

# Comparative effects of three methods of promoting breastfeeding among human immunodeficiency virus–infected women in Uganda: a parallel randomized clinical trial

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**Background:** The objective of this study was to evaluate the comparative effects of three breastfeeding promotion interventions on the duration of exclusive breastfeeding (EBF) and any breastfeeding (BF) among human immunodeficiency virus (HIV)-infected women in Uganda.

**Methods:** Between February 2012 and February 2013, 218 HIV-infected pregnant mothers were randomly assigned to (A) standard care (n=73), (B) enhanced family/peer support (n=72) or (C) enhanced nutrition education (n=73).

**Results:** The prevalence (%) of EBF/BF did not differ between intervention arms at the sixth (A, 85/92; B, 84/91; C, 87/89) and ninth (A, 17/91; B, 18/89; C, 16/87) postpartum month assessments ( $p>0.05$ ). However, the risk of early BF cessation differed between intervention arms depending on the mother's level of formal education ( $p=0.04$ ). Among women with no formal education, the risk of early BF cessation was 88% (adjusted hazard ratio [aHR] 0.12 [95% confidence interval {CI} 0.05–0.30]) and 93% (aHR 0.07 [95% CI 0.03–0.18]) lower in arms B and C, respectively, than in arm A ( $p<0.01$ ). HIV status disclosure to a partner was associated with a higher risk of early EBF ( $p=0.03$ ) and BF ( $p=0.04$ ) cessation.

**Conclusions:** In resource-limited settings, enhanced (vs standard care) EBF promotion interventions may not differentially influence EBF but reduce the risk of early BF cessation among women with no formal education. Targeted enhanced interventions among women with no formal education and a mother's partner may be critical to reducing the risk of early EBF/BF cessation.

**Keywords:** exclusive breastfeeding, breastfeeding cessation, HIV-infected women, randomized clinical trial

## Introduction

Although the negative consequences (e.g. higher risk of respiratory infections,<sup>1–3</sup> stunted growth<sup>3,4</sup> and infant mortality<sup>3</sup>) associated with failure to exclusively breastfeed (EBF) infants for at least 6 months postpartum are well established, mothers are often unable to reach this World Health Organization (WHO) recommendation.<sup>5</sup> Moreover, extended periods of breastfeeding (BF) are supported by dose-dependent long-term benefits for not just the child (e.g. lower obesity and type 2 diabetes rates, increased intelligence), but also the mother (e.g. lower breast/ovarian cancer and type 2 diabetes rates).<sup>6</sup>

In resource-limited settings, some studies suggest that cultural norms and limited or lack of knowledge are barriers to the

adoption of recommended EBF practices.<sup>7–9</sup> Before the WHO 2010 recommendations and guidelines,<sup>10</sup> among HIV-infected women, motivation to reduce the risk of mother to child transmission (MTCT) was also linked to early EBF cessation.<sup>9</sup> Preoccupied with thoughts about unintentionally infecting the child, it is plausible that mothers may pay less attention to the competing risks to infant health and survival.<sup>9,11</sup> Yet, with adherence to antiretroviral (ARV) treatment and appropriate BF practices, MTCT is substantially reduced (<5%) vs no treatment (range 15–45%).<sup>12</sup> Recent results from a multisite Promoting Maternal and Infant Survival Everywhere (PROMISE) 1077BF randomized clinical trial conducted in 14 sites in east and southern African show that MTCT is even lower (<1%) with the use of

either daily infant nevirapine (NVP) prophylaxis or maternal anti-retroviral therapy (ART) through up to 18 months of BF.<sup>13</sup>

Considering the aforementioned benefits of EBF and emerging evidence on MTCT through BF,<sup>14</sup> the 2016 WHO feeding guidelines recommend that HIV-infected mothers on lifelong ART should EBF for 6 months, followed by complementary feeding (i.e. introduction of non-breast milk liquids and/or solids while breastfeeding) until 24 months postpartum.<sup>15</sup> This is different from the 2010 WHO guidelines that recommended EBF for 6 months and continued BF while introducing complementary foods until at least 12 months postpartum.<sup>10</sup> Replacement feeding is only recommended when it is considered acceptable, feasible, affordable, sustainable and safe (AFASS).<sup>10</sup>

Mixed findings exist regarding the adoption of these ever-evolving WHO infant feeding recommendations in developing countries.<sup>14</sup> Some countries still fall short of these goals among HIV-infected mothers,<sup>16–18</sup> including Uganda.<sup>19</sup> In Uganda, the low rates of EBF among HIV-infected mothers prompted renewed national efforts to increase awareness and promote the adoption of WHO recommendations through social support and education programmes.<sup>20</sup> On a positive note, recent estimates show some parts of sub-Saharan Africa<sup>21–24</sup> are achieving >70% adherence based on self-reported EBF rates among HIV-infected women in prevention of MTCT (PMTCT) settings. However, when validated using a deuterium oxide dilution technique that measures non-human milk and water intake among infants, EBF rates have been shown to be lower among HIV-infected and uninfected women (75% vs 43% and 60% vs 24%, respectively).<sup>22</sup> This disparity in EBF rates between assessment methods in EBF promotion research underscores the negative role social desirability bias may play in the overestimation of EBF among HIV-infected women, suggesting a need for cautious optimism.

Globally, EBF promotion interventions (e.g. education, community health worker and peer support programmes) show promise with respect to increasing the duration of EBF in both high- and low-income countries.<sup>25,26</sup> However, contradictory findings exist among HIV-infected women in resource-limited settings. For example, results from a recent study in South Africa<sup>27</sup> showed EBF adherence at 3 months was 53% (adjusted risk ratio 1.53 [95% confidence interval {CI} 1.22–1.94]) higher among HIV-infected women randomized to a community health worker home visitation intervention (24%) than standard care (16%). In contrast, a different randomized trial in the same country showed there was no difference in EBF rates ( $p=0.67$ ) between mothers randomized to a peer support group (45%) vs standard care (43%).<sup>28</sup> Even wider EBF rate variations are reported for observational studies conducted in different African countries.<sup>29</sup> Evidently the effectiveness of different EBF promotion interventions varies in different contexts; however, literature on the comparative effects of these interventions in similar settings is limited.

The objective of this randomized study was to evaluate the comparative effects of three breastfeeding promotion interventions (enhanced peer support and nutrition education vs standard care) on the duration of EBF and BF among HIV-infected women in Uganda. We hypothesized that women randomly assigned to enhanced EBF promotion interventions would have a lower risk of early EBF and BF cessation than those receiving standard care.

## Materials and methods

### Study population

Participants referred to the study were pregnant women who had undergone routine counselling and testing, had positive HIV rapid test results and were either on PMTCT drug regimens (zidovudine [AZT], WHO option A) or Option B+ or highly active antiretroviral therapy (HAART) as recommended at the time by the Uganda Ministry of Health (MOH).

