

Adjustment of a Population of South African Children of Mothers Living With/and Without HIV Through Three Years Post-Birth

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Abstract Mothers living with HIV (MLH) and their children are typically studied to ensure that perinatal HIV transmission is blocked. Yet, HIV impacts MLH and their children lifelong. We examine child outcomes from pregnancy to 3 years post-birth among a peri-urban population of pregnant MLH and mothers without HIV (MWOH). Almost all pregnant women in 12 neighborhoods (98 %; N = 584) in Cape Town, South Africa were recruited and repeatedly assessed within 2 weeks of birth (92 %), at 6 months (88 %), 18 months (84 %), and 3 years post-birth (86 %). There were 186 MLH and 398 MWOH. Controlling for neighborhood and repeated measures, child and maternal outcomes were contrasted over time using longitudinal random effects regression analyses. For measures collected only at 3 years, outcomes were analyzed using multiple regressions. Compared to MWOH, MLH had less income, more informal housing and food insecurity, used alcohol more often during pregnancy, and were more depressed during pregnancy and over time. Only 4.8 % of MLH's children were seropositive; seropositive children were excluded from additional analyses. Children of MLH tended to have significantly lower weights ($p < .10$) over time (i.e., lower weight-for-age Z-scores) and were also hospitalized significantly more often than children of MWOH ($p < .01$). Children of MLH and

MWOH died at similar rates (8.5 %) and were similar in social and behavioral adjustment, vocabulary, and executive functioning at 3 years post-birth. Despite living in households with fewer resources and having more depressed mothers, only the physical health of children of MLH is compromised, compared to children of MWOH. In township neighborhoods with extreme poverty, social, behavioral, language, and cognitive functioning appear similar over the first three years of life between children of MLH and MWOH.

Keywords Mothers living with HIV · Maternal child health · Low and middle income countries · PMTCT · Community health workers

Introduction

Poverty, non-communicable and infectious diseases are common barriers to the healthy development of children in low and middle income countries (LMIC) [1]. These factors often compromise children's health by the time children are 1000 days old and continue to have negative consequences lifelong [1, 2].

In sub-Saharan Africa, maternal HIV often threatens children's health. One young women aged 15–24 years old becomes infected by HIV every minute [3–5] and HIV infection is twice as common among young women as compared to young men [6, 7]. Annually, approximately 375,000 seropositive South African women are offered services to prevent-mother-to-child-transmission (PMTCT) of HIV [4–6, 8]. About 30 % of mothers learn of their HIV infection while pregnant, when the probability of infecting their children is highest [5]. Therefore, the impact of HIV on children is most commonly evaluated from birth to

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12 months post-birth among clinic samples, with substantial loss-to-follow-up [9–11]. These studies typically focus on whether perinatal transmission has been averted or not [10, 11]. In contrast to previous research, this study examines all pregnant women and their children in 12 neighborhoods over time, mothers living with HIV (MLH) and mothers without HIV (MWOH).

Maternal HIV influences children on an ongoing basis [12] and is likely to affect children's long-term development [13, 14]. MLH have more tasks to accomplish in order to sustain their health over time, compared to MWOH. MLH must regularly seek HIV care, know their CD4 count, routinely seek, receive and adhere to antiretroviral therapies (ARV), and proactively be tested and treated for TB [15]. MLH must also decide to whom to disclose their serostatus and how, when, and what to share [16, 17]. Both issues of disclosure and the need to protect their sexual partners from acquiring HIV make women's partnerships more complex. HIV is often stigmatizing [18, 19], so MLH may avoid situations that could make them vulnerable with neighbors or extended family.

Physical health symptoms related to HIV may also make establishing and maintaining healthy daily routines more difficult for MLH (i.e., eating meals consistently, sleeping and rising at consistent times [20, 21]. MLH are also more likely to be depressed than MWOH [20, 21]. Depressed mothers tend to have more chaotic family routines and schedules [20]. When a mother is depressed, her ability to effectively parent is significantly compromised, reducing children's resiliency [22–26]. Children of depressed mothers typically demonstrate higher rates of psychopathology and antisocial behavior [27]. Given that MLH are more depressed and have health burdens, children of MLH were expected to have more social and behavioral problems than children of MWOH.

