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Development of children at risk for adverse outcomes participating in early intervention in developing countries: a randomized controlled trial

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Background: Previous research has indicated positive effects of early developmental intervention (EDI) on the development of children in developing countries. Few studies, however, have examined longitudinally when differential treatment effects may be observed and whether differential outcomes are associated with exposure to different risk factors and country of implementation. Also, birth asphyxia as a risk condition has not been well studied. To address these limitations, we conducted a randomized controlled trial to test the hypothesis that there will be differential developmental trajectories favoring those who receive EDI versus a health education intervention in children in rural areas of India, Pakistan, and Zambia. **Methods:** Children with and without birth asphyxia were randomized to EDI or control intervention, which was implemented by parents who received training in biweekly home visits initiated before child age 1 month and continuing until 36 months. Development was assessed in 376 children at ages 12, 24, and 36 months using the Bayley Scales of Infant Development and Ages & Stages Questionnaire administered by evaluators blind to intervention assignment and risk condition. **Results:** Longitudinal mixed model analysis indicated that EDI resulted in better development over 36 months in cognitive abilities, regardless of risk condition, maternal resources, child gender, or country. Psychomotor development and parent-reported general development showed similar trends as for cognitive abilities, but were not statistically different between intervention conditions. Developmental differences were observed first at 36 months of age. **Conclusion:** Early developmental intervention has promise for improving development in children across developing countries when exposed to various risk conditions. EDI should be one prominent approach used to begin to address long-term outcomes and intergenerational transmission of poverty. **Keywords:** Early developmental intervention, low resource countries, birth trauma, at risk.

Introduction

Many young children in low and low-middle income countries (L/LMIC) are exposed to multiple risks that can affect their psychosocial development, such as poverty, malnutrition, birth trauma, and home environments that are unable adequately to stimulate their development. A conservative estimate is that more than 200 million children under 5 years fail to reach their potential in cognitive development alone due to such risk factors (Grantham-McGregor et al., 2007), most of whom live in south Asia and sub-Saharan Africa. Early developmental intervention (EDI) can prevent or limit the declines in cognitive development that may occur in children exposed to risk conditions. EDI encompasses a broad array of activities designed to enhance a young child's development (Ramey & Ramey, 1998), directly via structured experiences and/or indirectly through influencing the care giving environment. The primary goals for EDI include improving the child's developmental trajectories and assisting the family in addressing the needs of a child at risk for adverse outcomes.

The potential for EDI to improve development of children in L/LMIC has been well recognized. For example, 15 of 16 studies that implemented randomized controlled trial (RCT) designs in the first 5 years of life in L/LMIC reported significantly higher cognitive functioning in young children provided EDI compared with children in control conditions (Walker et al., 2007). These trials have collectively targeted children exposed to a range of risk factors and residing in a variety of L/LMIC. Follow-up studies consistently have reported lasting effects of EDI, including up to 17 years later (Walker, Chang, Powell, & Grantham-McGregor, 2005).

Birth asphyxia as a developmental risk

One risk group has been argued to be newborns with neonatal respiratory depression or birth asphyxia (Perlman & Risser, 1995). Failure to initiate or sustain spontaneous breathing at birth is a leading cause of perinatal mortality, neonatal encephalopathy, intellectual disability and other childhood neurodevelopmental disorders (Al-Macki, Miller, Hall, & Shevell, 2009), particularly in L/LMIC (Halloran et al., 2009). Birth asphyxia accounts for about 23% of the 3.5 million neonatal deaths that occur

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each year worldwide, 98% of which occur in L/LMIC (Black et al., 2010). Although its availability is quite limited in many L/LMIC, resuscitation at birth decreases fresh stillbirths (Carlo, Goudar, et al., 2010) and early neonatal mortality (Carlo, McClure, et al., 2010). However, an estimated one million children who survive birth asphyxia each year develop learning difficulties, cerebral palsy, and other disabilities, resulting in a loss of over 41 million disability-adjusted life-years (World Health Organization, 2005, 2008). This burden disproportionately affects L/LMIC.