### Study sample and setting

We recruited HIV-positive pregnant women ( $\geq 18$  y) in their late second or third trimester from U.S. President's Emergency Plan for AIDS Relief (PEPFAR)-supported PMTCT sites, Mulago Hospital antenatal clinic and postnatal follow-up clinics located in Kampala, Uganda from February 2012 to February 2013. More than 33 000 pregnant women receive same-day rapid opt-out screening for HIV infection annually at Mulago Hospital antenatal clinics. These clinics identify about 3300 HIV-infected women annually (i.e. seroprevalence of 10%). All pregnant women recruited in this study continued to get routine antenatal and PMTCT follow-up clinic visits and ARV drugs as per the PMTCT schedule.

### Ethical considerations

Institutional review boards and ethics committees at the Joint Clinical Research Centre and Uganda National Council for Science and Technology and Johns Hopkins Medicine in the USA approved the study and study participants provided written consent.

### Eligibility and exclusion criteria

Mother–infant pairs were evaluated for study eligibility immediately after delivery. Eligible participants were HIV-positive mothers ( $\geq 18$  y) who had a live birth, received ARV treatment as part of the PMTCT programme or those who planned to receive HAART as recommended by the Uganda MOH guidelines, delivered at Mulago Hospital, planned to breastfeed their children immediately after birth, resided in Kampala City or planned to stay within the Kampala district for at least 9 months postpartum, were willing to be home visited during the postpartum period and were able to bring a close family member ( $\geq 18$  y) to the clinic who would be able to be in touch with the participant at least three times a week and to give support on EBF. Exclusion criteria were having a stillbirth or premature delivery and mother or infant sickness that did not allow for study participation as judged by the study staff (attending physician). Specifically, we excluded mothers if they had a breast abscess, mastitis, hepatitis B or C, psychosis or had a life-threatening illness or birth condition incompatible with life; had an infant who was unable to breastfeed due to health reasons (e.g. oral lesions); or refused to breastfeed after delivery.

### Study design

This was a single-centre, parallel group, three-arm randomized trial. Participants were randomly assigned to one of three intervention arms using a 1:1:1 ratio to standard care support (arm

A), enhanced family/peer support (arm B) or enhanced nutrition demonstrations (arm C).

### Randomization

Eligible participants who provided both verbal and written consent for study participation completed the baseline assessment and were randomized to study arm A, B or C. Following simple randomization procedures, random assignment was programmatically determined (using random number generators) immediately after the completion of baseline assessments. Blinding participants, family/peer support and study staff to intervention arm allocation was practically impossible because of the distinct observable intervention differences during study implementation (see descriptions below). However, outcome assessors and data analysts were blinded to study arm assignments to prevent detection and interpretation bias.

### Study interventions

All intervention messages were compliant with the 2010 WHO HIV and infant feeding guidelines<sup>10</sup> and Uganda's national guidelines.<sup>30</sup> For detailed descriptions of study interventions, see supplementary files.

Arm A: standard messages. This group received the current MOH PMTCT messages on HIV and infant feeding promoting EBF during scheduled antenatal and postnatal follow-up clinic visits with counselling and support from PMTCT counsellors. Standard MOH counselling messages on HIV and infant feeding included group sessions and videos that emphasized the importance of EBF, appropriate breastfeeding practice and maternal nutrition. Mothers also received printed materials on how to practise EBF.

Arm B: enhanced family/peer support. In addition to all arm A intervention activities described above, this group included family members (or friends) and hospital-based peer mothers who supported a mother's EBF practices for at least 6 months at home and in the hospital, respectively.

Arm C: enhanced nutrition education. In addition to all arm A intervention activities described above, this group received clinic-based coaching on techniques of BF and 'hands-on' demonstrations of safe preparation of locally available nutritious foods by a special infant feeding counsellor.

Across the intervention arms (A, B and C), training and information sessions were delivered at 2, 6, 10 and 14 weeks and at 6 months postpartum. The duration of sessions ranged from 30 to 45 min across intervention arms (but were longer in arm C than in arm A or B due to the additional hands-on demonstrations).

### Primary outcome

The operational definition of EBF was based on the WHO infant feeding recommendations in the context of HIV.<sup>10</sup> For our analyses we defined early EBF cessation as not meeting the WHO recommendations at anytime before the ninth postpartum month.

### Secondary outcome

Early BF cessation was operationally defined as starting replacement feeding (i.e. infant receives no breast milk and is being fed suitable breast milk substitutes in the form of commercial infant formula or animal milk) before the ninth postpartum month.

### Power and sample size

Our study sample size calculations were based on a superiority hypothesis with a 65% lower hazard (risk) of early EBF cessation among arm B or C than arm A participants (hazard ratio 0.65). To achieve 80% power, we needed at least 67 participants in each arm of the study (A, B and C) to be able to reject the null hypothesis that the experimental and control hazard rates are equal at a type I error probability of 0.05. We assumed an accrual period of 365 days and an additional 365 days for study follow-up.

### Data collection

Study interviews were conducted in a local Ugandan language (Luganda) by study counsellors at baseline (i.e. delivery) with follow-up data at 2, 6, 10 and 14 weeks and 6 and 9 months using structured questionnaires at the hospital during mother-infant dyad clinic visits. Data collected included sociodemographic characteristics, HIV status disclosure and infant feeding information.

Sociodemographic characteristics included maternal age (in years), education (years of formal education), self-reported religious affiliation, marital status, occupation, type of housing, number of household members, monthly household income, whether the participant earns income by working outside the home and pregnancy/live birth history. We also assessed for HIV status disclosure to a current partner and any family member (including friends).

We collected infant feeding information using a standardized WHO infant feeding questionnaire that included the type of infant feeding and the introduction of other liquids or solids since the last visit. At the baseline and 6-month visit, study counsellors assessed each mother for AFASS criteria needed for replacement or complementary feeding and intent to continue breastfeeding after 6 months.

All completed questionnaires were reviewed by the study coordinator/designer to ensure completeness in real time before participants left the clinic. Thereafter, double data entry was employed to ensure accurate data entry on all study-enrolled mother-infant dyads.

### Statistical methods

We followed study participants prospectively for 9 months postpartum to determine the time to EBF and BF cessation. Participants who did not stop EBF/BF during the study follow-up and those who dropped out of the study before EBF/BF cessation were right-censored. We compared the distribution of baseline participant characteristics between intervention arms to assess the integrity of randomization procedures. We implemented

intent-to-treat-based analyses to compare intervention effects on the risk of early EBF and BF cessation.

