



# Attention Test Improvements from a Cluster Randomized Controlled Trial of Caregiver Training for HIV-Exposed/Uninfected Ugandan Preschool Children

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**Objective** To report vigilance attention outcomes from a cluster randomized controlled trial of early childhood development caregiver training for perinatally HIV-exposed/uninfected preschool-age children in rural Uganda. The Early Childhood Vigilance Test (ECVT) provides a webcam recording of proportion of time a child views an animation periodically moving across a computer screen.

**Study design** Sixty mothers/caregivers received biweekly year-long training sessions of the Mediation Intervention for Sensitizing Caregivers (MISC), and 59 mothers received biweekly training about nutrition, hygiene, and health care. Children were tested for attention at baseline, 6 months, and 12 months with the ECVT, in terms of proportion of time spent viewing a 6-minute animation of animals greeting the child and moving across the computer monitor screen. Time viewing the animation were scored by trained observers using ProCoder program for webcam scoring of proportion of time the child faced the animation. Mixed-effects modeling was used to compare ECVT outcomes for the 2 intervention groups.

**Results** Unadjusted and adjusted (for age, sex, height, and ECVT at baseline) group differences on ECVT significantly favored the MISC arm at 6 months ( $P = .03$ ; 95% CI (0.01, 0.11), effect size = 0.46) but not at 12 months. Both groups made significant gains in sustained attention across the year-long intervention ( $P = .021$ ) with no significant interaction effects between time and treatment arms or sex.

**Conclusions** Caregiver early childhood development training enhanced attention in at-risk Ugandan children, which can be foundational to improved working memory and learning, and perhaps related to previous language benefits reported for this cohort. (*J Pediatr* 2021;235:226-32).

**Trial registration** Clinicaltrials.gov: NCT00889395.

Boivin et al have established that caregiver early childhood development training of impoverished Ugandan mothers with HIV can enhance the development of their children with HIV.<sup>1,2</sup> A similar intervention with mothers with HIV in these same communities demonstrated consistent findings with children exposed but not infected.<sup>2,3</sup> We have documented that even the older siblings (6-12 years of age) of the preschool children of Ugandan caregivers with HIV receiving early childhood development training can benefit neurocognitively from such an intervention.<sup>4</sup>

These earlier studies used the Mullen Scales of Early Learning (MSEL) language and visual-spatial analysis cognitive skills, as well as a color-object association test of working memory and learning to document the neurodevelopmental benefits of early childhood development intervention with their mothers living with HIV.<sup>2,5</sup> The MSEL does not measure attention, nor did we want to rely solely on caregiver report regarding their child's attentiveness for this neurocognitive domain. Therefore, we selected the Early Childhood Vigilance Test (ECVT) as a culturally and age appropriate performance-based measure of attention in Ugandan children 2-4 years of age at enrollment.

The ECVT, an experimental measure of sustained attention, was designed to evaluate vigilance in preschool children.<sup>6,7</sup> We deemed it to be a useful test for measuring early childhood attention in the sub-Saharan African context after pilot testing. We considered these test attributes important in the assessment of attention in at-risk children in low and middle income countries, after being unable to find any other validated measures of vigilance attention for preschool sub-Saharan African children.<sup>8</sup>

At the time that the present Mediation Intervention for Sensitizing Caregivers (MISC) early childhood development caregiver training intervention

ECVT	Early Childhood Vigilance Test
ES	Effect size
MISC	Mediation Intervention for Sensitizing Caregivers
MSEL	Mullen Scales of Early Learning
RCT	Randomized controlled trial
UCOBAC	Uganda Community Based Association for Child Welfare program