Despite its prevalence and burden, we are aware of only one RCT of EDI targeting birth asphyxia. Conducted in a single center in China (Bao, Sun, Yu, & Sun, 1997), the home-based, parent-provided EDI consisted of approximately 13 home visits by trainers during up to 2 years. Assessment with the Bayley Scales of Infant Development (BSID; Bayley, 1993) at 18–24 months showed significantly better Mental Development Index (MDI) for infants receiving EDI (EDI = 105 ± 15 vs. standard care =. 91 ± 11), but not Psychomotor Development Index (PDI). Although this trial suggests that a relatively low-intensity EDI may promote cognitive development in infants with birth asphyxia in L/LMIC, it remains unclear whether the benefits are reproducible and generalizable because of the small sample ($n = 64$) studied in a single country.

Limitations in prior research

Although there is a considerable body of research evaluating the efficacy of EDI with children at risk for adverse developmental outcomes, there are some limitations. Very few of these studies have examined the effects of EDI on development over time, examining rather outcome at a specified age. One exception is Walker et al. (2005), who showed graphically, at least, that stunted children in Jamaica receiving EDI demonstrated better mean development at the end of the 2-year intervention (ages 33–48 months), which was sustained through follow-up assessments through ages 17–18. We are not aware of any study using longitudinal analytical models (e.g., Rogosa, Brandt, & Zimowski, 1982; Willett, 1997) to examine data representing trajectories of development across time. Such methods can illuminate more clearly the impact of EDI on children's development over time.

Also, we are not aware of any RCT that has been conducted in more than one country, which makes it difficult to discuss whether a specific EDI is useful across countries. Moreover, evaluations of EDI have typically been conducted separately for children with different risk conditions, such as different medical or socioeconomic risk factors. If it can be demonstrated that the same EDI is effective for children with different risk conditions in the same trial, this would suggest that this EDI can be applied efficiently to different groups at risk.

Aims

We address here the hypothesis that trajectories in development will favor those who receive EDI versus a control intervention over the first 36 months of life in children in socioeconomically disadvantaged, rural areas of three L/LMIC. In addition, we examine whether differential treatment effects may be observed at 12, 24, or 36 months of age and if differences are associated with (a) exposure to different risk factors, including birth asphyxia and preterm birth; (b) maternal age and education; (c) child gender; and (d) country of implementation.

This study is embedded in a RCT, the Brain Research to Ameliorate Impaired Neurodevelopment: Home-based Intervention Trial (clinicaltrials.gov ID# NCT00639184), which had as the primary hypothesis that an EDI improves cognitive abilities at 36 months among children with resuscitated birth asphyxia, compared with a control intervention. As reported elsewhere (Carlo et al., 2013), this hypothesis was supported in analyses solely focused on outcome at the end of the 36-month RCT. Those analyses did not examine effects of EDI over the course of the trial, nor whether differential improvements would be observed prior to the 36-month end point or in different groups of children.

Methods

Procedures and trial design

Details on the procedures have been published (Wallander et al., 2010). This parallel design RCT was implemented in rural communities marked by poverty in defined rural regions in India, Pakistan, and Zambia in two populations born from January 2007 to June 2008: (a) infants with birth asphyxia unresponsive to stimulation who received bag and mask ventilation; and (b) infants without asphyxia who did not require any resuscitation. Infants in each cohort were randomized individually, using 1:1 concealed parallel allocation, matched for country and chronological time using variable block sizes to assure allocation concealment, to either: (a) EDI plus health education; or (b) Control intervention consisting of health education only (Figure 1). Allocation sequence was generated centrally and distributed using sealed envelopes to the local investigators, who obtained consent for the trial. Written informed consent was obtained during the second week after birth following the 7-day neurological assessment and before randomization. Interventions were initiated within the first month of life and ended at 36 months. Continuing biweekly home visits past 12 months was the only change in trial design. Although plans had been to decrease home visits to every fourth week after 12 months, this change was implemented to increase the intensity of the intervention. The trial was approved by IRBs at all research sites

Study populations

Birth asphyxia. Infants with birth asphyxia unresponsive to stimulation, who received bag and mask ventilation for resuscitation at birth, were screened for enrollment into this RCT. Birth asphyxia was defined as the inability to initiate or sustain spontaneous breathing at birth using the WHO (1997) definition. Exclusion criteria were as follows: the infant's (a)