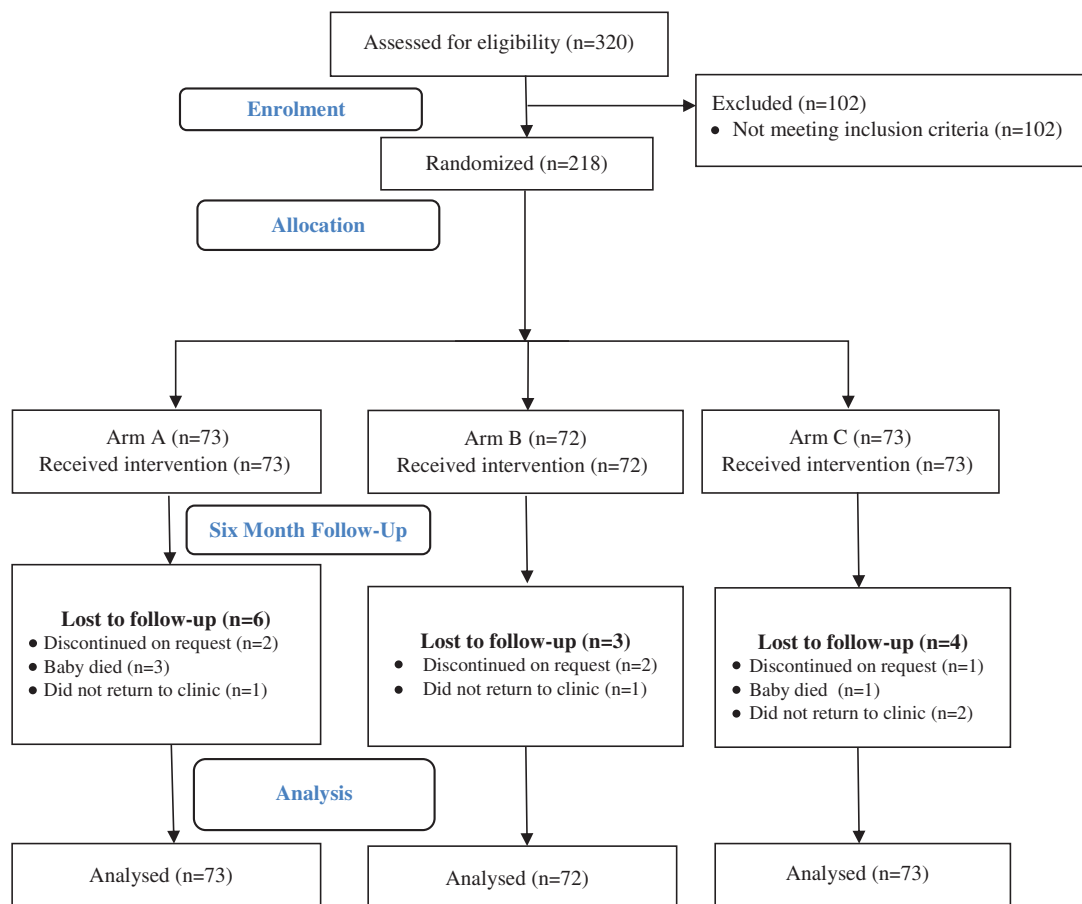
Differences in the overall survival experiences (i.e. probability of time to EBF and BF cessation) between intervention arms and participant characteristics were examined using non-parametric Kaplan–Meier (KM) procedures with appropriate adjustments for multiple group comparisons at a 0.05 level of significance. We used Cox proportional hazards regression models to examine whether intervention effects on the risk of early EBF and BF cessation differed by study arm while controlling for differences in other participant characteristics. The adequacy of modelling assumptions (e.g. constant hazard ratio over time and a multiplicative relationship between covariates and the hazard) were tested and confirmed to be adequate in our final models. In the absence of significant two-way interactions, main and potential confounder effects were examined. We conducted confounder-adjusted analysis to control for selection bias introduced due to differential loss of follow-up related to participant characteristics. A covariate was considered a confounder if its inclusion or deletion from a model resulted in a >10% difference in the regression parameter of the variable of interest (i.e., main effect). All Cox proportional hazards models were adjusted for missing data bias under the assumption that data were missing

at random, and partial likelihood was used to estimate regression parameters employed to generate hazard ratios. All statistical analyses were implemented using SAS 9.4 (SAS Institute, Cary, NC, USA).

## Results

### Summary of study participants and follow-up

Of the 1571 referred and screened pregnant mothers, only 320 (20%) agreed to study participation; 68% (n=218) of the mothers were eligible and 32% (n=102) were excluded (Figure 1). There was an equal assignment to intervention arms (A, 73; B, 72; C, 73). The median follow-up time between intervention arms was not different (p=0.87); overall participants were followed for a median of 252 days (interquartile range 7 d). Study attrition was 7% and 21% at the 6- and 9-month follow-ups, respectively. All participants assessed at 6 months (n=203) met AFASS criteria for replacement or complementary feeding. Table 1 summarizes the distribution of study participant characteristics by intervention arm. With the exception of monthly household income (p=0.02), other baseline participant characteristics did not differ between the intervention arms



**Figure 1.** Study flow diagram showing eligibility assessment, randomized intervention arm assignments, participant follow-up and number of participants included in the analysis.

