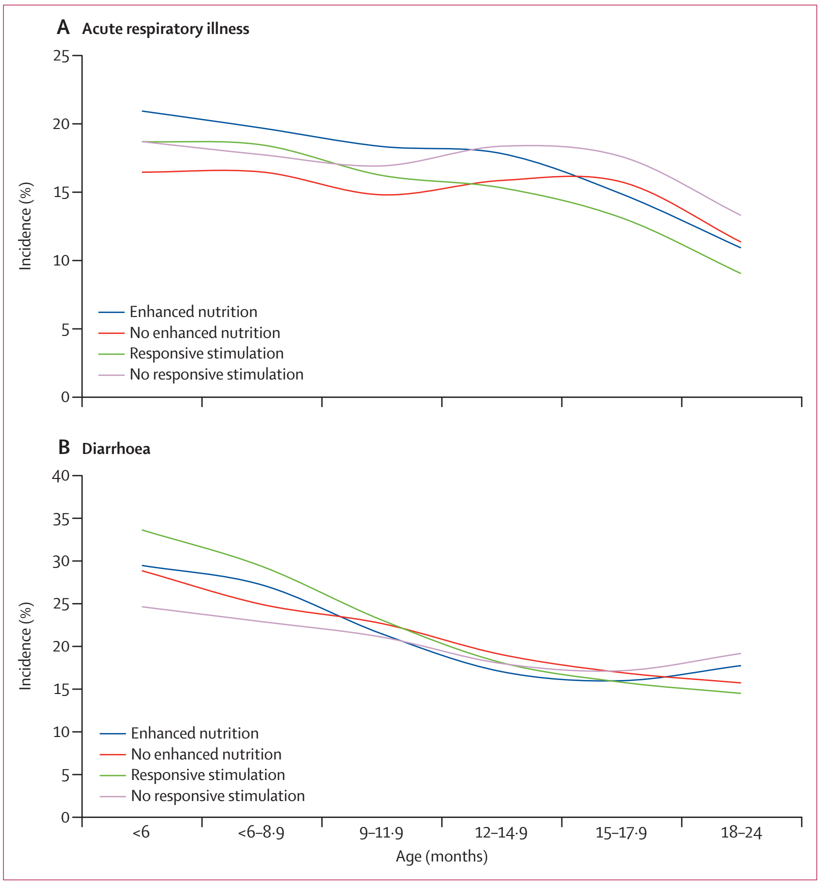


***Figure 4:*** **Incidence of child morbidity in the study**
Incidence of (A) acute respiratory illness and (B) diarrhoea. Incidence was calculated as the number of visits in which morbidity is reported divided by the total number of visits. Cluster-adjusted generalised estimating equation analyses showed that both acute respiratory illness and diarrhoeal disease decreased over time (p<0·0001 for both). For acute respiratory illness, the responsive stimulation intervention had a lower incidence trend over time than no responsive simulation (p<0·0001), and the enhanced nutrition group also had a lower incidence trend over time than did the group with no enhanced nutrition (p=0·0076). For diarrhoeal disease, responsive stimulation intervention had a lower incidence trend over time than did no responsive stimulation, whereas the children who received enhanced nutrition had a higher incidence trend over time than did those who received no enhanced nutrition (p<0·0001).

| | Combined responsive stimulation and enhanced nutrition | Responsive stimulation | Enhanced nutrition |
|---|---|---|---|
| Cognition | 0·5 (0·3–0·6) | 0·6 (0·5–0·8) | 0·2 (0·0–0·4) |
| Language | 0·6 (0·4–0·7) | 0·7 (0·5–0·8) | 0·4 (0·3–0·6) |
| Motor | 0·4 (0·2–0·6) | 0·5 (0·4–0·7) | 0·2 (0·0–0·4) |

Data are Cohen's d effect size for each intervention group (95% CI). The child development outcomes were all assessed at 24 months on Bayley Scales for Infant and Toddler Development, Third Edition. Effect size is calculated as the difference in mean scores between the treatment groups and control group over the pooled SD score. Analysis is adjusted for clustering and controlled for covariates of socioeconomic status, household food security, maternal education, and number of siblings by generalised estimating equations. The 95% CIs indicate a significant difference in the intervention groups compared with the control group.

***Table 5:*** **Treatment effect size on significant child development outcomes after 2 years of intervention exposure**

children not exposed to enhanced nutrition (mean [SD]: 6 months enhanced nutrition −1·2 [1·3] *vs* no enhanced nutrition −1·4 [1·2], p<0·0001; 18 months enhanced nutrition −2·2 [1·2] *vs* no enhanced nutrition −2·4 [1·1], p=0·02). In the longitudinal analysis, with a linear mixed model adjusted for clustering and controlling for covariates, height-for-age *Z* score showed a significant benefit from enrolment to 24 months in the enhanced nutrition intervention group (p=0·026) (data not shown).