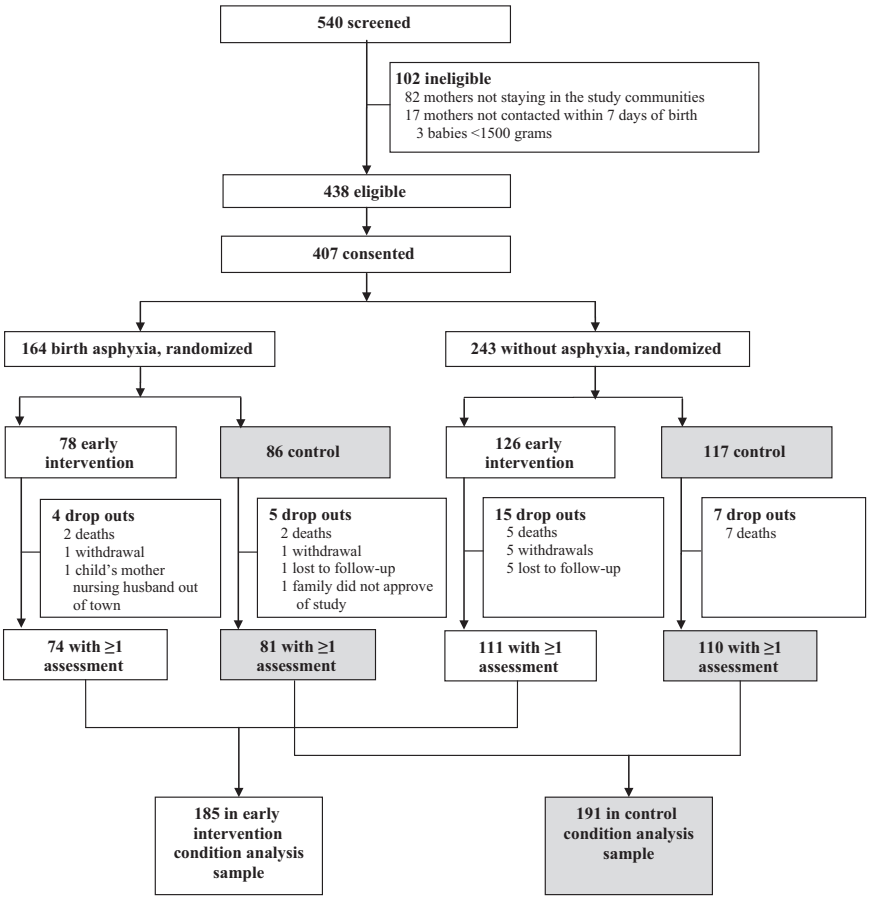

Figure 1 Participant flowchart of screening, randomization, and completion of developmental assessments, resulting in analysis sample for each intervention condition

birthweight <1500 g or (b) neurological examination at 7 days was severely abnormal (grade III by criteria from Ellis et al., 2000), or the mother was (c) <15 years of age, (d) unable/unwilling to participate, or (e) not planning to stay in the study communities for the following 3 years.

Birth without asphyxia. Infants who did not require any resuscitation and had normal neurological exams at 7 days of age, but otherwise met the same criteria as infants with birth asphyxia, were randomly identified from the next one or two births following the infant with asphyxia, matched for country and chronological time, and enrolled into this trial.

Intervention conditions

Participants and parent trainers in both conditions were masked to the objectives and hypotheses of the study. Both interventions were delivered using a biweekly schedule of home visits, starting before age 1 month and ending at 36 months of age

Early development intervention. A home-based, parent-implemented EDI model was the active intervention (detailed in Wallander et al., 2010). Following the *Partners for Learning* (Sparling & Lewis, 1984) curriculum, parent trainers introduced playful interactive learning activities and modeled them for the parents during home visits. This curriculum covers: (a) cognitive and fine motor, (b) social and self-help, (c) gross motor, and (d) language skills. Each research site employed EDI parent trainers who were trained in an initial 5-day workshop held at each research site. A second 3-day workshop was conducted before any children reached 18 months. The same trainer was assigned to each parent throughout the trial whenever possible.

