The Impact of Safer Breastfeeding Practices on Postnatal HIV-1 Transmission in Zimbabwe

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Objectives. We assessed the association between exposure to an educational intervention that emphasized safer breastfeeding practices and postnatal HIV transmission among 437 HIV-positive mothers in Zimbabwe, 365 of whom did not know their infection status.

Methods. Mothers were tested for HIV and were encouraged—but not required—to learn their HIV status. Intervention exposure was assessed by a questionnaire, Turnbull methods were used to estimate postnatal HIV transmission, and multivariate Cox proportional hazard models were constructed to assess the association between intervention exposure and postnatal HIV transmission.

Results. Cumulative postnatal HIV transmission was 8.2%; each additional intervention contact was associated with a 38% reduction in postnatal HIV transmission. HIV-positive mothers who were exposed to both print and video materials were 79% less likely to infect their infants compared with mothers who had no exposure. These findings were similar for mothers who did not know their HIV status.

Conclusions. The promotion of exclusive breastfeeding has the potential to reduce postnatal HIV transmission among women who do not know their HIV status, and child survival and HIV prevention programs should support this practice. (*Am J Public Health.* 2007;97:1249–1254. doi:10.2105/AJPH.2006.085704)

Each year, an estimated 700 000 children are infected with HIV by their mothers,[1] and at least 40% of these transmissions occur during breastfeeding.[2–3] The vast majority of HIV-infected children live in sub-Saharan Africa, where universal and prolonged breastfeeding protects children against diarrhea and other infections and contributes to birth spacing (i.e., intervals between pregnancies).[4–6] Hence, the transmission of HIV through breastfeeding has created one of the most challenging dilemmas of the HIV pandemic and has contributed to reduced support for breastfeeding in some areas where there is a high prevalence of HIV.[7]

International guidelines currently state that HIV-positive mothers should avoid all breastfeeding when replacement feeding is acceptable, feasible, affordable, sustainable, and safe. Otherwise, HIV-positive mothers are advised to breastfeed exclusively during the first months of life and to stop breastfeeding as soon as the conditions for replacement feeding are met.[8] Counselors should provide information on the risks and benefits of exclusive breastfeeding and replacement feeding so that HIV-positive mothers can make fully informed decisions.[9]

We developed an education and counseling intervention to fully inform women about infant feeding in the context of HIV. We then implemented it within an ongoing postpartum vitamin A supplementation trial, Zimbabwe Vitamen A for Mothers and Babies Trial, hereafter "ZVITAMBO," in Harare, Zimbabwe. As part of the trial, participating mothers were tested for HIV within 96 hours of delivering their babies and were encouraged—but not required—to learn their HIV status. The intervention promoted exclusive breastfeeding to mothers who were HIV-negative, mothers who were HIV-positive and chose to breastfeed, and mothers who chose not to learn their HIV status. We evaluated the association between the mothers' exposure to this intervention and their HIV-related knowledge, infant-feeding practices, postnatal HIV transmission, and child mortality.

In 2005, we reported that women who enrolled in the trial after the intervention was implemented were more knowledgeable about HIV and were 8.4 times more likely to practice exclusive breastfeeding compared with women who enrolled in the trial before the intervention began.[10] Furthermore, exclusive breastfeeding for at least 3 months was associated with significantly lower postnatal transmission and higher HIV-free survival compared with partial breastfeeding (i.e., animal milks or solid foods in addition to breastmilk).[11] Our findings were consistent with previous reports from South Africa.[12,13]

In this study, we examined the association between the amount of exposure mothers had to the educational intervention and their infants' risk for postnatal HIV transmission or death. The analysis examined HIV-positive women whose infants were alive and were HIV polymerase chain reaction (PCR)–negative at 6 weeks, which put them at risk for postnatal HIV transmission. We hypothesized that exposure to the intervention would be inversely associated with HIV transmission and that this association would be attenuated after we adjusted for breastfeeding exclusivity. Previous studies on breastfeeding and HIV have included only HIV-infected women who made feeding decisions after learning their HIV status. The ZVITAMBO is unique in that both HIV-negative and HIV-positive women were enrolled and the majority declined to learn their test results.[10] Thus, our analysis reflects the potential impact of a public health intervention that promotes exclusive breastfeeding in settings where HIV prevalence is high, yet the majority of mothers do not know their HIV status. These conditions are common throughout Africa.[1]

METHODS

The ZVITAMBO study was a clinical trial of postpartum maternal and neonatal vitamin

A supplementation; study methods have been published elsewhere.[10,11,14,15] Briefly, from November 1997 to January 2000, 14 110 postpartum mothers and their neonates were enrolled within 96 hours of delivery and were randomized to 1 of 4 vitamin A treatment arms. Recruitment took place at maternity clinics and hospitals in Greater Harare. Mother–infant pairs were eligible if neither had an acute life-threatening condition, if the baby was a singleton who weighed 1500 grams or more at birth, and if the mother planned to stay in Harare after delivery. We obtained written informed consent.

