8-Year Follow-up of a Maternal Education Trial in a Low-Resource Setting

Paul Kakwangire, MSc,[a] Grace Muhoozi, PhD,[b] Moses Ngari, PhD,[c] Nicholas Matovu, PhD,[d] Ane Cecilie Westerberg, PhD,[e,f] Per Ole Iversen, MD,[a,g,h] Prudence Atukunda, PhD[i]

abstract

OBJECTIVES: Nutrition and stimulation interventions promote early childhood development, but little is known about their long-term benefits in low- and middle-income countries. We conducted a follow-up study of a cluster-randomized maternal education trial performed in children aged 6 to 8 months to assess the sustainability of developmental benefits after 8 years.

METHODS: The education intervention lasted 6 months and consisted of nutrition, hygiene, sanitation, and child stimulation aspects. We assessed child processing and cognitive abilities using the Kaufman Assessment Battery for Children Second Edition (KABC-II) and attention and inhibitory control using the Test of Variables of Attention after 8 years. The original trial included 511 mother-child pairs (intervention, $n = 263$; control, $n = 248$), whereas in the current study, 361 (71%; intervention, $n = 185$; control, $n = 176$) pairs were available for analyses.

RESULTS: The intervention group scored higher than the controls (all $P < .001$) on all 5 KABC-II subscales and on the KABC-II global score (mean difference: 14; 95% confidence interval, 12–16; $P < .001$). For all 5 Test of Variables of Attention variables, the intervention group scored higher than the controls on both the visual and auditory tasks (all $P < .05$). Because the intervention was delivered as a package, a limitation is that we cannot pinpoint the individual contribution of each component (nutrition, hygiene, and stimulation) to the developmental benefits.

CONCLUSIONS: The intervention group consistently scored markedly higher on both neuropsychological tests. Thus, even 8 years after the original maternal education intervention, the developmental benefits that we observed at child age of 1, 2, and 3 years, were sustained.

[a]Department of Nutrition, IMB, University of Oslo, Oslo, Norway; [b]Department of Nutritional Sciences and Dietetics, Kyambogo University, Kampala, Uganda; [c]KEMRI Wellcome Trust Research Programme, Kilifi, Kenya and Department of Public Health, School of Health & Human Sciences, Pwani University, Kilifi, Kenya; [d]Centre for Public Health, Institute of Clinical Sciences Block B, Queen's University, Belfast, UK; [e]Division of Obstetrics and Gynecology, Department of Obstetrics, Oslo University Hospital Rikshospitalet, Oslo, Norway; [f]School of Health Sciences, Kristiania University College, Oslo, Norway; [g]Department of Haematology, Oslo University Hospital, Oslo, Norway; [h]Division of Human Nutrition, Stellenbosch University, Tygerberg, South Africa; and [i]Center for Crisis Psychology, Faculty of Psychology, University of Bergen, Bergen, Norway

Mr Kakwangire collected and analyzed the data, drafted the initial manuscript, and critically reviewed and revised the manuscript; Drs Muhoozi and Iversen and Ms Atukunda conceptualized and designed the study, supervised data collection, and critically reviewed and revised the manuscript; Dr Ngari performed statistical analyses of the data and critically reviewed and revised the manuscript; Dr Matovu collected data and critically reviewed and revised the manuscript; Dr Westerberg conceptualized and designed the study and critically reviewed and revised the manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

The study is registered at ClinicalTrials.gov (ID: NCT02098031).

WHAT'S KNOWN ON THIS SUBJECT: Nutrition and stimulation interventions may promote early childhood development. However, little is known about the long-term benefits of such interventions, particularly in low- and middle-income countries.

WHAT THIS STUDY ADDS: Eight years after a randomized maternal education trial in rural Uganda, child development outcomes remained improved in the intervention compared with controls. Our study supports interventions in the early months of life to promote adequate developmental trajectories in small children.

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ARTICLE

Progress of any society is highly dependent on its human resources and therefore appropriate attention given to development of children at an early age is vital for a future productive generation.[1,2] Strategies to ensure that every child thrives and attains full developmental potentials, are in line with the United Nations' Sustainable Development Goals, in particular Sustainable Development Goal 3: "Good health and well-being."[3,4] Development includes progressive changes in the functioning capacity of emotional, physical, mental, and social skills.[5] Adequate nutrition, hygiene, and stimulation, especially from conception and throughout the first 2 years of life, are critical for good development and health in later life.[6] The biological and psychological changes that occur during these early years of life comprise rapid development of brain structures, volumes, neuronal connectivity, myelination as well as language, cognitive, social-emotional, and motor skills.[7]

Nutrition plays a crucial role in brain development, and any nutritional deficiencies during the first years of life can result in delayed and impaired neurodevelopment.[8] In particular, the need for sufficient nutrient supply has been linked to the development of executive functions,[9] a term used to describe the ability to consciously control thoughts, actions, and emotions to achieve goals.[10] The 3 core dimensions of executive functions are inhibitory control, working memory, and cognitive flexibility.[10] Therefore, optimal nutrition during infancy and childhood to facilitate healthy neurologic and cognitive development is crucial. In addition, the importance of stimulation from both the caregivers/parents and the child's environment has become evident.[11] Thus, a combination of nutritional support and stimulation interventions during early life is key to promote early childhood development.[12]

Despite this knowledge, poverty and undernutrition, especially stunting (reduced height-for-age, a marker for chronic undernutrition), have left millions of children in low- and middle-income countries (LMICs) unable to attain their full development potential.[13] For example, Uganda faces high rates of childhood undernutrition with nearly one third of its children younger than age 5 years stunted.[14]

Research shows that parenting interventions, including child nutritional support and stimulation in the first years of life, promote early childhood development.[15–17] Although such interventions are beneficial in the early stages of life, their long-term outcomes are not well understood, particularly in LMICs.[18]

In 2013–2014, we conducted the Child Nutrition and Development (CHNUDEV) study, a 2-armed, cluster-randomized controlled trial (RCT) among children aged 6 to 8 months in rural Uganda.[19] We examined child stunting and development outcomes after a 6-month maternal education intervention focusing on nutrition, hygiene, sanitation, and child stimulation. Whereas the prevalence of stunting remained fairly constant until school start (children aged 6 years),[20,21] concurrent stunting and overweight was significantly reduced in the intervention group compared with the controls.[22]

Notably, follow-up studies of the CHNUDEV cohort at child ages of 1 ($n = 467$), 2 ($n = 467$), and 3 ($n = 155$) years demonstrated that the maternal education intervention promoted and maintained development domains in cognitive, language, and motor skills.[20,23] The aim of the current follow-up study was to assess whether these positive effects on child development were sustained at age 8 years (ie, after commencing education in primary school).

METHODS

Approvals

The CHNUDEV study was approved by the Uganda National Council for Science (no. HS1809), Makerere University School of Public Health, Higher Degrees Research and Ethics Committee (no. IRB 000353), and the Norwegian Regional Committee for Medical and Health Research Ethics (no. 2013/1833).

