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Prenatal nutrition, stimulation, and exposure to punishment are associated with early child motor, cognitive, language, and socioemotional development in Dar es Salaam, Tanzania

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Abstract

Background: Despite growing evidence that early life experiences and exposures can impact child development, there is limited research on how prenatal and early life nutrition and early life parenting practices predict specific domains of child development in resource-limited settings. This study examines the association between prenatal factors, birth outcomes, and early life characteristics with motor, cognitive/language, and socioemotional development in Tanzania.

Methods: We assessed motor, cognitive/language, and socioemotional development among a cohort of 198 children aged 20–39 months in Dar es Salaam, Tanzania, whose mothers were previously enrolled in a randomized, placebo-controlled trial of prenatal vitamin A and zinc supplementation. Linear regression models were used to assess standardized mean differences in child development scores for randomized prenatal regimen and pregnancy, delivery, and early childhood factors.

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CONFLICTS OF INTEREST
None to report.

SUPPORTING INFORMATION
Additional supporting information may be found online in the Supporting Information section at the end of the article.

Results: Children born to mothers randomized to prenatal vitamin A had significantly lower reported motor scores in minimally adjusted and multivariate analyses, −0.29 SD, 95% CI [−0.54, −0.04], p = 0.03, as compared with children whose mothers did not receive vitamin A. There was no significant effect of randomized prenatal zinc on any development domain. Greater caregiver–child stimulation was associated with 0.38 SD, 95% CI [0.14, 0.63], p < 0.01, better cognitive/language scores, whereas children who experienced both verbal and physical punishment had 0.29 SD, 95% CI [−0.52, −0.05], p = 0.02, lower scores in socioemotional development. Maternal completion of primary school was associated with higher reported motor and cognitive/language development. Further, children of mothers who were <155 cm tall had lower cognitive and language scores.

Conclusion: Prenatal vitamin A supplements in a setting with low levels of vitamin A deficiency may not provide child development benefits. However, integrated environmental, educational, parenting, and stimulation interventions may have large positive effects across child development domains in resource-limited settings.

Keywords

child development; developing countries; early assessment; psychosocial factors; randomized trials

1 | INTRODUCTION

In 2010, an estimated 33% of 3- and 4-year-olds in low- and middle-income countries (LMICs)—80.8 million children in total—failed to meet basic milestones in cognitive and/or socioemotional development (McCoy et al., 2016). Early motor, cognitive, language, and socioemotional development are predictive of later life outcomes, including educational attainment, economic earnings, and violent behaviour in early adulthood, which highlights the urgent need to alter the developmental trajectory early in life to ensure children have the opportunity to thrive (Gertler et al., 2014; Heckman, Pinto, & Savelyev, 2013; Peet et al., 2015; Piek, Dawson, Smith, & Gasson, 2008; Walker, Chang, Vera-Hernández, & Grantham-McGregor, 2011).

Research on global child development has increased over the last decade, and it is well documented that early experiences and exposures can have a lifelong impact on cognitive and social functioning (Shonkoff, Boyce, & McEwen, 2009; Shonkoff, Phillips, & National Research Council (U.S.), 2000). A multitude of risk factors for early child development have been identified, including those related to early life nutrition, the home caregiving environment, and disease burden (Britto et al., 2017; Walker et al., 2007; Walker et al., 2011). Further, recent work has highlighted the positive effects of integrated interventions that include early child nutrition and stimulation components on cognitive development outcomes (Grantham-McGregor, Fernald, Kagawa, & Walker, 2014; Yousafzai, Rasheed, Rizvi, Armstrong, & Bhutta, 2014). However, the ways in which prenatal and early life nutrition and early life parenting practices predict specific domains of child development remain understudied in LMICs. In particular, there is sparse evidence on the effect of prenatal nutrition supplementation on child development.

In order to address some of these research gaps, we examined the effect of prenatal vitamin A and zinc supplements, as well as the association between birth outcomes and early life factors and motor, cognitive/language, and socioemotional development among a prospective cohort of children 20–39 months of age living in Dar es Salaam, Tanzania. We hypothesized that undernutrition in pregnancy, poor birth outcomes, linear growth faltering, and exposure to verbal or physical punishment would be associated with lower cognitive, motor, and socioemotional development scores.