Baseline data were collected via interviews and medical record transcriptions. We estimated gestational age using the Capurro method,[16] and we measured infant birthweight and maternal mid–upper arm circumference using methods described by Gibson.[17] Infant plasma and cell pellets (Amplicor whole blood PCR sample preparation method; Roche Diagnostics Systems, Alameda, Calif) were prepared and were stored at −70° C. Mothers were tested for HIV at baseline using an algorithm of 2 enzyme-linked immunosorbent assays (ELISAs), which were run parallel to each other, and Western blot confirmation.[14] We enumerated maternal CD4 cells with Facscount (Becton Dickinson International, Erembodegem, Belgium), and we measured hemoglobin on the day of blood collection (HemoCue, Mission Viejo, Calif).

We conducted follow-up clinic visits at 6 weeks and 3 months and then at 3-month intervals thereafter for up to 24 months. Infant plasma and cell pellets were archived for all HIV-exposed infants; after all follow-up visits were completed, we tested the last available blood specimen. If samples were collected at or after 18 months, plasma was tested using GeneScreen ELISA (Roche Diagnostic Systems). If samples were collected before 18 months, cell pellets were tested by prototype using the Roche Amplicor version 1.5 qualitative PCR assay (Roche Diagnostic Systems). If the last available sample was HIV negative, the baby was classified as uninfected. If the last sample was positive, we tested intervening samples to determine the timing of infection.

We collected breastfeeding initiation data at baseline, and breastfeeding duration and intensity were assessed during all follow-up visits. At baseline, 6 weeks, 3 months, and 6 months, mothers were asked whether the infant had ever been fed any liquids (water, juice, tea, cooking oil), milks (formula, fresh, tinned), solid foods (porridge, maize meal, fruits, vegetables, meat, eggs), or medicines (traditional, prescribed, oral rehydration solution). We classified infants as exclusively breastfed, predominantly breastfed, or partially (mixed) breastfed at each visit in accordance with World Health Organization definitions.[18] We encouraged mothers to learn their HIV test results at any time during the study during pretest and posttest counseling. Intrapartum and postnatal antiretroviral prophylaxis were not available in Zimbabwe at the time of the study.

Education and Counseling Intervention

When the study began in 1997, breastfeeding was recommended for all HIV-positive mothers in accordance with national and international policy at the time.[19] After the release of new guidelines on HIV and infant feeding in 1998,[9] we developed an intervention to educate all study mothers about mother-to-child HIV transmission and the implications for infant feeding. The intervention encouraged mothers to learn their HIV test results and it provided HIV-positive mothers with information and skills for making and safely implementing their best infant-feeding choice.

The intervention was introduced in September 1999. Study nurses had group talks with antenatal mothers at the ZVITAMBO recruitment sites, with new mothers in postnatal wards during trial recruitment and at ZVITAMBO follow-up clinics during follow-up visits. Two videos on mother-to-child HIV transmission and ways to prevent it were produced for the intervention and were shown during group talks. Two pamphlets were also produced and distributed. The first pamphlet described the risk for mother-to-child transmission of HIV and the implications for infant feeding; the second described the 4 safer breastfeeding practices—breastfeeding exclusively[12]; breastfeeding techniques for avoiding cracked nipples, milk stasis, and mastitis and encouraging prompt treatment of breast problems[20]; seeking medical care quickly, especially for breast problems; and promoting safer sexual practices during the breastfeeding period.[21] The pamphlets were promoted during group sessions to all women who chose not to learn their HIV test results.

During individual posttest counseling sessions, HIV-negative mothers were advised about safer breastfeeding and HIV-positive mothers were advised about the risks, benefits, and costs of several infant-feeding options. HIV-positive women who chose to breastfeed were counseled about safer breastfeeding and early breastfeeding cessation at 6 months.