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study was being developed, Boivin et al had adapted the ECVT with preschool Ugandan children (2-4 years of age) in a neurodevelopmental study of the effects of severe malaria at preschool-age.<sup>9,10</sup> In this study, the ECVT was well accepted by the children and proved sensitive in documenting the neurocognitive attention effects of this exposure consistently over a 2-year period follow-up period following acute illness.<sup>10</sup> We previously found using the tests of variables of attention that diminished vigilance attention was one of the most prevalent and robust effects of cerebral malaria in school-age Ugandan children.<sup>11-13</sup> With preschool severe malaria survivors in Uganda, the ECVT also had good correspondence other more comprehensive performance-based measures of development such as the MSEL.<sup>10,14</sup> Therefore, our effective use of the ECVT in gauging the persistent neurocognitive effects of severe malaria in Ugandan preschoolers in the domain of vigilance attention further supported our use of the ECVT in the present intervention study in children affected by HIV.<sup>15</sup>

The ECVT has also been used to evaluate the benefits of early antiretroviral treatment in Ugandan children with HIV.<sup>5,16</sup> The present report presents ECVT findings from our previously published study of the benefits of MISC early childhood development caregiver training for exposed but uninfected children in an impoverished rural area of eastern Uganda.<sup>2</sup>

## Methods

After Human Subjects Research Protection (institutional review board) approval by Michigan State University and Makerere University School of Medicine, all subcounties (unit of randomization) in Tororo district (within a 30 km catchment area of Tororo town) were randomly assigned to one of 2 treatment arms. As previously reported at the time of this clinical trial, these districts in eastern Uganda have 24% of the population living under the poverty line and a 5.8% HIV prevalence.<sup>1,17</sup> This cluster randomized controlled trial (RCT) evaluated whether a year-long biweekly caregiver training intervention could improve caregiver mental health, quality of caregiving, and child neurodevelopmental outcomes in children affected by HIV.

As described in our previously published findings for this early childhood development intervention cluster RCT study (clustered by neighborhood) with HIV-exposed/uninfected children in Tororo,<sup>2</sup> child/caregiver dyads ( $n = 120$ ) were enrolled when the children were 2-4 years of age. This was after completing a previous malaria prevention clinical trial.<sup>18</sup> They were clustered in this manner to prevent spillover of caregiver training intervention arm. By clustering by neighborhood, the non-MISC childhood development caregivers were less likely to learn from the caregiver trainings others have in the intervention arm (eg, immediate neighbors) or to feel neglected in not receiving the same training. Clusters were successively assigned to each trial arm until we had 60 child/caregiver dyads in each of the 2 trial arms. One child who was exposed/uninfected with HIV seroconverted to

HIV positive after enrollment with the mother withdrawing from this study, so the final tally at baseline assessment after cluster randomization to the 2 treatment arms was 60 children in the MISC caregiver training arm and 59 in the “treatment as usual” (or “active control” caregiver training arm). The treatment as usual caregivers received the same number of training sessions, but rather than MISC early childhood development, the sessions were comprised of nutrition/hygiene/health training (Table I).<sup>2</sup>

Following cluster RCT to either MISC early childhood development or treatment as usual intervention arms, we were able to obtain and score ECVT webcam measures across all 3 time points (baseline, 6 months, 12 months) for 56 children in each group (Table II). A few ECVT webcams in each caregiver training arm at each time point were not of sufficiently good quality (eg, lighting, child seating placement) to allow for scoring of eye gaze direction, as determined by the Ugandan research assistant doing the ProCoder scoring. The principal female caregiver provided written consent for her and her child. HIV-exposed/uninfected children were eligible to participate if they had no history of neurologic insult and a female caregiver able to participate in the year-long biweekly early childhood development training.

Participants in both study arms received a biweekly nutritional supplement.<sup>2</sup> The interventions were provided in 1-hour sessions with each caregiver alternating biweekly between home and the project office at Tororo District Main Hospital. All intervention providers were Ugandan Makerere University psychology or social work graduates who received a 2-week training in their respective intervention and participated in weekly supervision and a week-long refresher training.