Most of the research on children of MLH has focused on their infected children living with HIV. Uninfected children of MLH have been expected to have compromised immune systems. Yet, the immune systems of perinatally-exposed, but HIV uninfected children appear relatively normal [28]. Children's responses to vaccinations and immunizations are similar to non-perinatally-exposed children [29]. However, there are few studies of the social, behavioral, language or cognitive consequences of maternal HIV on the uninfected children of MLH. This study compares uninfected children of MLH to children experiencing similar neighborhood and family stressors, but whose mothers do not have HIV.

We have a highly representative sample of pregnant women from 12 peri-urban neighborhoods, with 98 % of pregnant MLH and MWOH recruited. Almost all of these mothers and their children have been repeatedly reassessed at five time points over the first 3 years of life. This paper

examines child outcomes between MLH and MWOH, documenting the similarities and differences in the lives of MLH and MWOH, which may account for children's adjustment. Therefore, we examined children's cognitive, behavioral, and social outcomes over 3 years, comparing children of MLH and MWOH. We hypothesized that child outcomes would be worse for children and their MLH compared to children and their MWOH. We also documented the initial and ongoing maternal stressors that may add to the maternal disease burden and, thus, poor child outcomes.

Methods

The Institutional Review Boards of the University of California, Los Angeles (UCLA), Stellenbosch University, and Emory University approved the study. The study protocol has been published previously [30]. Independent teams conducted the assessment (Stellenbosch) and data analyses (UCLA). The study was conducted in 12 neighborhoods in three Cape Town townships. These neighborhoods constituted the control condition in a larger randomized controlled trial [31–33]. Each neighborhood had health care accessible within 5 km, and these clinics provided HIV testing, dual regimen antiretroviral therapies for MLH, consistent access to milk tins (i.e., formula), TB and CD4 testing, co-trimoxazole for infants until HIV testing was possible with polymerase chain reaction (PCR) for infants at 6 weeks, postnatal visits within 2 weeks post-birth, treatment for MLH, and HIV testing for partners of MLH. Each neighborhood consisted of about 450–600 families and had 5–6 shebeens (i.e., alcohol bars). The presence of electricity, running water and indoor toilets on the premises varied across neighborhoods.

Participants

From May 2009 to September 2010, local recruiters (township women from different neighborhoods) went house-to-house to identify all adult pregnant women at least 18 years of age and obtained consent to contact; 98 % were then assessed by a different interviewer. The sample was highly mobile; 24 % had moved nearly 1000 km to the Eastern Cape within the first 3 years post-birth. Yet, mothers and children were reassessed in person, even if families had moved.

Assessments

Assessments were conducted at 1 week post-birth (98.7 %; $M = 2.1$ weeks; $SD = 2.42$); 6 months (89.4 %;

M = 6.3 months, SD = 0.95); 18 months (91.9 %; M = 18.5 months; SD = 1.55); and 3 years (84.9 %; M = 36.6 months, SD = 2.24). All assessments were completed by 73 % of mothers. Only 3 % were assessed at one follow-up point. Among the 24 % of children living in the Eastern Cape of South Africa by 3 years of age, 62 % of these children were there without their mothers. Some assessments included interviews to be completed by mothers only, without an independent assessment of their child.

Child Measures

At each assessment, interviewers weighed and measured infants' length and head circumference. Data on growth and development were also transcribed from their government-issued, Road-to-Health card. The infant anthropometric data was converted to Z-scores based on the World Health Organization's (WHO) age-adjusted norms for height-for-age, weight-for-age, and weight-for-height-for-age. A Z-score below -2 SD was considered a serious health deficit [34], reflecting stunting (height-for-age Z-score < -2 SD) or malnourishment (weight-for-age Z-score < -2 SD). Low birth weight (LBW) was reported as < 2500 grams.

Health Clinic visits and hospitalizations were reported by mothers and transcribed from the Road-to-Health card.

Language was assessed at 3 years only using a version of the Peabody Picture Vocabulary Test (PPVT) for children [35], adapted for South Africa [36]. With the PPVT, children are shown four pictures and asked to identify an object named by the interviewer. The responses are summed to create a composite score.

Executive functioning was assessed by three types of tasks [37, 38]: (1) "something's the same," which presents a series of match-to-sample tasks from among three choices; (2) "silly sounds" tasks, which ask children to mimic animal sounds when presented with pictures of animals; and, (3) "operational span," which tests working memory by asking children to recall figures presented to them on a previous page, without looking. The number of correct responses across tasks are combined for an overall score.