2 | METHODS

2.1 | Study population

This study was composed of children whose mothers were enrolled in a randomized, factorial-designed prenatal supplementation trial of vitamin A and zinc (NCT01115478). The aim of the parent trial was to measure the effect of prenatal vitamin A and zinc supplementation on placental malaria as well as birth outcomes. The full details of recruitment and data collection for this trial are presented elsewhere (Darling et al., 2017).

Briefly, the parent randomized, double-blind, placebo-controlled trial enrolled 2,500 women at eight antenatal care clinics in the urban Temeke and Ilala districts of Dar es Salaam, Tanzania, between September 21, 2010 and September 17, 2013. Pregnant women were eligible for enrollment if they were in their first trimester of pregnancy, primigravida or secundigravida, human immunodeficiency virus uninfected, and intended to stay in Dar es Salaam for at least 6 weeks post-delivery. Participants were recruited either at their first antenatal care visit or through a demographic surveillance system established to identify early pregnancies in the population. Enrolled pregnant women were randomized to receive a daily oral dose of either 2,500 IU of vitamin A as retinyl palmitate, 25 mg of zinc, both 2,500 IU of vitamin A and 25 mg of zinc, or a placebo. Additionally, all women were given a daily dose of 60 mg of iron and 5 mg of folic acid in accordance with Tanzanian standard of care. The mean compliance rate across all women in the parent trial was 84.5% (median 97.6%; Darling et al., 2017).

2.2 | Recruitment for child development follow-up study

Children of mothers enrolled in the parent trial were eligible for the child development follow-up study if they were 18–36 months of age at the time of recruitment selection. We contacted a random selection of eligible mothers with available contact information for participation in the child development follow-up study between July and October 2015. Written informed consent for the follow-up study was obtained from all caregivers who participated in the study.

2.3 | Child development follow-up visit

Child motor, cognitive/language, and socioemotional development were assessed by the early Tanzanian version of the Caregiver Reported Early Childhood Development Index (CREDI; McCoy et al., 2017). The CREDI is a simple, low-cost, caregiver-reported tool that is feasible to include in large household surveys to monitor and measure child development cross-culturally. The version of the CREDI used in the present study was validated against the 3rd edition of the Bayley Scales of Infant Development in Ifakara, Tanzania, and is included in Table S3 (McCoy et al., 2017). Four native Swahili-speaking research assistants were trained on the CREDI as well as anthropometric assessment of both adults and children. Research assistants were selected based on their performance as data collectors in previous clinical trials and studies and participated in a 3-day training on the CREDI, anthropometry, and other study procedures. All research assistants were monitored by the study coordinator on a weekly basis to ensure continued adherence to study protocols. Research assistants also rated their perceptions of caregivers' understanding of and honesty in responding to the CREDI items. In addition, the research assistants recorded any questions or concerns stated by the caregivers during the interview and met at least once a week to discuss these issues. The CREDI was administered orally to the child's primary caregiver and contained yes/no questions related to the child's development that were grouped into three domains (motor, cognitive/language, and socioemotional) according to the original validation study's protocol (McCoy et al., 2017). Research assistants conducting the child development assessments were blinded to the randomized regimen, and all data were collected using an Android tablet. CREDI subscale scores were calculated by taking an average of the responses to questions included in each subscale, resulting in a score with a possible range from 0 to 1 for each subscale. The final scores for the motor, cognitive/language, and socioemotional subscales include 5, 19, and 20 items, respectively. During the child development assessment visit, we also collected anthropometric information from the children and mothers, as well as information about caregiver stimulation and verbal and physical punishment. The questions used to assess caregiver stimulation and verbal and physical punishment are presented in Table S4. The height of children and mothers was measured to the nearest 0.1 cm on a portable stadiometer (Seca, Hamburg, Germany), and weight was measured to the nearest 0.1 kg using a digital scale (Seca, Hamburg, Germany).

2.4 | Statistical analyses

The analyses included 198 children who were assessed with the CREDI tool between July and October 2015. For analyses on each subscale, we included only individuals who answered >75% of the questions within the respective subscale. Baseline characteristics of the study population were compared with individuals in the parent trial who were not included in the current study using two-tailed t tests and χ^2 tests for continuous and binary outcomes, respectively.