Study Area and Participants

Mothers and their infants aged 6 to 8 months' old were recruited to the original RCT between October 2013 and February 2014 in the rural districts of greater Kabale and Kisoro in Southwestern Uganda (Supplemental Information; Supplemental Fig 5). Children who had physical or congenital malformations that would affect food intake, growth, mental, or brain function as evidenced by mother or health worker were excluded.

Sample size calculation, enrollment, and randomization of the study participants in the original RCT has been detailed in the Supplemental Information and elsewhere.[20] Briefly, simple random sampling was performed to allocate 10 subcounties (clusters) in the 2 districts (6 from Kabale and 4 from Kisoro) to either the intervention or control group. All villages in each subcounty (intervention or control) were listed alphabetically and computer-generated random numbers were then used to obtain the villages; finally, complete enumeration was used to obtain participating households. The youngest eligible child was selected from each household and for twins, 1 of the 2 was selected by simple random sampling.

Intervention in the Original RCT

The intervention consisted of an education package containing information on nutrition, hygiene, sanitation, and child stimulation delivered to groups of mothers by trained personnel. Details are given in the Supplemental Information and by Muhoozi et al.[20] Briefly, behavioral change communication techniques were used to deliver the messages and demonstrations on the guiding principles of complementary feeding, food preparation, good hygiene practices, and child stimulation. Graduate nutritionists and a psychologist trained in the education package delivered the intervention and were supervised by the principal investigators. Each group of mothers had a leader who, in most cases, would be a member of the village health team. This team leader was responsible for following up the group members and encouraging them to put the educational messages into practice. The intervention was delivered on a monthly basis for 6 months followed by booster sessions. As detailed in the Supplemental Information, the booster sessions were conducted to keep reminding mothers about the intervention messages. The sessions were delivered on a 3-monthly basis, each lasting about 6 hours and given until the children were 3 years of age. The control group received routine health care (nutritional assessment, deworming, immunization, and vitamin A supplementation).

Assessment of Outcomes

Trained bachelor's degree graduates in psychology blinded to group allocation, assessed the child development outcomes, from January to July 2022. This assessment team was not part of the previous data collection teams. The age-appropriate Kaufman Assessment Battery for Children Second Edition (KABC-II) and the Test of Variables of Attention (TOVA) were used. For every child, these 2 neuropsychological tests were administered on 2 separate days, with KABC-II done first because it is more extensive than TOVA.

The Kaufman Assessment Battery for Children

KABC-II is an individually administered test of cognitive and processing capabilities for individuals aged 3 to 18 years.[24] The test comprehensively assesses cognitive ability and has previously been validated in a Ugandan setting similar to our study area.[25] KABC-II is organized in a number of subtests on which children are assessed and scored, higher score means better performance. The subtest raw scores are then grouped into 5 scales: (1) sequential, (2) simultaneous, (3) learning, (4) planning, and (5) knowledge. Our assessments were based on the Cattell-Horn-Carroll model of KABC-II which combines all the 5 scales into a global scale (Fluid-Crystallized Index [FCI]).[24] The Cattell-Horn-Carroll model terms the 5 scales as: (1) Short-Term memory, (2) Visual processing, (3) Long-Term Storage and Retrieval, (4) Fluid Reasoning, and (5) Crystallized Ability (Supplemental Table 5). The scores from the FCI were used to group the children into 5 different categories: upper extreme (scores 131 or higher), above average (scores 116–130), average (scores 85–115), below average scores (70–84), and lower extreme (scores 69 or below).[24] Further details are given in the Supplemental Information.

Test of Variables of Attention

We used the computerized TOVA visual and auditory continuous performance test to measure attention and impulse control processes in four areas: (1) response time variability, (2) response time, (3) impulse control (commission errors), and (4) inattention (omission errors). Each of the visual and auditory tests (Supplemental Information) lasted 22 minutes for each child. During the test, responses to visual or auditory stimuli were recorded by the TOVA device (software version 9.1). Whereas this device generates a number of response parameters and variables, z-scores were considered for this study.[26] The z-scores are generated by comparing individual performances with a normative sample (individuals with no attention deficits) by age and gender and presented on 5 variables including: (1) Omission Errors, the sum of incorrect nonresponses to the target stimulus divided by the total number of target stimuli presented; (2) Commission Errors, the sum of incorrect responses to the nontarget stimuli divided by the number of presented nontarget stimuli; (3) Response Time Variability, estimates the time differences for accurate (correct) responses registered by the child. It measures how consistent the child's speed is in responding correctly, the slower the child responds, the higher the variability is; (4) Mean Response Time, the average amount of time a child takes to make correct responses from when target stimuli are presented. It is derived from the sum of correct response time divided by the number of target stimuli presented, and (5) the calculated "D prime." Interpreted as a measure of "perceptual sensitivity," the D prime denotes the ratio of correct response rate to a "false alarm" rate. It highlights how accurate the child is in differentiating target and nontarget stimuli. Further details are given in the Supplemental Information. Results from the TOVA sessions are presented in 4 quarters (5.4 minutes), 2 halved sessions (10.8 minutes), and the total session (22 minutes) for each of the 5 variables.[26,27] We used the total session scores in our analysis. Each child was first given about 3 minutes of practice for each of the visual and auditory tasks to help them get familiar with the test and understand the target and nontarget stimuli. The TOVA test has been used in similar settings as a reliable assessment of attention and identification of attention deficits.[28,29]

Study Sample Size Calculation

The original RCT was powered at 80%, with an α of 0.05 to detect changes in continuous height-for-age z scores.[20] The current follow-up study used the intention-to-treat approach where all children assessed were included in the analysis; hence, no new sample size was estimated.

Statistical Analysis

Statistical analyses were conducted using Stata version 17.0 (StataCorp, College Station, TX). Statistical significance was assessed using a 2-tailed $P < .05$ and cluster-adjusted 95% confidence interval (CI). Because approximately one third of the children recruited in the original RCT were not assessed in the current follow-up study, we present baseline characteristics (ie, when the children were aged 6–8 months) for both the original RCT cohort and for the current follow-up cohort to show that the latter cohort was quite similar to the original RCT cohort. Moreover, to examine if the baseline characteristics of the 2 study groups (intervention and control) were well balanced in the follow-up study cohort, we calculated cluster-adjusted *P* values.