**Table 1.** Baseline characteristics of the study population by study arm

	Total (N=218)	Standard (n=73)	Family/peer (n=72)	Nutrition (n=73)	p-Value
Maternal age (y), mean (SD)	34 (6)	34 (6)	34 (7)	34 (6)	0.635
Formal level of education <sup>a</sup> , n (%)					
None	14 (6.5)	3 (4.2)	6 (8.3)	5 (6.9)	0.329
Some primary school	90 (41.5)	31 (43.1)	35 (48.6)	24 (32.9)	
Some secondary school	104 (47.9)	35 (48.6)	30 (41.7)	39 (53.4)	
Some tertiary/university or higher	9 (4.2)	3 (4.2)	1 (1.4)	5 (6.9)	
Years in school, n (%)					
<5	27 (12)	9 (13)	10 (14)	8 (11)	0.870
≥5	190 (88)	63 (87)	62 (86)	65 (89)	
Religion <sup>a</sup> , n (%)					
Protestant	65 (29.8)	16 (21.9)	22 (30.6)	27 (37)	0.158
Catholic	75 (34.4)	24 (32.9)	24 (33.3)	27 (37)	
Muslim	52 (23.8)	23 (31.5)	18 (25)	11 (15.1)	
Born again	21 (9.6)	9 (12.3)	5 (6.9)	7 (9.6)	
Adventist	4 (1.8)	1 (1.4)	3 (4.2)	0 (0)	
Other	1 (0.5)	0 (0)	0 (0)	1 (1.37)	
Marital status <sup>a</sup> , n (%)					
Never married	29 (13.3)	9 (12.3)	9 (12.5)	11 (15.1)	0.884
Married	15 (6.9)	5 (6.9)	4 (5.6)	6 (8.2)	
Cohabiting	161 (73.9)	56 (76.7)	55 (76.4)	50 (68.5)	
Separated	12 (5.5)	3 (4.1)	3 (4.2)	6 (8.2)	
Widow	1 (0.5)	0 (0)	1 (1.4)	0 (0)	
Monthly household income (Ugandan shillings) <sup>a</sup> , n (%)					
≤100 000 (<US\$28)	63 (29.0)	14 (19.4)	23 (31.9)	26 (35.6)	0.019
100 000–500 000 (US\$28–138)	44 (20.3)	11 (15.3)	13 (18.1)	20 (27.4)	
≥500 000 (>US\$138)	1 (0.5)	1 (1.4)	0 (0)	0 (0)	
Didn't know (unknown)	109 (50.2)	46 (63.9)	36 (50)	27 (37)	
Does mother earn income by working outside the home? <sup>b</sup> , n (%)					
Yes	118 (53.9)	32 (43.8)	39 (53.4)	47 (64.4)	0.055
No	101 (46.1)	41 (56.2)	34 (46.6)	26 (35.6)	
Occupation <sup>a</sup> , n (%)					
Skilled	26 (22.2)	4 (12.5)	8 (21.1)	14 (29.8)	0.137
Unskilled	23 (19.7)	8 (25)	4 (10.5)	11 (23.4)	
Small business	68 (58.1)	20 (62.5)	26 (68.4)	22 (46.8)	
Type of housing, n (%)					
Own house	44 (20.5)	11 (15.5)	14 (19.4)	19 (26.4)	0.248
Rent house	23 (10.7)	12 (16.9)	8 (11.1)	3 (4.2)	
Rent room/apartment	138 (64.2)	44 (61.9)	47 (65.3)	47 (65.3)	
Other (employment-based housing or stay with relative) <sup>c</sup> , n (%)	10 (4.7)	4 (5.6)	3 (4.2)	3 (4.2)	
Number of household members, median (IQR)	4 (2)	4 (2)	4 (2)	4 (2)	0.245
HIV status disclosed to current partner, n (%)	123 (57.8)	42 (59.2)	42 (59.2)	39 (54.9)	0.841
HIV status disclosed to a family member/friend <sup>d</sup> , n (%)	152 (70.4)	54 (75.0)	54 (75.0)	44 (61.1)	0.109
Type of ARVs <sup>b</sup> , n (%)					
AZT only	31 (14.2)	10 (13.7)	9 (12.5)	12 (16.4)	0.951
HAART	112 (51.4)	37 (50.7)	37 (51.4)	38 (52.1)	
Option B+	75 (34.4)	26 (35.6)	26 (36.1)	23 (31.5)	
Previous pregnancies, median (IQR) <sup>e</sup>	3 (2)	3 (2)	3 (3)	3 (2)	0.413
Live births, median (IQR) <sup>e</sup>	1 (2)	2 (2)	2 (1)	1 (3)	0.873
Follow-up (d), median (IQR) <sup>e</sup>	252 (3)	252 (3)	252 (4)	253 (3)	0.868

<sup>a</sup>Fisher's exact test.<sup>b</sup> $\chi^2$  test.<sup>c</sup>Other: employment-based housing (n=6) or stay with relative (n=4).<sup>d</sup>At least one family member knows, including parents, grandparents, siblings, aunt, uncle, mother-in-law, father-in-law, other family members and friends.<sup>e</sup>Kruskal–Wallis test.

( $p > 0.05$ ). However, this income differential across intervention arms is confounded by the fact that 50% of the participants did not report their income.

### Risk of early EBF cessation

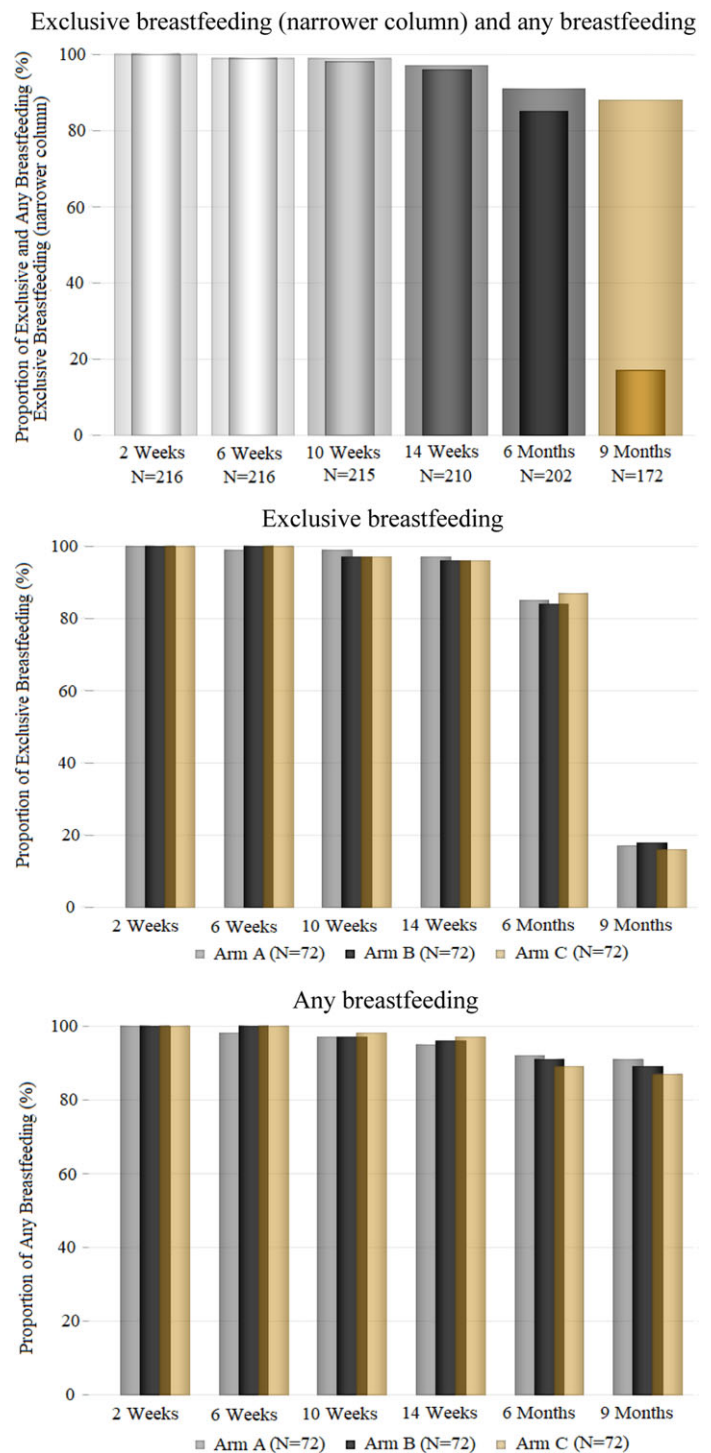
EBF rates were not different between the intervention arms at the 6-month (A, 85%; B, 84%; C, 87%;  $p = 0.47$ ) and 9-month (A, 17%; B, 18%; C, 16%;  $p = 0.97$ ) follow-ups (Figure 2). KM plots showed that the probability of time to EBF cessation did not differ between intervention arms during follow-up (Figure 3).