We examined the prospective association between prenatal and birth characteristics as well as the cross-sectional association between child characteristics at follow-up and children's motor, cognitive/language, and socioemotional development. Height-for-age z-scores (HAZ), weight-for-height z-scores (WHZ), and weight-for-age z-scores (WAZ) were calculated using the 2006 WHO child growth standards (WHO Multicentre Growth Reference Study Group, 2006). Stunting, underweight, and wasting were defined by a child scoring more than 2 SDs below the median for HAZ, WAZ, and WHZ scores, respectively. Small-for-gestational-age (SGA) births were defined as a weight-for-gestational-age by sex below the 10th percentile using the Oken reference (Oken, Kleinman, Rich-Edwards, & Gillman, 2003). To assess caregiver stimulation of the child in the past 3 days, six questions from the Early Child Development Index introduced in round 4 of UNICEF's Multiple

Indicator Cluster Survey were used. High stimulation was classified as having a stimulation score above 3, meaning the caregiver had completed 4–6 of the six stimulation activities (e.g., reading, counting, and playing) in the past 3 days. Verbal and physical punishment was classified as being present if the mother reported that the child had been both yelled at or scolded and spanked or hit by an adult in the last 3 days. Household asset scores were reported during the mothers' first trimester of pregnancy and were represented by the sum of the number of household assets (e.g., electricity generator, bike, fridge, and couch) out of a total of 10. The distribution of asset scores was divided into tertiles for analysis.

We first ran minimally adjusted linear regression models with robust standard errors for all variables of interest, including adjustment for child sex, child age category, and interviewer, to account for the potential relationship of these factors with child development measures. We then ran fully adjusted linear regression models with robust standard errors for each subscale for prenatal maternal and early childhood characteristics separately in order to avoid adjusting for mediators. The fully adjusted regression models for prenatal maternal characteristics and early child characteristics both included child sex, child age category, interviewer, asset score tertile, maternal education, prenatal supplement regimen, and all of the prenatal maternal or early child characteristics that were significant at $p < 0.20$ when included separately in the minimally adjusted regression models for each subscale. The missing indicator method was used to retain individuals with missing covariates in the analyses (Miettinnen, 1985). All statistical analyses were conducted in Stata version 12 (Stata Corp, College Station, TX).

2.5 | Ethics

Institutional review boards at the Harvard T.H. Chan School of Public Health, the National Institute of Medical Research, and Muhumbili University for Health and Allied Sciences approved the parent trial and the child development follow-up study.

3 | RESULTS

3.1 | Participants

Of the 2,500 women enrolled in the parent study, 1,112 had a child who was alive at 6 weeks of age (time of discharge from parent trial) and was 18–36 months of age at the time of recruitment for the current study. Attempts were made to enroll 608 of these eligible children, of whom 198 participated in child development follow-up study. The sample size was limited by those that had available contact information and funding constraints. A flow chart outlining participant selection is shown in Figure S1.

Maternal and child characteristics are reported in Table 1. The average age of mothers during pregnancy was 23.4 years (SD ± 3.8), 60% of mothers had completed some primary education, and half of the mothers were under 155 cm tall. Just over half of the children included in the follow-up were female, and the average child age at follow-up was 27.5 months (*SD* ± 4.5). Around 20% of the children for whom we had both weight and gestational age information at birth were born SGA. Means and SDs for scores on each of the CREDI subscales are reported in Table 1. We also present baseline characteristics of the study population by randomization arm in Table S1, which suggests balance between arms. No participants were excluded from analyses for the cognitive or socioemotional domains, and 20% of women had incomplete data and were excluded from the motor domain analysis.

Table S2 displays a comparison of characteristics of the mothers and children included in the child development follow-up study sample with those from the parent trial who were not included. When compared with the mothers not in our sample, mothers in our sample were older and had children with higher birthweights, though these differences were small in magnitude. Additionally, preterm births were underrepresented in follow-up study participants as compared with the trial population ($p < 0.05$).