The KABC-II standard scores (short-term memory, visual processing, long-term storage and retrieval, fluid reasoning, and crystallized ability) were not normally distributed and therefore medians and interquartile ranges are reported. Cluster-adjusted absolute differences between the 2 study groups are reported and *P* values calculated as outlined previously. The means and standard deviation of both auditory and visual TOVA *z*-scores are presented because they are standardized scores with a normal distribution. Cluster-adjusted *t* tests were used to calculate mean differences in both auditory and visual TOVA *z*-scores and *P* values comparing the 2 study groups were from a multilevel mixed effect linear regression model explicitly accounting for the cluster as a random effect. The *P* values for the KABC-II standard scores and TOVA *z*-scores are adjusted for false discovery rate using the Benjamini-Hochberg method.[30]

RESULTS

Baseline Characteristics of the Study Participants

In the original RCT, we enrolled 511 children aged 6 to 8 months (intervention, 263; control, 248). In the current follow-up study, 361/511 (71%) children (intervention, 185/361, 51%; and control, 176/361, 49%) were available for analyses (Fig 1). The attrition overall was 150/511 (29%) and not significantly different ($P = .53$) between the intervention 87/263 (33%) and control 72/248 (29%).

Table 1 shows the baseline characteristics by study group for both the original RCT ($n = 511$) and the current follow-up study ($n = 361$). The child, maternal, and household characteristics were well balanced between the 2 study groups both in the original RCT[20] and in the current follow-up study. Importantly, at baseline, child growth and development characteristics did not differ significantly between the intervention and control groups in the original RCT or in the current follow-up study, indicating that adequate randomization at start of the original RCT was maintained for the current follow-up study. Because of COVID-19 disruptions, children delayed school enrollment and the majority were in the first school year at the time of data collection. There were no significant age differences between the intervention and control children.

Child Development Outcomes as Assessed With the KABC-II Test

All the KABC-II standard scores (short-term memory, visual processing, long-term storage and retrieval, fluid reasoning and crystallized ability) were significantly higher among children randomized to the intervention compared with the controls (cluster-adjusted $P < .001$) (Table 2; Supplemental Fig 6). The FCI global score was 14 (95% CI, 12–16; $P < .001$) points higher in the intervention group compared with the control group, indicating improved cognition and better processing abilities (Table 2; Fig 2B). The proportion of children with scores below the average/lower extreme on the FCI global score, combining the 5 subscales, was significantly lower in the intervention (72%) compared with the control (97%) group by 25 (95% CI, 18–32) (Fig 2A). With regard to the proportion of children categorized in the average, above average, or upper extreme groups, we found no significant differences between the 2 study groups.

Child Development Outcomes as Assessed With the TOVA Test

For all 5 variables of the TOVA test, children in the intervention group had significantly higher *z*-scores than the controls on both the auditory and visual tasks (Table 3; Supplemental Fig 7). Hence, the intervention children consistently responded correctly to the target stimuli faster than the control children. Furthermore, the intervention children made fewer errors in their responses than the control children. The mean *z*-score difference for commission errors shows that the control children were more impulsive (ie, they were more likely to press on the micro-switch based on the wrong stimulus [ie, nontarget]). Similarly, the difference in mean omission errors *z*-score implies that control children were less attentive (ie, less likely to press on the micro-switch when the target stimuli were presented). Moreover, the significant D prime *z*-score difference between the 2 study groups indicates that the intervention children more accurately discriminated between correct and incorrect stimuli compared with control children (Fig 3).

DISCUSSION

We report here that an education intervention delivered to mothers of 6- to 8-month-old children in a low-resource setting led to sustained child developmental benefits 8 years later. The intervention group performed significantly better than the control group on 2 independent neuropsychological tests (TOVA and KABC-II). On the KABC-II, the intervention children had better short-term and long-term memory abilities; in other words, they were better at

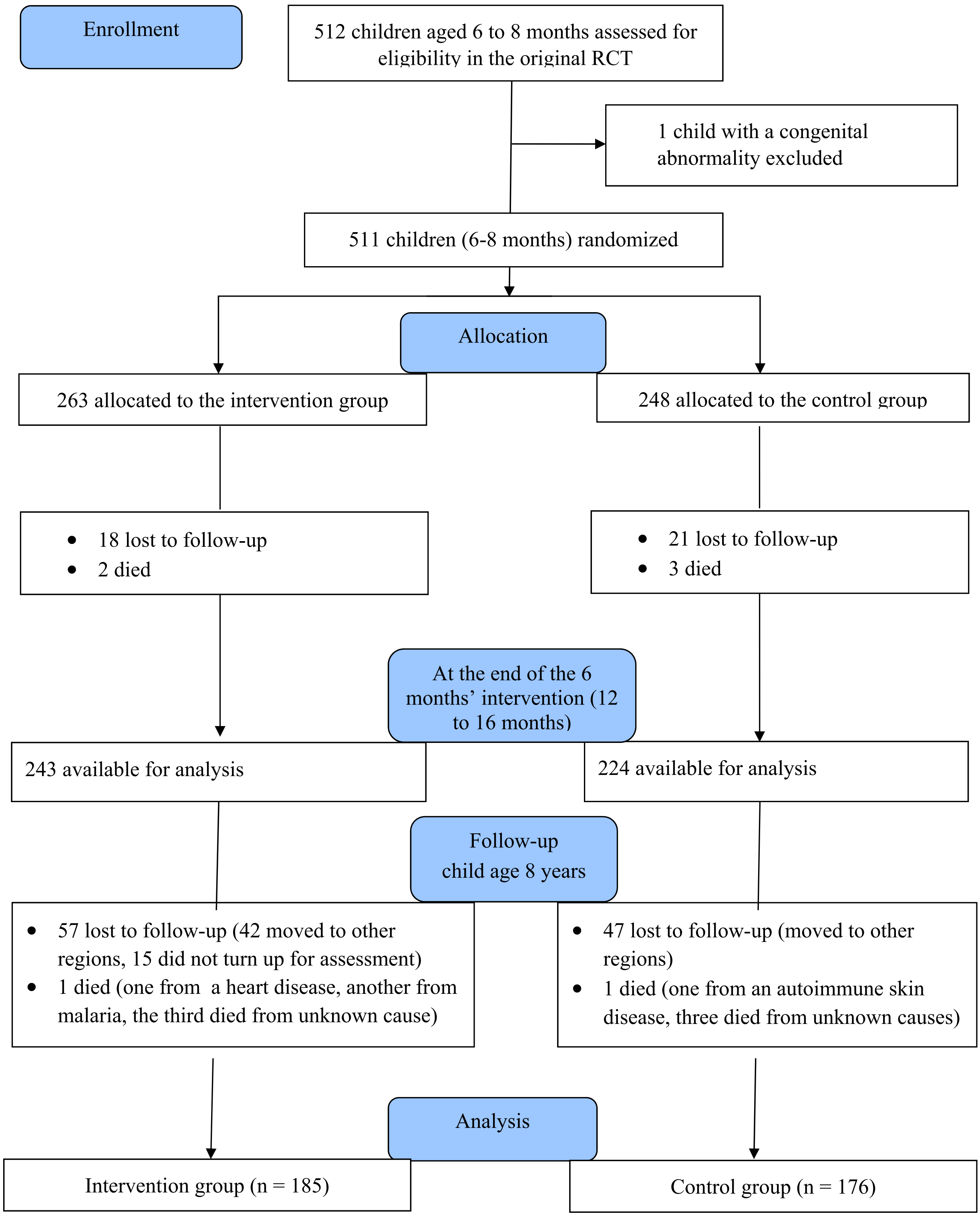

FIGURE 1
CONSORT flowchart. The flowchart illustrates the inclusion into the original cluster-randomized trial and current follow-up study.