Behavior was rated by parents using Achenbach's (1992) [39] *Preschool Behavior Checklist*, a 99-item questionnaire rating their children's comportment on a 0–2 scale, resulting in scales for internalizing behaviors, externalizing behaviors, and an overall summary score. The Strengths and Difficulties Questionnaire [40] is a 25-item maternal interview which reports prosocial and difficult child behaviors. This measure has been previously shown to have both high internal and external validity on

samples in the United States, as well as among South Africans [41–43].

Family Issues Fathers must formally present children to their families in order to be considered "legitimate"; presentation was scored as present (1) or not (0). We also documented whether the father lived with the mother (or not); mothers received the government child support grant (or not); childcare was provided in a crèche (i.e., childcare facility; or not); and, mothers were employed (or not).

Maternal Measures

HIV continuum of care. MLH were asked to self-report their HIV status (which was also documented on the child's Road-to-Health card), HIV-related clinic appointments, and prescriptions received for ARV medication.¹

Partnerships and HIV prevention strategies included recent partnerships (i.e., in the last 3 months), intimate partner violence, maternal disclosure of serostatus to partners; asking partners to test for HIV; and, consistent condom use (on 10 of the last 10 sexual encounters, or not).

Health was assessed by self-reports of HIV (1 yes, 0 no), and reports of tuberculosis, diabetes and high blood pressure [presence of any of three conditions (1) or not (0)]. Mothers reported subsequent pregnancies and births.

Depressive symptoms were reported on the Edinburgh Postnatal Depression Scale (EPDS) at each assessment [44]. The EPDS is a 10-item scale which is rated on a 4-point rank order and summed across items. A score of greater than 13 indicates probable clinical depression. This scale has been validated among South African women [45]. The EPDS was designed for women who are pregnant or have just had a baby, but has also been shown to be an effective measure for general depression in the larger population [44]. At 3 years only, the Hopkins Symptom Checklist (HSCL-25) [46] was administered. This is a 25-item scale with each item having a range of 1–4.

Alcohol and substance use was self-reported, including the frequency of alcohol use, the number of drinks per episode, and symptoms of withdrawal from alcohol. The Derived AUDIT-C, a three-item reliable questionnaire of alcohol abuse was administered [47, 48]. This scale has been used extensively among Cape Town residents. A score greater than 2 on the AUDIT indicates harmful alcohol use.

Analyses

We conducted an analysis comparing those lost to follow-up at the 3 year assessment ($n = 82$) with those retained

¹ The adherence rates to PMTCT milestones have been previously reported and are not included in this report [31].

($n = 455$). There were only two significant differences: those who were lost to follow-up were less likely to have a recent sexual partner at the baseline interview and more likely to have a monthly income less than 2000 rand.² Our primary analysis compared MLH and MWOH using random effects regression models, with MWOH as the reference group. For the purpose of the analysis, a MLH is defined as a mother that reported a positive HIV status at least once during the study (during pregnancy or at any follow-up assessment). Logistic random effects regression models were used for binary outcomes and a Poisson random effects regression model was used for count outcomes. All models were adjusted for neighborhood clustering and for repeated measures, where appropriate. The developmentally sensitive measures of language and executive functioning were also adjusted for children's age in months. Comparisons of MLH and MWOH utilized a random participant effect to control for the longitudinal nature of the assessments of partner relationships, physical and mental health, and family issues. The random effects regression was carried out using SAS PROC MIXED or GLIMMIX for continuous or binary/count variables, respectively (version 9.4; SAS Institute Inc., Cary, North Carolina).

Results

Contrasts During Pregnancy

Table 1 compares the MWOH and the MLH at the time of recruitment, i.e., during pregnancy (26 weeks). Similar to the national profile, 32 % of the study participants were MLH. The pregnant women were about 26 years old on average, almost all (87.7 %) had a sexual partner, but only about half (54.5 %) lived with their partner. MLH and MWOH were equally likely to live with a partner. MWOH went to school about 6 months longer than MLH (i.e., 10th grade; $p < .01$), were more likely to have ever been employed (19.6 % vs. 12 %, $p < .05$), had higher incomes (i.e., above 2000 rand; 52.1 % vs. 39.9 %, $p < .01$), were less likely to experience food insecurity (47 % vs. 57 %, $p < .05$), and tended to live in formal housing, rather than informal housing (34.4 % vs. 28.5 %, $p < .10$). The probability of having water, electricity, or of having a toilet that flushes on the premises were similar between MWOH and MLH. MWOH and MLH were recruited at about the same point in their pregnancy and were equally likely to receive antenatal care. MWOH tended to be primiparous (36.2 % vs. 28 %, $p < .054$) more often than MLH. Partners of MLH were significantly more likely to be