Evaluation of the Intervention and Statistical Analysis

Because all mothers who enrolled in the study after September 1, 1999, had an opportunity for intervention exposure, we compared knowledge, behaviors, and outcomes in accordance with reported levels of intervention exposure; we controlled for confounding variables using a plausibility evaluation design.[22] A questionnaire was administered to mothers during the 3-month follow-up clinic visit to elicit information about HIV-related knowledge, the total number of contacts with the intervention (maximum of 4 contacts: antenatal, delivery, 6-week visit, or 3-month visit), and the total number and type of educational materials received at all time points (maximum 4 materials; 2 videos and 2 pamphlets).

We used data from 437 HIV-positive postintervention mothers who completed the 3-month questionnaire and whose infants were alive and PCR-negative at 6 weeks for our analysis. Restricting the analysis to infants who were PCR-negative at 6 weeks allowed us to focus on the intervention's impact on postnatal HIV transmission.[23] Infant survival to 12 months was estimated using Kaplan–Meier methods[24]; we used Turnbull methods, which are recommended for interval censored data when the exact time of the event (HIV infection) is unknown,[25] to estimate cumulative risk for postnatal HIV transmission. Infants who never had a positive HIV test were censored at the age of their last negative test. Infants of mothers who

died (n=4) or who reported stopping breastfeeding (n=57) were censored 60 days after the mother's date of death or breastfeeding cessation.[26]

The number of educational materials mothers saw was highly correlated with the reported number of intervention contacts (Spearman $R=0.61$; $P<.001$). Therefore, we constructed Cox proportional hazards models with stepwise backward elimination to estimate the additive effect on postnatal HIV transmission and postnatal HIV transmission or death of 3 different forms of intervention exposure: (1) the number of contacts, (2) the number of educational materials seen or received, and (3) the timing of first intervention exposure. Variables that measured exposure to the intervention were forced into the models, and other covariates retained in the final model for postnatal HIV transmission in the overall study population (i.e., maternal age; mid–upper arm circumference, CD4 cell count, and hemoglobin at baseline from the mother; and maternal death during follow-up)[11] were entered and retained at the $\alpha \leq 0.20$ and 0.10 levels, respectively. Because breastfeeding exclusivity was hypothesized to be part of the causal pathway, we omitted early breastfeeding patterns from these models to evaluate the impact of intervention exposure on study outcomes.

As a way of checking for the possibility that inherently lower-risk women were self-selecting increased exposure to the intervention, we ran a parallel series of Cox models and added dummy variables for the quartiles of estimated propensity scores for the probability of a woman having at least 1 intervention contact. Propensity scores are used to correct baseline imbalances among exposure groups in nonrandomized trials,[27,28] and we estimated these scores in logistic regression models with terms for family income, infant gender, and maternal age, maternal marital status, maternal educational attainment, maternal baseline hemoglobin, maternal mid–upper arm circumference, maternal CD4 cell count, and maternal death during follow-up, (a proxy for advanced disease state at baseline). We conducted statistical analyses using SAS version 8.2 (SAS Institute Inc, Cary, NC).

TABLE 1—Baseline Characteristics of Mothers and Infants (n = 437): ZVITAMBO, Harare, Zimbabwe, 1999–2000

Variable	Total, Mean (SD) or % (n)
Birth Weight, g	2976 (434)
Gestational age under 37 weeks	3.9 (n = 17)
Male infant	54.7 (n = 239)
Maternal mid-upper arm circumference, cm	25.8 (2.5)
Maternal CD4 cell count, μ/L	416.9 (221)
<200	10.8 (n = 47)
200–399	33.2 (n = 145)
≥400	35.9 (n = 157)
Missing CD4 at baseline	20.1 (n = 88)
Maternal hemoglobin, g/L	112.8 (18.6)
Maternal education, y	9.7 (1.9)
Maternal age, y	25.8 (4.6)
Maternal parity	2.3 (1.1)
Household income/day, US $	3.23 (3.2)
Maternal unemployment	21.7 (n = 95)
Maternal marital status–married	88.8 (n = 388)
Vitamin A treatment arm	
Mother A, baby A	24.9 (n = 109)
Mother A, baby P	25.9 (n = 113)
Mother P, baby A	24.0 (n = 105)
Mother P, baby P	25.2 (n = 110)

Note. A = vitamin A; P = placebo.