taking in, holding, and using information immediately and after some time. Higher visual processing scores indicated that the intervention children had improved ability to use visual patterns to perceive, store, manipulate, and think compared with control children. Furthermore, the intervention group had acquired more knowledge and they applied better reasoning abilities to solve problems, as indicated by the differences in crystalized ability and

TABLE 1 Characteristics of the Enrolled and Follow-Up Participants					
	Original RCT Cohort (n = 511)		**Follow-Up Study Cohort (n = 361)**		
	Intervention (n = 263)	Control (n = 248)	Intervention (n = 185)	Control (n = 176)	P
Baseline					
Child characteristics					
Child sex					
Male	139 (53)	123 (50)	95 (51)	89 (51)	.90[a]
Female	124 (47)	125 (50)	90 (49)	87 (49)	
Child age (mo), mean (SD)	7.4 (0.8)	7.3 (0.9)	7.4 (0.9)	7.3 (0.9)	.28[b]
Exclusive breastfeeding					
Yes	184 (70)	178 (72)	124 (67)	130 (74)	.42[a]
No	79 (30)	70 (28)	61 (33)	46 (26)	
Length-for-age z-score, mean (SD)	−1.07 (1.15)	−1.21 (1.24)	−1.06 (1.20)	−1.17 (1.30)	.39[b]
Weight-for-age z-score, mean (SD)	−0.63 (1.10)	−0.72 (1.13)	−0.64 (1.10)	−0.70 (1.10)	.64[b]
Weight-for-length z-score, mean (SD)	0.12 (1.21)	0.15 (1.26)	0.10 (1.20)	0.16 (1.30)	.76[b]
Cognitive composite score, median (IQR)	100 (15)	105 (20)	100 (15)	105 (20)	.43[c]
Language composite score, median (IQR)	104 (14)	100 (14)	103 (21)	100 (20)	.14[c]
Motor composite score, median (IQR)	105 (14)	104 (15)	105 (21)	103 (21)	.61[c]
Maternal characteristics					
Maternal age (y), median (IQR)	25 (9)	26 (9)	26 (8)	27 (8)	.37[c]
Maternal education level					
None/primary	173 (66)	166 (67)	123 (67)	125 (71)	.83[a]
Lower secondary	64 (24)	62 (25)	47 (25)	39 (22)	
Tertiary	26 (10)	20 (8)	15 (8)	12 (7)	
Number of biological children					
$<$5	187 (71)	184 (74)	129 (70)	119 (68)	.66[a]
$\geq$5	76 (29)	64 (26)	56 (30)	57 (32)	
Household characteristics					
Household head age (y), median (IQR)	30 (11)	30 (13)	30 (10)	30 (13)	.17[c]
Household head education level					
None/primary			132 (71)	143 (81)	.13[a]
Secondary/tertiary			53 (29)	33 (19)	
Poverty score, median (IQR)	49 (17)	49 (18)	49 (13)	49 (17)	.55[c]
Household member size					
3–5 members	150 (57)	139 (56)	105 (57)	92 (52)	.39[a]
6–13 members	113 (43)	109 (44)	80 (43)	84 (48)	
Current					
Age at follow-up, mo			107.2 (0.35)	106.9 (0.25)	.46[b]
Child education					
Primary one			140 (76)	139 (79)	.63[a]
Primary two			41 (22)	35 (20)	
Primary three			4 (2)	2 (1)	

Values are n (%) unless otherwise stated. All P values (cluster-adjusted) refer to comparisons between the 2 study groups in the follow-up cohort. The anthropometrical z-scores were calculated according to World Health Organization recommendations, whereas the developmental composite scores were assessed using the Bayley Scales of Infant and Toddler Development Test-III. IQR, interquartile range; RCT, randomized controlled trial; SD, standard deviation.
[a] P values obtained via χ^2 tests.
[b] P values obtained via t tests.
[c] P values obtained via rank-sum tests.

fluid reasoning scales, respectively. On the TOVA test, the intervention children consistently responded faster to the target stimuli and made fewer errors in their responses, indicating that they more accurately distinguished between correct and incorrect stimuli than the control children.

The CHNUDEV study was designed as a pragmatic RCT, applying a low-cost (maternal education intervention in a challenging study area [remote parts of rural Uganda]) to improve child growth and development. There was no impact on child anthropometrical measures from end of the original RCT (child approximately

TABLE 2 KABC-II Scale Scores Between the 2 Study Groups

KABC-II Scale Scores	Intervention (n = 185) Median (IQR)	Control (n = 176) Median (IQR)	Difference (n = 361) Mean (95% CI)	P	FDR Adjusted P
Fluid-Crystallized Index global score	79 (12)	65 (11)	14 (12–16)	<.001	.001
Short-term memory	85 (17)	74 (15)	10 (8–13)	<.001	.001
Visual processing	93 (16)	72 (17)	20 (17–24)	<.001	.001
Long-term storage and retrieval	84 (14)	70 (17)	12 (10–15)	<.001	.001
Fluid reasoning	80 (15)	69 (11)	11 (9–14)	<.001	.001
Crystallized ability	81 (12)	72 (9)	10 (8–11)	<.001	.001

The values are median scores with interquartile range (IQR) or means with cluster-adjusted 95% confidence interval (CI). The P values are from a multilevel model accounting for the clustering effect. The FDR adjusted P values were adjusted using the Benjamini-Hochberg method. FDR; false discovery rate; KABC-II, Kaufman Assessment Battery for Children Second Edition.

aged 1 year) until school start (child approximately aged 6 years).[20,21] However, children in the intervention group over time consistently scored markedly better on various development outcomes using the tests of Bayley Scales of Infant and Toddler Development-III (BSID-III), Ages and Stages Questionnaire (ASQ), and Mullen Scales of Early Learning (Fig 4). Specifically, at 2 years of age, the intervention group had higher cognitive, language, and motor composite development scores than the controls on the BSID-III as well as higher ASQ scores on communication, gross motor, fine motor, problem solving, and personal–social development.[20] At 3 years, the intervention group still scored higher on all BSID-III development outcomes and the ASQ fine motor scores compared with the controls.[23] Notably, using the Mullen Scales of Early Learning, the fine motor, language, cognitive, and early learning composite standard scores were significantly higher in the intervention group at 3 years compared with the controls.[23]

