Effects of parenting classes and economic strengthening for caregivers on the cognition of HIV-exposed infants: a pragmatic cluster randomised controlled trial in rural Zimbabwe

Helen Mebrahtu,1 Victoria Simms,2 Zivai Mupambireyi,3 Andrea M Rehman,2 Rudo Chingono,3 Edward Matsikire,3 Rickie Malaba,4 Helen A Weiss,2 Patience Ndlovu,4 Frances M Cowan,3,5 Lorraine Sherr1

ABSTRACT

Introduction HIV-exposed children show signs of developmental delay. We assessed the impact of a pragmatic multicomponent intervention for caregivers of HIV-exposed children aged 0–2 years in Zimbabwe.

Methods We conducted a cluster-randomised trial from 2016 to 2018. Clusters were catchments surrounding clinics, allocated (1:1) to either National HIV guidelines standard of care or standard care plus an 18-session group intervention comprising i) early childhood stimulation (ECS) and parenting training with home visits to reinforce skills and retention in HIV care; ii) economic strengthening. Primary outcomes measured 12 months after baseline (4.5 months postintervention completion) included: i) global child development measured using the Mullen early learning composite score; ii) retention in HIV care. Analysis used mixed effects regression to account for clustering and adjusted minimally for baseline prognostic factors and was by intention to treat.

Results Thirty clusters, 15 in each arm, were randomised. 574 dyads were recruited with 89.5% retained at follow-up. Ninety one of 281 (32.4%) were recorded as 14 ECS sessions. There was no evidence of an intervention effect on global child development (intervention mean 88.1 vs standard of care mean 87.6; adjusted mean difference = 0.69; 95% CI 0.35 to 1.03; p=0.001). There was weak evidence that the proportion of caregivers with parental stress was reduced in the intervention arm (adjusted OR (aOR)=0.69; 95% CI 0.45 to 1.05; p=0.08) and stronger evidence that parental distress specifically was reduced (intervention arm 17.4% vs standard of care 29.1% scoring above the cut-off; aOR=0.56; 95% CI 0.35 to 0.89; p=0.01).

Conclusion This multicomponent intervention had no impact on child development outcomes within 4.5 months of completion, but had an impact on parental distress. Maternal mental health remains a high priority.

Trial registration number PACTR201701001387209.

Key questions

What is already known?

► HIV-exposed children in resource-limited settings face multiple and complex stressors associated directly and indirectly with HIV infection.

► Early interventions for HIV-exposed children have led to documented improvements in child outcomes in the short term and long term.

What are the new findings?

► The intervention trialled here did not have an impact on child cognitive development, but reduced parental distress which could directly and indirectly impact child trajectories.

► The prevalence of reported symptoms of common mental disorder was extremely high among participating caregivers.

What do the new findings imply?

► Cognitive development outcomes may take longer to improve following parental child stimulation training.

► Comprehensive interventions to address childhood development may need to include screening and intervention for poor mental health in caregivers.

INTRODUCTION

Early childhood development (ECD) covering the first 3 years of a child’s life marks a time of gradual development of a child’s sensorimotor, social-emotional, cognitive and language capacities. These processes are shaped by many factors, including interactions between the child and their environment, exposure to experiences and genetics.1 During this period of rapid physical growth, the child acquires a complex set of skills and functional competencies facilitating achievement of their potential in life and laying the
foundation for long-term physical, emotional and psychological health in childhood and adulthood.

During this period, children’s brains develop rapidly and can be modified by their environment influencing their ability to learn and develop over time.\(^3\) Thus, early childhood is a key time to maximise the opportunity for children to develop their full potential. Researchers have shown that appropriate stimulation, good quality parenting provided by a consistent, responsive caregiver, coupled with adequate nutrition and access to health and psychosocial care can contribute to optimal development.\(^4\) Conversely, adversities during this period, such as poverty, malnutrition, poor health, low stimulation, exposure to stressful conditions and impoverished environment can disrupt brain development, attachment, and early learning.\(^2\)

HIV infection in both the parent and the child represents a multifaceted life challenge.\(^6\) HIV can impact child growth and development in a variety of ways including their cognitive development.\(^7\) Several studies have described the risk of developmental delay and impairment in both children living with HIV,\(^9\) and HIV-exposed uninfected (HEU) infants\(^7\) compared with HIV-unexposed infants,\(^8\) with the risk apparently heightened in low-income and middle-income countries (LMICs).\(^10\) Children infected with HIV perinatally face greater risk of neurological and neuropsychological deficits compared with HEU infants, either due to direct effects of HIV on the central nervous system,\(^2\) exposure to treatment or other HIV-related factors. These risks can be mitigated; research illustrates the importance of early antiretroviral therapy (ART) initiation, and virological suppression during infancy or early childhood and its association with improved neurocognitive outcomes in children with perinatally acquired HIV.\(^11\) HIV can also impact the neurodevelopment of children indirectly through its influence on the child’s living environment,\(^8\) including community stigma and discrimination, caregiver unemployment, caregiver illness and bereavement or caregiver mental health.\(^10\) However, in some cases despite facing significant adversities, HEU children can develop resiliency and demonstrate positive developmental trajectories, similar to those HIV-unexposed uninfected.\(^15\)

Early interventions for disadvantaged children have led to documented improvements in child outcomes such as survival, health, growth and cognitive and social development.\(^16\) Several studies have demonstrated the benefits of caregiver or child targeted interventions over the long term and showed improvements in developmental outcomes of children from LMICs.\(^2\) Home visits and support to HIV-positive caregivers by community health workers was found to improve developmental outcome for HEU children.\(^17\) Parenting and child stimulation programmes taught to the caregiver can significantly improve cognitive and motor development in young children infected with HIV.\(^18\) In addition, microfinance programmes (which includes the provision of loans, savings and insurance) in rural settings can have a positive impact on various household indicators, improve food security and the health of children.\(^19\) Research shows that combination interventions can have accelerated benefits.\(^20\) Theoretical models\(^22\) suggest that internal assets, family resources and community support can promote the resilience process and temper negative impacts of parental HIV. The need for an evaluation of more complex, broader and integrated interventions is timely.

Zimbabwe is one of the countries most severely affected by HIV globally, with prevalence estimated at 14.6% among those aged 15–64 years.\(^23\) Over a million children have been orphaned due to AIDS-related deaths since the start of the epidemic.\(^24\) Prevention of mother to child transmission (PMTCT) programmes have dramatically reduced perinatal transmission and ART rollout has reduced mortality and morbidity in caregivers.\(^25\) However, despite improved health and survival of infants born to mothers living with HIV, interventions to improve the well-being and development of these children are needed. The Child Health Intervention for Developmental Outcomes (CHIDO) trial aimed to determine the real-world effectiveness of a multicomponent community-based intervention on child development and HIV.

**METHODS**

The methods have been previously published.\(^26\) A brief overview is provided here.

**Study design and participants**

The CHIDO trial is a pragmatic parallel-arm cluster randomised controlled trial conducted in 30 primary care clinic catchment areas in two districts in Zimbabwe (Goromonzi and Mudzi). Detailed mapping of all health facilities and their communities was conducted to select trial sites, which are at least 15 km apart.

