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Family Matters: Co-enrollment of Family Members Into Care Is Associated With Improved Outcomes for HIV-Infected Women Initiating Antiretroviral Therapy

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Background: Although there is widespread interest in understanding how models of care for delivering antiretroviral therapy (ART) may influence patient outcomes, family-focused approaches have received little attention. In particular, there have been few investigations of whether the co-enrollment of HIV-infected family members may improve adult ART outcomes over time.

Methods: We examined the association between co-enrollment of HIV-infected family members into care and outcomes of women initiating ART in 12 HIV care and treatment programs across sub-Saharan Africa. Using data from the mother-to-child transmission-(MTCT) Plus Initiative, women starting ART were categorized according to the co-enrollment of an HIV-infected partner and/or HIV-infected child within the same program. Mortality and loss to follow-up were assessed for up to 5 years after women's ART initiation.

Results: Of the 2877 women initiating ART included in the analysis, 31% (n = 880) had at least 1 HIV-infected family member enrolled into care at the same program, including 24% (n = 689) who had an HIV-infected male partner, and 10% (n = 295) who had an HIV-infected child co-enrolled. There was no significant difference in the risk of death of women by family co-enrollment status (P = 0.286). However, the risk of loss to follow-up was greatest among women who did not have an HIV-infected family member co-enrolled (19% after 36 months on ART) compared with women who had an HIV-infected family member co-enrolled (3%–8% after 36 months on ART) ($P < 0.001$). These associations persisted after adjustment for demographic and clinical covariates and were consistent across countries and care programs.

Discussion: These data provide novel evidence for the association between adult outcomes on ART and co-enrollment of HIV-infected family members into care at the same program. Interventions that build on women's family contexts warrant further consideration in both research and policies to promote retention in ART services across sub-Saharan Africa.

Key Words: antiretroviral therapy, family care, loss to follow-up, women's health, models of care, Africa

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INTRODUCTION

Over the past decade, there has been a dramatic increase in the numbers of HIV-infected individuals receiving antiretroviral therapy (ART) across sub-Saharan Africa. At the end of 2012, there were more than 7 million individuals receiving ART, an increase of >90% over the preceding decade.[1] With increasing numbers of individuals on treatment, there is widespread interest in understanding how the design and implementation of health care services to deliver ART may influence patient outcomes.[2] Although morbidity and mortality are key outcomes for patients on treatment, there is recognition that loss to follow-up (LTF) presents a fundamental challenge to maximizing the benefits of HIV care and treatment services.[3] In turn, there is ongoing interest in how service delivery models may influence the risk of

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death or LTF among HIV-infected patients, independent of patient characteristics. Studies over the past decade have identified aspects of ART service implementation that were associated with improved patient outcomes. For example, studies have compared outcomes of primary care versus hospital-based ART services, the role of task-shifting of ART services to nurses, and more recently, the effectiveness of community-based models of ART provision.[4–6]

Despite the attention devoted to different models of service delivery, there has been relatively little attention given to the potential of family-focused approaches for enhancing outcomes of HIV care and treatment.[7] Most ART services engage patients as individuals, with little attention to their families or other social contexts, despite evidence from other chronic conditions that family support can be a key determinant of outcomes,[8–10] and to the reality that many HIV-infected individuals in sub-Saharan Africa live in households where immediate family members are also likely to be infected as well.[11] Thus, it is plausible that health care services that engage families may offer advantages in terms of improving retention in care and adherence with ART over the long run.[12] To date, most research on the role of family support in influencing HIV care and treatment outcomes has centered on outcomes for HIV-infected children.[13–15] This literature suggests that care for HIV-infected children may be strengthened by a family-friendly service environment; however, there is paucity of data on the role of family-focused ART services on adult treatment outcomes.[16,17]

We investigated the effect of providing HIV care and treatment services to HIV-infected family members on HIV-related outcomes of women initiating ART. Using data from the mother-to-child transmission (MTCT)-Plus Initiative, a multicountry HIV care and treatment program in sub-Saharan Africa, we tested the hypothesis that HIV-infected women with other HIV-infected family members co-enrolled in care at the same service delivery site would have significantly different outcomes when compared with women who did not have family members in care at the same site.