RESULTS

After the education and counseling intervention was introduced to the ZVITAMBO trial, 2749 mother–infant pairs were enrolled in the trial. Of these, 845 mothers (30.7%) were HIV-positive at delivery, and 514 of their infants were alive and were PCR-negative at 6 weeks. Intervention exposure data were available for 437 mothers (85%), who comprised the sample for our analysis (Table 1). Compared with mothers who had exposure data, eligible mothers who were excluded from the analysis because they lacked intervention exposure data (n=77) also had infants with lower birthweights (2856 grams [n=441] vs 2976 grams [n=435]; $P=.03$) and lower baseline hemoglobin (108.1 g/L vs 112.8 g/L; $P=.05$). Excluded mothers were more likely to have died during the follow-up period and thus be unavailable for interviews (14.3% of eligible but excluded mothers vs 1.8% of eligible and included mothers; $P<.001$). All other characteristics were similar (data not shown). Of the 437 women in our sample, 72 (16%) chose to receive their HIV test results; there were no differences in baseline characteristics among mothers who learned their HIV status compared with those who did not.

TABLE 2—Timing, Frequency, and Type of Intervention Exposure: ZVITAMBO, Harare, Zimbabwe, 1999–2000

Exposure variable	No. (%)
Timing of first exposure	
Antenatal	83 (19.0)
Recruitment	205 (46.9)
6 weeks	73 (16.7)
3 months/other	1 (0.2)
None	75 (17.2)
Frequency of reported contacts[a]	
0	75 (17.2)
1	234 (53.6)
2	108 (24.7)
3	20 (4.6)
4	0 (0)
Number of materials seen or received	
0	119 (27.2)
1–2	248 (56.8)
3–4	70 (16.0)
Type of material seen or received	
Print only	222 (50.8)
Video only	20 (4.6)
Both	76 (17.4)
Neither	119 (27.2)

[a]Number of study visits when information on safer breastfeeding was observed or received.

Exposure to the Intervention and Safer Breastfeeding Practices

Reported timing, type, and frequency of intervention exposure are shown in Table 2. Seventy-five mothers (17.2%) reported having never seen or received any educational materials, and 234 (53.6%), 108 (24.7%), and 20 (4.6%) reported having been exposed to 1 or more components of the intervention during 1, 2, and 3 follow-up clinic

TABLE 3—Association Between Intervention Exposure and Safer Breastfeeding Knowledge and Practices: ZVITAMBO, Harare, Zimbabwe, 1999–2000

	Number of Visits When Information on HIV and Infant Feeding Was Provided, No. (%)				
	0 (n = 75)	1 (n = 234)	2 (n = 108)	3 (n = 20)	P[a]
Reported knowledge of specific safer breastfeeding practices to prevent HIV transmission[b]					
Importance of exclusive breastfeeding	0 (0)	36 (15.4)	26 (24.1)	8 (40)	<.001
How to prevent and treat breast problems	4 (5.3)	50 (21.4)	26 (24.1)	4 (20.0)	.005
Safer sexual practices	4 (5.3)	28 (12.0)	30 (27.8)	7 (35.0)	<.001
Safer breastfeeding practices[c]					
Exclusive breastfeeding					
6 weeks[d]	6 (8.0)	35 (15.0)	16 (14.8)	6 (30.0)	.02
3 months[d]	5 (6.7)	30 (12.8)	19 (17.6)	5 (25.0)	.005
6 months[d]	3 (4.0)	14 (6.0)	5 (4.6)	1 (5.0)	.48
Breast health problems reported or diagnosed					
6 weeks[d]	6 (8.0)	10 (4.3)	5 (4.6)	1 (5.0)	.22
3 months[d]	2 (2.7)	8 (3.4)	5 (4.6)	2 (10.0)	.09
6 months[d]	4 (5.3)	10 (4.3)	4 (3.7)	2 (10.0)	.42
Postpartum condom use (among sexually active mothers)	16 (21.3)	56 (23.9)	31 (29.7)	5 (25.0)	.15

[a]χ^2 test for trend; 1-sided test.
[b]Knowledge data obtained using a questionnaire that was administered during the 3-month follow-up clinic visit.
[c]Practice data obtained prospectively during each follow-up clinic visit.
[d]Indicates age of infant.

visits, respectively. Most mothers reported that their first exposure was during delivery of their babies (n=205; 46.9%). Frequency of intervention contact was associated with safer breastfeeding knowledge and exclusive breastfeeding practices, but it was not associated with breast health or postpartum condom use (Table 3).