Community sensitisation was carried out in phases. First, the local leaders (including traditional and political leaders, health and educational professionals) were given information about the study, its objectives, the target population and encouraged to ask questions or raise any concerns. They were then invited to take part in the site randomisation process. The caregivers were identified from the HIV-exposed infant registers kept at trial clinics and were eligible for inclusion if they were the primary caregivers (biological and non-biological), the biological mother had been living with HIV and cared for a child aged 0–24 months. Caregivers who gave written informed consent/assent in English or Shona were enrolled into the trial, completed a baseline assessment and were followed up after 12 months. In intervention communities, caregiver-infant dyads were encouraged to engage in all CHIDO intervention activities. While they attended the clinic specifically for the intervention sessions, they could also attend clinic services if scheduled/required.
Extended Consolidated Standards of Reporting Trials guidelines were followed for reporting the results of this trial.

**Patient involvement**

Patients and village health workers were involved in formative work undertaken at which the CHIDO intervention was developed.

**Randomisation and masking**

Clinics were randomised in a 1:1 allocation ratio to the CHIDO intervention or Ministry of Health and Child Care (MoHCC) standard of care. Restricted randomisation was used to ensure balance by district (20 in Goromonzi district and 10 in Mudzi district) and on the number of HIV-exposed infants aged between 0 and 24 months per clinic by stratifying the clinics into those able to run one group of 12 dyads (12 clusters) and those of sufficient size to run two groups of 12 dyads (18 clusters). To maximise transparency and buy-in from stakeholders, a public randomisation procedure was undertaken in each district (on 19 January 2016 in Goromonzi and on 31 May 2016 in Mudzi) involving MoHCC, and district-level government and medical representatives. Assessors conducting the endline survey procedures were blind to trial arm.

**Intervention components**

The intervention included three elements: (i) an 18-session health, nutrition and early childhood stimulation (ECS) parenting programme (table 1); (ii) an internal savings and lending scheme (ISALS) with ISALS sessions held immediately after each ECS session and (iii) village health workers who visited participants at home each month (or more frequently in the case of non-attendance at group sessions or other problems). The parenting programme content evolved out of formative work and the number of sessions was set after piloting and feedback from participants about preferred length and frequency of sessions.

**Baseline and endline assessments and data collection**

Participant enrolment was conducted in parallel in intervention and standard of care communities between 16 January and 8 September 2016. At enrolment, all participating caregiver-child dyads were allocated a unique identifier. Questionnaire data which included demographic, socioeconomic, maternal mental health and household food security information were collected using an interviewer-administered questionnaire with data entered directly onto tablets preprogrammed using Open Data Kit with range and consistency checks incorporated. Maternal mental health was measured using the Edinburgh Postnatal Depression Scale (EPDS), which is a diagnostic tool that has been locally validated in Zimbabwe, plus the 8-item Shona Symptoms Questionnaire (SSQ-8), a locally developed and validated scale which determines risk of common mental disorders (including anxiety and depression). Finally, parental stress was measured using the Parental Stress Index Short Form (PSI-SF).

### Table 1 Parenting programme content

| Session number | Delivered by | Parenting programme content |
|----------------|--------------|-----------------------------|
| 1              | CHW          | Relationships with people around you and your child |
| 2              | CHW          | The role of good parent—responsive parenting practices (session I) |
| 3              | CHW          | The role of good parent—responsive parenting practices (session II) |
| 4              | Nurse        | A healthy infant and young child (session I) |
| 5              | Nurse        | A health infant and young child (session II) |
| 6              | Nurse        | A well-nourished infant and young child |
| 7              | CHW          | Physical/motor development (session I) |
| 8              | CHW          | Physical/motor development (session II) |
| 9              | CHW          | Social and emotional development (session I) |
| 10             | CHW          | Social and emotional development (session II) |
| 11             | Nurse        | A health infant and young child (focus on PMTCT and treatment adherence) |
| 12             | Nurse        | Complementary feeding (session I) |
| 13             | Nurse        | Complementary feeding (session II) |
| 14             | CHW          | Communication and language development (session I) |
| 15             | CHW          | Communication and language development (session II) |
| 16             | CHW          | Developing thinking and understanding of the world (cognitive) (session I) |
| 17             | CHW          | Developing thinking and understanding of the world (cognitive) (session II) |
| 18             | CHW          | Positive discipline |

CHW, Community Health Worker; PMTCT, Prevention of mother to child transmission.
The more sensitive questions were self-completed using audio computer-assisted survey instrument to maximise validity. This was followed by a developmental assessment of the child conducted by one of two trained research nurses. Developmental assessments were videoed, and a small randomly selected sample was reviewed by a highly experienced assessor. This was done as part of quality control and assurance, and to minimise differences between assessors.

Intervention implementation commenced within 3 months of participant enrolment in all communities and ran over 12 months between 7 March 2016 and 7 July 2017.

An endline assessment was conducted between 10 April 2017 and 18 January 2018 among enrolled caregiver-child dyads 12 months after the baseline survey and within 0–5 months after completion of intervention delivery. The endline survey was conducted in parallel, with pairs of intervention and control trial sites being assessed at the same survey venue to minimise unblinding of assessors. Survey procedures were as described at baseline.

At endline a dried blood spot sample was collected from all biological mothers to determine HIV viral load and infants to test for HIV antibody status and viral load. Programme attendance records and village healthcare worker diaries were reviewed, and data double entered into password protected Access databases.

Laboratory assessments
Dried blood spot samples were air dried, stored at room temperature and submitted weekly to the respective laboratories. Infant samples were sent to the National Microbiology Reference Laboratory in Harare for HIV-1 antibody testing using COBAS AmpliPrep/COBAS TaqMan. Samples confirmed HIV positive were sent for viral load testing. Caregiver samples were sent to flow cytometry laboratory for viral load testing using Biomerieux NucliSENS easyMag and EasyQ.

### Outcome measures

There were two primary outcomes for the trial: (i) change in the mean age-standardised Mullen early learning composite (ELC) score of children; (ii) the proportion of HIV-exposed or HIV-positive children with full retention in care (>80%) of scheduled HIV treatment and care visits at 12 months. In the absence of locally validated robust child development measures, the Mullen ELC score was chosen as it had been used to determine impact of caregiver interventions over a similar time period in Africa. We assessed seven prespecified secondary end points as previously reported, reflecting factors intended to be affected by the intervention, which were analysed by the same analytical framework as the primary outcome (table 2).