METHODS

Data for this analysis were derived from the MTCT-Plus Initiative, which supported the enrollment of patients across 12 sites in 8 sub-Saharan African countries: Cameroon, Cote d'Ivoire, Kenya, Mozambique, Rwanda, South Africa, Uganda, and Zambia. The program has been described in detail previously.[18–20] In brief, pregnant or postpartum HIV-infected women (here referred to as index women) were recruited from prevention of mother-to-child transmission (PMTCT) programs and enrolled into ongoing HIV care and treatment services. Women were enrolled regardless of ART eligibility and received comprehensive care during follow-up, including ART when indicated based on national guidelines. At enrollment and throughout follow-up, women were encouraged to have their partners and children tested for HIV and such testing was available at all sites. Family members found to be HIV infected were encouraged to join the program; however, this was not required.

HIV care, including ART, was provided according to WHO and national guidelines. Although specific ART regimens varied between countries as well as over time, they typically included 2 nucleoside reverse transcriptase inhibitors and a nonnucleoside reverse transcriptase inhibitor as the first-line regimen. Standardized clinical data collection forms were used to collect basic clinical and sociodemographic information at all sites, and the clinical forms of family members were linked to the index woman by the use of her unique program identification number.

Data were analyzed using Stata (version 12.0; Stata Corporation, College Station, TX). We restricted analyses to women initiating ART within MTCT-Plus (index women), and classified each woman according to whether any type of family member (child or partner) was also enrolled into the program before or after the woman's date of ART initiation. This variable was divided into 4 categories: women with no co-enrolled family member, with co-enrolled HIV-infected child only, with co-enrolled HIV-infected partner only, or with co-enrollment of both HIV-infected children and partners. In subanalyses, these categories were collapsed into a binary measure: women with co-enrolled family members versus none. In examining factors associated with these categories, bivariate comparisons used Fisher exact tests (for proportions), Student *t* tests (for mean values), and Wilcoxon rank-sum tests (for medians); all statistical tests are 2 sided at $\alpha = 0.05$.

The primary outcomes for this study were death or LTF, defined as more than 6 months since the last clinic visit without program contact. Kaplan–Meier methods were used to examine the proportions of women who died or were lost to follow-up, after ART initiation, according to the co-enrollment of family members. Cox's proportional hazards models were used to estimate the relative hazard of each outcome separately, with family member co-enrollment included as time-varying covariate. Multivariable models were used to examine the association between family member co-enrollment and outcomes among index women while adjusting for the following: women's age, education level, WHO clinical stage, and nadir $CD4^+$ cell count before ART initiation. All models were stratified by site of enrollment, and results are presented as hazard ratios (HRs) with 95% confidence intervals (CIs).

RESULTS

Overall, 2877 women initiated ART across the 12 sites between 2003 and 2007. Table 1 describes the characteristics of index women initiating ART by age category. The median age was 28 years (interquartile range [IQR], 25–32). Levels of parity, employment, and marriage/cohabitation were lower among younger women, whereas older women had lower $CD4^+$ cell counts and higher WHO clinical stage, on average, at the time of ART initiation.