## Caregiver Training Interventions

**Mediational Intervention for Sensitizing Caregivers.** As described in detail in our previous publication,<sup>2</sup> MISC is a model for training caregivers to enhance their children’s development (early childhood development) based on the Feuerstein theory of cognitive modifiability.<sup>19,20</sup> Caregivers were training individually every other week, alternating

**Table I. Descriptive statistics for study groups at baseline**

Characteristics	MISC training arm ( $n = 60$ )	Control training arm ( $n = 59$ )
	Mean (SD) or $n$ (%)	Mean (SD) or $n$ (%)
Age	2.81 (0.35)	2.79 (0.33)
HAZ	-0.58 (1.66)	-0.34 (1.56)
WAZ	-1.14 (1.48)	-1.00 (1.14)
ECVT at baseline	0.60 (0.15)	0.51 (0.14)
Sex		
Boys	32 (53%)	32 (54%)
Girls	28 (47%)	27 (46%)
Primary caregiver		
Mother	56 (93%)	53 (90%)
Other	4 (7%)	6 (10%)

HAZ, height-for-age z scores; WAZ, weight-for-age z scores.

**Table II.** Unadjusted and adjusted (for age, sex, HAZ, and ECVT at baseline) group differences on ECVT at 6 and 12 months: *P* values, 95% CIs, and ES

ECVT assessments	Unadjusted			Adjusted		
	Group 1, mean (SE)	Group 2, mean (SE)	<i>P</i> value 95% CI ES	Group 1, LS mean (SE)	Group 2, LS mean (SE)	<i>P</i> value, 95% CI ES
6 mo	0.71 (0.02)	0.65 (0.02)	<b>.03</b> (0.01, 0.11) <b>0.46</b>	0.70 (0.02)	0.67 (0.02)	.33 (−0.03, .08) <b>.25</b>
12 mo	0.73 (0.02)	0.68 (0.02)	.13 (−0.01, 0.11) 0.31	0.71 (0.02)	0.70 (0.02)	.82 (−0.05, 0.06) .08

ES, effect size; LS, least squares; SE, standard error.  
*P* values <.05 and ES ≥1/4 are bolded.

between home and clinic, and not within a small group. Office trainings were regularly observed by the study site coordinator to ensure fidelity of intervention.

The training of the caregiver was focused on the acquisition of knowledge and skills necessary for effective intervention to enrich the child's home-based learning environment. The intervention used naturally occurring situations and objects in the environment to train caregivers in a structured process. The training included a variety of techniques (ie, role playing, videotaping, and analysis) for clarifying basic issues related to caregiver-child interaction, with the training objectives including (1) understanding of the philosophy of child rearing and recognition of the family views on what is an ideal child and ideal caregiver; (2) helping caregivers read the child's communication and understand it; (3) knowing how to raise the caregivers' awareness of their interactive behaviors and the immediate and potential effects on the child; (4) learning how to identify and use the most suitable ways to foster quality interactions and mediation of learning in everyday life with the children; (5) and encouraging caregivers to value their own ideas for meaningful, challenging, and affectionate interactions with the children. This approach to MISC training was consistent with previous work in Ethiopia.<sup>20,21</sup>