We did not record any intervention effects on haemoglobin concentration (and thus anaemia status) for either intervention (mean [SD]: responsive stimulation 89 g/L [17] *vs* no responsive stimulation 91 g/L [16], p=0·06; enhanced nutrition 91 g/L [17] *vs* no enhanced nutrition 89 g/L [17], p=0·11; interaction p=0·09). Maternal reports of child morbidity showed that the incidence of diarrhoeal disease and acute respiratory illness decreased over time (p<0·0001). The incidence of diarrhoeal disease was significantly lower in infants who received responsive stimulation than in those who did not (p<0·0001), but was significantly higher in the enhanced nutrition groups than in those with no enhanced nutrition (p<0·0001). Compared with the groups not exposed to the interventions, the occurrence of acute respiratory illness was significantly lower over time in the responsive stimulation (p<0·0001) and enhanced nutrition groups (p=0·076) (figure 4).

Table 5 shows the treatment effect sizes on the significant outcomes when the children were 24 months of age. Treatment effects are moderate to large for cognition, language, and motor development for groups exposed to responsive stimulation, and are slightly higher for responsive stimulation alone than for the combined intervention group. Treatment effects, on the same outcomes, were low to moderate for the enhanced nutrition group (table 5).

## Discussion

We designed this study to investigate the effect of the delivery of a model of integrated early child development interventions with community health workers in a public sector effectiveness setting. Our results show that the responsive stimulation intervention had significant benefits on early child cognitive, language, and motor development outcomes, but not on social-emotional development. The treatment effect sizes (moderate to large) of responsive stimulation at 24 months of age were similar to those in previous efficacy studies.[12,13] Many of the recommended effectiveness factors could be implemented in the programme design (eg, parents trying activities with their children and receiving feedback); however, the intensity of delivery was lower than in previous studies because the frequency of contacts and their duration per caregiver–child dyad was less than that reported in previous efficacy studies, which were typically a weekly or a fortnightly home visit of up to 1 h duration.[8–11,18–20] In a large-scale community health programme, weekly or fortnightly visits were not feasible; however, a longer programme duration, which makes use of community groups and the potentials of group dynamics, uses problem solving, imparts mothers with the skills to continue practice at home, and builds the skills of the community workers with effective supervision strategies, might have compensated for the loss of intensity. In further research, analysis of how implementation features (eg, skills of delivery agents), community demand, child and caregiver characteristics, and doses interact to moderate outcome will be crucial. These data are essential to identify features to take effective programmes to scale and support advocacy.[13,33]

Between 12 and 24 months, language, motor, and social-emotional development scores increased in infants in all intervention groups; however, cognitive developmental scores declined. Evidence suggests an association between low socioeconomic status and poor cognitive outcome,[1] and a decline in cognitive development scores over time has been shown as early delays become worse in children who are poor[34] and as the effects of several risk factors accumulate.[2] Although the decline in cognitive development scores was less in children exposed to the responsive stimulation intervention than in those who were not, which suggests that the intervention offers some protection, it does raise questions about how to strengthen curriculum design to support and promote early learning. For example, are families able to provide a sufficient variety of developmentally appropriate learning materials or can they build up activities appropriately to target cognitive development as children become older?

With respect to our study hypothesis, although we recorded independent benefits of the responsive stimulation intervention and the enhanced nutrition intervention on development outcomes, we did not note additive benefits as a result of combining the two interventions. Few studies have reported additive or synergistic effects of combined interventions (panel 2).[8,10] However, the combination did not harm early child outcomes, and many reasons still exist to consider integrating child health, nutrition, and development interventions, such as an efficient use of resources, cost savings, an opportunity to coordinate messages and activities for families, and the chance to affect several child outcomes.[36] To move forward with integrated approaches, delivery platforms will need to be optimised through implementation science research.

The enhanced nutrition intervention had modest benefits on early linear growth. Further analysis is warranted to better understand how the treatment effect on growth was moderated by several contextual factors reported in this study, such as household food security and potential associations with maternal undernutrition and high rates of births that were small for gestational age. Similarly small effects of plausible nutrition interventions on linear growth have been noticed in other studies of complementary feeding, even with food provision.[37] The enhanced nutrition intervention, specifically the multiple micronutrient powder, also did not affect anaemia status. Other recent trials of micronutrient powders have also shown them to have little effect on anaemia.[38] However, the overall poor intake of micronutrient powders and high rates of inflammation and infection might have contributed to this absence of effect. Additionally, in this study, although most families reported giving the micronutrient powders to their young children, some families had concerns and did not give the powder to their children, which suggests that improvements might be needed in the communication strategy for micronutrient powder uptake, which is especially important for children who could well have benefited from this targeted intervention.