Across all sites, 31% of women (n = 880) had at least 1 HIV-infected family member enrolled into care at the same site, including 24% of women (n = 689) who had an HIV-infected partner, and 10% (n = 295) who had an HIV-infected child co-enrolled. Four percent (n = 104) of women had both an HIV-infected child and an HIV-infected partner co-enrolled. Sixty-nine percent of HIV-infected partners, and 87% of HIV-infected children, were co-enrolled before or

TABLE 1. Characteristics of Index Women Initiating ART, Overall and by Age Category*

	All Index Women Starting ART (N = 2877)	<25 yrs (N = 697)	25–29 yrs (N = 1047)	30–34 yrs (N = 779)	≥35 yrs (N = 354)
Median age (IQR)	28 (25–32)				
Median parity (IQR)	3 (2–4)	2 (1–3)	3 (2–4)	4 (3–5)	5 (3–6)
Primaparous	416 (15)	220 (32)	149 (14)	39 (5)	8 (2)
Marital status: married/cohabiting	1891 (67)	422 (61)	711 (68)	523 (67)	235 (66)
Employed	697 (24)	109 (16)	276 (74)	209 (27)	103 (29)
Water in the home	1100 (38)	236 (34)	412 (40)	307 (40)	145 (41)
Electricity in the home	1766 (61)	392 (57)	682 (65)	487 (63)	205 (58)
Median yrs of education (IQR)	9 (7–12)	8 (7–11)	9 (7–12)	9 (6–12)	8 (7–11)
WHO stage at ART initiation					
I/II	1856 (65)	480 (69)	674 (64)	484 (62)	218 (62)
III	875 (30)	185 (27)	313 (30)	261 (34)	115 (33)
IV	146 (5)	31 (5)	60 (6)	34 (4)	21 (6)
Median $CD4^+$ count at ART initiation (IQR)	195 (119–234)	184 (138–264)	173 (117–230)	169 (110–213)	167 (115–217)
Family member enrolled in the program					
No family member enrolled	1997 (69)	495 (71)	722 (69)	532 (68)	248 (70)
HIV+ partner enrolled into the program	689 (24)	167 (24)	265 (25)	180 (23)	77 (22)
HIV+ child enrolled into the program	295 (10)	54 (8)	100 (10)	100 (13)	41 (12)
Only HIV+ partner co-enrolled	585 (20)	148 (21)	225 (21)	147 (19)	65 (18)
Only HIV+ child co-enrolled	191 (7)	35 (5)	60 (6)	67 (9)	29 (8)
Both HIV+ partner and HIV+ child co-enrolled	104 (4)	19 (3)	40 (4)	33 (4)	12 (3)
Either HIV+ partner or HIV+ child co-enrolled	880 (30)	202 (29)	325 (31)	247 (32)	106 (30)

*All cells are n (%) unless otherwise specified.

at the time of index woman's ART initiation. Among partners, the median age was 35 years (IQR, 30–39); among children, the median age at enrollment was 2 years (maximum, 4 years), and 49% of the children were male. For both categories of HIV-infected family member, the majority of the remainder of co-enrollments took place within 180 days after ART initiation by the index woman.

Table 2 compares the index women who had an HIV-infected partner or HIV-infected child co-enrolled to women who had no family member co-enrolled in care at the site. The proportion of women who had an HIV-infected partner co-enrolled varied from 1% at the site in Cape Town, South Africa, to 14% at the sites in Cameroon and Soweto, South Africa. The proportion of women who had an HIV-infected child co-enrolled varied from 1% in Mozambique to 23% in Kampala, Uganda.

Co-enrollment of family members was strongly patterned with respect to demographic and clinical characteristics at the time of women's ART initiation. Women who had HIV-infected family members co-enrolled were older (although this was only statistically significant for co-enrollment of HIV-infected children, $P < 0.001$) and less likely to be nulliparous ($P < 0.001$). Measures of socioeconomic status, such as education, employment, access to piped water, and electricity in the home, all appeared lower in women who co-enrolled family members, although differences did not reach statistical significance for all comparisons. In addition, women who had HIV-infected partners and/or HIV-infected children co-enrolled into care were more likely to be married or cohabiting at the time of ART initiation, compared with women who did not (91% and 61%, versus 59%; $P < 0.001$ and 0.080, respectively).