Because our intervention did not significantly improve child stunting,[20] it is unlikely that the observed improvement in development among the intervention children was related to growth itself. It is possible that the stimulation component of the education intervention was the most important contributor to the sustained child developmental benefits as interventions focusing only on nutrition have apparently had minimal effect on child developmental outcomes,[16] but incorporating stimulation and nurturing aspects to the interventions profoundly promoted child development.[31] In support of this, we observed reduced self-reported maternal depression symptoms in the intervention group, and this reduction was associated with improved child cognitive and language development at 2 and at 3 years of age.[32] Based on group dynamics theory, the mothers may have been empowered by the intervention, leading to fewer depressive symptoms, and thus improved parenting skills.[33]

Interventions during early life, including parenting interventions on child nutritional support and/or stimulation in the first years of life, have improved early childhood development in various settings.[15–17] A 2021 meta-analysis of RCTs highlighted the benefits of parenting and stimulation among children younger than age 2 years in LMICs,[34] thus providing evidence that combined nutrition and stimulation interventions can improve early childhood development. However, the long-term benefits of such interventions have not been sufficiently explored. In Jamaica, Grantham-McGregor et al used various child developmental tests to assess if early nutrition supplementation and stimulation interventions given to stunted children aged 9 to 24 months was still beneficial in children aged 7 to 8 years.[35] They found that stimulation and nutrition supplementation were beneficial to development, but the benefits from nutrition supplementation alone were smaller compared with when the children were younger.[36] Interestingly, when these children reached the age of 11 to 12 years, nutrition supplementation had no apparent benefits to child development, whereas stimulation was still beneficial.[37] Notably, the most recent assessment of this cohort found that the stimulation aspect still proved to be beneficial when the study participants reached 31 years of age.[38]

It is possible that our results can be explained at least in part by the fact that the nutrition component of the education intervention encouraged the mothers to feed their children a variety of foods from different food groups, thus enhancing their dietary diversity. This could have increased the intake of various nutrients, especially micronutrients that are linked to brain development and function, such as iodine.[39] Notably, although Uganda does not experience iodine deficiency (probably because of national salt iodization), we found that the urinary iodine/creatinine ratio (a marker of iodine uptake) was associated with BSID-III cognitive development scores, but not growth when the children were aged 2 years.[40] Furthermore, as previously reported for the CHNUDEV cohort, improved child dietary diversity at age 6 to 8 months was associated with better motor skills at age 2 years,[41] which is in line with findings in Nepal[42] and China.[43]

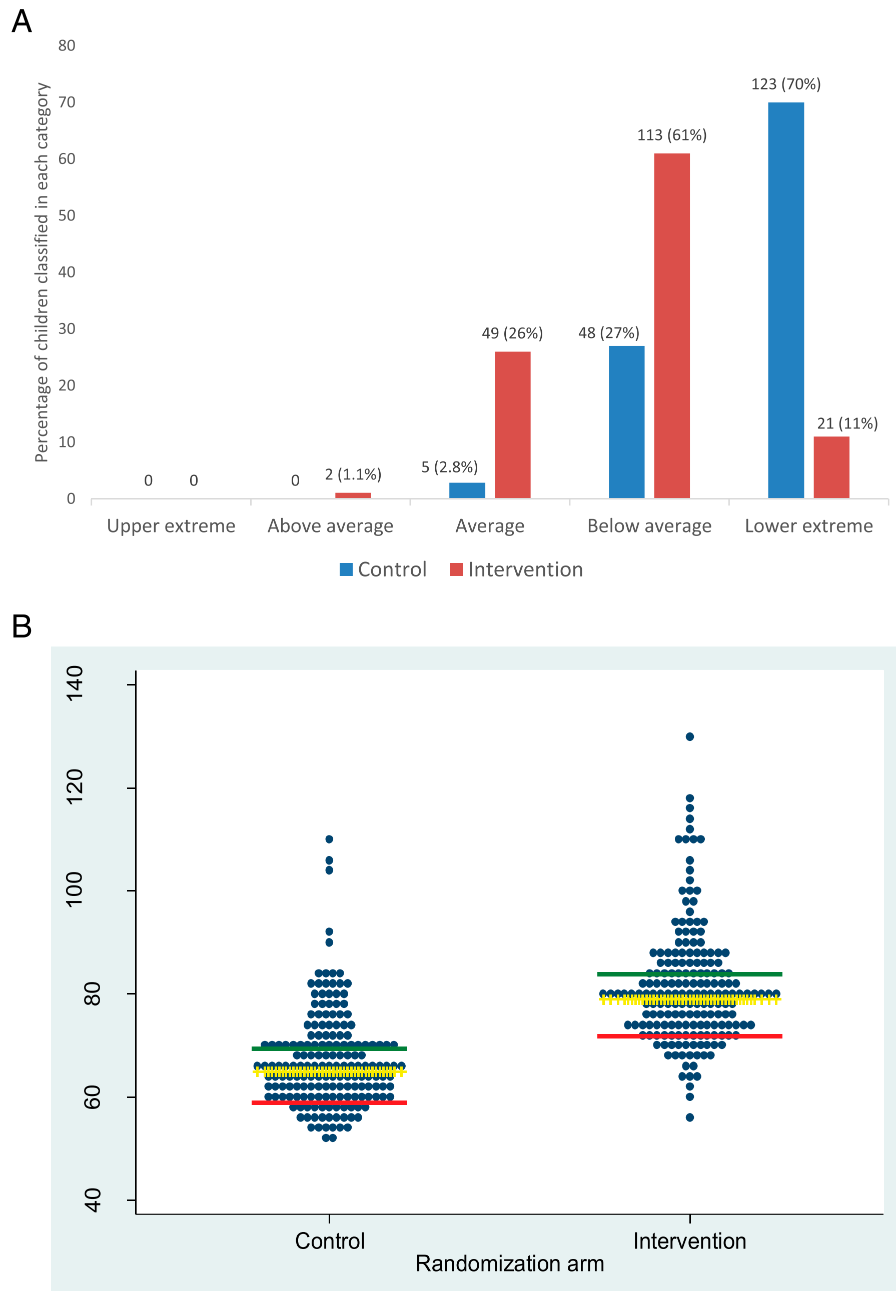

FIGURE 2
Child performance on the KABC-II test. (A) Categorization of child performance as measured with the KABC-II test. Values above the bars are *n* (%). (B) Dot plots comparing FCI global scores between the 2 study groups. Each dot represents the score from 1 child. The horizontal yellow lines in the middle represent the median scores, whereas the red and green lines represent the corresponding interquartile ranges. FCI, Fluid-Crystallized Index; KABC-II, Kaufman Assessment Battery for Children Second Edition.