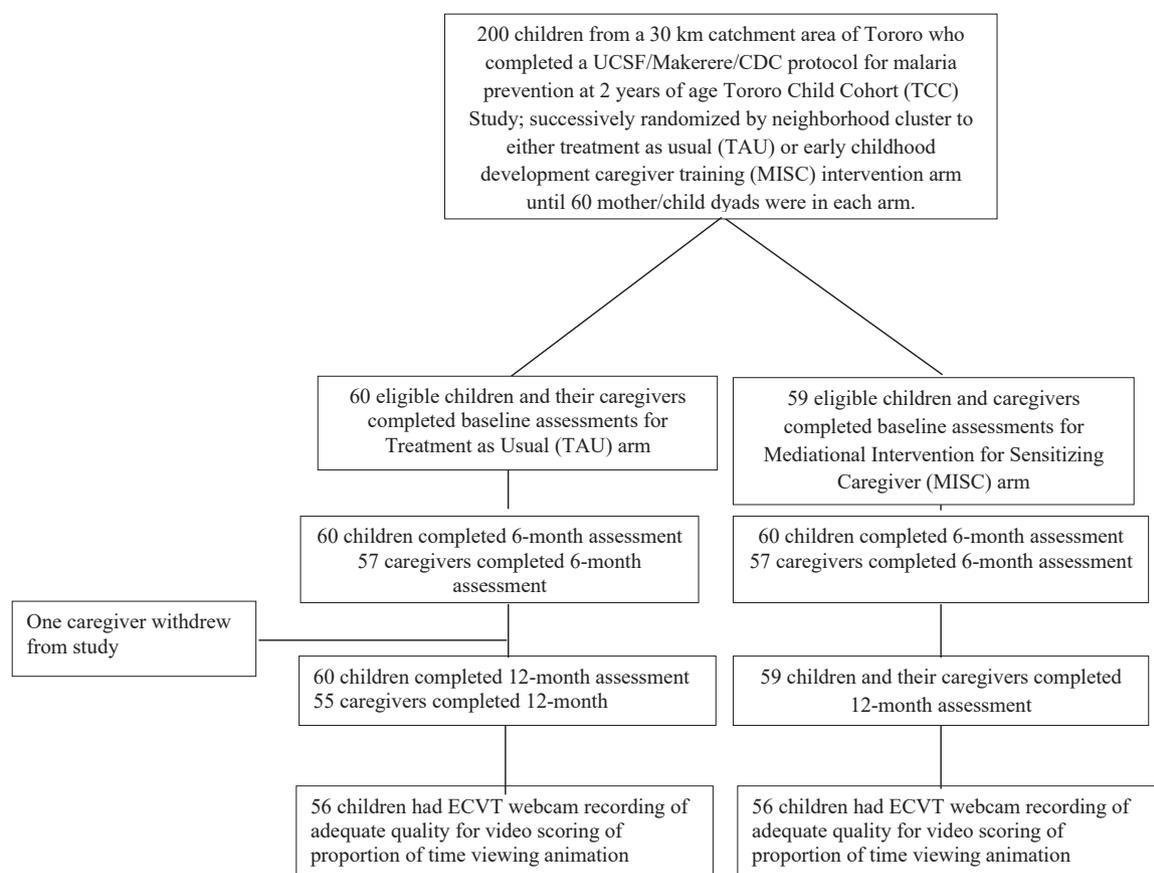
**Treatment as Usual Training Arm.** The treatment as usual comparison condition was a manualized nutrition and hygiene information program designed for impoverished households by the Uganda Community Based Association for Child Welfare program (UCOBAC; <http://ucobac.org/>) with support from United Nations International Children's Emergency Fund.<sup>3</sup> For the treatment as usual dyads, intervention sessions consisted of a 30- to 45-minute nutrition and medical training session using a standard curriculum. This ensured that the treatment as usual group receives a comparable number of contact/support hours by the field teams, alternating between home and clinic every other week, as was the case with the MISC intervention caregiver training arm. The UCOBAC treatment as usual program differed from MISC early childhood development in that it did not explicitly train caregivers on how to facilitate the cognitive development of their child. The purpose of this program is to sustain adequate nutritional and health care for the child. Because the district ministry of health for Tororo had made

this intervention available to all households requesting this in the village areas of Tororo, we could not ethically withhold this program for study women in the form of a passive control arm. Instead, for local IRB approval we needed to include UCOBAC intervention as our treatment as usual arm and considered it an active control condition so as to gauge the "value added" benefits to ECVT attention for the MISC early childhood development children.

### Measures

Study data were collected at baseline (enrollment), at 6 months (midway through training), and 1 year (completion of training) (Figure). Child and caregiver demographics for this cohort have been previously described<sup>2</sup> and are summarized in Table I. We present here findings for the ECVT test only because these have not been previously reported.<sup>6,22</sup> Because it was previously validated for the present study setting,<sup>23</sup> the ECVT was used in the present study to measure sustained attention, with the principal outcome being the proportion of time looking at an animation video as scored from a computer-mounted webcam video.<sup>3</sup> We also included weight-for-age z scores and height-for-age z scores based on World Health Organization 2018 norms as our adjustment for child growth measures (Tables I and II).