Overall, there were 320 women lost to follow-up and 141 deaths during up to 5.2 years of follow-up. The median duration of follow-up of index women from the time of ART initiation was 1.9 years (IQR, 0.7–3.3). Figure 1 shows the Kaplan–Meier curves for death and LTF for women with and without an HIV-infected family member co-enrolled into care. There was no significant difference in the risk of death between women who did and did not have an HIV-infected family member co-enrolled (log-rank $P = 0.286$). However, the risk of LTF was greatest among women who did not have an HIV-infected family member co-enrolled (19% after 36 months on ART) compared with women who had an HIV-infected family member co-enrolled (3%–8% after 36 months on ART) (log-rank $P < 0.001$).

Table 3 shows the results of proportional hazards models of the association between co-enrollment of an HIV-infected partner and/or HIV-infected child and the outcomes of index women on ART, stratified by site. There was no association between co-enrollment of HIV-infected family members and women's risk of death in crude or adjusted analyses. However, risks of LTF were significantly lower in women who had an HIV-infected partner co-enrolled (adjusted HR, 0.36; 95% CI: 0.24 to 0.55), and HIV-infected child co-enrolled (adjusted HR, 0.23; 95% CI: 0.09 to 0.63) or both (adjusted HR, 0.40; 95% CI: 0.16 to 0.97) after adjusting for women's age, $CD4^+$ cell count, and WHO stage at the time of ART initiation. When the final

TABLE 2. Characteristics of Index Women by Co-enrollment of HIV-Infected Partners and/or HIV-Infected Children at Same Site*

	No HIV-Infected Partner/Child Enrolled (N = 1988)	HIV-Infected Partner Enrolled Into the Program at Any Time (N = 699)	*P* (vs No Family Member Enrolled)	HIV-Infected Child Enrolled Into the Program at Any Time (N = 295)	*P* (vs No Family Member Enrolled)
Median age (IQR)	28 (25–32)	28 (25–32)	0.568	29 (26–32)	<0.001
Mean parity (SD)	3.1 (1.7)	3.3 (1.6)	<0.001	3.6 (1.6)	<0.001
Primaparous	330 (17)	70 (10)	<0.001	18 (6)	<0.001
Marital status: married/cohabiting	1179 (59)	624 (91)	<0.001	180 (61)	0.080
Employed	494 (25)	156 (23)	0.307	67 (23)	0.520
Water in the home	787 (40)	242 (25)	0.060	98 (33)	0.070
Electricity in the home	1265 (64)	384 (56)	<0.001	174 (59)	0.312
Median yrs of education (IQR)	9 (7–11)	8 (7–12)	0.851	9 (7–12)	0.206
WHO stage at ART initiation: I/II	1309 (66)	452 (66)	0.787	156 (53)	<0.001
III	590 (30)	204 (30)		117 (40)	
IV	98 (5)	33 (5)		22 (8)	
Median $CD4^+$ count at ART initiation (IQR)	175 (118–238)	174 (125–230)	0.382	171 (115–212)	0.333
Country/site					
South Africa					
Soweto	189 (9)	94 (14)	<0.001	28 (9)	<0.001
Durban	158 (8)	40 (6)		27 (9)	
Cape Town	128 (6)	3 (1)		4 (1)	
Uganda					
Mulago	93 (5)	78 (11)		69 (23)	
Nsambya	130 (7)	85 (12)		33 (11)	
Mozambique	42 (2)	24 (3)		1 (1)	
Cameroon	485 (24)	94 (14)		28 (9)	
Rwanda	62 (3)	62 (9)		18 (6)	
Kenya					
Kisumu	123 (6)	69 (10)		19 (6)	
Eldoret	105 (5)	65 (9)		19 (6)	
Cote d'Ivoire	290 (15)	57 (8)		32 (11)	
Zambia	189 (9)	69 (10)		17 (6)	
Median duration of follow-up (IQR)	594 (209–1115)	926 (413–1340)		1100 (545–1474)	
Index woman's outcome					
Died	101 (5)	35 (5)	<0.001	15 (5)	<0.001
Loss to follow-up	288 (14)	44 (6)		12 (4)	
In care at data closeout	1608 (81)	610 (89)		268 (91)	