Our results support the notion that early life exposures affect later child developmental outcomes.[44] The education intervention given to mothers with children early in life (6–8 months) led to sustained improvements in child development even after 8 years. This emphasizes the need to intervene early for long-term benefits for children, in particular those residing in low-resource settings. Our data suggest that interventions directed at educating mothers regarding the importance of nutrition, hygiene, sanitation, and stimulation are likely to improve child health and thereby reduce the many burdens mothers in low-resource settings face every day. Moreover, because nutritional deficiencies start at an early stage,[45] early interventions are vital to avoid

TABLE 3 TOVA *z*-Scores Among the 2 Study Groups

TOVA *z*-Scores	Intervention (n = 185) Mean (SD)	Control (n = 176) Mean (SD)	Difference (n = 361) Mean (95% CI)	*P*	FDR Adjusted *P*
Auditory variables					
Response time variability	−0.60 (1.0)	−1.23 (1.1)	0.63 (0.18 − 1.07)	<.001	.0014
Mean response time	−0.38 (1.2)	−0.81 (1.2)	0.43 (0.10 − 0.75)	.001	.0014
Commission errors	−1.89 (2.0)	−2.86 (2.7)	0.97 (0.08 − 2.13)	.03	.034
Omission errors	−0.95 (1.5)	−2.27 (2.2)	1.32 (0.49 − 2.16)	<.001	.0014
D prime	−1.27 (0.7)	−1.81 (0.8)	0.55 (0.17 − 0.92)	<.001	.0014
Visual variables					
Response time variability	−1.84 (1.8)	−2.80 (2.0)	0.95 (0.22 − 1.68)	.001	.0014
Mean response time	−1.66 (1.8)	−2.43 (1.7)	0.77 (0.09 − 1.44)	.006	.0075
Commission errors	−0.53 (1.5)	−1.31 (2.1)	0.78 0.03 − 1.54)	.01	.011
Omission errors	−5.51 (8.5)	−9.98 (13.2)	4.47 (1.70 − 7.24)	<.001	.0014
D prime	−1.51 (0.6)	−1.96 (0.8)	0.45 (0.16 to 0.74)	<.001	.0014

All reported means and 95% confidence interval (CI) differences are cluster-adjusted. The *P* values are from a multilevel model accounting for the clustering effect. The FDR adjusted *P* values were adjusted using the Benjamini-Hochberg method. FDR, false discovery rate; SD, standard deviation; TOVA, Test of Variables of Attention.

negative trajectories of child development. However, we recognize that vulnerable children who miss interventions early in life could later benefit from school-age interventions regarding their nutritional health and development.[46,47]

Our study has a number of strengths. The design of the original pragmatic RCT adjusted for the cluster effect and with assessors blinded to allocation most likely minimized confounding and measurement bias. The intervention and control subcounties are geographically far apart, which probably minimized "contamination" of the education components from the intervention group to the controls. The booster education sessions that followed the intervention period may have contributed to improved adherence to the intervention among the participants. In support of this, nearly three-quarters (71%) of the original RCT cohort participants were available for the current follow-up study. Furthermore, the assessment of developmental outcomes was performed with 2 neuropsychological tools that are internationally recognized and have been validated in similar settings to our study area.[25,28,29] Moreover, we recently showed that our RCT proved to be cost-effective: the incremental cost-effectiveness ratio for the education intervention compared with current (ie, the control group) practice was USD 16.50 per cognitive composite score gained.[48]

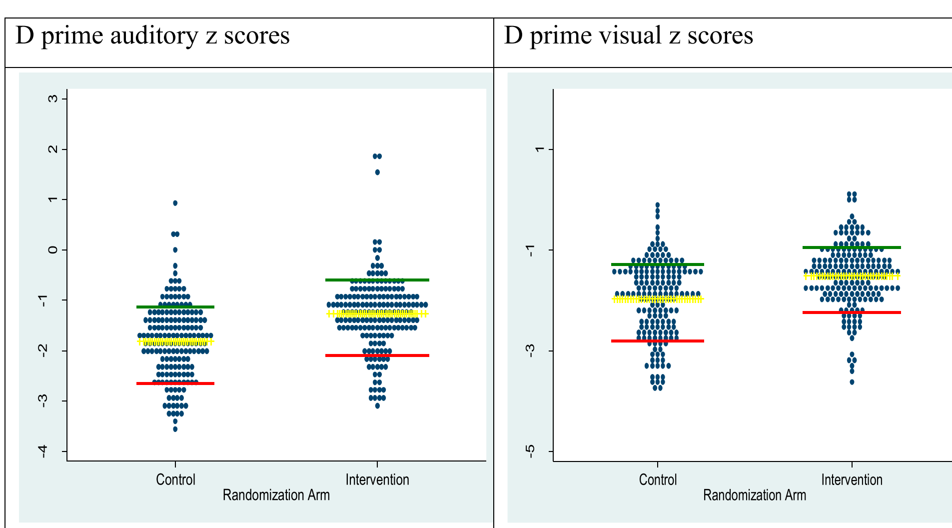

FIGURE 3
Visual and auditory D prime *z*-scores in the 2 study groups. Each dot represents the *z*-score from 1 child. The horizontal yellow lines represent the mean *z*-scores, whereas the red and green lines represent the lower and upper 95% confidence interval of the mean, respectively.