**The ECVT.** The ECVT, a test of vigilance attention, is originally described by Zelinsky et al<sup>6,7</sup> and was previously used by Boivin et al to assess attention in Ugandan preschool survivors of severe malaria<sup>10</sup> and HIV.<sup>3,15,23</sup> A colorful rabbit periodically greeted a child audibly to attract the child's attention to the computer screen, and then disappears after a few seconds. This was almost immediately followed by another colorful animal that appeared and moved across the screen silently with the expectation that the child would visually track it. A different colorful animal appeared for 10 seconds as it moved across the screen and then disappeared for either 5, 10, or 15 seconds. A different creature then appeared each time and alternated moving left to right or right to left across the screen. The length of time the creatures were absent was arranged such that each interval of time occurred 6 times. A webcam on top of the computer screen recorded the child's face throughout the duration of the test (6.5 minutes in duration).



**Figure.** Consort diagram from the cluster RCT for children in Tororo Uganda born to mothers with confirmed HIV infection but who themselves were confirmed uninfected (HIV-exposed/uninfected). These were based on a sampling pool of 200 children who eligible at 2 years of age after completing a study on the “Interactions between HIV and malaria in African children” conducted by a University of California–San Francisco (UCSF), Makerere University, and Center for Disease Control (CDC) collaboration entitled the Tororo Child Cohort Study.

The principal ECVT outcome score was the total proportion of time during the animation presentation that the child could clearly be seen to have been facing the computer screen; the total number of seconds looking at the video screen divided by the total number of seconds in the video (420 seconds). In earlier developmental work for the ECVT, descriptive statistics of preschool American children indicated that the average time spent looking at the video was 67%, which corresponded to just over 4.5 minutes.<sup>7</sup> The median score for these children was 70% and the SD of time spent looking at the screen was 19%, corresponding to 1.33 minutes. These would be considered normative for this test.

**Validation of the ECVT as a Vigilance Measure of Attention.** In the original validation of the ECVT, it was administered along with several attention and cognitive measures to normal Midwestern US samples of children ranging from 24 to 30 months of age.<sup>6,7</sup> In terms of the webcam scoring, the ECVT had adequate internal consistency, demonstrated by correlations for each third of the test ranging from .56 to .81. Interscorer reliability ProCoder scores for propor-

tion of total time viewing the screen during the animation had a correlation of .98, indicating excellent inter-rater reliability.

The validity of the ECVT was demonstrated through examining correlations between the ECVT and parent/caregiver rating measures of attention.<sup>15</sup> ECVT performance was significantly correlated ( $r^2 = .33$ ,  $P < .01$ ) with the Behavior Rating Scale from the Bayley Scales of Infant Development-Second Edition.<sup>24</sup> This rating scale included items pertaining to attention, persistence, motor regulation, adaptability, and negative affect. In addition, the ECVT was found to significantly correlate ( $r^2 = -.35$ ) with a free play session coded according to the Self-Regulation scale of Minnesota Preschool Affect Rating Scale,<sup>25</sup> which provided child observer ratings for attention, orientation to objects, persistence, and adaptability. Finally, the ECVT was significantly correlated with the proportion of time the child played with toys during an 8-minute free-play session.

In sum, initial psychometric testing of this measure suggested that the measure could be a reliable and valid tool for measuring sustained attention in very young children. The present study evaluated the utility of the ECVT for

measuring vigilance attention in preschool Ugandan children perinatally exposed to, but not infected with, HIV.