Similar to KM analyses, multivariable Cox proportional hazards regression results (Table 2) showed that the risk of early EBF cessation did not differ between intervention arms ( $p = 0.67$ ) even after adjusting for household size, type of housing, HIV status disclosure to current partner and HIV treatment regimen effects. Independent of intervention effects, the risk of early EBF cessation was 56% lower among participants on AZT HIV-related treatment vs those on Option B+ treatment (adjusted hazard ratio [aHR] 0.44 [95% CI 0.20–0.96]) and 10% lower in households with one additional household member (aHR 0.90 [95% CI 0.81–0.99]). On the other hand, participants who disclosed their HIV status to current partners had a 93% higher risk of EBF cessation than those who did not (aHR 1.93 [95% CI 1.10–3.41]). The risk of early EBF cessation was 3.6 times higher among participants who lived in employment-based housing or with relatives than those who lived in houses they owned (aHR 3.62 [95% CI 1.03–12.74]). Other participant characteristics were not associated with the risk of early BF cessation (Table 2).

### Risk of early BF cessation

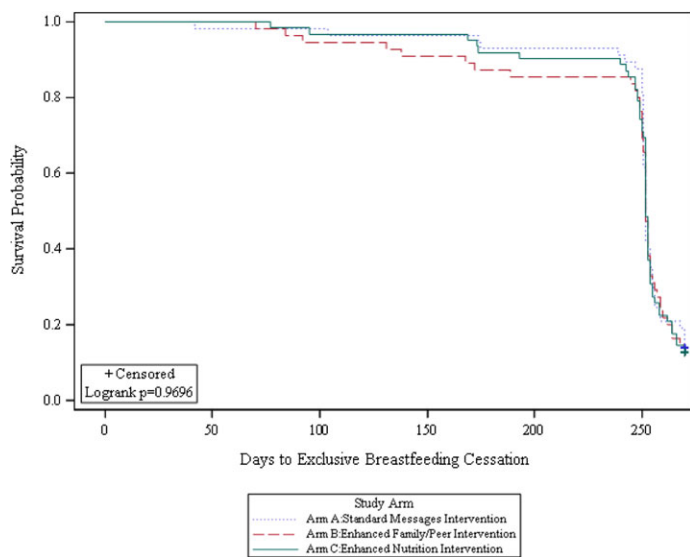
In contrast to EBF, any BF rates remained high (>87%) throughout the follow-up in all study arms (Figure 2). The probability of time to BF cessation differed between intervention arms depending on the participant’s level of formal education (Figure 4). Among participants with no formal education, the probability of longer BF duration was higher in the enhanced intervention arms (B and C) than in arm A ( $p = 0.05$ ). In intervention arm A, the probability of longer BF duration was higher among participants with some formal education than participants who had no formal education (Figure 5).

Multivariable Cox proportional hazards regression results (Table 3) showed that the risk of early BF cessation differed between intervention arms depending on the mother’s level of education (intervention  $\times$  education interaction;  $p = 0.04$ ). Among mothers with no formal education, the risk of early BF cessation was 88% (aHR 0.12 [95% CI 0.05–0.30]) and 93% (aHR 0.07 [95% CI 0.03–0.18]) lower in arm B and C than arm A, respectively, adjusted for religious affiliation and HIV status disclosure to a current partner. At higher levels of education, the risk of early BF cessation was not different between intervention arms (Table 3). After controlling for intervention effects, Catholic religious affiliation was associated with a higher risk of early BF cessation than Protestant affiliation (aHR 2.31 [95% CI 1.27–4.20]).



**Figure 2.** Overall and intervention-specific rates of EBF and any BF among study participants during a 9-month follow-up, 2012–2013.

Participants who disclosed their HIV status to their current partner had a 66% higher risk of early BF cessation than those that did not (aHR 1.66 [95% CI 1.02–2.69]).



**Figure 3.** Plot of the KM estimate of the survival function (probability) of EBF by intervention arm assignment.

## Discussion

Our findings show that enhanced intervention (involving family/peer support and nutrition-based education) effects on EBF promotion are not different when compared with standard practice in PMTCT programme settings. However, these enhancements lower the risk of early BF cessation among women with no formal education. Independent of intervention effects, disclosure of HIV status to a partner and living in employment-based housing or with a relative were associated with a higher risk of early EBF cessation. The risk of early BF cessation was higher among mothers who self-reported Catholic religion affiliation and disclosed their HIV status to their partners. In contrast, the receipt of AZT HIV-related treatment and larger household size were associated with a lower risk of early EBF cessation.

### Risk of early EBF cessation

The null finding regarding the effect of enhanced intervention (vs standard care) on EBF promotion is consistent with some<sup>28</sup> but not all<sup>24,27</sup> existing randomized trial results in sub-Saharan Africa. Moreover, intervention effect sizes examined in previous studies are different compared with our study at 6 months postpartum despite being carried out within the context of country-level PMTCT programmes. For example, intervention vs standard care EBF rates involving community health worker (CHW) home visits were 24% vs 16%,<sup>27</sup> peer home visits were 43% vs 45%<sup>28</sup> and peer counsellors were 73% vs 22% (in Burkina Faso), 59% vs 15% (in Uganda) and 2% vs 1% (in South Africa).<sup>24</sup> These interventions also involved a different frequency/intensity and timing of delivery contacts. The fact that our intervention effects are different when compared with similar interventions in other countries underlines the argument for differential effects of culture and norms on EBF behaviour and promotion. For interventions that involve PMTCT counsellors, our findings suggest enhanced peer support and nutrition education do not accrue additional

benefit. Future research needs to examine the comparative effects of CHW, peer support and nutrition education with and without PMTCT counsellor support, the background condition that was common to all our intervention arms. These comparisons will need to control for the potential differential effects of frequency/intensity and timing of intervention activities.<sup>29</sup>

In our study, the relatively high prevalence of EBF at 6 months across study arms (compared with recent global<sup>5</sup> and national estimates<sup>31</sup>) may be explained by our restrictive eligibility criteria that required a self-reported intention to breastfeed after delivery, receipt of prenatal care and hospital delivery, factors known to be associated with EBF adherence.<sup>31</sup> Moreover, all study participants were exposed to general infant feeding messages and education offered by hospital midwives/nurses and PMTCT counsellors during routine antenatal and postpartum care visits.