During each home visit, the trainer presented one or two learning activities. Each activity targeted a developmentally appropriate skill. The parent practiced the activity in the presence of the trainer who provided feedback. Cards depicting the activities were then left with the parent, who was encouraged to apply the activities in daily life with the child until the next home visit. The trainer introduced new activities in subsequent visits to enhance the child's developmental competencies. The trainers were supervised during weekly group meetings and observations during home visits. Implementation was measured by home visits completed on schedule within its assigned 2-week window following the preceding visit.

Control intervention. Parents in both trial conditions received health education during every home visit as the sole content of the control intervention, which was based on a WHO (2014) curriculum that addressed, for example, breast feeding, nutrition, hygiene, and vaccinations. The health education was provided by both the EDI and control trainers who completed a 5-day training program at each research site conducted separately from the EDI training.

Developmental Outcome Measures

Local evaluators familiar with the language and culture were masked to the children's birth history and intervention condition. Evaluators from the three countries were trained jointly in three 4-day workshops, each held before commencing the yearly assessments. Assessments occurred at or close to each child's 12-, 24-, and 36-month birthday.

The *Bayley Scales of Infant Development-II* (BSID; Bayley, 1993) was selected as the primary outcome measure because at the start of this trial, it had been used extensively in numerous studies in L/LMIC that support its psychometric quality. The BSID underwent extensive pretesting at each site to verify validity in the local context, and a few items were slightly modified to make each more culturally appropriate (e.g., image of a sandal instead of a shoe). The BSID Mental (MDI) and Psychomotor (PDI) Development Index were administered directly to each child in the appropriate language using standard material.

Ages and Stages Questionnaire, 2nd edition (ASQ; Squires, Potter, & Bricker, 1999): Total score was used as a secondary outcome measure to assess parent-reported child development observed in the home environment. It consists of 30 items addressing communication, gross motor, fine motor, problem solving, and personal–social development using age-specific forms. To reduce the impact of variation in literacy, ASQ was administered in an interview with the parent, who was instructed to report on the child's behavior observed in the home or community. The ASQ has been widely used in research on early development, supporting its psychometric quality, including in numerous L/LMIC (e.g., Heo, Squires, & Yovanoff, 2008; Tsai, McClelland, Pratt, & Squires, 2006).

Child and maternal characteristics

Health variables were obtained from medical research records regarding birth asphyxia (yes vs. no) and gestational age (preterm vs. term). Information on child, maternal and family demographics was collected at enrollment in the trial through a structured interview. Of relevance here were child gender, maternal age (25+ vs. ≤24), and education (illiterate vs. literate). Additional information was recorded to fully describe the sample, which has been presented elsewhere (Carlo et al., 2013).

Sample size

To test the main hypothesis, at least 40 children in each of the four groups (see Figure 1) needed to complete the intervention and the 36-month assessment (assuming a 5% one-tailed significance level) to detect a difference between groups comparable to that observed in previous studies (e.g., Grantham-McGregor, Powel, Walker, & Himes, 1991; Nahar et al., 2009) of 10 points (SD = 15) on a standardized developmental measure such as the BSID with a power of 90%.

Statistical analysis

Trajectories of developmental measures (MDI, PDI, and ASQ) collected at the three assessments were compared between conditions using linear mixed effect models with SAS PROC MIXED to account for repeated measurements over time. This analysis uses maximum likelihood estimates that can include all cases with a measurement on at least one of the three assessment occasions and are not missing data on the covariates. It will produce unbiased estimates if the data are missing at random. Because children's exact ages varied at the time of the assessments, exact age was included as a continuous variable in the models. Each model included intervention condition, birth asphyxia, gestational age, maternal age and education, child gender, and country (designated A, B, and C here) and interactions of age with the other factors. Interactions were retained if significant for at least one of the three outcomes. Of particular interest was the interaction between age and intervention condition, which tests whether developmental trajectories over time differed between the two conditions.