**_Panel 2:_ Research in context**

**Systematic review**

In the development of the study protocol, we reviewed recently published systematic reviews about child development in developing countries.[1,3,12,13] We did our initial search of PubMed in April, 2008, and our updated formal search in January, 2013. Our search terms included: "feeding behaviors", "malnutrition", "protein energy malnutrition", "nutritional status", "body weight", "infant feeding", "nutrition", "nutrition education", "food supplements", "nutrition programs", "micronutrient", "child development", "play", "parental behavior", "parents", "parenting", "mothers", "maternal behavior", "responsive care", "psychosocial", "psychosocial stimulation", and "intervention". Our inclusion criteria for the systematic review were studies done in developing countries, interventions for children younger than 5 years old, and interventions that included both nutrition and psychosocial stimulation. During the course of the trial, we supplemented these reports with new reviews on risks to early child development and interventions to promote early child development,[2] along with new studies of integrated stimulation and nutrition intervention published between 2011 and 2012 from Bangladesh,[18,19] India,[20] and Uganda.[35] These studies have shown that home visits, group and clinic-based parenting programmes, parent–child interaction programmes, and play programmes can benefit early and longer term development. These programmes tend to have high intensity, which cannot always be replicated on a large scale. However, other important effectiveness factors identified include implementation of a structured curriculum, a parent and child focus, opportunities for parents to experience play with their children and receive feedback, and integration with health, nutrition, education, and family support programmes. Synergies with early development and nutrition are especially crucial and can work together to promote survival, development, and growth. However, few studies have assessed integrated early child development interventions in community-based effectiveness settings.

**Interpretation**

Our results show that the integration of new responsive stimulation and care for development intervention in an existing community-based health service is feasible, and benefits early child cognitive, language, and motor development with similar outcomes to previous efficacy studies. Despite the challenges faced by the service providers (Lady Health Workers), they were able to deliver a good-quality programme that was accepted by the community and engaged families to develop positive practices for early childcare. Further strengthening of the nutrition component of the package is necessary to also see benefits to growth outcomes and significant reductions in malnutrition; these include more attention to preconception health, birth spacing, early maternal nutrition health, and targeted support for food-insecure households. These findings add to the efficacy and effectiveness of community-based approaches to promote early child development in the first 2 years of life. More assessments are needed to analyse the effectiveness features of programmes with potential to be scaled up (eg, the different degrees of effect of quality, intensity, and community demand).

With respect to morbidity, our data suggest that the prevalence of diarrhoeal disease and acute respiratory illness decreased over time as a result of exposure to both responsive stimulation and enhanced nutrition compared with non-exposure. Several plausible explanations might exist, including overall improved integration of nutrition messaging and more time spent by LHWs in home visits to counsel families in the intervention groups than with the control group. The responsive stimulation curriculum also promoted responsive care, and the enhancement of these basic caregiving skills, learned during play interactions, might also have protected children's health by helping families to respond early to signs of illness in their children.[7]

Our study design and implementation have several strengths. The three main strengths were: our data collection team were masked to the intervention allocation of clusters, we noted no differential recruitment in our enrolled sample, and the attrition rate was low. However, a key limitation in our study was the measurement of social-emotional development, which is complex for this age group and relies largely on maternal report. The adaptation of methods to different cultural contexts and low literacy populations needs specific attention to what mothers can report reliably about their children's behaviours. The quality of our adaptation for the maternal report assessment in this study could be improved. In further research, it might also be worthwhile to consider the use of biomarkers (eg, cortisol) to assess levels of stress in infants and young children.[39] Finally, with respect to intervention design, we focused our intervention on the period from birth to 24 months of age. This period is an important window of opportunity for early intervention to build the necessary strong foundations in early brain development; however, the longer term outcomes will be affected by the life course. In other words, although action in this sensitive period is crucial, we also need to recognise and explore further how risk and protective factors can moderate treatment effects along the life course (eg, pre-conception, pregnancy, toddlerhood, and adolescents) to understand what further interventions are needed to protect the early benefits to development recorded in our study.

In summary, although further research is needed to explore how the implementation features moderate outcomes, the pragmatic nature of this study shows that LHWs can integrate responsive stimulation successfully into their routine work in a context of poverty and household food insecurity, which may be generalisable to community health workers in similar programmatic and community contexts. The long-term successful scale-up of a responsive stimulation intervention in the LHW programme partly depends on the willingness to strengthen the basic programme infrastructure to ensure catchments are functional and home visits are enabled on a regular basis and to optimise the timing of, number of, and links between health, growth, and development messages. Nonetheless, these findings indicate a promising direction for the further integration of psychosocial stimulation interventions in community health services.

#### Contributors

AKY and ZAB conceptualised the study with inputs from RA. AKY developed the protocol, study design, and data collection materials, coordinated the implementation of the study and oversaw training of the research team, planned analysis, interpreted findings, and drafted the report. MAR trained the community-based child development assessors, oversaw quality assurance of child development data collection, contributed to the literature review, helped with interpretation of findings, and critically reviewed drafts of the report. AR was the statistician for the study, and participated in the study design, data analysis and interpretation, and critically reviewed drafts of the report. ZAB and RA critically reviewed drafts of the report. AKY and ZAB are guarantors for the research.

#### Declaration of interests

We declare no competing interests.

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