3.2 | Prenatal characteristics and child development

The relationships between prenatal maternal characteristics and child development are presented in Table 2. In the fully adjusted prenatal maternal characteristics model, children whose mothers were randomized to receive prenatal vitamin A were reported to have significantly lower scores on the motor subscale of the CREDI, −0.29 SD, 95% CI [−0.54, −0.04], as compared with those who did not receive vitamin A. Maternal stature <155 cm was associated with lower reported scores on the cognitive/language subscale, −0.26 SD, 95% CI [−0.52, −0.00], and children whose mothers completed primary school education achieved 0.32 SD, 95% CI [0.05, 0.60], higher motor scores and 0.37 SD, 95% CI [0.11, 0.64], higher cognitive/language scores, as compared with children whose mothers did not complete primary school education. Mothers' age during pregnancy, mothers' body mass index in the first trimester, wealth during pregnancy, and anaemia during first trimester were not significantly associated with outcomes on any of the three subscales.

3.3 | Birth and early child characteristics and development

The relationships between birth and early child characteristics and child development are presented in Table 3. In the fully adjusted birth and early child characteristics models, children who were reported to experience high stimulation were also reported to show significantly higher scores on the cognitive/language subscale, 0.38 SD, 95% CI [0.14, 0.63], whereas children who were reported to experience verbal and physical punishment had significantly lower scores on the socioemotional subscale, −0.29 SD, 95% CI [−0.52, −0.05]. Preterm birth, birthweight, SGA, HAZ, WAZ, WHZ, and stunting were not significantly associated with child development outcomes on any of the three subscales.

In all fully adjusted models, child age group was significantly ($p < 0.03$) associated with child development score for all developmental domains.

4 | DISCUSSION

We identified several prenatal and early childhood characteristics associated with caregiver reported motor, cognitive/language, and socioemotional development among children 20–39 months of age in Dar es Salaam, Tanzania. Overall, our results suggest that different types of biological and environmental factors convey unique risk for different early developmental outcomes. On the motor development subscale, we found that randomized prenatal vitamin A supplementation was associated with lower scores whereas greater maternal education was associated with higher scores. On the cognitive/language development subscale, we found that children of mothers with greater schooling, children who experience high levels of parental stimulation, and those whose mothers were ≥155 cm tall obtained higher scores. On the socioemotional subscale, children who were reported to have experienced verbal and physical punishment obtained lower scores, indicating that they had more difficulty getting along with others as well as controlling their emotions and behaviours.

We found that children whose mothers received prenatal vitamin A supplements were reported to perform significantly worse on the motor development subscale. We found no significant effect of prenatal vitamin A supplementation on cognitive/language or socioemotional development. The effect of vitamin A on motor development scores was not expected and adds to a body of research showing mixed effects of maternal vitamin A supplementation on maternal and child health. In Bangladesh, there was no effect of maternal vitamin A supplementation on general intelligence, memory, or motor function at 8 years of age, though there was a small improvement in scholastic achievement amongst the children who received both antenatal and newborn supplementation (Ali et al., 2017). In a vitamin A sufficient population in Nepal, there was no difference in developmental status between prenatal vitamin A supplemented and placebo groups at 10–13 years of age (Buckley et al., 2013). Previous work in Tanzania examined the relationship between maternal vitamin A supplementation and development outcomes at 6 months of age in a trial of children born to human immunodeficiency virus-infected mothers and found a beneficial association between maternal vitamin A supplementation with motor development scores at 6 months for children whose mothers' baseline CD4 count was <200 cells/mm3 (McGrath et al., 2006). To our knowledge, our work is the first to assess prenatal vitamin A supplementation and child development outcomes between 1.5 and 3 years of age.

There are several potential explanations for our finding that maternal vitamin A supplementation produced harmful effects on motor function and did not provide benefits on cognitive/language and socioemotional development in the Tanzanian setting. Notably, we recently determined the prevalence of moderate vitamin A deficiency (defined as serum retinol <0.07 μmol/L) in Dar es Salam to be low (8%) in a separate pregnancy cohort (Masanja et al., 2015). In the parent trial, we found no effect of prenatal vitamin A on placental malaria, small-for-gestational age birth, or prematurity (Darling et al., 2017). As a result, the low level of deficiency in this population may have led to no effect of supplementation on maternal and child health, cognitive/language, and socioemotional outcomes. There are also known teratogenic concerns of high vitamin A intake and supplementation in pregnancy (Dibley & Jeacocke, 2001). Retinoic acid embryopathy can cause underdevelopment of the cerebellum and structural malformations of the cerebral cortex (Brent, Hendrickx, Holmes, & Miller, 1996; Dibley & Jeacocke, 2001). There is also evidence in rats that high-dose vitamin A supplementation reduces both locomotor and exploratory behaviours (de Oliveira et al., 2007). We did not find any association between prenatal zinc supplementation and any domain of early child development. Although our negative motor developments findings for vitamin A are not definitive, they support the need for more research on the long-term effects of vitamin A and other micronutrient supplementation interventions in LMICs.