Results

Sample constitution and implementation of intervention

As detailed in Figure 1, of 540 births screened over 18 months, 438 (81% of screened) were eligible. Informed consent was obtained for 407 participants (93% of eligible; 164 birth asphyxia, 243 birth without asphyxia), who were randomized into the two trial conditions (EDI = 204, control = 203). The analysis sample is constituted by 376 (92% of randomized participants, EDI = 185, control = 191) who provided a valid assessment on at least one of the three occasions. As shown in Table 1, the EDI and control conditions did not differ significantly in the distributions of birth asphyxia, gestational age, maternal age and education, and gender, nor on a range of other family, maternal, and infant characteristics detailed elsewhere (Carlo et al., 2013). Following the trial protocol, a total of 77 home visits

Table 1 Child and maternal characteristics and developmental outcomes by intervention condition

Characteristic	All (N = 376) N (%)	EDI (N = 185) N (%)	Control (N = 191) N (%)	p[a]
Child and maternal characteristics				
Birth asphyxia				
With	155 (41)	74 (40)	81 (42)	.635
Without	221 (59)	111 (60)	110 (58)	
Gestational age				
Preterm	111 (30)	49 (27)	62 (33)	.216
Term	260 (70)	133 (73)	127 (67)	
Maternal age				
25+	180 (48)	93 (50)	87 (46)	.360
≤24	196 (52)	92 (50)	104 (54)	
Maternal education				
Illiterate	172 (48)	86 (49)	86 (47)	.721
Literate	185 (52)	89 (51)	96 (53)	
Gender				
Male	218 (59)	104 (57)	114 (61)	.494
Female	150 (41)	77 (43)	73 (39)	
Country				
A	94 (25)	48 (26)	46 (24)	.839
B	123 (33)	58 (31)	65 (34)	
C	159 (42)	79 (43)	80 (42)	
Developmental outcomes(n)				
MDI				
12 months (376)	96 (15)	96 (16)	97 (95)	.477
24 months (294)	96 (15)	97 (15)	96 (16)	.521
36 months (293)	99 (12)	101 (10)	98 (12)	.014
PDI				
12 months (376)	96 (20)	96 (20)	95 (21)	.743
24 months (294)	95 (16)	95 (16)	95 (16)	.988
36 months (293)	104 (16)	107 (14)	101 (17)	.002
ASQ Total				
12 months (291)	242 (57)	243 (58)	241 (56)	.811
24 months (275)	231 (50)	234 (46)	227 (53)	.230
36 months (354)	245 (53)	249 (49)	240 (56)	.111

EDI, early developmental intervention; MDI, Mental Development Index; PDI, Psychomotor Development Index; ASQ, Agest & Stages Questionnaire.

[a]Chi-square tests for comparisons of child and maternal characteristics and t-tests for comparisons of outcomes.

could be completed for each participant until child age 36 months. On average, 96% and 98% of the home visits were completed in the EDI and control conditions, respectively.

Effects of intervention on developmental trajectories

Results of mixed effects models for each developmental outcome are shown in Table 2 (raw means are shown in Table 1). The age-by-intervention condition interaction for Mental Development Index (MDI) was significant ($p = .020$), indicating that children in EDI had a more positive trajectory across the three assessment occasions (12, 24, 36 months of age). Figure 2 presents the mean MDI for the EDI and control condition over time after adjusting for the variables in the model (birth asphyxia, gestational age, maternal age and education, child gender, country and interactions of age with the other factors). EDI children displayed a linear increase in MDI over time with model-adjusted mean scores ranging from 93.7 at 12 months to 100.6 at 36 months. The control condition displayed a smaller linear increase in MDI with values ranging from 94.7 at 12 months to 97.7 at 36 months. Whereas the adjusted mean MDI did not differ significantly between conditions at 12 or 24 months, those in the EDI condition had significantly higher MDI at 36 months ($p = .026$).

Although not statistically significant ($p = .057$), the age-by-treatment condition interaction for Psychomotor Development Index (PDI) suggests a similar trend as for MDI (Figure 2); children in the EDI condition experiencing greater improvements over time (Table 2) and the difference favoring the EDI over the Control condition reached significance ($p = .017$) at 36 months. Likewise, the age-by-treatment effect for the Ages and Stages Questionnaire (ASQ) total scores shows a trend favoring EDI (Figure 2), but it was not statistically significant ($p = .349$; Table 2) in part due to the large standard error (*SE*) of measurement.