12-Month Infant Mortality and Postnatal HIV Transmission

There were 32 postnatal HIV infections and 9 deaths; 5 of the deaths were infants whose last HIV test was PCR-negative. The Kaplan–Meier estimate of mortality (with or without HIV infection) from 6 weeks to 12 months was 2.1% (95% confidence interval [CI]=0.7, 3.4), with no difference by number of reported intervention contacts (χ^2 log rank test P=.5; Fisher exact test [1 *df*]). Overall cumulative risk for postnatal HIV transmission was 8.2% (95% CI=4.6, 14.3), and for postnatal HIV transmission or death, it was 8.7% (95% CI=6.0, 11.4). Postnatal HIV transmission rates declined in a dose–response manner with increasing frequency of intervention contact (χ^2 log rank test P=.03), and postnatal HIV transmission rates among mothers who reported 0, 1, 2, and 3 intervention contacts were 11.5% (95% CI=4.8, 25.2), 9.1% (95% CI=3.9, 19.7), 5.0% (95% CI=1.0, 21.6), and 0%, respectively.

Findings were similar when the analysis was restricted to mothers whose HIV status was unknown. There were 29 infections and 8 deaths among this subgroup; the Kaplan–Meier estimate of mortality was 2.2% (95% CI=0.7, 3.7). Postnatal HIV transmission rates among mothers who reported 0, 1, 2, and 3 intervention contacts were 13.3% (95% CI=5.5, 28.6), 8.8% (95% CI=3.9, 18.6), 6.2% (95% CI=1.2, 26.0), and 0% (χ^2 log rank test P=.04), respectively.

Cox Proportional Hazard Regression Models

Each additional intervention contact was associated with a proportionate 38% reduction in postnatal HIV transmission (P=.045) and a 33% reduction in postnatal HIV transmission or death (P=.07), after we adjusted for maternal baseline CD4 and hemoglobin, which were the only 2 variables that were retained in the stepwise regression models (Table 4). Adjusted hazard ratios were similar in the models that had propensity score variables (data not shown). In the second model, in which exposure to the intervention was assessed as the number of educational materials seen or received, postnatal HIV transmission was 88% lower (adjusted hazard ratio [HR]=0.12; 95% CI=0.02, 0.90) and 35% lower (HR=0.65; 95% CI=0.32, 1.33) among women who had received 3–4 materials and 1–2 materials, respectively. Mothers who were exposed to both print and video materials had significantly lower postnatal

TABLE 4—Risk for Postnatal HIV Transmission and Postnatal HIV Transmission or Death Associated With Intervention Exposure: ZVITAMBO, Harare, Zimbabwe, 1999–2000

	Postnatal HIV Transmission		Postnatal HIV Transmission or Death	
	Adjusted HR (95% CI)	P	Adjusted HR (95% CI)	P
Reported intervention contacts, no.	0.62 (0.39, 0.99)	.045	0.67 (0.44, 1.04)	.07
Maternal baseline CD4 cell count (μ/L)				
<200	5.94 (1.98, 17.86)	.003	4.94 (1.72, 14.10)	.003
200–399	2.60 (1.00, 6.77)	.05	2.64 (1.08, 6.42	.03
≥400	1.00 (. . .)		1.00 (. . .)	
Maternal hemoglobin (g/L)	0.98 (0.96, 0.99)	.02	0.98 (0.97, 0.99)	.03

Note. HR=hazard ratio; CI=confidence interval. Variables considered but not retained in all models include maternal knowledge of HIV status, age, mid-upper arm circumference (cm), death during the follow-up period, education, and vitamin A treatment arm.

HIV transmission rates (HR=0.21; 95% CI=0.05, 0.95) compared with mothers who had no exposure to any educational material. All of the protective effect of intervention exposure was for antenatal and delivery-based exposure; among women who were first exposed to the intervention at 6 weeks or later, there was no effect on postnatal HIV transmission (HR=1.00; 95% CI=0.38, 2.61) or postnatal HIV transmission or death (HR=1.28; 95% CI=0.52, 3.18). In all models, inclusion of maternal knowledge of HIV status was not retained and had no effect on exposure estimates. Adding safer breastfeeding knowledge and exclusive breastfeeding practices to the model attenuated the benefit of intervention exposure on postnatal HIV transmission and postnatal HIV transmission or death.