Maternal stature is affected by a confluence of factors over a woman's lifetime including genetics, nutrition, and infectious disease exposures (Christian, 2010). We found children born to women with a height of <155 cm had lower cognitive/language scores than their peers born to taller mothers. These findings are consistent with our previous work in rural Tanzania where children whose mothers were <150 cm tall had 0.10 SD lower cognitive development scores as compared with a >155 cm reference group (Sudfeld et al., 2015). This finding highlights the importance of focusing on nutrition and health throughout early life and adolescence, as there may be intergenerational effects of maternal nutrition and growth. In our study, we found no statistically significant association between child HAZ, stunting status, WHZ or WAZ, and child development outcomes; however, we may have been underpowered. The direction and magnitude of the results for stunting status are similar to the results found in the most recent meta-analysis on linear growth and child development outcomes, which found robust evidence that children's HAZ is associated with cognitive and motor development (Sudfeld et al., 2015).

Maternal education and child stimulation were both strong predictors of reported cognitive/language development. We also found that reported motor development scores were higher with more maternal education and greater stimulation, though results were not statistically significant for the latter relationship. It is well documented that maternal education is associated with child development in high-income and LMIC settings (e.g., Fernald, Weber, Galasso, & Ratsifandrihamanana, 2011). In a recent meta-analysis, the weighted mean effects of stimulation interventions were 0.42 and 0.47 SDs for language and cognitive development scores, respectively (Aboud & Yousafzai, 2015). As such, our effect size of 0.38 SD is aligned with previous intervention work and reinforces the potential for stimulation interventions to provide large effects on early child development. We also found that children who were reported to have experienced verbal and physical punishment were reported to perform worse on the socioemotional subscale. Child maltreatment is considered to be a risk factor for child development outcomes globally (Britto et al., 2017). A cross-sectional observational study in Mozambique found that an intervention that was related to a reduction in harsh punishment was also related to fewer conduct problems in preschool-aged children (Skar, Sherr, Clucas, & von Tetzchner, 2014). Furthermore, evidence from the Netherlands and the Ukraine demonstrates that verbal and physical punishment is associated with internalizing and externalizing symptoms in children (Burlaka, 2016; van der Sluis, van Steensel, & Bögels, 2015). However, there is limited research on harsh disciplining practices in LMICs, and to our knowledge, this is the first study to examine the association between caregiver-reported verbal and physical punishment and development in children under the age of three living in a low-income country.

We acknowledge several limitations. First, the small sample size reduces power to detect factors that have moderate to small associations with child development. Second, the sociodemographic questionnaire and child development assessment were conducted as a caregiver report, allowing for both recall and social desirability bias, especially for questions about parenting practices. However, 57% of caregivers report verbal and physical punishment indicating that social desirability bias may not have a large effect on the reporting of this indicator. In addition, there is also a risk of selection bias because only a subset of the trial participants that we attempted to contact were reachable, consented, and had child development assessed (~35%). Nevertheless, we found that mothers and children who were enrolled in the follow-up study were similar to those who were unable to be assessed, possibly indicating low risk of selection bias. In addition, this study was conducted among Tanzanian women residing in Dar es Salaam who were enrolled in the first trimester of pregnancy, therefore the results may not be directly generalizable to women who start antenatal care late in pregnancy (or who do not seek care at all) and those who live in rural areas or other contexts. Finally, there are several unmeasured factors related to the home environment, parenting practices, and delivery and neonatal conditions that we were not able to capture, such as maternal depression, social and emotional neglect, neonatal infection, delivery complications, and an observation of mother–child interaction, which may be strongly associated with child development outcomes. Future research is needed to explore the mediating and moderating roles of these related constructs and conditions.