Independent of intervention effects, our findings also highlight the benefits of larger households on EBF adherence. Specifically, our results suggest that even after adjusting for other indicators of socio-economic status (e.g. maternal occupation, housing and education), having additional family support reflected in household size may be beneficial for EBF adherence among HIV-infected women. This benefit, however, may not be apparent in scenarios where extended family influence may function to undermine EBF adherence through misconceptions about an HIV-infected nursing mother's breast milk (e.g. superiority of formula) and the risk to an infant.<sup>32,33</sup>

The lower risk of EBF cessation among mothers receiving AZT vs Option B+ HIV treatment regimens is a new finding that warrants further research. Existing evidence on the side effects of HIV treatment among infants born to HIV-infected mothers suggests daily NVP in an infant's saliva may irritate a mother's nipple.<sup>34</sup> Additionally, other side effects such as oral lesions, conjunctivitis and blistering may contribute to the risk of early EBF cessation due to their influence on quality and frequency of breastfeeding.<sup>35</sup> Further, because both Option A (includes AZT) and Option B+ HIV treatment regimens require NVP for 4–6 weeks or until BF cessation, it is unclear why EBF cessation would be different between these treatment groups. The potential influence of drug interactions and side effects of NVP involving Option A vs B and their effect on BF quality needs further research.

The negative effect of HIV status disclosure to a partner on the risk of early EBF (and BF) cessation is consistent with previous studies.<sup>17,21,36</sup> Nursing mothers may have reduced autonomy in decision making about infant feeding, especially if a partner/spouse has divergent views on the need for BF or the risk it poses to an infant's health and is the sole financial provider.<sup>9,33</sup> If this is true, in addition to empowerment of women, EBF/BF promotion interventions should target both a nursing mother and her current partner.

### Risk of early BF cessation

The enhanced intervention benefit (i.e. lower risk of early BF cessation) observed among mothers with no formal education might be explained by the additional study contacts and activities involving peers or counsellors received in the enhanced study arms (B and C). This argument is supported by findings from a previous cross-sectional study in Uganda that showed a dose-response gradient for longer BF duration as the number of

**Table 2.** Cox proportional hazards model regression results of the association between time to EBF and BF cessation and selected covariates summarized as crude and adjusted hazard ratios (with 95% CI)

Characteristics	Risk of early EBF cessation		Risk of early BF cessation	
	Crude HR (95% CI)	aHR (95% CI)	Crude HR (95% CI)	aHR (95% CI)
Study arm				
A: standard intervention	Reference	Reference	Reference	Reference
B: family/peer intervention	1.21 (0.74–2.00)	1.39 (0.74–2.60)		
C: nutrition intervention	0.95 (0.58–1.55)	1.20 (0.66–2.21)		
Formal education				
None (0 y)	Reference	Reference	Reference	Reference
Some primary school (1–7 y)	0.97 (0.49–1.93)	1.26 (0.56–2.82)		
Some secondary school (8–13 y)	0.89 (0.45–1.77)	1.52 (0.64–3.58)		
Some university or higher (>13 y)	0.87 (0.27–2.78)	1.83 (0.38–8.63)		
HIV treatment indication				
Option B+	Reference	Reference	Reference	Reference
AZT	0.57 (0.29–1.13)	<b>0.44 (0.20–0.96)</b>	1.08 (0.56–2.09)	0.97 (0.46–2.08)
HAART	1.01 (0.67–1.54)	0.74 (0.42–1.31)	1.38 (0.89–2.14)	1.15 (0.65–2.02)
Religion				
Protestant	Reference	Reference	Reference	Reference
Catholic	1.10 (0.68, 1.77)	1.21 (0.71, 2.07)	<b>1.83 (1.11–3.02)</b>	<b>2.31 (1.27–4.20)</b>
Muslim	1.58 (0.93–2.69)	1.94 (1.06–3.59)	1.69 (0.99–2.92)	1.78 (0.94–3.37)
Born again	0.66 (0.29–1.50)	0.89 (0.33–2.46)	0.72 (0.30–1.68)	1.25 (0.41–3.84)
Adventist	3.02 (0.72–12.78)	2.00 (0.38–10.47)	2.58 (0.77–8.58)	2.55 (0.62–10.42)
Other	0.95 (0.13–6.96)	1.50 (0.11–21.02)	1.05 (0.14–7.74)	0.21 (0.01–12.20)
Marital status				
Married	Reference	Reference	Reference	Reference
Never married	0.92 (0.35–2.46)	1.51 (0.45–5.04)	0.99 (0.36–2.41)	1.09 (0.35–3.45)
Cohabiting	1.27 (0.55–2.92)	1.22 (0.48–3.10)	0.96 (0.42–2.21)	1.06 (0.40–2.64)
Separated	1.62 (0.54–4.82)	1.89 (0.52–6.89)	1.21 (0.41–3.61)	1.03 (0.29–3.64)
Widow	2.89 (0.34–24.32)	2.18 (0.19–24.64)	1.50 (0.18–12.49)	0.90 (0.08–9.94)
Monthly household income (Ugandan shillings)				
≤100 000 (<US\$28)	Reference	Reference	Reference	Reference
100 000–500 000 (US\$28–\$138)	0.99 (0.65–1.51)	0.94 (0.55–1.58)	0.96 (0.63–1.46)	0.89 (0.55–1.46)
≥500 000 (>US\$138)	–	–	–	–
Didn't know (unknown)	0.96 (0.53–1.73)	1.24 (0.56–2.75)	1.05 (0.59–1.89)	1.96 (0.87–4.40)
Mother's occupation				
Unskilled	Reference	Reference	Reference	Reference
Skilled	1.03 (0.56–1.89)	1.25 (0.63–2.48)	0.86 (0.47–1.56)	0.92 (0.40–2.11)
Small business	1.02 (0.61–1.71)	1.43 (0.75–2.73)	0.82 (0.49–1.37)	0.70 (0.36–1.36)
Type of housing				
Own house	Reference	Reference	Reference	Reference
Rent house	0.72 (0.34–1.52)	1.53 (0.58–4.05)	0.82 (0.38–1.79)	0.88 (0.34–2.24)
Rent room/apartment	0.79 (0.47–1.30)	1.33 (0.70–2.52)	0.90 (0.55–1.49)	0.83 (0.46–1.53)
Other (employment-based housing or stay with relative)	1.04 (0.39–2.78)	<b>3.62 (1.03–12.74)</b>	2.52 (0.94–6.79)	2.63 (0.82–8.36)
Number of household members	0.99 (0.92–1.06)	<b>0.90 (0.81–0.99)</b>	1.02 (0.92–1.14)	1.01 (0.88–1.17)
Disclosed HIV status to current partner				
No	Reference	Reference	Reference	Reference
Yes	1.48 (0.99–2.21)	<b>1.93 (1.10–3.41)</b>	<b>1.53 (1.01–2.32)</b>	<b>1.66 (1.02–2.69)</b>
Disclosed HIV status to at least one family member				
No	Reference	Reference	Reference	Reference
Yes	0.85 (0.55–1.31)	0.74 (0.42–1.28)	0.89 (0.58–1.38)	0.74 (0.44–1.25)
Number of live births	1.17 (1.01–1.36)	1.18 (0.95–1.48)	1.13 (0.97–1.31)	1.06 (0.85–1.31)