seropositive (31.1 % vs. 0 %), although women of different serostatuses were equally likely to ask their partners to get tested for HIV (83.3 %). MLH tended to use alcohol more often before realizing they were pregnant (30.9 % vs. 23.5 %; $p < .06$), and had significantly more problematic drinking during pregnancy compared to MWOH (25.9 % vs. 17.7 %; $p < .01$).

Child Outcomes Over time

Only 4.8 % ($n = 9$) of children were seropositive. These children were excluded from further analyses. The developmental trajectories of seropositive children have been repeatedly studied over time. There are no community samples of MLH whose children are seronegative. Table 2 summarizes the child outcomes for MWOH and MLH. Over 3 years, 8.5 % ($n = 43/507$) children died, with rates similar across serostatus. MWOH and MLH were equally likely to have a low birth weight baby (i.e., <2500 grams; 17.5 %). The weight-for-age Z-score and the weight-for-height-by-age Z-scores tended to be significantly lower among children of MLH compared to children of MWOH (-0.0 vs. 0.1 and 1.0 vs. 1.2 respectively, $p < .10$). The entire sample is more than 1 SD below the WHO mean height-for age Z-score and weight-by-height for age Z-score for healthy children, as determined by Z-scores calculated at 3 years post-birth. The seronegative children of MLH were significantly more likely to be hospitalized than children of MWOH (37.7 % vs. 29.1 %, $p < .05$). There were no significant differences between children of MWOH and MLH in vocabulary, executive functioning, or on two indices of behavioral adjustment (Achenbach's Preschool Behavior Checklist and the Strengths and Difficulties Questionnaire).

Maternal Differences Between MLH and MWOH Over Time

Table 3 compares MWOH and MLH over 3 years. Partner relationships were similar across mothers with different serostatus, including not having a current partner (16 %), having a recent partner (i.e., in the last 3 months; 84 %), having more than one recent partner (2.2 %), and the likelihood of intimate partner violence (or not, 15.4 %). Over time, significantly more MLH wanted their partners to be tested for HIV (89.1 %). MLH were far more likely to consistently use a condom (OR = 6.3, $p < .01$), to ask their partner to test their HIV status (OR = 3.73, $p < .01$), and to disclose their serostatus to their partner (OR = 4.9, $p < .01$) than MWOH. MLH were significantly more likely to have active TB cases (17.7 % vs. 5.4 %, $p < .05$) compared to MWOH. MLH and MWOH were equally likely to have a subsequent child reported (18.5 %).

² Results available upon request from authors.

Table 1 Baseline characteristics of the sample (N = 584)^a summarized by HIV status: MWOH (N = 398) and MLH (N = 186)