4.1 | CONCLUSION

The current study suggests that different types of risk factors (e.g., environmental and biological) may be differentially related to children's reported developmental outcomes early in life. The range of prenatal and early life factors determined to be associated with motor, cognitive, language, and socioemotional development of Tanzanian children in this study provides additional evidence for the need for integrated interventions that target the diverse set of factors associated with child development. Randomized trials and implementation evaluations of integrated environmental, nutritional, educational, and stimulation intervention packages are needed in resource-limited settings.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Key messages

- Prenatal vitamin A supplementation in a setting with low levels of vitamin A deficiency may not provide child development benefits.
- Children who experienced verbal and physical punishment had significantly lower scores on the socioemotional subscale.
- The range of prenatal and early life factors determined to be associated with motor, cognitive, language, and socioemotional development of Tanzanian children in this study provides additional evidence for the need for integrated interventions that target the diverse set of factors associated with child development.
- Randomized trials and implementation evaluations of integrated environmental, nutritional, educational, and stimulation intervention packages are needed in resource-limited settings.

TABLE 1

Maternal and child characteristics of assessed participants

Characteristic	Mean ± SD or Frequency (%)
Maternal characteristics	
Maternal age at birth (years)	23.4 ± 3.8
Maternal education	8.1 ± 2.98
<5 years	14 (7.1)
5–7 years	119 (60.1)
8+ years	65 (32.8)
Subsequent child	19 (9.6)
Maternal height (cm)	155.0 ± 5.8
Maternal height <155	99 (50.0)
Maternal prenatal supplementation regimen	
Vitamin A	53 (26.8)
Zinc	46 (23.2)
Both	38 (19.2)
Placebo	61 (30.8)
Anaemia in first trimester (Hb < 11)	64 (33.7)
Anaemia at delivery (Hb < 11)	77 (56.2)
Asset index score	3.76 (2.4)
0–2	66 (35.7)
3–5	74 (40.0)
6+	45 (24.3)
Delivery characteristics	
Female	98 (51.6)
Birthweight (kg)	3.1 (0.5)
Low birthweight, (<2,500 g)	7 (3.7)
Preterm (<37 weeks)	29 (14.7)
Small-for-gestational age (<10%)	38 (20.3)
Characteristics at follow-up	
Age at follow up (months)	27.5 ± 4.5
Anthropometry	
Height-for-age *z*-score (HAZ)	−1.4 ± 1.1
Stunted (HAZ < −2)	53 (27.9)
Weight-for-height *z*-score (WHZ)	0.24 ± 1.2
Wasted (WHZ < −2)	4 (2.1)
Weight-for-age *z*-score (WAZ)	−0.55 ± 1.0
Underweight (WAZ < −2)	14 (7.4)
Stimulation and punishment at follow-up	
Verbal and physical punishment	113 (57)
Stimulation score (0–6)	3.46 ± 1.23
High stimulation (>3)	94 (47.47)

Characteristic	Mean ± SD or Frequency (%)
CREDI scores	
Motor domain	0.72 ± 0.26
Cognitive domain	0.69 ± 0.18
Socioemotional domain	0.65 ± 0.17

Note. CREDI: Caregiver Reported Early Childhood Development Index.

TABLE 2

Standardized mean differences (SMDs) in motor, cognitive/language, and socioemotional development for prenatal maternal characteristics