Continued

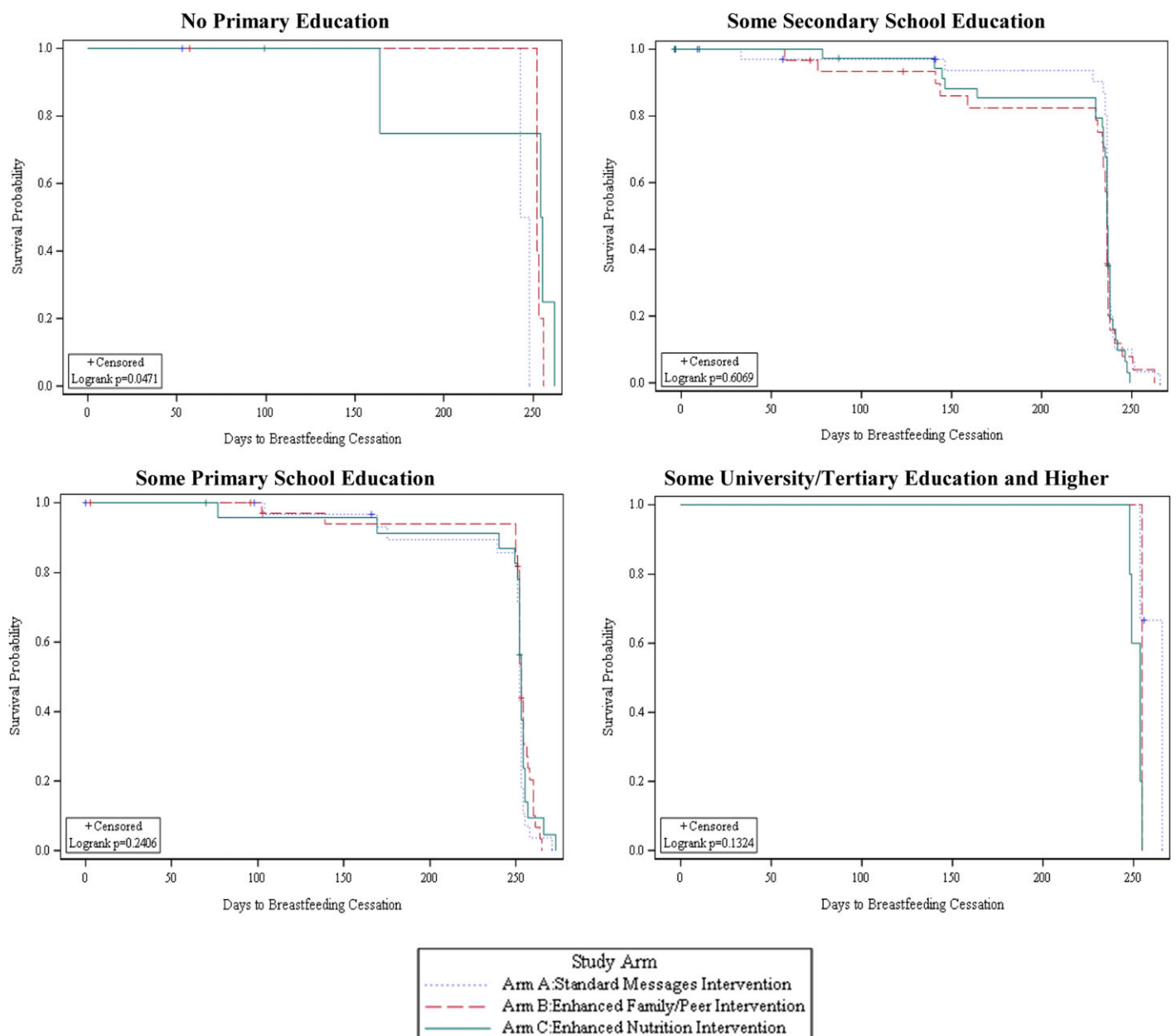


**Table 2.** *Continued*

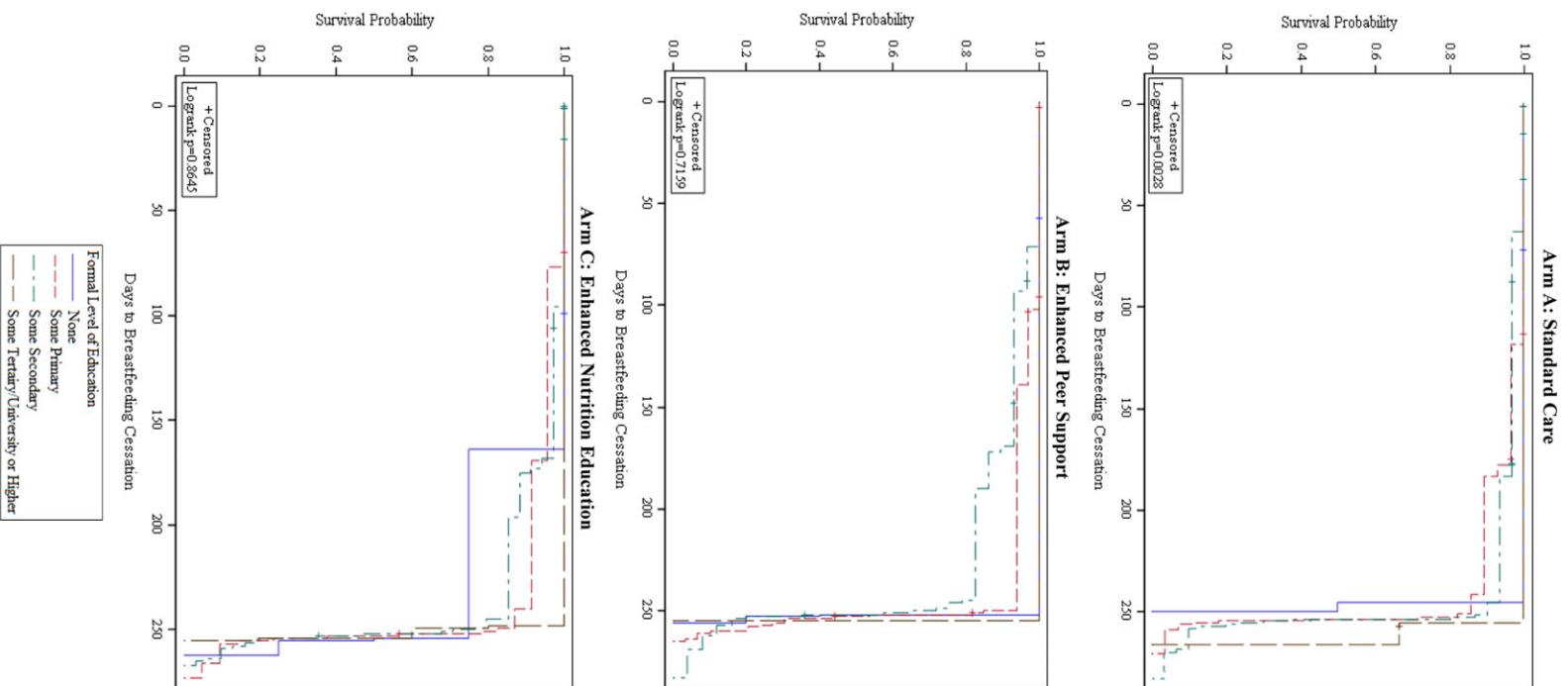
Characteristics	Risk of early EBF cessation		Risk of early BF cessation	
	Crude HR (95% CI)	aHR (95% CI)	Crude HR (95% CI)	aHR (95% CI)
Number of previous pregnancies	1.09 (0.96–1.24)	1.10 (0.89–1.36)	1.07 (0.94–1.23)	1.01 (0.79–1.28)
Maternal age	1.03 (0.99–1.07)	1.01 (0.96–1.07)	1.00 (0.96–1.04)	0.98 (0.92–1.03)