**ECVT Coding and Analysis.** Raw ECVT data (video files) were coded by a single Ugandan research assistant in which he had scored ECVT webcam videos using ProCoder. Each of the 3 Ugandan research assistants at this study site originally enlisted to score the ECVT webcams for this previous R01 MISC early childhood development cluster RCT study practiced scoring the ECVT until achieving an inter-rater reliability of 0.80 over 10 successive webcam recordings.<sup>1,3</sup>

Ultimately, 1 research assistant scored all the ECVT webcams in the present study blinded to the intervention group and the assessment time (baseline, 6 months, 12 months) for each of these webcam videos. ECVT scoring for our principal attention measure outcome in this study involved tracking the amount of time in seconds the child was looking at the screen and turning that amount into a percentage representing the amount of time spent attending to the screen out of the total time of the animation. ProCoder for Digital Video (ProCoderDV; Tapp 2003)<sup>26</sup> is a software program developed at Vanderbilt University for gathering observational data from video and/or audio files, was used to code all of the ECVT videos.<sup>15,23</sup>

**ECVT Study Outcome Analysis.** Baseline characteristics of study participants were summarized (Table I). Linear mixed effects models were employed to analyze the ECVT measures at 6 and 12 months in relation to trial arm while adjusting for ECVT at baseline, age, and sex. Correlations arising from repeated measures were accounted for by specifying an autoregressive covariance structure. Time-by-intervention interactions were included to capture potential changes in differences by intervention arm over time. The least squares (adjusted) means for each time point and trial arm were output from the linear mixed effects models, and differences between them by trial arm were tested. Inclusion of a random effect for clusters (unit of randomization) was explored, but the resulting intraclass correlation coefficients were virtually zero. Effect sizes were estimated as differences between means by study group (unadjusted or adjusted) divided by the SD (unadjusted) or square root of residual variance (adjusted).

## Results

Children in both interventions improved significantly from baseline to 6 and 12 months ( $F = 4.41, P = .013$ ) with the interaction effects by age ( $F = 2.49, P = .09$ ) and intervention arm ( $F = 0.65, P = .52$ ) being insignificant, although the main effect of group (MISC vs control) across the 3 time points was significant ( $F = 7.50, P = .007$ ). Controlling for ECVT baseline performance, age at assessment, and sex, MISC performance on the ECVT was significantly better with moderate effect sizes compared with the control arm at 6 months for both the adjusted and unadjusted analyses (Table II).

However, this difference was not significant at 12 months, although the unadjusted comparison has a moderate effect size (ES) difference ( $ES = 0.31$ ; Table II). The effects of age, sex, and height-for-age z scores were not significant over the baseline ECVT.

We analysed the comparison between the MISC and treatment as usual children with and without adjusting for ECVT at baseline (Table II). This allowed us to see, in our unadjusted findings, whether children with weaker scores could have benefited more from MISC intervention and controlling for baseline ECVT performance would mask that finding. Depending on the structure of data in these unadjusted between-group comparisons, additional analyses could specifically evaluate utility of training in weaker and stronger performers on the ECVT. However, this seemed to not be the case in our preliminary evaluation, so these further analyses were not necessary.

## Discussion

The present study showed that MISC was a valuable treatment modality among this population. HIV-exposed/uninfected children receiving MISC showed significant improvements in attention at 6-month follow-up and continued to improve their performance at the 12-month follow-up, although not statistically different than that of the control intervention arm by 12 months. Therefore, the “value-added” attention benefits of MISC early childhood development relative to treatment as usual were transient.

The MISC children had significantly greater gains by the end of the training year compared with controls on the MSEL receptive and expressive language development, and on the MSEL composite score of cognitive ability. Color-Object Association Test total memory for MISC children was marginally better than controls (moderate ES although not quite statistically significant). The differing time course of improvements in different cognitive domains in response to MISC early childhood development intervention (eg, language vs Color-Object Association Test memory) may be due to the period of neurocognitive development most responsive to an early childhood development between 2 and 3 years of age. That was within the age range of our present HIV-exposed/uninfected cohort of children (2-4 years of age).

No Achenbach Child Behavior Checklist differences between the groups were noted. Caldwell Home Observation for Measurement of the Environment scores and observed mediational interaction scores from videotapes measuring caregiving quality also improved significantly more for the MISC group, indicating fidelity of intervention in terms of caregiving quality from the caregiver training.