	Motor				Cognitive/language				Socioemotional			
	Minimally adjusted SMD[a]	***p***	**Fully adjusted SMD[b]**	***p***	**Minimally adjusted SMD[a]**	***p***	**Fully adjusted SMD[b]**	***p***	**Minimally adjusted SMD[a]**	***p***	**Fully adjusted SMD[b]**	***p***
Maternal age												
20 years & under	0.03 (−0.29–0.35)	0.85	–		−0.04 (−0.38–0.30)	0.82	–		−0.02 (−0.35–0.30)	0.82	−0.07 (−0.40–0.25)	0.66
21–24 years	Ref		–		Ref		–		Ref		Ref	
25 years & over	−0.08 (−0.40–0.25)	0.63	–		0.06 (−0.24–0.36)	0.70	–		0.20 (−0.07–0.47)	0.15	0.25 (−0.02–0.53)	0.07
Maternal education												
No primary (0–4 years)	−0.09 (−0.44–0.26)	0.62	−0.13 (−0.47–0.22)	0.48	0.12 (−0.35–0.58)	0.62	0.07 (−0.41–0.56)	0.77	0.21 (−0.23–0.65)	0.34	0.29 (−0.14–0.72)	0.19
Some primary (5–7 years)	Ref		Ref				Ref		Ref		Ref	
Primary + (8+ years)	0.33 (0.06–0.59)	0.02 *	0.32 (0.05–0.60)	0.02 *	0.41 (0.15–0.68)	<0.01 *	0.37 (0.11–0.64)	0.01 *	0.03 (−0.23–0.28)	0.84	0.05 (−0.20–0.30)	0.67
Asset tertiles (asset sum)												
T1 (Poorest, 0–2)	Ref		Ref		Ref		Ref		Ref		Ref	
T2 (3–5)	0.01 (−0.31–0.33)	0.95	−0.05 (−0.37–0.27)	0.76	0.07 (−0.23–0.37)	0.65	0.07 (−0.24–0.38)	0.64	−0.04 (−0.31–0.22)	0.75	−0.03 (−0.31–0.23)	0.77
T3 (Richest, 6+)	0.12 (−0.23–0.47)	0.52	0.05 (−0.32–0.40)	0.81	0.32 (−0.01–0.64)	0.06	0.28 (−0.04–0.60)	0.09	−0.13 (−0.46–0.19)	0.42	−0.21 (−0.55–0.12)	0.21
BMI in first trimester (kg/m^2)												
<20	−0.12 (−0.43–0.19)	0.45	–		−0.05 (−0.33–0.24)	0.78	–		−0.02 (−0.38–0.35)	0.93	–	
20–25	Ref		–		Ref		–		Ref		–	
25+	0.13 (−0.16–0.42)	0.37	–		−0.12 (−0.41–0.18)	0.44	–		0.13 (−0.13–0.39)	0.32	–	
Randomized regimen												
Vitamin A	−0.23 (−0.53–0.07)	0.13	−0.25 (−0.55–0.05)	0.10	−0.00 (−0.32–0.31)	0.98	−0.00 (−0.31–0.31)	0.90	−0.16 (−0.48–0.16)	0.34	−0.22 (−0.53–0.09)	0.17
Zinc	−0.03 (−0.38–0.32)	0.87	−0.03 (−0.39–0.33)	0.88	−0.07 (−0.39–0.26)	0.68	−0.06 (−0.39–0.27)	0.73	−0.05 (−0.35–0.26)	0.77	−0.05 (−0.35–0.24)	0.72

	Motor				Cognitive/language				Socioemotional			
	Minimally adjusted SMD[a]	***p***	**Fully adjusted SMD[b]**	***p***	**Minimally adjusted SMD[a]**	***p***	**Fully adjusted SMD[b]**	***p***	**Minimally adjusted SMD[a]**	***p***	**Fully adjusted SMD[b]**	***p***
Both	−0.39 (−0.80–0.01)	0.06	−0.37 (−0.78–0.03)	0.07	0.01 (−0.34–0.35)	0.96	−0.02 (−0.37–0.33)	0.91	0.24 (−0.14–0.62)	0.21	0.22 (−0.15–0.60)	0.25
Placebo	Ref		Ref		Ref		Ref		Ref		Ref	
Dichotomized regimen[c]												
Zinc containing regimen vs. placebo	−0.08 (−0.36–0.20)	0.57	−0.05 (−0.33–0.22)	0.70	−0.03 (−0.28–0.22)	0.80	−0.04 (−0.30–0.21)	0.74	0.03 (−0.21–0.27)	0.81	0.18 (−0.07–0.42)	0.15
Vitamin A containing regimen vs. placebo	−0.28 (−0.54 to −0.03)	0.03*	−0.29 (−0.54 to −0.04)	0.03*	0.03 (−0.22–0.28)	0.80	0.02 (−0.23–0.26)	0.88	0.16 (−0.08–0.40)	0.19	−0.01 (−0.25–0.23)	0.95
Anaemia in first trimester												
<11 g/dl	−0.12 (−0.38–0.15)	0.40	–		−0.11 (−0.37–0.16)	0.45	–		0.14 (−0.10–0.38)	0.25	–	
Maternal height												
<155 cm	−0.12 (−0.39–0.14)	0.37	–		−0.27 (−0.52 to −0.12)	0.04*	−0.26 (−0.52 to −0.00)	0.05*	−0.13 (−0.37–0.11)	0.28	–	

Note. BMI: body mass Índex.