DISCUSSION

We implemented a health center–based intervention to educate mothers about HIV and infant feeding. We have previously reported that postintervention mothers were more likely to breastfeed exclusively[10] and that exclusive breastfeeding was associated with reduced risk for postnatal HIV transmission and postnatal HIV transmission or death.[11] With each additional intervention contact, HIV-positive mothers were 38% less likely to infect their infants during breastfeeding. Although the intervention emphasized 3 messages (exclusivity of breastfeeding, prevention and treatment of breast problems, and safer sexual practices), only exclusive breastfeeding was associated with intervention exposure, which suggests that the observed association was primarily mediated through increasing the proportion of HIV-positive women who exclusively breastfed. Our findings also suggest that breastfeeding patterns may be more amenable to change through education than adoption of health-seeking and safer sexual practices.

We observed no statistical differences between HIV-positive mothers who knew their status and HIV-positive mothers who did not know their HIV status. This finding contradicts another study in Zimbabwe that reported knowledge of HIV status influenced infant-feeding decisions.[29]

There were several limitations to our study that should be considered. To comply with Zimbabwean national policy, our intervention was made available to all mothers and was not randomized. Thus, we are unable to conclude a causal association between intervention exposure and reduced postnatal HIV transmission. Possible explanations for our findings were that healthier mothers were more likely to attend follow-up clinic visits, they may have better recall of intervention exposure, and they were less likely to transmit HIV. However, inclusion of the propensity score to adjust for baseline differences did not affect the results, nor did adjusting models for the number of missed follow-up clinic visits. It also is possible that our findings are biased because of systematic differences between those who were included and those who were excluded from the analysis. At 6 weeks, 143 infants were missing PCR data, including 57 whose mothers had intervention exposure data. We assumed these 57 infants were PCR-negative at 6 weeks, and including them in the analysis had little effect on the adjusted hazard ratios. Excluded mothers may have been sicker than those who were included, which potentially may have biased our estimate of postnatal HIV transmission. This is suggested by the lower hemoglobin and higher incidence of maternal death among the 77 eligible mothers who were missing intervention exposure data. However, cumulative postnatal HIV transmission was only 2.3% among excluded mothers, which suggests no systematic underestimation. Taken together, these observations suggest that maternal health and selection bias are not the primary explanations for our results.

Our study is the first to suggest that an intervention to encourage exclusive breastfeeding reduces postnatal HIV transmission among mothers who do not know their HIV status. These findings are important because even in populations where mother-to-child HIV transmission programs are rapidly expanding, many mothers are not tested for HIV and there are no other interventions to protect their infants. Exclusive breastfeeding is beneficial for noninfected mothers and can be promoted in the general population without targeting or stigmatizing those who are infected with HIV.

Our findings also suggest that group education alone can improve infant outcomes. Although mothers who were exposed to the intervention once had lower transmission rates compared with mothers who had no exposure, our results suggest that early and more frequent intervention contacts that use both video and print materials are most effective. It is important to note that our intervention was health center–based only. Had we included a community component, it is possible that the impact would have been even greater[30,31] by reaching those high-risk mothers who do not regularly access antenatal and postnatal care.

Although intervention exposure was not associated with reduced infant mortality, in part because of the small number of deaths between 6 weeks and 12 months, it was associated with significantly reduced postnatal HIV transmission. Up to 80% of untreated HIV-infected children die before their 5th birthday.[32] Therefore, promotion of exclusive breastfeeding to the general population, prevention of mother-to-child HIV transmission, and availability of pediatric antiretroviral treatment should be policy priorities in all settings where HIV contributes to child mortality. As suggested by the World Health Organization[33] and the World Health Assembly,[34] governments should scale up their support for infant and young-child feeding rather than scale them back because of the tragic HIV pandemic. ■

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E.G. Piwoz participated in study origination, design, and implementation; conducted most of the analysis; and drafted the article. J.H. Humphrey participated in all aspects of the study, including origination, design, implementation, analysis, and drafting the article. N.V. Tavengwa participated in study design, implementation, and interpretation. P.J. Iliff participated in the origination and design of the study, its implementation, and drafting the article. E.T. Marinda and L.H. Moulton contributed to the statistical analysis. C.D. Zunguza contributed to study interpretation. K.J. Nathoo participated in study design, implementation, and interpretation. K. Mutasa was responsible for all laboratory analyses. B.J. Ward contributed to the study's origination, design and interpretation. All primary authors reviewed the final draft of the article.

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Human Participant Protection

This study was approved by the Medical Research Council of Zimbabwe, the Medicines Control Authority of Zimbabwe, the Johns Hopkins Bloomberg School of Public Health Committee on Human Research, and the Montreal General Hospital Research Ethics Committee.

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