### Statistical analysis
Our sample-size calculations have been described previously. We estimated that we would need 15 clusters per arm with a harmonic mean of 16 caregiver-child dyads per cluster at endline, and assuming 20% loss to follow-up over 12 months to have 80% power to detect an effect size (difference in means/SD) of 1.23 for the Mullen ELC score and 82% power to detect a risk difference in retention in care of HIV-exposed children of at least 17% assuming 65% are retained in the control arm. The overall recruitment target was therefore

---

**Table 2.** Secondary outcomes of the CHIDO trial

| Outcome measures                      | Assessment tools used                                      |
|---------------------------------------|------------------------------------------------------------|
| Child HIV outcomes: viral load        | Viral load tests conducted using Biomerieux NucliSENS easyMag and EasyQ on dried blood spot samples |
| Child development outcomes:          |                                                            |
| ► Visual reception                    | Mullen early learning composite score                      |
| ► Fine motor                         |                                                            |
| ► Receptive language                 |                                                            |
| ► Expressive language                |                                                            |
| Nutritional outcomes: weight-for-age, height-for-age, weight-for-height (BMI) z-scores | Midupper arm circumference tape measure, height mate/board |
| Parental stress                      | Parental Stress Index Short Form                           |
| Adherence outcomes:                  |                                                            |
| ► Retention in care                  | Medical Adherence Rating Scale                             |
| ► Viral load                         | Viral load tests conducted using Biomerieux NucliSENS easyMag and EasyQ on dried blood spot samples |
| Food security outcome                | Household hunger (food deprivation) scale—modified HFIAS (one item from each domain of the scale: i) uncertainty about household food supply; ii) insufficient quality and iii) insufficient food intake |
| Mental health outcomes:              |                                                            |
| ► Postnatal depression               | Edinburgh Postnatal Depression Scale                      |
| ► Common mental disorders            | Shona Symptom Questionnaire 8                             |

BMI, body mass index; CHIDO, Child Health Intervention for Developmental Outcomes; HFIAS, Household Food Insecurity Access Scale.
528 caregiver-child dyads in total from 30 clinics. We recruited 574 dyads to ensure a harmonic mean of 24 dyads was enrolled from the larger seven clinics (to allow two groups to run at these sites) and a harmonic mean of 12 dyads was enrolled from the smaller eight clinics, where just one ECS/ISALS group was run.

The statistical analysis followed a prespecified analytical plan differing from the published protocol by using individual-level analysis (see online supplementary materials), which allowed for greater flexibility. Data were analysed in STATA V.15.1 (StataCorp, College Station, Texas, USA) using intention-to-treat principles incorporating random effects for clusters and adjusting minimally for baseline prognostic factors. Mean differences and 95% CIs were used to estimate the effect of the intervention for quantitative outcomes using mixed effects linear regression. ORs and 95% CI were used to estimate the effect of the intervention for binary outcomes using mixed effects logistic regression. Mental health questions were categorised as at risk or not at risk, with cut-points of 12/30 for the EPDS,

Evidence for effect modification in the ELC score was assessed by incorporating interaction terms with baseline Mullen ELC score or with baseline caregiver’s mental health as measured by EPDS, SSQ-8 and PSI-SF. The effect of the intervention was also examined in a per-protocol analysis comparing those in the intervention arm who attended most ECS sessions (either at least 14/18 sessions in total, or at least 7/9 sessions addressing child development) with those in the standard of care arm.

RESULTS
All 30 clusters were randomised (15 to each trial arm) and all remained in the trial until the end (figure 1). Number of participants recruited (n=574) exceeded target enrolment (n=528). Retention was 89.5% (514/574) (261: 91.5% in the intervention arm and 253: 85.0% in the standard of care arm), of whom 506 of 514 had endline data on the Mullen score. Six Mullen scores were missing because the child had died. The other two children were found and tested for HIV but the Mullen test was not performed. At follow-up, 18 children had a different primary caregiver from the person who completed the baseline interview.

Descriptive characteristics at baseline
Baseline characteristics were generally comparable between trial arms (table 3); the intervention arm had a greater percentage of infants aged under 6 months (26.3% vs 15.0%), infants stunted at baseline (38.4% vs 34.3%) and households of lower socioeconomic status (37.0% vs 30.0%). Only two of seven HIV-infected babies had been started on ART within 6 weeks of birth. Almost all caregivers (562/574; 97.9%) were biological mothers, and about half (304/574; 53.0%) had secondary education or higher. Reported food insecurity was high. Mental health of caregivers was poor with 230/574 (40.1%) caregivers at risk of common mental disorders (SSQ-8 >6) and about half (304/574; 53.0%) above the threshold for postnatal depression (EPDS >12) at baseline. High parental distress (PSI-SF parental distress subscale >90th percentile) was reported by 185/574 (32.2%) caregivers.

Infants were 291/574 (50.1%) female, and 207/574 (36.1%) were stunted (WHO height-for-age z-score <–2). The mean composite score on the Mullen ELC score at baseline was 102.3 (95% CI 98.6 to 106.0), which was similar to the US reference norms (table 3). Characteristics of those lost to follow-up were similar to those who completed follow-up (online supplementary appendix table 1).

Programme implementation
The CHIDO intervention was initiated in all 15 intervention clusters, with 281 participants enrolled. There are missing attendance data from one cluster. In the 14 clusters with attendance data, 21 ECS groups were run with each group intended for up to 12 participants. Seven clusters ran one group and seven clusters ran two groups.
| Measure and level                              | Intervention arm | Standard of care arm |
|------------------------------------------------|------------------|----------------------|
| Total N (% of total)                          | 281 (49.0%)      | 293 (51.0%)          |
| Infant's characteristics                      |                  |                      |
| Age (years) Median (IQR)                      | 1.04 (0.48–1.49) | 1.00 (0.68–1.47)     |
| Age (months) 0 to <6                          | 74 (26.3%)       | 44 (15.0%)           |
| 6 to <12                                       | 61 (21.7%)       | 100 (34.1%)          |
| 12–24                                         | 146 (52.0%)      | 149 (50.9%)          |
| Sex N (%)                                      |                  |                      |
| Male                                           | 141 (50.2%)      | 142 (48.5%)          |
| Female                                         | 140 (49.8%)      | 151 (51.5%)          |
| HIV status as reported at baseline N (%)       |                  |                      |
| True positive                                  | 2 (0.7%)         | 3 (1.0%)             |
| False positive                                 | 7 (2.5%)         | 1 (0.3%)             |
| Unconfirmed positive                           | 3 (1.1%)         | 2 (0.7%)             |
| True negative                                  | 155 (55.2%)      | 184 (62.8%)          |
| False negative                                 | 6 (2.1%)         | 2 (0.7%)             |
| Unconfirmed negative                           | 11 (3.9%)        | 31 (10.6%)           |
| Prefers not to say                             | 2 (0.7%)         | 0 (0%)               |
| Unknown                                        | 95 (33.8%)       | 70 (23.9%)           |
| HIV status as reported at 12 months N (%)      |                  |                      |
| True positive                                  | 5 (1.8%)         | 4 (1.4%)             |
| False positive                                 | 1 (0.4%)         | 2 (0.7%)             |
| True negative                                  | 236 (84.0%)      | 231 (78.8%)          |
| False negative                                 | 5 (1.8%)         | 2 (0.7%)             |
| Unconfirmed negative                           | 1 (0.4%)         | 2 (0.7%)             |
| Prefers not to say                             | 1 (0.4%)         | 2 (0.7%)             |
| Unknown (negative)                             | 9 (3.2%)         | 7 (2.4%)             |
| Lost to follow-up                              | 23 (8.2%)        | 43 (14.7%)           |
| HIV status as known at 12 months N (%)         |                  |                      |
| Infected                                       | 10 (3.6%)        | 6 (2.0%)             |
| Exposed uninfected                             | 247 (87.9%)      | 242 (82.6%)          |
| Unknown                                        | 1 (0.4%)         | 2 (0.7%)             |
| Lost to follow-up                              | 23 (8.2%)        | 43 (14.7%)           |
| Birth weight (kg) Mean (95% CI) n=272          | 2.99 (2.90 to 3.08) | 2.93 (2.86 to 3.00) |
| Weight-for-age z-score Mean (95% CI) n=283     | −0.86 (−1.15 to −0.57) | −0.86 (−0.99 to −0.72) |
| Underweight (z-score <−2) Yes                  | 44 (15.7%)       | 43 (14.7%)           |
| No                                             | 237 (84.3%)      | 250 (85.3%)          |
| Length-for-age z-score Mean (95% CI)           | −1.56 (−1.87 to −1.25) | −1.46 (−1.71 to −1.21) |
| Stunted (z-score <−2) Yes                      | 107 (38.4%)      | 100 (34.3%)          |
| No                                             | 172 (61.7%)      | 192 (65.8%)          |
| BMI z-score                                     |                  |                      |
| Low BMI z-score                                 | 15 (5.4%)        | 17 (5.8%)            |
| No                                             | 264 (94.6%)      | 275 (94.2%)          |
| MUAC z-score                                    |                  |                      |
| Low MUAC z-score <−2                           | 14 (6.0%)        | 15 (5.8%)            |