p<0.05 in bold.

Covariates examined as potential confounders in the final models included maternal age, HIV treatment indication, religion, marital status, personal income, occupation, type of housing, number of household members, disclosure of HIV status–current partner or any family member, number of live births and number of pregnancies.



**Figure 4.** Plot of the KM estimate of survival function (probability) of any BF by intervention arm assignment and level of education.



**Figure 5.** Plot of the KM estimate of survival function (probability) of any BF by level of education within intervention arms.

**Table 3.** Cox proportional hazards model regression results of intervention effects on risk of early BF cessation by education level summarized using aHR (95% CI)

Arm	No formal education		Some primary school		Some secondary school		Some university	
	Crude HR (95% CI)	aHR (95% CI)	Crude HR (95% CI)	aHR (95% CI)	Crude HR (95% CI)	aHR (95% CI)	Crude HR (95% CI)	aHR (95% CI)
A	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
B	<b>0.14 (0.06–0.35)</b>	<b>0.12 (0.05–0.30)</b>	0.79 (0.38–1.71)	0.91 (0.43–1.94)	0.78 (0.35–1.75)	0.89 (0.39–2.02)	2.75 (0.17–45.47)	1.44 (0.08–27.03)
C	<b>0.08 (0.03–0.19)</b>	<b>0.07 (0.03–0.18)</b>	0.81 (0.39–1.73)	0.90 (0.39–2.05)	0.77 (0.37–1.62)	0.79 (0.37–1.68)	5.75 (0.50–66.62)	17.01 (0.88–33.28)

p<0.05 in bold.  
Adjusted for confounding by religious affiliation.

counselling visits increased.<sup>36</sup> It is also plausible that the increased health care contact as a function of the additional study contacts and activities may have mediated a longer duration of BF in the enhanced intervention arms vs standard care. The lack of enhanced intervention benefit among women with at least some formal education is consistent with previous general population studies that show higher levels of education are independently associated with a longer duration of BF.<sup>37-39</sup>

The lower risk of early BF cessation among mothers with some (vs no) formal education in the standard care arm (A) but no education effect in the enhanced intervention arms (B and C) suggests two things. One, standard care among mothers with some formal education may be sufficient to achieve desired BF goals. Two, enhancing standard care with family/peer support or nutrition education attenuates the risk of early BF cessation among mothers with no formal education. On the other hand, it is also plausible that formal education may be a proxy for other factors (e.g. culture and norms) that may be associated with the risk of early BF cessation; this should be explored further in future research.

The higher risk of early BF cessation among Catholic- vs Protestant-affiliated mothers in our study may be explained by the low rates of contraceptive use among Catholic women.<sup>40</sup> These low rates of contraceptive use are associated with shorter birth intervals and consequently early BF cessation.<sup>41</sup> Still, qualitative research is needed to understand why Catholic-affiliated mothers are at higher risk of early BF cessation than other religions. This information could be useful in designing targeted BF promotion strategies in this population.

### Study limitations

This study has some limitations. First, EBF/BF was determined based on self-reports, which are prone to both recall and social desirability bias (misclassification). Secondly, although we had different appointment days for participants in the different arms during follow-up to decrease the likelihood of intervention mixing between study arms, we cannot rule out the potential for contamination bias due to information sharing between participants in different intervention arms. Thirdly, given that 50% of the participants did not report their monthly household income (further analyses involving income effects were not instituted), it remains unclear what effect income may have had on the risk of early EBF/BF cessation. Still, the higher risk of early EBF cessation among mothers who live in employment-based housing or with a relative points to known negative effects associated with low socio-economic status.<sup>9</sup> Fourthly, we did not examine some factors such as spouse education, income and religion of family members (including spouse) known to influence BF behaviour.<sup>9,42</sup> Finally, the relatively small sample sizes and low power related to some of our stratified analyses call for a cautious interpretation of study findings and warrant replication in larger-scale studies.

### Conclusions

In summary, our results suggest that enhanced (vs standard care) EBF promotion interventions may not differentially influence EBF but reduce the risk of early BF cessation among women with no formal education in resource-limited PMTCT

program settings. Targeted interventions among women with no formal education and a nursing mother's partner are critical to reducing the risk of early EBF and BF cessation. Further research is needed to understand the contexts that mediate the relationships between religious beliefs, HIV treatment regimen (i.e. side effects on breast or infant health) and BF practices to inform intervention programming.

### Supplementary data

Supplementary data are available at *International Health* online (<https://academic.oup.com/inthealth>).

**Authors' contributions:** JNM, AHO, CO, MM, PEN, MMO, PM, MN and MGF conceived the study. All authors contributed to the design of the study. AHO analysed the data. JNM, AHO, CO, MM, PEN, MMO, PM, MN and MGF interpreted the data. JNM and AHO drafted the manuscript. All authors critically revised the manuscript for intellectual content and read and approved the final manuscript. JNM and AHO are guarantors of the paper.

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