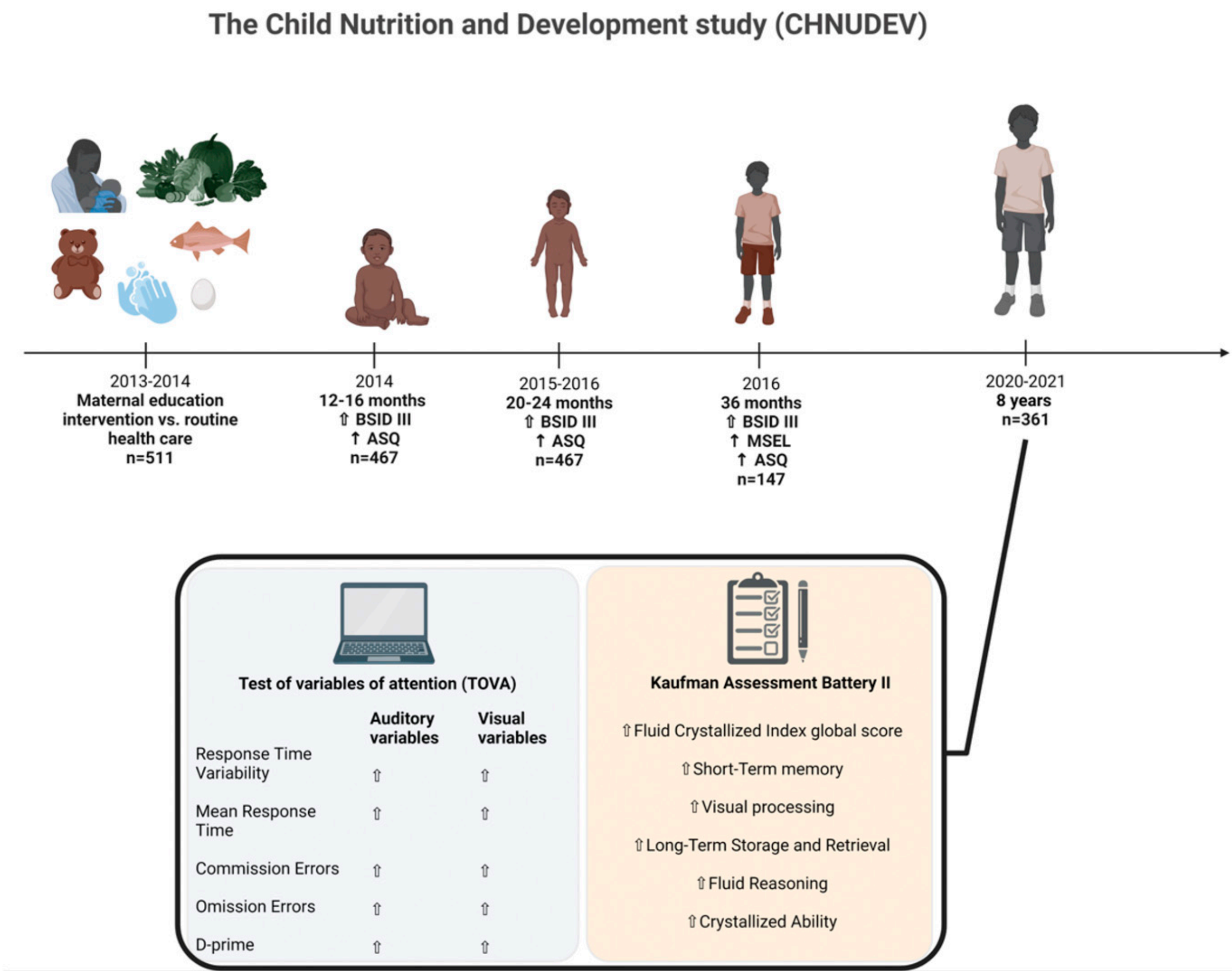

FIGURE 4
The long-term follow-up of the CHNUDEV study. The maternal education intervention was performed when the infants were aged 6 to 8 months and lasted for 6 months. Developmental assessments have since been performed regularly. Arrows indicate improved (↑) or similar (↔) scores in the intervention group compared with the control group. ASQ, Ages and Stages Questionnaire; BSID III, Bayley Scales of Infant and Toddler Development third ed.; CHNUDEV, Child Nutrition and Development; MSEL; Mullen Scales of Early Learning.

The study also has several limitations. The original RCT was powered to test differences in length-for-age z scores, so the current follow-up study may have been underpowered to evaluate differences in developmental outcomes and not growth. When assessing the developmental outcomes, several tests were performed. However, we performed adjustments for multiple testing by use of the Benjamini-Hochberg method.[30] Moreover, because the education intervention consisted of a combined package of several components (nutrition, hygiene, sanitation, and stimulation), we cannot determine the exact individual contribution of each of these components to child development benefits.

In summary, 8 years after our low-cost maternal education intervention was conducted in low-resourced rural Uganda, the developmental benefits observed at child ages 1, 2, and 3 years were still sustained. Our study supports implementation of nutrition, hygiene, sanitation, and stimulation interventions in the early months of life to promote adequate developmental trajectories in small children. We aim to conduct further follow-up studies on this cohort to understand how long the observed benefits last. Long-term studies that evaluate similar education components, both individually and in combination, are warranted.

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ABBREVIATIONS

ASQ: Ages and Stages Questionnaire
BSID-III: Bayley Scales of Infant and Toddler Development-III
CHNUDEV: Child Nutrition and Development study
CI: confidence interval
FCI: Fluid-Crystallized Index
KABC-II: Kaufman Assessment Battery for Children Second Edition
LMIC: low- and middle-income country
RCT: randomized controlled trial
TOVA: Test of Variables of Attention

Data Sharing Statement: Data are available from the Dryad data repository (doi:10.5061/dryad.n8pk0p31r). The study protocols will be made available on publication to researchers who provide a methodologically sound proposal for use in achieving the goals of the approved proposal. Proposals should be submitted to the corresponding author.

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Address correspondence to Prudence Atukunda, PhD, Center for Crisis Psychology, Faculty of Psychology, University of Bergen, Jekteviksbakken 31, 2nd floor 5006 Bergen, Norway. E-mail: Prudence.Friberg@uib.no

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REFERENCES

1. Victora CG, Hartwig FP, Vidaletti LP, et al. Effects of early-life poverty on health and human capital in children and adolescents: analyses of national surveys and birth cohort studies in LMICs. *Lancet.* 2022;399(10336):1741–1752
2. Attanasio O, Cattan S, Meghir C. Early childhood development, human capital, and poverty. *Annu Rev Econ.* 2022;14:853–892
3. *United Nations Sustainable Development Goals.* New York: 2015
4. United Nations. *The Global Strategy for Women's, Children's and Adolescents' Health.* Every Woman Every Child; 2015:2016–2030
5. Keenan T, Evans S, Crowley K. *An introduction to child development.* 3rd ed. Vol. 1. *Sage.* 2016;4-5
6. Garner AS, Shonkoff JP; Committee on Psychosocial Aspects of Child and Family Health; Committee on Early Childhood, Adoption, and Dependent Care; Section on Developmental and Behavioral Pediatrics. Early childhood adversity, toxic stress, and the role of the pediatrician: translating developmental science into lifelong health. *Pediatrics.* 2012;129(1):e224–e231
7. Miguel PM, Pereira LO, Silveira PP, Meaney MJ. Early environmental influences on the development of children's brain structure and function. *Dev Med Child Neurol.* 2019;61(10):1127–1133
8. Prado EL, Dewey KG. Nutrition and brain development in early life. *Nutr Rev.* 2014;72(4):267–284
9. Costello SE, Geiser E, Schneider N. Nutrients for executive function development and related brain connectivity in school-aged children. *Nutr Rev.* 2021;79(12):1293–1306
10. Diamond A. Executive functions. *Annu Rev Psychol.* 2013;64:135–168
11. Aboud FE, Yousafzai AK. Global health and development in early childhood. *Annu Rev Psychol.* 2015;66:433–457
12. Yousafzai AK, Rasheed MA, Rizvi A, Armstrong R, Bhutta ZA. 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. *Lancet.* 2014;384(9950):1282–1293
13. Black MM, Walker SP, Fernald LCH, et al; Lancet Early Childhood Development Series Steering Committee. Early childhood development coming of age: science through the life course. *Lancet.* 2017;389(10064):77–90
14. Uganda Bureau of Statistics. Uganda demographic and health survey 2016. Key indicators report. Available at: https://www.dhsprogram.com/pubs/pdf/FR333/FR333.pdf. Accessed January 12, 2024

15. Jeong J, Franchett EE, Ramos de Oliveira CV, Rehmani K, Yousafzai AK. Parenting interventions to promote early child development in the first three years of life: a global systematic review and meta-analysis. *PLoS Med.* 2021;18(5):e1003602