Continued
Table 3  Continued

| Measure and level                  | Intervention arm | Standard of care arm |
|------------------------------------|------------------|----------------------|
| No                                 | 218 (94.0%)      | 246 (94.3%)          |
| Mullen scales (T-scores)           |                  |                      |
| Mean (95% CI)                      |                  |                      |
| Expressive language                | 52.4 (49.7 to 55.1) | 53.1 (51.3 to 55.0) |
| Fine motor                         | 51.1 (47.9 to 54.4) | 50.2 (47.4 to 53.0) |
| Gross motor                        | 50.1 (47.7 to 52.6) | 50.8 (49.2 to 52.4) |
| Receptive language                 | 47.6 (44.5 to 50.8) | 47.6 (44.8 to 50.4) |
| Visual reception                   | 53.5 (49.3 to 57.8) | 52.6 (50.2 to 55.1) |
| Early learning composite score     | 102.6 (96.5 to 108.7) | 102.0 (97.8 to 106.3) |

Caregiver's characteristic

| Caregiver type | N (%)      |          |
|----------------|------------|----------|
| Mother         | 272 (96.8%)| 290 (99.0%) |
| Other          | 9 (3.2%)   | 3 (1.0%)  |

Age (years)

| Marital status | N (%)      |          |
|----------------|------------|----------|
| Married        | 227 (81.1%)| 228 (77.8%) |
| Divorced/separated | 32 (11.4%)| 42 (14.3%)  |
| Widowed        | 16 (5.7%)  | 15 (5.1%) |
| Never married  | 5 (1.8%)   | 8 (2.7%)  |

Education

| Parental stress score (PSI-SF) | N (%)      |          |
|--------------------------------|------------|----------|
| Secondary or above             | 152 (54.1%)| 152 (51.9%) |

Employment

| Employment | N (%)      |          |
|------------|------------|----------|
| Employed   | 90 (32.0%) | 120 (41.0%) |

SES

| Parental stress subscale n=565 | N (%)      |          |
|--------------------------------|------------|----------|
| Not stressed (<90th percentile) | 188 (68.4%)| 192 (66.2%) |
| Stressed (≥90th percentile)    | 87 (31.6%) | 98 (33.8%) |

| Parent-child interaction dysfunction subscale n=565 | N (%)      |          |
|------------------------------------------------------|------------|----------|
| Not stressed (<90th percentile)                      | 169 (61.2%)| 182 (63.0%) |
| Stressed (≥90th percentile)                          | 107 (38.8%)| 107 (37.0%) |

| Difficult child subscale n=563 | N (%)      |          |
|--------------------------------|------------|----------|
| Not stressed (<90th percentile) | 241 (87.3%)| 240 (83.6%) |
| Stressed (≥90th percentile)    | 35 (12.7%) | 47 (16.4%) |

| PSI-SF total score n=564 | N (%)      |          |
|-------------------------|------------|----------|
| Not stressed (<90th percentile) | 180 (65.7%)| 185 (63.8%) |
| Stressed (≥90th percentile)    | 94 (34.3%) | 105 (36.2%) |

| Mother's viral load copies/mL n=485 | Geometric mean (SD) | N (%) | (≥1000 copies/mL) |
|-------------------------------------|---------------------|-------|-------------------|
|                                      | 126.2               | 33/246 (13.4%) | 25/239 (10.5%) |
Table 3  Continued

| Measure and level                   | Intervention arm | Standard of care arm |
|-------------------------------------|------------------|----------------------|
| Maternal mental health (EPDS) n=562 |                  |                      |
| Not depressed (score 0–11)          | 132 (48.5%)      | 146 (50.3%)          |
| Depressed (score≥12)                | 140 (51.4%)      | 144 (50.0%)          |
| Common mental disorders (SSQ-8) n=573|                  |                      |
| No CMD (score 0–5)                 | 168 (60.0%)      | 175 (60.0%)          |
| CMD (score 6–8)                     | 112 (40.0%)      | 118 (40.0%)          |
| Household food security (HFIAS)     |                  |                      |
| Little to no hunger                 | 116 (41.3%)      | 126 (43.0%)          |
| Moderate-to-severe hunger           | 165 (58.7%)      | 167 (57.0%)          |
| Medical Adherence Rating Scale n=560|                  |                      |
| Not adherent                        | 8 (3.0%)         | 5 (1.7%)             |
| Adherent                            | 263 (97.1%)      | 284 (98.3%)          |

BMI, body mass index; CMD, Common mental disorders; EPDS, Edinburgh Postnatal Depression Scale; HFIAS, Household Food Insecurity Access Scale; MUAC, mid-upper arm circumference; PSI-SF, Parental Stress Index Short Form; SES, socioeconomic status; SSQ-8, 8-item Shona Symptoms Questionnaire.

Of 268 caregivers in the intervention arm from the 14 clusters with records, 232 (86.6%) attended any ECS session. There were 43/268 (16.0%) participants who attended all 18 ECS sessions, and 118/268 (44.0%) who attended 14–17 sessions. Of the nine sessions addressing child development (table 1 and figure 2), 79/268 (29.5%) participants attended all nine sessions, and 79/268 (29.5%) attended seven or eight sessions, median per group who attended seven to nine child development sessions was 7.5 (IQR 6–9).