Table 2 Mixed effects models of developmental outcomes

	Mental Developmental Index		Psychomotor Developmental Index		Ages & Stages Questionnaire	
Variable	Raw Regression Coefficient (*SE*)	*p*	Raw Regression Coefficient (*SE*)	*p*	Raw Regression Coefficient (*SE*)	*p*
Age-corrected (months)[a]	0.02 (0.07)	.741	0.33 (0.09)	**<.001**	1.14 (0.25)	**<.001**
Intervention condition[a]						
EDI	−2.94 (2.31)	.204	−2.65 (3.06)	.387	−1.71 (8.21)	.835
Control	REF		REF		REF	
Age × Intervention Condition	0.16 (0.07)	**.020**	0.18 (0.09)	.057	0.25 (0.26)	.349
12 months: EDI vs. Control	−0.98 (1.65)	.550	−0.47 (2.12)	.823	1.25 (5.92)	.834
24 months: EDI vs. Control	0.97 (1.23)	.430	1.70 (1.50)	.259	4.19 (4.74)	.377
36 months: EDI vs. Control	2.92 (1.31)	**.026**	3.87 (1.61)	**.017**	7.14 (5.45)	.191
Birth asphyxia						
Yes	0.04 (1.23)	.972	1.76 (1.49)	.239	2.84 (4.86)	.559
No	REF		REF		REF	
Gestational age						
Term	0.24 (1.33)	.856	−0.45 (1.61)	.782	1.91 (5.32)	.720
Preterm	REF		REF		REF	
Maternal age						
25+	0.42 (1.31)	.748	1.36 (1.60)	.395	4.65 (5.19)	.371
≤24	REF		REF		REF	
Maternal education						
Illiterate	−1.91 (1.74)	.275	0.22 (2.13)	.916	−2.86 (6.96)	.681
Literate	REF		REF		REF	
Gender						
Male	0.82 (1.22)	.499	2.16 (1.48)	.145	−0.43 (4.80)	.929
Female	REF		REF		REF	
Country						
A	−14.75 (3.34)	**<.001**	8.11 (4.35)	.063	21.64 (11.75)	.070
C	7.69 (3.00)	**.011**	11.58 (3.92)	**.003**	82.30 (11.12)	**<.001**
B	REF		REF		REF	
Age × Country						
Age: Country A	0.39 (0.09)	**<.001**	−0.10 (0.12)	.405	−1.10 (0.32)	<.001
Age: Country C	−0.09 (0.08)	.286	−0.04 (0.11)	.722	−2.69 (0.32)	<.001
Age: Country B	REF		REF		REF	

Model adjusts all comparisons for all other variables listed here. Only interactions that were significant for any of the developmental outcomes were retained in the final model. EDI, early developmental intervention; *SE*, standard error; REF, reference category.
[a]Because the model includes an interaction between Intervention Condition and Age, main effects cannot be meaningfully interpreted.
Bold value denotes significant *p*-value.