16. Prado EL, Larson LM, Cox K, Bettencourt K, Kubes JN, Shankar AH. Do effects of early life interventions on linear growth correspond to effects on neurobehavioural development? A systematic review and meta-analysis. *Lancet Glob Health.* 2019;7(10):e1398–e1413

17. Grantham-McGregor SM, Fernald LCH, Kagawa RMC, Walker S. Effects of integrated child development and nutrition interventions on child development and nutritional status. *Ann N Y Acad Sci.* 2014;1308:11–32

18. Jeong J, Pitchik HO, Fink G. Short-term, medium-term and long-term effects of early parenting interventions in low- and middle-income countries: a systematic review. *BMJ Glob Health.* 2021;6(3):e004067

19. University of Oslo Institute of Basic Medical Sciences. The Child Nutrition and Development Study (CHNUDEV). Available from: https://www.med.uio.no/imb/english/research/projects/chnudev-study/. Accessed January 12, 2024

20. Muhoozi GKM, Atukunda P, Diep LM, et al. Nutrition, hygiene, and stimulation education to improve growth, cognitive, language, and motor development among infants in Uganda: a cluster-randomized trial. *Matern Child Nutr.* 2018;14(2):e12527

21. Atukunda P, Ngari M, Chen X, Westerberg AC, Iversen PO, Muhoozi G. Longitudinal assessments of child growth: a six-year follow-up of a cluster-randomized maternal education trial. *Clin Nutr.* 2021;40(9):5106–5113

22. Iversen PO, Ngari M, Westerberg AC, Muhoozi G, Atukunda P. Child stunting concurrent with wasting or being overweight: a 6-y follow up of a randomized maternal education trial in Uganda. *Nutrition.* 2021;89:111281

23. Atukunda P, Muhoozi GKM, van den Broek TJ, et al. Child development, growth and microbiota: follow-up of a randomized education trial in Uganda. *J Glob Health.* 2019;9(1):010431

24. Lichtenberger EO, Sotelo-Dynega M, Kaufman AS. *The Kaufman Assessment Battery for Children*, 2nd ed. 2009

25. Bangirana P, Seggane-Musisi P, Allebeck P, et al. A preliminary examination of the construct validity of the KABC-II in Ugandan children with a history of cerebral malaria. *Afr Health Sci.* 2009;9(3):186–192

26. Greenberg LM, Kindschi C, Dupuy T, Hughes S. *TOVA Clinical Manual.* TOVA Company; 2020

27. Leark RA, Dupuy TR, Greenberg LM, Kindschi CL, Hughes SJ. *TOVA professional manual.* Available at: https://files.tovatest.com/documentation/9/Professional%20Manual.pdf. Accessed January 12, 2024

28. Boivin MJ. Effects of early cerebral malaria on cognitive ability in Senegalese children. *J Dev Behav Pediatr.* 2002;23(5):353–364

29. John CC, Bangirana P, Byarugaba J, et al. Cerebral malaria in children is associated with long-term cognitive impairment. *Pediatrics.* 2008;122(1):e92–e99

30. Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. *J Royal Stat Soc.* 1995;57:289–300

31. Dulal S, Prost A, Karki S, Saville N, Merom D. Characteristics and effects of integrated nutrition and stimulation interventions to improve the nutritional status and development of children under 5 years of age: a systematic review and meta-analysis. *BMJ Glob Health.* 2021;6(7):e003872

32. Atukunda P, Muhoozi GKM, Westerberg AC, Iversen PO. Nutrition, hygiene and stimulation education for impoverished mothers in rural Uganda: effect on maternal depression symptoms and their associations to child development outcomes. *Nutrients.* 2019;11(7):1561

33. Forsyth DR. *Group dynamics.* Cengage Learning; 2018

34. Zhang L, Ssewanyana D, Martin M-C, et al. Supporting child development through parenting interventions in low-to middle-income countries: an updated systematic review. *Front Public Health.* 2021;9:671988

35. Grantham-McGregor SM, Powell CA, Walker SP, Himes JH. Nutritional supplementation, psychosocial stimulation, and mental development of stunted children: the Jamaican Study. *Lancet.* 1991;338(8758):1–5

36. Walker SP, Grantham-Mcgregor SM, Powell CA, Chang SM. Effects of growth restriction in early childhood on growth, IQ, and cognition at age 11 to 12 years and the benefits of nutritional supplementation and psychosocial stimulation. *J Pediatr.* 2000;137(1):36–41

37. Grantham-McGregor SM, Walker SP, Chang SM, Powell CA. Effects of early childhood supplementation with and without stimulation on later development in stunted Jamaican children. *Am J Clin Nutr.* 1997;66(2):247–253

38. Walker SP, Chang SM, Wright AS, Pinto R, Heckman JJ, Grantham-McGregor SM. Cognitive, psychosocial, and behaviour gains at age 31 years from the Jamaica early childhood stimulation trial. *J Child Psychol Psychiatry.* 2022;63(6):626–635

39. Gómez-Pinilla F. Brain foods: the effects of nutrients on brain function. *Nat Rev Neurosci.* 2008;9(7):568–578

40. Atukunda P, Muhoozi GKM, Diep LM, Berg JP, Westerberg AC, Iversen PO. The association of urine markers of iodine intake with development and growth among children in rural Uganda: a secondary analysis of a randomised education trial. *Public Health Nutr.* 2021;24(12):3730–3739

41. Kakwangire P, Moss C, Matovu N, et al. The association between dietary diversity and development among children under 24 months in rural Uganda: analysis of a cluster-randomised maternal education trial. *Public Health Nutr.* 2021;24(13):4286–4296

42. Thorne-Lyman AL, Shrestha M, Fawzi WW, et al. Dietary diversity and child development in the far west of Nepal: a cohort study. *Nutrients.* 2019;11(8):1799

43. Li S, Chen K, Liu C, et al. Association of dietary diversity and cognition in preschoolers in rural China. *Nutrition.* 2021;91-92:111470

44. Stein AD, Adair LS, Donati G, et al; COHORTS Group. Early-life stature, preschool cognitive development, schooling attainment, and

cognitive functioning in adulthood: a prospective study in four birth cohorts. *Lancet Glob Health*. 2023;11(1):e95–e104

45. Victora CG, de Onis M, Hallal PC, Blössner M, Shrimpton R. Worldwide timing of growth faltering: revisiting implications for interventions. *Pediatrics*. 2010;125(3):e473–e480

46. Saavedra JM, Prentice AM. Nutrition in school-age children: a rationale for revisiting priorities. *Nutr Rev*. 2023;81(7):823–843

47. Prentice AM, Ward KA, Goldberg GR, et al. Critical windows for nutritional interventions against stunting. *Am J Clin Nutr*. 2013; 97(5):911–918

48. Ahmed M, Muhoozi GKM, Atukunda P, Westerberg AC, Iversen PO, Wangen KR. Cognitive development among children in a low-income setting: cost-effectiveness analysis of a maternal nutrition education intervention in rural Uganda. *PLoS One*. 2023;18(8):e0290379