ISALS ran immediately after the ECS sessions and all women who attended an ECS session were assumed to have attended an ISALS session. Women were recorded in the ISALS register if they made a financial contribution to the ISALS (ie, actively participated in the ISALS process). The target was for women to participate in 12 ISALS over the course of the trial. ISALS registers were not available for five clusters. Where records were kept, 184 of the 232 caregivers (79.3%) participated in at least one ISALS session and 155 (67%) made a financial contribution. The median number of sessions attended at which a financial contribution was made was 5 (IQR 2–9), and 14/232 (6.0%) made a financial contribution at least 12 times (equivalent to once monthly). Overall, 198/232 (85.3%) received at least one home visit and the median number of home visits per caregiver was seven (IQR 0–9). Impact evaluation was assessed a median 134 (IQR 98–163) days after participants attended their last ECS session among 232 participants who attended any session and were followed up.

Among all intervention participants, only 32.4% (91/281) were recorded as having received the full intervention package as devised (>14 ECS, >6 ISALS and >6 home visits) (figure 3).

Primary outcomes

Early learning composite score

At the endline survey the Mullen ELC mean score was 87.9, a reduction of 14.4 points from baseline. There was no evidence of a difference in Mullen composite score after programme implementation between trial arms (mean of 88.1 in the intervention arm and 87.6 in standard of care arm; adjusted mean difference (aMD)=0.06; 95% CI −2.68 to 2.80). The estimated coefficient of variation (k) was 0.09. Cluster-level means showed departure from normality, but results were comparable (aMD=0.11; 95% CI −2.90 to 3.11). There was also no evidence of difference in Mullen subscales by trial arm (table 4). Individual child trajectories showed that 80% of infants had lower ELC scores at follow-up compared with baseline in both arms.

There was no evidence for effect modification for the prespecified baseline covariates on the intervention
Mebrahtu H, et al. BMJ Global Health 2019;4:e001651. doi:10.1136/bmjgh-2019-001651

Figure 3  Venn diagram of trial participant attendance at intervention sessions. ECS, early childhood stimulation; HV, home visit; ISALS, internal savings and lending scheme.

Table 4  Primary outcomes

| Outcome                              | Intervention arm | Standard of care arm | Adjusted mean difference* (95% CI) | Measure of effect (95% CI) | Coefficient of variation (k) |
|--------------------------------------|------------------|----------------------|------------------------------------|---------------------------|------------------------------|
| Mullen scales (T-scores), mean (95% CI), adjusted mean difference | n=257            | n=249                |                                    |                           |                              |
| Early learning composite score       | 88.1 (84.0, 92.2) | 87.6 (83.1, 92.1)    | 0.06 (−2.68 to 2.80)               | p=0.97                    |                              |
| Expressive language Mullen scale     | 44.9 (43.1, 46.7) | 45.3 (43.3, 47.3)    | −0.44 (−2.03 to 1.14)              | p=0.58                    | −0.44 (−2.03 to 1.14)        |
| Receptive language Mullen scale      | 45.3 (43.1, 47.5) | 45.8 (43.1, 48.4)    | −0.11 (−1.82 to 1.60)              | p=0.90                    | −0.11 (−1.82 to 1.60)        |
| Fine motor Mullen scale              | 41.7 (39.3, 44.2) | 41.0 (38.5, 43.6)    | −0.23 (−2.38 to 1.92)              | p=0.83                    | −0.23 (−2.38 to 1.92)        |
| Gross motor Mullen scale             | 50.2 (47.7, 52.6) | 48.2 (45.4, 51.0)    | 1.99 (−0.54 to 4.51)               | p=0.12                    | 1.99 (−0.54 to 4.51)         |
| Visual reception Mullen scale        | 42.8 (40.1, 45.5) | 41.5 (38.6, 44.4)    | 0.84 (−1.44 to 3.12)               | p=0.47                    | 0.84 (−1.44 to 3.12)         |
| Child retention in HIV care          | 201/257 (78.2%)   | 207/249 (83.1%)      | –                                  | OR=0.73 (0.47 to 1.14)    | p=0.16                       |
| Virological failure children as proportion of those HIV positive | 4/8 (50%)        | 4/6 (67%)            | –                                  | –                         |                              |
| Virological failure mothers          | 33/246 (13.4%)    | 25/239 (10.5%)       | –                                  | OR=1.33 (0.72 to 2.46)    | p=0.36                       |

*Positive mean difference indicates that those in the intervention arm have higher Mullen scores.
Table 5  Effect modification of the intervention effect by baseline characteristics

| Covariate ELC score | Level                          | Mean Mullen ELC after programme implementation | Intervention arm | Standard of care arm | P value for effect modification |
|---------------------|--------------------------------|-------------------------------------------------|------------------|----------------------|---------------------------------|
|                     | Below average (Mullen ELC <85) |                                                 | 78.5             | 79.2                 |                                 |
|                     | Average+(Mullen ELC≥85)        |                                                 | 90.1             | 89.1                 | 0.91                            |
| Baseline EPDS       | Not showing signs of depression (EPDS score <12) |                                                 | 89.7             | 88.5                 |                                 |
|                     | Showing signs of depression (EPDS score≥12)   |                                                 | 86.5             | 86.5                 | 0.78                            |
| Baseline SSQ-8      | No CMD (SSQ-8<6)               |                                                 | 89.7             | 88.6                 |                                 |
|                     | CMD (SSQ-8≥6)                 |                                                 | 85.7             | 86.1                 | 0.51                            |
| Baseline PSI-PD parental distress subscale | Not showing signs of distress (PSI-PD<90th percentile) |                                                 | 87.7             | 88.3                 |                                 |
|                     | Showing signs of distress (PSI-PD≥90th percentile) |                                                 | 89.2             | 85.9                 | 0.54                            |
| Baseline infant’s age (month) | 0 to <6                      |                                                 | 88.5             | 89.1                 |                                 |
|                     | 6 to <12                      |                                                 | 89.6             | 86.7                 |                                 |
|                     | 12–24                         |                                                 | 87.3             | 87.8                 | 0.70                            |

ELC, early learning composite; EPDS, Edinburgh Postnatal Depression Scale; PSI-PD, Parental Stress Index parental distress subscale; SSQ-8, 8-item Shona Symptoms Questionnaire.

In the intervention arm 21.8% of infants had missed the most recent test, compared with 16.9% in the standard of care arm (adjusted OR (aOR)=1.25; 95% CI 0.77 to 2.01, p=0.37).

At baseline, 165/574 (28.7%) of caregivers said they did not know the child’s HIV status and by follow-up only 16/506 (3.1%) said they did not know (table 3). There was no difference between arms in reported knowledge of HIV status at follow-up. At follow-up in the intervention arm 79/85 (92.9%) of caregivers who at baseline reported not knowing child’s status reported they now knew it, compared with 55/58 (94.8%) in the standard of care arm.

Secondary outcomes
Nutritional outcomes
There was no evidence of any impact of the intervention on weight-for-age z-score, height-for-age z-score or body mass index (table 6), although there was strong evidence that infants in the intervention arm had a reduced mean MUAC for z-score (−0.60 vs −0.49; aMD=−0.20; 95% CI −0.35 to 0.06; p=0.01).

Parenting stress
There was weak evidence of an intervention effect on parental stress overall (aOR=0.69; 95% CI 0.45 to 1.05; p=0.08). There was strong evidence that the intervention had an impact on the parental distress subscale of the PSI (17.4% vs 29.1%; aOR=0.56; 95% CI 0.35 to 0.89; p=0.01).