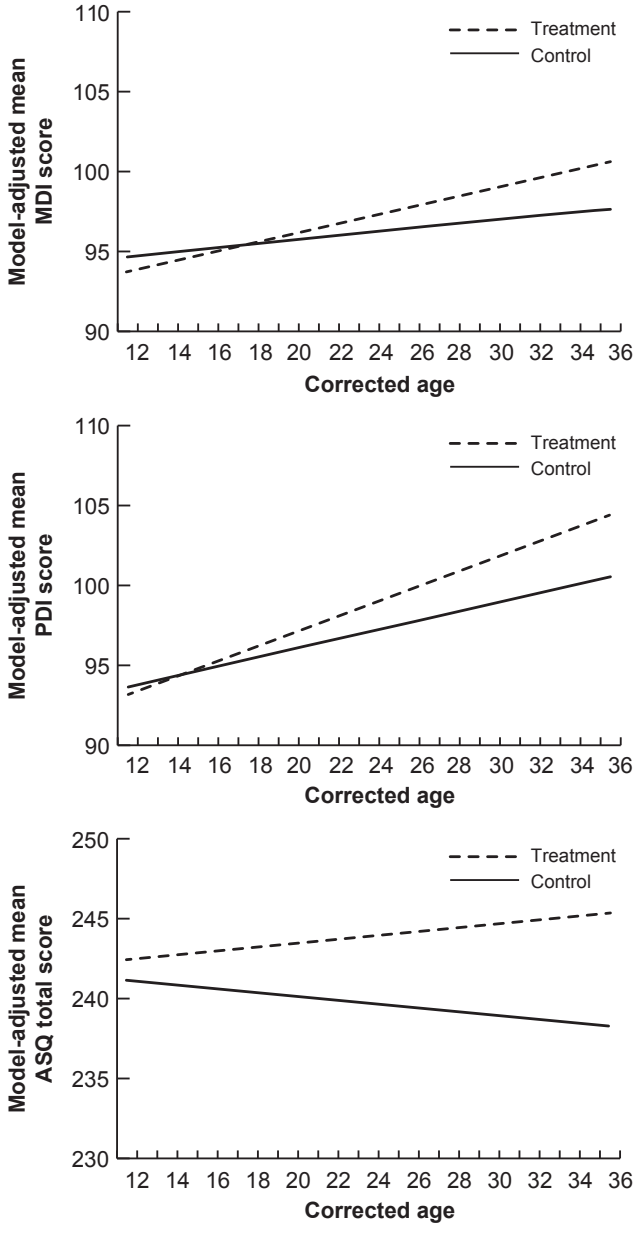

Figure 2 Model-Adjusted Mean by Intervention Condition for MDI (upper), PDI (middle), and ASQ Total Scores (lower). Means are adjusted for corrected age, intervention condition, age x intervention condition, birth asphyxia, gestational age, maternal age and education, child gender, country, and age x country interaction

Moderation of intervention effects

Interactions between age and variables indicating the risk conditions of birth asphyxia or preterm birth, maternal age or education, or child gender were not significant, which indicated that the developmental trajectories were not different across any of these factors. However, there were several differences among the three countries. The age-by-country interaction was significant ($p < .001$) with children in Country A experiencing significantly greater increases in MDI over the intervention period than those in Country B. Children in Country A had significantly lower adjusted mean MDI at 12 months than those in Country B or C ($p < .001$). While their MDI remained significantly lower than those in Country C at 36 months ($p = .005$), their scores no longer differed significantly from those in Country B ($p = .810$). As judged from the nonsignificant three-way interaction, however, the intervention effect on MDI trajectories did not differ among countries ($p = .143$).

The age-by-country interaction was not significant for PDI. Although children in Country C generally had higher scores than those in Country B, patterns of change in PDI over the intervention period were similar across the countries. There was a significant age-by-country effect for ASQ Total scores ($p < .001$). Country C had significantly higher ASQ scores at 12 months than Country A or B after adjusting for other factors, but these differences were no longer significant at 24 and 36 months. However, intervention effects on PDI ($p = .090$) or ASQ ($p = .636$) developmental trajectories did not differ significantly among countries.

Discussion

Longitudinal analysis of yearly assessments of a RCT indicates that EDI resulted in better cognitive development in children in L/LMIC over the first 36 months of life compared with a control intervention. The positive effect occurred regardless whether children were exposed to birth asphyxia, preterm birth, or an essentially healthy birth, or different maternal age or education, child gender, or country. This absence of moderation suggests that EDI can have a positive effect across a range of children. Significantly improved cognitive development due to the EDI was first observed at 36 months, with a modest effect (3.9 points on MDI). Although trajectories for psychomotor development and parent reports of general development showed the same positive trend due to EDI as for cognitive development, these were not significantly different from the control condition.

One previous smaller RCT (Bao et al., 1997) of EDI for birth asphyxia reported similar effects, including on cognitive but not psychomotor development. Although this other trial implemented a less intensive home-visiting schedule over a shorter period (18–24 months), the effect on cognitive development was larger than in our trial. This may be due to our trial employing a more intensive control condition than the standard care condition used by Bao et al. (1997), which did not involve any home visits. Our control intervention consisted of over 75 home visits over 3 years, which provided social resources to the mothers and information to maintain the general health of the child. The nature of the control intervention thus may partly explain the relatively small advantage attributed to the EDI here. The positive effect on cognitive but not psychomotor development observed in both Bao et al.'s (1997) and our trial may be because most EDI curricula empha-

size learning mental concepts and processes. In addition, physical development may be more biologically based and dependent on every day activities, and be challenging to stimulate through relatively few assigned activities.