[a] Minimally adjusted models include child sex, interviewer, and child’s age group.

[b] Fully adjusted models include child sex, interviewer, child’s age group, maternal education, asset tertiles, randomized regimen, and all characteristics included in the table with $p < 0.20$ in minimally adjusted model.

[c] Dichotomized regimen, zinc and vitamin A versus placebo were included separately in a model that did not include randomized regimen. Results for all variables other than the dichotomous regimen variables include the randomization regimen.

* $p < 0.05$.

TABLE 3

Standardized mean differences (SMDs) in motor, cognitive/language, and socioemotional development for early life child characteristics

	Motor				Cognitive/language				Socioemotional			
	Minimally adjusted SMD[a]	*p*	Fully adjusted SMD[b]	*p*	Minimally adjusted SMD[a]	*p*	Fully adjusted SMD[b]	*p*	Minimally adjusted SMD[a]	*p*	Fully adjusted SMD[b]	*p*
Female	0.11 (−0.15–0.37)	0.01*	0.12 (−0.14–0.39)	0.36	0.23 (−0.02–0.48)	0.07	0.21 (−0.04–0.46)	0.09	0.11 (−0.15–0.36)	0.42	0.08 (−0.17–0.34)	0.51
Birth characteristics												
Preterm (<37 weeks)	−0.03 (−0.39–0.32)	0.87	–		0.20 (−0.11–0.53)	0.21	–		0.12 (−0.23–0.46)	0.51	–	
Birthweight per 100 g	0.01 (−0.01–0.04)	0.36	–		−0.00 (−0.03–0.02)	0.88	–		−0.02 (−0.05–0.01)	0.17	−0.02 (−0.05–0.01)	0.19
SGA (<10%)	−0.07 (−0.36–0.21)	0.61	–		0.02 (−0.23–0.31)	0.87	–		0.12 (−0.16–0.41)	0.40	–	
Anthropometry												
HAZ	0.05 (−0.06–0.17)	0.37	–		0.07 (−0.04–0.19)	0.22	–		0.04 (−0.07–0.15)	0.52	–	
WAZ	0.05 (−0.06–0.17)	0.37	–		0.00 (−0.14–0.14)	0.98	–		0.06 (−0.06–0.17)	0.35	–	
WHZ	0.02 (−0.09–0.15)	0.66	–		−0.05 (−0.18–0.08)	0.45	–		0.03 (−0.07–0.12)	0.56	–	
Stunted	−0.21 (−0.49–0.07)	0.14	−0.11 (−0.41–0.18)	0.44	−0.26 (−0.56–0.05)	0.10	−0.19 (−0.49–0.11)	0.21	−0.24 (−0.50–0.02)	0.07	−0.22 (−0.49–0.06)	0.12
High stimulation score (>3)	0.24 (−0.01–0.50)	0.06	0.18 (−0.07–0.43)	0.16	0.52 (0.29–0.72)	<0.01*	0.38 (0.14–0.63)	<0.01*	0.14 (−0.10–0.38)	0.26	–	
Books in home	0.17 (−0.08–0.43)	0.17	0.06 (−0.20–0.32)	0.66	0.37 (0.12–0.62)	<0.01*	0.14 (−0.14–0.42)	0.31	0.15 (−0.09–0.39)	0.22	–	
Verbal and physical punishment	0.20 (−0.05–0.45)	0.11	0.18 (−0.07–0.44)	0.16	−0.04 (−0.30–0.21)	0.75	−0.03 (−0.27–0.21)	0.82	−0.33 (−0.56 to −0.10)	<0.01*	−0.29 (−0.52 to −0.05)	0.02*

Note. HAZ: height-for-age z-scores; SGA: small-for-gestational-age; WAZ: weight-for-age z-scores; WHZ: weight-for-height z-scores.

[a] Minimally adjusted models include child sex, interviewer, and child's age group.

[b] Fully adjusted models include child sex, interviewer, child's age group, maternal education, asset tertiles, randomized regimen, and all characteristics included in the table with $p < 0.20$ in minimally adjusted model. Birthweight and stunted were included in sepárate models to avoid adjusting for upstream factors. Results presented for other variables are from model including stunting.

* $p < 0.05$.