It may be that the MISC-enhanced cognitive performance, especially in language development, was undergirded by the enhanced ECVT attention in the first 6 months of the year-long training especially, as witnessed in the greater MISC ECVT attention benefits reported here. These neurocognitive benefits were possibly mediated by improved caregiving and

positive emotional benefit to the caregiver.<sup>17</sup> MISC training does emphasize caregiver-child verbal interactions as a core part of the early childhood development program, and this could also explain the language benefit over time during a developmental period (2-3 years) when both expressive and receptive language blossom in children whether developmentally delayed or not.<sup>19-21,27,28</sup>

Because our MISC early childhood development intervention trial did previously report developmental benefits for child language and caregiver well-being,<sup>2,5</sup> future studies could include assessing the extent of enhanced language development. Improved language would be further demonstrated to come about from improved caregiving for impoverished HIV-affected African children, and added benefit for school achievement, especially in terms of early stage literacy education.<sup>29</sup>

In a subsequent cluster RCT comparing the same interventions with new cohorts of HIV-exposed/uninfected children 2-3 years of age at the same site as the present study, twice the number of child/caregiver dyads (n = 120) were initially enrolled in a year-long biweekly training program.<sup>3</sup> The same child development outcomes were administered at baseline, 6 months, and 12 months. However, a 12-month post-training follow-up evaluation was also administered. In this more highly powered study, caregivers who participated in MISC demonstrated significantly improved caregiving quality, but this did not result in better child cognitive outcomes. However, caregiving quality was significantly correlated with MSEL composite cognitive performance 1-year post training for the MISC trial arms, like our post-training ECVT benefit in the present study. Likewise, physical growth was significantly related to child development outcomes,<sup>3</sup> as was the case with our ECVT findings with children with HIV and in the present study.<sup>15</sup>

In a MISC early childhood development clinical trial study at the present study site with a cohort of preschool-age children perinatally infected with HIV, the MISC caregiver training arm evidenced significant postintervention receptive language benefits compared with the treatment as usual control arm. These benefits persisted at 1-year follow-up post-training.<sup>1</sup> MISC caregivers reported significantly less functional impairment related to activities of daily child caregiving. Thus, greater functionality for these caregivers living with HIV may have mediated the language benefits from MISC training because of better care of the child with HIV in general (including anti-retroviral therapy treatment and seeking medical care support). The improved outcomes for the MISC children with HIV may also have been due to better implementation of MISC training for healthier moms living with HIV who were also more functional. Therefore, our present study findings extend the emphasis on early assessment to sub-Saharan African children in impoverished rural settings also at risk from the effects of HIV on their caregiving and overall developmental milieu.

Accurate identification of attention problems at the preschool level with performance-based and culturally adaptable

tests such as the ECVT can be an important screening and surveillance tool for identifying children whose caregivers might benefit from a MISC early childhood development intervention. The key would be adapting such an intervention for scalability, such as a shorter version adapted to the small-group setting and led by community woman peer leaders.<sup>17,29</sup>

MISC can lead to enhanced vigilance attention within the first 6 months of our year-long biweekly training program for caregivers living with HIV. We propose that this improved attention during the first 6 months of caregiver training intervention may subsequently reinforce improvements evident in child receptive language acquisition,<sup>29</sup> and intend to explore this relationship more fully with ECVT measures enhanced by eye tracking technology.<sup>23,30</sup> Establishing such a relationship would help justify using ECVT as a short screening measure of neurocognitive development for at-risk children in low and middle income countries resource-constrained settings as a means of determining those who may be lagging in school-readiness. Such children could then be helped by a scaleable early childhood development intervention such as MISC, strategically targeting caregiver interactions for enhancing the child's preliteracy foundational skills during a critical phase of language development during a critical phase of cognitive and social development for these children. Such screening and services could then become part of the standard of care for public health outreach services to such resource-constrained communities.<sup>31</sup> ■

*This work is dedicated to Professor Pnina Klein (1945-2014), who dedicated her professional life to the development and promotion of the MISC, and without whose efforts this study would never have been possible.*

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