One aim of this study was to examine the timing of EDI effects. Developmental improvements were not apparent until 36 months. This was later than reported for children with low birthweight, where positive effects from weekly home visits were evident already at 2 months in one study (Meeks Gardener, Walker, Powell, & Grantham-McGregor, 2003) and 15 months in another (Walker, Chang, Powell, & Grantham-McGregor, 2004). Studies with children with growth retardation (Grantham-McGregor et al., 1991) or undernourishment (Hamadani, Huda, Khatun, & Grantham-McGregor, 2006; Powell, Baker-Henningham, Walker, Gernay, & Grantham-McGregor,2004) also showed positive effects earlier in life (average ages 27–31 months) after 12 months of primarily weekly home visits. In addition to targeting different conditions in different social–cultural contexts, it is possible that the more intensive schedule of home visits accounts for observing earlier effects. Because these studies also differ at what age EDI was initiated (1–30 months), direct comparisons become difficult. Further research is needed evaluating when the developmental improvements due to EDI emerge related to the initiation and intensity of intervention.

Another aim was to examine if effects of EDI were moderated by different factors. Whether children were exposed to birth asphyxia or not did not alter the effects of EDI, nor did gestational age. Beyond these medical conditions, all children in this trial resided in rural areas in L/LMIC marked by socioeconomic deprivation, which may negatively affect child development. Others (e.g., Eickmann et al., 2003) have documented positive effects of EDI also for children in L/LMIC who are exposed to socioeconomic deprivation rather than a medical risk. Our findings that children without birth asphyxia also benefited from EDI are consistent with this literature and supports the argument that EDI may benefit children who are disadvantaged for any reason (Grantham-McGregor et al., 2007). This RCT of EDI was conducted in three countries. Even though there were some developmental differences in the participating children in these countries, the positive effect of EDI was not different across them. This suggests that the same EDI can be effective in quite varied sociocultural contexts.

Among the strengths of this research is the longitudinal analysis of the effect of EDI in one of the largest samples enrolled in an RCT in L/LMIC countries. Being implemented in different countries and with different risk groups, this study can more directly address generalizability of the effects of EDI. Limitations include the modest gain due to EDI, which may question the clinical relevance. However, we are encouraged by the upward trajectories of development over time (see Figure 2), which may suggest that differentiation would continue. Also, independent observation was not obtained of the quantity or quality of parents' implementation of the developmental activities. Therefore, the intervention may have been less intense than desirable. Children were evaluated across the first 3 years when neurodevelopmental assessments may be less predictive of long-term outcomes than at later ages. It is conceivable that larger benefits will be observed at school age or that survivors of birth asphyxia will have problems that manifest only later.

The positive cognitive development due to EDI is consistent with the collective findings from many controlled evaluations with children exposed to a variety of risk conditions and contexts. The particular EDI used here is based on a standard curriculum and can, with modest resources, be implemented as a public health intervention. Beyond affecting early development, it has been well documented that exposure to early risk conditions has significant long-term adverse effects on children. Such children are likely to achieve poorly in school (Grantham-McGregor et al., 2007), which is likely to lead to low incomes in adulthood and difficulty providing for their own children (Walker et al., 2005). It is important for the health and development of many countries to disrupt this cycle of intergenerational transmission of poverty in which early childhood development plays an important role. Much evidence accumulated to date suggests that EDI should be one of the approaches used to improve early development in L/LMIC.

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Key Points

- Substantial research supports the efficacy of early developmental intervention (EDI) for children in low/low-middle resource countries (L/LMIC);
- Yet, few studies have examined impact on development over time, or in more than one country or one risk condition at the time;
- In this study, EDI resulted in better cognitive development over 36 months, regardless of risk condition, maternal resources, or child gender. Developmental differences were observed first at 36 months of age;
- Much evidence suggests that EDI should be one prominent approach used in L/LMIC to improve early development in children and begin to address long-term outcomes and intergenerational transmission of poverty.

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