	MWOH (N = 398) n (%)	MLH (N = 186) n (%)	Total (N = 584) n (%)
Demographic characteristics			
Mean age (SD)	26.1 (5.7)	26.8 (5.2)	26.3 (5.6)
Married or lives with partner	220 (55.3)	98 (52.7)	318 (54.5)
Mean highest grade level (SD)	10.4 (1.8)	10.0 (1.8)	10.3 (1.8)**
Ever employed	79 (19.8)	24 (12.9)	103 (17.6)*
Monthly household income >2000 rand	202 (52.1)	73 (39.9)	275 (48.2)**
Mother hungry past week	187 (47.0)	106 (57.0)	293 (50.2)*
Children hungry past week	118 (29.6)	62 (33.3)	180 (30.8)
Formal housing	137 (34.4)	53 (28.5)	190 (32.5) [†]
Water on site	223 (56.0)	98 (52.7)	321 (55.0)
Electricity	370 (93.0)	164 (88.2)	534 (91.4)
Flush toilet	233 (58.5)	104 (55.9)	337 (57.7)
Maternal health			
Mean weeks pregnant at assessment (SD)	26.2 (8.0)	25.7 (8.7)	26.0 (8.2)
Non-primipara	254 (63.8)	134 (72.0)	388 (66.4)*
Previous Low Birth Weight infant	45 (18.1)	22 (16.4)	68 (17.5)
Mean number of live births (SD)	1.8 (1.2)	1.6 (1.1)	1.7 (1.1)
Antenatal clinic appointment			
Tested for TB, lifetime	127 (31.9)	79 (42.5)	206 (35.3)
Test positive TB, lifetime	20 (5.7)	29 (16.8)	49 (9.4)***
Partnerships			
Recent ^b sexual partner	351 (88.2)	161 (86.6)	512 (87.7)
Partner HIV+	0 (0.0)	50 (31.1)	50 (9.8)**
Partner HIV–	254 (72.4)	37 (23.0)	291 (56.8)
Partner serostatus unknown	97 (27.6)	74 (46.0)	171 (33.4)
Request partner to test for HIV	242 (82.3)	108 (85.7)	350 (83.3)
Mental health			
Mean EPDS score >13	113 (28.4)	76 (40.9)	189 (32.4)**
Alcohol			
Drank any alcohol, month prior to pregnancy discovery	77 (23.5)	50 (30.9)	127 (25.9) [†]
AUDIT-C > 2, month prior to pregnancy discovery	58 (17.7)	42 (25.9)	100 (20.4)*
Drank any alcohol after pregnancy discovery	32 (9.8)	17 (10.6)	49 (10.0)
AUDIT-C > 2, after pregnancy discovery	16 (4.9)	8 (5.0)	24 (4.9)
Drank any alcohol, anytime during pregnancy	95 (23.9)	57 (30.6)	152 (26.0) [†]

p values from linear (continuous variables), logistic (binary), or multinomial (categorical, >2 levels) random effects regressions, adjusted for neighborhood clustering

[†] *p* < .10; * *p* < .05; ** *p* < .01; *** *p* < .001

^a 10 mothers did not report their HIV status at recruitment and are excluded

^b “Recent” always refers to the last 3 months

MLH reported significantly higher depression scores on both the EPDS and the HSCL-25 over 3 years. A significantly higher percentage of MLH had EPDS scores greater than 13 compared to MWOH (27.1 % vs. 18 %). Over 3 years, MLH and MWOH were equally likely to use alcohol and have symptoms of alcohol abuse in the harmful range

on the AUDIT-C (15.2 %), secure the child support grant (80.9 %), place their child in a crèche (58.1 %), or to be employed (44.3 %). Mothers of different serostatus also moved their residences at similar rates: 28.1 % moved from childbirth to 3 years later. Almost all moved to the Eastern Cape.

Table 2 Child outcomes at 36 months, stratified by HIV status: MWOH (N = 316) and MLH (N = 131)

	MWOH (N = 316) mean (SD)	MLH ^b (N = 131) mean (SD)	Total (N = 447) mean (SD)
Growth			
Weight-for-age Z	0.1 (1.1)	-0.0 (1.1)	0.1 (1.1) [†]
Height-for-age Z	-1.3 (1.2)	-1.3 (1.2)	-1.3 (1.2)
Weight for height Z for age Z	1.2 (1.2)	1.0 (1.2)	1.2 (1.2) [†]
Head circ. for age Z	1.1 (1.1)	0.9 (1.1)	1.0 (1.1)
Weight-for-age Z < -2 (N/ %)	5 (1.7)	3 (2.5)	8 (1.9)
Height-for-age Z < -2 (N/ %)	88 (30.1)	30 (24.6)	118 (28.5)
Health			
Child Admitted to Hospital (N/ %)	92.0 (29.1)	49.0 (37.7)	141.0 (31.6) [†]
Number of times child admitted (N/ %)			
Zero	224.0 (70.9)	81.0 (62.3)	305.0 (68.4)*
One	64.0 (20.3)	31.0 (23.9)	95.0 (21.3)
Two	16.0 (5.1)	10.0 (7.7)	26.0 (5.8)
Three	6.0 (1.9)	3.0 (2.3)	9.0 (2.0)
Four	4.0 (1.3)	2.0 (1.5)	6.0 (1.4)
Five+	2.0 (0.6)	3.0 (2.3)	5.0 (1.1)
Child cognitive^a			
Language	19.3 (8.5)	18.7 (7.8)	19.2 (8.2)
Something's the same	31.6 (37.5)	27.7 (38.0)	30.4 (37.7)
Silly sounds	31.9 (28.7)	34.9 (30.8)	32.8 (29.3)
Operational span	13.8 (19.8)	13.1 (18.6)	13.6 (19.4)
Overall score	25.8 (21.7)	25.2 (20.3)	25.6 (21.3)
Child behavior checklist^a			
Internalizing	20.0 (11.4)	19.9 (10.4)	20.0 (11.1)
Externalizing	5.2 (4.1)	5.1 (3.9)	5.2 (4.1)
Sum	47.1 (22.2)	48.5 (23.5)	47.5 (22.6)
Strengths and difficulties^a			
Prosocial	7.6 (2.1)	7.5 (2.2)	7.5 (2.1)
Difficulties	9.4 (4.5)	9.8 (4.8)	9.5 (4.6)