Maternal adherence outcomes
The proportion of women with viral loads of >1000 copies/mL was similar by arm (13.4% in the intervention arm vs 10.5% in the standard of care arm; aOR=1.33; 95% CI 0.72 to 2.46). Self-reported adherence on the Medical Adherence Rating Scale was high at follow-up and also similar between trial arms (97.6% in the intervention arm vs 98.4% in the standard of care arm; online supplementary appendix table 1).

Household food security
There was no evidence of difference in household food security by trial arm, with 24.9% in the intervention arm and 21.7% in the standard of care arm reporting experiencing food insecurity (aMD=1.19; 95% CI 0.62 to 2.26; p=0.52).

Maternal mental health outcomes
There was no evidence of a difference between trial arms in the proportion of biological mothers with at least mild postnatal depression measured using the EPDS (39.8% vs 43.9%; aOR=0.79; 95% CI 0.50 to 1.25; p=0.32), despite symptoms of postnatal depression being common (table 6). There was also no difference observed among...
Table 6 Secondary outcomes

| Outcome | Intervention arm n=257 | Standard of care arm n=249 | Measure of effect (95% CI) |
|---------|------------------------|-----------------------------|---------------------------|
| Weight-for-age z-score, mean (95% CI), adjusted mean difference | -0.96 (-1.09 to -0.84) | -0.85 (-0.97 to -0.72) | -0.13 (-0.28 to 0.03) p=0.10 |
| Underweight, n (%), adjusted OR | | | |
| No | 224 (86.8%) | 222 (88.8%) | 1 |
| Yes | 34 (13.2%) | 28 (11.2%) | 1.24 (0.62 to 2.47) p=0.54 |
| Height-for-age z-score, mean (95% CI), adjusted mean difference | -1.36 (-1.61 to -1.12) | -1.34 (-1.49 to -1.20) | -0.06 (-0.24 to 0.11) p=0.49 |
| Stunted, n (%), adjusted OR | | | |
| No | 184 (71.3%) | 189 (75.6%) | 1 |
| Yes | 74 (28.7%) | 61 (24.4%) | 1.23 (0.79 to 1.93) p=0.36 |
| BMI-for-age z-score, mean (95% CI), adjusted mean difference | -0.16 (-0.48 to 0.15) | -0.01 (-0.20 to 0.18) | -0.14 (-0.39 to 0.10) p=0.26 |
| Low BMI-for-age z-score, n (%), adjusted OR | | | |
| No | 239 (92.6%) | 237 (94.8%) | 1 |
| Yes | 19 (7.4%) | 13 (5.2%) | 1.45 (0.68 to 3.05) p=0.34 |
| MUAC-for-age z-score, mean (95% CI), adjusted mean difference | -0.60 (-0.75 to -0.45) | -0.49 (-0.61 to -0.38) | -0.20 (-0.35 to -0.06) p=0.006 |
| Low MUAC-for-age z-score, n (%), adjusted OR | | | |
| No | 245 (95.0%) | 244 (97.6%) | 1 |
| Yes | 13 (5.0%) | 6 (2.4%) | 1.63 (0.53 to 4.96) p=0.39 |
| PSI-SF percentile≥90%, n (%), adjusted OR | | | |
| No | 185 (71.7%) | 161 (63.6%) | OR=1 |
| Yes | 73 (28.3%) | 92 (36.4%) | OR=0.69 (0.45 to 1.05) p=0.08 |
| PSI-SF percentile, mean (95% CI), adjusted mean difference | 76.8 (73.0 to 80.4) | 76.2 (70.5 to 81.9) | 0.44 (-5.18 to 6.05) p=0.88 |
| Parental distress subscale percentile≥90%, n (%), adjusted OR | | | |
| No | 213 (82.6%) | 178 (70.9%) | OR=1 |
| Yes | 45 (17.4%) | 73 (29.1%) | OR=0.56 (0.35 to 0.89) p=0.01 |
| Parental distress subscale, mean (95% CI), adjusted mean difference | 65.0 (60.1 to 70.0) | 66.6 (60.2 to 72.9) | -0.15 (-7.16 to 6.86) p=0.97 |
| Parent-child dysfunctional interaction subscale percentile≥90%, n (%), adjusted OR | | | |
| No | 157 (60.6%) | 152 (60.1%) | OR=1 |
| Yes | 102 (39.3%) | 101 (39.9%) | OR=1.00 (0.63 to 1.59) |
| Parent-child dysfunctional interaction subscale, mean (95% CI), adjusted mean difference | 74.0 (68.3 to 79.7) | 72.7 (65.8 to 79.6) | -0.02 (-6.16 to 6.12) p=0.99 |

Continued
Table 6 Continued

| Outcome | Intervention arm n=257 | Standard of care arm n=249 | Measure of effect (95% CI) |
|---------|------------------------|-----------------------------|---------------------------|
| Difficult child subscale percentile≥90%, n (%) | | | |
| No | 203 (78.3%) | 186 (73.5%) | OR=1 |
| Yes | 56 (21.6%) | 67 (26.5%) | OR=0.79 (0.46 to 1.38) p=0.41 |
| Difficult child subscale, mean (95% CI), adjusted mean difference | | | |
| No | 70.0 (65.5 to 74.5) | 70.0 (66.0 to 73.2) | 0.73 (−4.34 to 5.79) p=0.78 |
| High EPDS, n (%), adjusted OR | | | |
| No | 148 (60.2%) | 134 (56.1%) | 1 |
| Yes | 98 (39.8%) | 105 (43.9%) | 0.79 (0.50 to 1.25) p=0.32 |
| High SSQ-8, n (%), adjusted OR | | | |
| No | 144 (55.2%) | 138 (54.6%) | 1 |
| Yes | 117 (44.8%) | 115 (45.5%) | 0.90 (0.62 to 1.32) p=0.59 |
| Household food security (HFIAS), n (%), adjusted OR | | | |
| Little to no hunger | 196 (75.1%) | 198 (78.3%) | 1 |
| Moderate-to-severe hunger | 65 (24.9%) | 55 (21.7%) | 1.19 (0.62 to 2.26) p=0.52 |

BMI, body mass index; EPDS, Edinburgh Postnatal Depression Scale; HFIAS, Household Food Insecurity Access Scale; MUAC, mid-upper arm circumference; PSI-SF, Parental Stress Index Short Form; SSQ-8, 8-item Shona Symptoms Questionnaire.

those at risk for common mental disorders (44.8% vs 45.5%; aOR=0.90, 95% CI 0.62 to 1.32; p=0.59).

**DISCUSSION**

We undertook a pragmatic evaluation of a multicomponent group intervention combining sessions addressing early childhood stimulation and more general childcare with household economic strengthening to improve food security and economic barriers to clinic attendance. We aimed to improve global child development and retention in HIV care of infants born to HIV-positive mothers both by targeting these outcomes and some of their structural drivers. There was no effect of the intervention on global child development within 4.5 months of completing the intervention. HIV retention in care was almost universal in both arms of the trial by endline. Only 32% of those in the intervention arm were confirmed to have received the full intervention package. Participants reported high levels of food insecurity, symptoms of anxiety and depression and parenting stress at baseline, all factors which are likely to impede participation. The intervention had no effect on any of these secondary outcomes except parental distress. Of note, the intervention was evaluated in rural communities requiring some participants to travel considerable distances to attend sessions.