p values from linear (continuous variables), logistic (binary), or poisson (count) longitudinal random effects regressions, adjusted for neighborhood clustering and child's age difference

[†] *p* < .10; * *p* < .05

^a Measured at 36 month assessment only

^b Excludes *n* = 9 HIV + children

Discussion

We examined differences between children of MWOH and MLH from a population in 12 neighborhoods. Children's cognitive, behavioral, and emotional well-being appear very similar over time, whether or not their mothers had HIV. Internalizing (e.g., anxiety) and externalizing symptoms (e.g., disobedience) occur at similar rates among children whose mothers have different serostatus. Their cognitive functioning is similar on tests monitoring executive functioning (e.g., match-to-sample tasks, whether visual or auditory). Children were equally likely to die prematurely. These findings are important and suggest that

children of MLH may be similar to neighborhood peers. We had expected more deficits among children of MLH, compared to MWOH.

The only differences between children of MWOH and MLH are in physical health. Children of MLH are significantly more likely to be hospitalized and tended to lag behind their peers in weight compared to children of MWOH. Perhaps, due to their HIV, MLH are more engaged with the health care system and take children to the hospital with less severe symptoms. However, in a related publication [49], we have shown that MLH only slowly re-engage in HIV care following childbirth. By 3 years post-birth, only 62 % of MLH have reengaged in

Table 3 Maternal outcomes at 36 months post birth, stratified by HIV status: MWOH (N = 316) and MLH (N = 140)

	MWOH (N = 316) n (%)	MLH (N = 140) n (%)	Total (N = 456) n (%)
Maternal partners			
Father in household	172 (54.4)	57 (41.0)	229 (50.3)
Any violence with intimate partner	47 (14.9)	23 (16.6)	70 (15.4)
Recent^a partners:			
0	45 (14.2)	28 (20.1)	73 (16.0)
1	265 (83.9)	106 (76.3)	371 (81.5)
≥2	6 (1.9)	5 (3.6)	11 (2.2)
Serostatus disclosure to partner	N/A	91 (87.5)	N/A
Ask partners to test	192 (70.9)	98 (89.1)	290 (76.1)**
Consistent condom use	82 (30.6)	76 (69.1)	159 (41.7)***
Maternal health			
TB, high BP, or diabetes	30 (9.5)	19 (13.6)	49 (10.8)
Positive TB test	4 (5.4)	9 (17.7)	13 (10.40)*
Subsequent child	56 (17.7)	28 (20.1)	84 (18.5)
Maternal depression			
Mean EPDS score (SD)	6.3 (7.6)	8.4 (8.6)	7.0 (7.9)*
EPDS > 13	57 (18.0)	38 (27.1)	95 (20.8) [†]
Mean SF-36 total score (SD) ^b	86.1 (14.1)	84.3 (16.0)	85.5 (14.7)
Mean Hopkins score (SD)	35.0 (16.2)	38.9 (19.6)	36.2 (17.4)*
Alcohol use			
Recent ^a use	56 (17.7)	29 (20.9)	85 (18.7)
AUDIT > 2	45 (14.2)	24 (17.3)	69 (15.2)
Family issues			
Child grant	261 (82.6)	108 (77.1)	369 (80.9)
Child in Creche ^b	185 (60.7)	72 (52.6)	257 (58.1)
Employment	139 (44.0)	63 (45.0)	202 (44.3)
Family relocates	88 (27.9)	40 (28.6)	128 (28.1)

p values from linear (continuous variables), logistic (binary), or multinomial (categorical, >2 levels) longitudinal random effects regressions, adjusted for neighborhood clustering

[†] *p* < .10; * *p* < .05; ** *p* < .01; *** *p* < .001

^a “Recent” always refers to the last 3 months

^b Measured at 36 month assessment only

health care. Therefore, MLH appear engaged in health care at the same rate and intensity as MWOH. We do not have access to hospital or clinic records, so we are unclear why children of MLH were hospitalized more often. We do have children’s Road-to-Health cards to validate the hospital visits, however.