Although evidence from LMIC is limited, studies have demonstrated that ECS programmes targeting young children in these settings can improve global child development both in the short term and long term. However, few have been delivered to HEU children. Many of these interventions have focused just on single interventions (such as nutrition, positive parenting practices) while this trial has looked at a more comprehensive package which addressed the wider structural barriers to early childhood development in addition to global child development per se.

This intervention implemented by the Bantwana Initiative of World Education was innovative in seeking to reach groups of caregivers rather than individuals and combine ECS training with training on more general child care issues. In addition, the intervention aimed to strengthen household economic security through ISALS both to improve food security (and thereby nutritional status of the child) and reduce economic barriers to clinic attendance. In practice, uptake of the intervention was suboptimal possibly reflecting the acceptability of the intervention to some of the potential beneficiaries. Process evaluation suggested that using a group approach for mothers living with HIV was potentially stigmatising, in that some women feared participation might result in deductive disclosure within the community. The distance caregivers had to travel to take part in intervention sessions in some sites also undermined attendance. In addition, although the majority of women attended ISALS sessions relatively few opted to participate in the savings and lendings process perhaps reflecting their...
reluctance to trust women in a group they were assigned to. Outside of the trial this intervention is offered to all mothers/caregivers of small children in a community and mothers are free to choose whether or not to join an ISALS and with whom. By evaluating the intervention we impose artificial constraints on its delivery.

The trial occurred while the Zimbabwe Ministry of Health and Child Care and partners were strengthening prevention of mother to child transmission programmes. Option B+ was scaled up across Zimbabwe in 2014 and several studies have shown increasing engagement of mothers with services although engagement of infants in the care cascade has been less marked. Our findings suggest substantial improvements in knowledge of infant HIV status over the trial with knowledge of status near universal after 12 months in both arms. Reassuringly few children are HIV positive (3%) post-breast feeding, although among the few with HIV, a substantial proportion in both arms had a detectable viral load, implying suboptimal engagement with care. Over 90% of women in both arms were virologically suppressed, higher than among women living with HIV in Zimbabwe generally (86%). This suggests that Zimbabwean mothers are optimally engaged in care and that our intervention could not substantially contribute to this.

There was some evidence of an intervention effect on parenting stress overall and distress specifically. However, the intervention did not affect risk of other common mental disorders. Of note, the intervention was not designed to address maternal mental health specifically. Caregivers in this trial had a high prevalence of risk of common mental disorder symptoms; around 50% of women were above the cut-off for mild postnatal depression at baseline and endline. Previous studies suggest that maternal depression negatively impacts both parenting and child development and this may have undermined our ability to demonstrate an impact. Future interventions may need to incorporate a specific mental health component. The treatment gap for mental health in much of Africa is extremely high community-based lay health worker problem-solving therapy, such as the Friendship Bench which has been widely scaled up in urban Zimbabwe presents a method of closing the gap. Implementation of an adapted Friendship Bench through primary health clinics in rural areas is currently being explored.

We assessed global child development using the Mullen ELC score which is widely used but not validated or normed among African children of this age. It is a complex instrument and despite comprehensive training and limiting the number of trained assessors our independent review of instrument implementation found that assessment of children was suboptimal. Of note though, the Mullen ELS has been successfully used elsewhere in Africa to determine the impact of a caregiver intervention after 12 months. When compared with normative data (US-based), the baseline data on child development score ranges were comparable, but by 12 months follow-up the scores were lower than normative groups. All children in the study were, by definition, HIV-exposed and there is a solid evidence base that both HIV exposure and infection are associated with child development challenges.

Although there were no short-term effects on cognitive development for children, the fact that the endline data collection occurred a median of 4.5 months after intervention completion may be important. The child development benefit of parenting training may need more time to influence child development outcomes, particularly as the child stimulation components of the course were scheduled at the end of the package and the impact of reduced parental stress on parenting behaviours may take time to be observed.

Strengths of our study included that we piloted research and intervention components to optimise our implementation and evaluation approach. We ran a large trial and had a high retention rate (90%) over 12 months. The trial was conducted independently of programme implementers. We measured child development outcomes using assessors blinded to trial arm and undertook an independent validation of these measures. HIV retention in care was validated using biological markers. Mental health outcomes were all assessed using locally validated scales.

However, there are some limitations. By recruiting from the HIV-exposed infant registry, children who were not engaged in care were not included. This could have introduced some bias, excluding those least engaged in care and potentially most vulnerable. Measurement of global child development was suboptimal and we are uncertain as to what impact this has had on the global child development outcomes. However, we minimised number of Mullen ELC assessors and assessors determined outcomes in intervention and control arms. More time and resources for training and validation of assessment procedures was required. Programme uptake was measured using programme implementer data and the apparently low programme uptake may reflect incomplete data collection by lay facilitators rather than poor attendance. As outlined above, the intervention design was adapted to fit the constraints of the trial evaluation design which may have adversely affected outcomes. A shorter ECS programme may be more practical to implement. The nature of the intervention was ambitious both in complexity and duration. Our study suggests that fidelity to the lengthy programme may be a challenge, but that the intertwining of interventions was feasible. Single interventions may flounder when real-life complexity is not addressed. Parenting in poverty and the presence of HIV is a complex reality. Our hypothesis was that a multi-component intervention which addresses both ECD and its structural drivers was feasible and acceptable to some; the data on attendance can serve as a guide to future intervention planning. HIV-specific interventions, even if they are not labelled as such, may be stigmatising and may hinder attendance.
Our trial has important implications for programmers and policy makers. Causes of poor child development in HIV-affected children are clearly multifactorial, but the feasibility and scalability of addressing multiple factors in a single multicomponent intervention is challenging. Given the high rates of poor mental health, effective community-based mental health interventions need to be scaled up beyond urban areas and potentially run alongside ECS interventions. Design and implementation of evaluations of real-world interventions face several challenges including fitting within donor funding cycles, limited by implementer priorities and political realities, all of which are crucial factors.

Author affiliations
1Institute of Global Health, University College London, London, UK
2MRC Tropical Epidemiology Group, Faculty of Epidemiology and Population Health, London School of Hygiene & Tropical Medicine, London, UK
3Centre for Sexual Health HIV/AIDS Research (CeSHHAR) Zimbabwe, Harare, Zimbabwe
4MRC Tropical Epidemiology Group, World Education Inc./Bantwana, Harare, Zimbabwe
5International Public Health, Liverpool School of Tropical Medicine, Liverpool, UK

Acknowledgements The authors would like to thank various partners like USAID-PEPFAR (funding organisation), the PEPFAR OVC Technical Working Group (technical support) and World Education Zimbabwe (implementing partner), CESSHAR, Mavambe and UCL. The authors would also like to thank Professors Lucie D. Cluver, Mark Tomlinson and Michael J Boivin for their contribution during the initial stages of trial design. The authors would also like to thank the families and children who participated in the trial.