MLH have worse health and mental health over time, compared to MWOH. MLH have less income and education, and more food insecurity. MLH had fewer structural supports (education, income, formal housing, enough food) compared to MWOH. We expected that having fewer resources, as well as HIV, would lead to more deficits than we actually observed among the children of MLH. The impact of having an HIV-affected mother on children appears isolated to physical health issues. While initially

MLH are significantly more likely to use alcohol than MWOH, by 3 years post-birth, alcohol use and abuse are similar. It is also surprising that the indices of external family supports (the child support grant, childcare at a crèche, and maternal employment) are similar across mothers with different HIV statuses. The child support grant—valued at 350 rand per month—serves as an essential safety net for South African children, ensuring that they do not starve. Yet, the acquisition of the child support grant is delayed; by 18 months post-birth, only 60 % of mothers received the child support grant [33] and by 3 years, 81 % of mothers have secured the child support grant. Throughout this paper, we have chosen to use South African currency (rand, ZAR) instead of converting it to US dollars (USD) because of the extreme fluctuation over

the last ten years and in particular, over the last 4 years, in the value of the ZAR. The USD to ZAR conversion ratio has fluctuated between 1:6 and 1:16 since 2012, yet the purchasing power of poor South Africans has remained largely constant within the country.

Women's relationships with men also appear very similar. Most women, MLH and MWOH, have recent sexual partners and the same number of partners over the last 3 years. MLH are significantly more likely to use condoms, which is to be expected and reflects protecting their partners from HIV. At baseline, at least 31 % of MLH know their partner is HIV seropositive and another 23 % know they are in serodiscordant relationships. This contrasts sharply with MWOH. No MWOH thinks or knows their partner is seropositive. It would be surprising if the perceptions of MWOH are realistic. It appears that having HIV leads to greater disclosures and perhaps testing by partners of MLH. Thus, we expected that having HIV, in combination with less income and education, and more depression, would result in worse child outcomes. Yet, compared to the children of MWOH, the children of MLH appear similar in adjustment. As noted above, the problems observed are only in the area of physical health. These data suggest the importance of maintaining clinic visits among children of MLH over time compared to children of MWOH.

The sample is particularly robust, as 98 % of pregnant women in 12 neighborhoods were recruited and only 3 % were not reassessed over the last 3 years. All five assessments were completed by 73 % of mothers. While we are presenting the differences at 3 years post-birth, these results adjust for the longitudinal measures collected over five time points with this sample. At 3 years, only about 15 % of mothers or children were not reassessed. Yet, those lost to follow-up are highly similar to those maintained over time. The rates are substantially higher than those observed in PMTCT trials [11].

We also had multiple measures of children's functioning: language, social behaviors, executive functioning, and reports of children's physical health. Child outcomes were informed by maternal reports, the government Road-to-Health card, and interviewers' assessments. The standardized measures of childhood adjustment have been used previously in South Africa [43, 50]. It would have been desirable to have more biological measures of children's current health and to validate the hospital records of children to know the types of illnesses children had. However, we did not have the resources to access these data.

In the United States, we observed that being diagnosed with HIV mobilized MLH, especially MLH who had a history of serious drug use, to improve the quality of their life [51, 52]. MLH stopped using drugs and significantly improved their parenting skills. Perhaps a similar process is

occurring in South Africa among MLH. Antiretroviral therapies (ARV) are now broadly available to MLH, providing hope that mothers can live a normal lifespan, without serious illnesses [53]. Even though the social circumstances of MLH are more challenging than MWOH while pregnant, MLH are becoming less depressed over time. All mothers, regardless of their HIV status, want the best for their children. Five to 10 years ago, South African MLH would have anticipated that their children would be orphaned. Now, MLH can anticipate sharing their children's lives—perhaps leading to MLH investing more time and energy in becoming better parents than they might have if not a MLH. While unsure about the mechanism, children of MLH appear well adjusted and as ready for school as their peers.

The broad availability of PMTCT has often focused the attention of the HIV community on children's outcomes during the post-partum period [54]. Far less attention has been given to the MLH or her children during the preschool years. This paper bridges that gap.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all individual participants included in the study.

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