Contributors LS and FMC led the trial design, with involvement from VS and HAW. FC and LS conceived and designed the study protocol. PN and FMC developed the intervention programme. FMC, RC, PN, RM and ZM led the trial implementation, data collection and process evaluation. AMR carried out the statistical analysis. VS and HAW oversaw trial analysis and data interpretation. LS and FMC led data interpretation with involvement from VS and HAW.

Competing interests None declared.

Patient consent for publication Not declared.

Ethics approval The trial (registration number PACTR201701001387209) has been approved by the Medical Research Council of Zimbabwe and Research Council of Zimbabwe approval code MRCZA/19/43, University College London (6789/002) and London School of Hygiene and Tropical Medicine (9912) approvals were also obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, any changes made indicated, and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/.

REFERENCES
1. Youssafzai A, Bhutta Z. Integrating early child development interventions in child health services: opportunities and challenges in developing countries. In: Kamat D, ed. American Academy of Pediatrics textbook of global child health. 1st edn. Washington DC: American Academy of Pediatrics, 2012.
2. Grantham-McGregor S, Cheung YB, Cueto S, et al. Developmental potential in the first 5 years for children in developing countries. The Lancet 2007;369:60–70.
3. Hertzman C. The biological embedding of early experience and its effects on health in adulthood. Ann Y Acad Sci 1999;896:85–95.
4. Engle PL, Fernald LCH, Alderman H, et al. Strategies for reducing inequalities and improving developmental outcomes for young children in low-income and middle-income countries. The Lancet 2011;378:1339–53.
5. Black MM, Hurley KM. Investment in early childhood development. The Lancet 2014;384:1244–5.
6. Sherr L, Croome N, Parra Castaneda K, et al. A Systematic Review of Psychological Functioning of Children Exposed to HIV: Using Evidence to Plan for Tomorrow’s HIV Needs. AIDS Behav 2014;18:2059–74.
7. Hutchings J, Porton J. Developmental delay in HIV-exposed infants in Harare, Zimbabwe. Vulnerable Child Youth Stud 2014;9:43–55.
8. Van Rie A, Mupuata A, Dow A. Impact of the HIV/AIDS epidemic on the neurodevelopment of preschool-aged children in Kinshasa, Democratic Republic of the Congo. Pediatrics 2008;122:e123–8.
9. Blanchette N, Smith ML, Fernandes-Penney A, et al. Cognitive and motor development in children with vertically transmitted HIV infection. Brain Cogn 2001;46:50–3.
10. Sherr L, Croome N, Parra Castaneda K, et al. Developmental challenges in HIV infected children—An updated systematic review. Child Youth Serv Rev 2014;45:74–89.
11. Crowell CS, Hsu Y, Tasiosopoulos K, et al. Early viral suppression improves neurocognitive outcomes in HIV-infected children. AIDS 2015;29:295–304.
12. Crowell CS, Malee KM, Yoege R, et al. Neurologic disease in HIV-infected children and the impact of combination antiretroviral therapy. Rev Med Virol 2014;24:318–31.
13. Richter LM, Sherr L, Adato M, et al. Strengthening families to support children affected by HIV and AIDS. AIDS Care 2009;21 Suppl 1:3–12.
14. Wingood GM, DiClemente RJ, Mikhail I, et al. HIV discrimination and the health of women living with HIV. Women Health 2007;46:99–112.
15. Rotheram-Borus MJ, Christodoulou J, Hayati Rezvan P, et al. Maternal HIV does not affect resiliency among uninfected/HIV exposed South African children from birth to 5 years of age. AIDS 2019;33 Suppl 1:S5–S16.
16. UNICEF. Why early childhood development? 2013. Available: https://www.unicef.org/earlychildhood/index_40748.html. [Accessed 3 Aug 2017].
17. Rotheram-Borus MJ, Tomlinson M, le Roux IM, et al. A cluster randomised controlled effectiveness trial evaluating perinatal home visiting among South African mothers/infants. PLoS One 2014;9:e105934.
18. Potterton J, STEWART A, COOPER P, et al. The effect of a basic home stimulation programme on the development of young children infected with HIV. 2010;52:547–51.
19. van Rlooeyen C, Stewart R, de Wet T. The impact of microfinance in sub-Saharan Africa: a systematic review of the evidence. World Dev 2012;40:2249–62.
20. Cluver L, Pantelic M, Toska E, et al. Stracking the odds for adolescent survival: health service factors associated with full retention in care and adherence amongst adolescents living with HIV in South Africa. J Int AIDS Soc 2018;1758–52.
21. Sherr L, Macedo A, Tomlinson M, et al. Could cash and good parenting affect child cognitive development? A cross-sectional study in South Africa and Malawi. BMC Pediatr 2017;17:123.
22. Li X, Chi P, Sherr L, et al. Psychological resilience among children affected by parental HIV/AIDS: a conceptual framework. Health Psychol Behav Med 2015;3:217–35.
23. UNAIDS. The gap report 2016, 2016. Available: http://www.unaids.org/en/regionscountries/countries/zimbabwe [Accessed 17 Nov 2017].
24. UNAIDS. Global AIDS response country progress report Zimbabwe 2014. Harare, Zimbabwe: Government of Zimbabwe, 2014.
25. UNAIDS. Joint United nations programme on HIV/AIDS, UNAIDS data 2017. Geneva, 2017.
26. Chingono R, Mebrahtu H, Mupambiriso K, et al. Evaluating the effectiveness of a multi-component intervention on early childhood development in paediatric HIV care and treatment programmes: a randomised controlled trial. BMC Pediatr 2018;18:222.
28. Chibanda D, Mangezi W, Tshimanga M, et al. Validation of the Edinburgh postnatal depression scale among women in a high HIV prevalence area in urban Zimbabwe. Arch Womens Ment Health 2010;13:201–6.

29. Patel V, Simunyu E, Gwanzura F, et al. The Shona symptom questionnaire: the development of an Indigenous measure of common mental disorders in Harare. Acta Psychiatr Scand 1997;95:469–75.

30. Abidin RR. Parenting stress index, third edition: professional manual. Odessa, FL: Psychological Assessment Resources, Inc, 1995.

31. Mullen EM. Mullen scales of early learning: AGS circle pines, Mn 1995.

32. Bass JK, Opoka R, Familiar I, et al. Randomized controlled trial of caregiver training for HIV-infected child neurodevelopment and caregiver well being. AIDS 2017;31:1877–83.

33. Boivin MJ, Nakasujja N, Sikorskii A, et al. A randomized controlled trial to evaluate if computerized cognitive rehabilitation improves Neurocognition in Ugandan children with HIV. AIDS Res Hum Retroviruses 2016;32:743–55.10.1089/aid.2016.0026

34. Hayes R, Moulton L. Cluster randomised trials. New York: Chapman and Hall/CRC, 2017.

35. Aboud FE, Singla DR, Nahil MI, et al. Effectiveness of a parenting program in Bangladesh to address early childhood health, growth and development. Soc Sci Med 2013;97:250–8.

36. Ministry of Health and Child Care. MOHCC guidelines and operational service delivery standards. Zimbabwe, 2017.