*All cells are N (%) unless otherwise specified.

multivariable models for LTF were restricted to women who had an HIV-infected family member co-enrolled before the date of ART initiation, these associations remained (data not shown). When the analysis was restricted to women who had at least 1 family member co-enrolled, women who had only an HIV-infected child co-enrolled were less likely to be lost to follow-up than women who had only an HIV-infected partner co-enrolled (HR, 0.43; 95% CI: 0.16 to 1.13, $P = 0.088$), although this association did not reach statistical significance.

In stratified analyses (Table 4), the association between co-enrollment of an HIV-infected family member and reduced risk of LTF was persistent across subgroups of marital/cohabiting status, age categories, and parity categories. In a site-specific analysis, the corresponding HRs varied from 0.12 (at the Cameroon site) to 0.95 (at one of the Ugandan sites), with broad CIs.

DISCUSSION

Although the concept of family-focused HIV care has been discussed previously, largely in the context of pediatric HIV treatment, there have been few empirical investigations into how co-enrollment of HIV-infected family members within a single ART program may influence adult treatment outcomes. Our study provides novel evidence for the association between outcomes in HIV-infected adults and co-enrollment of HIV-infected family members into care. Although there was no link in our study between women's mortality in ART programs and co-enrollment of a family member, there was a strong and persistent association between co-enrollment of an HIV-infected partner and/or child and reduced risk of LTF on ART.

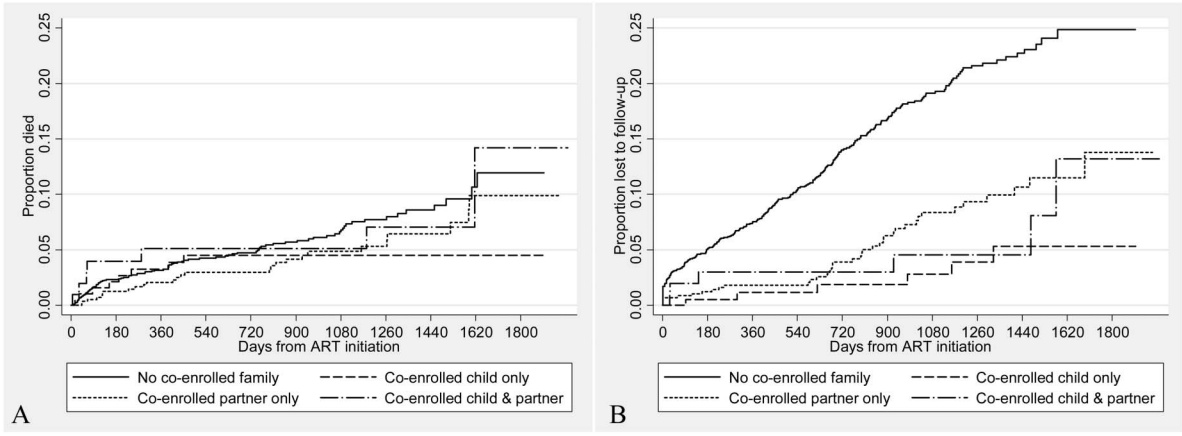

FIGURE 1. Kaplan–Meier plots of time to death (A) or LTF (B) comparing index women with and without an HIV-infected partner and/or HIV-infected child co-enrolled into care at site.

The paucity of data on this issue is itself notable and is likely a reflection of the overriding orientation of HIV programs, as with most health services, toward the management of individual patients.[12] However, as one of the unique features of the MTCT-Plus Initiative was the focus on family-centered care, the programs strongly encouraged HIV testing of family members of index women enrolled from PMTCT services and the enrollment of those found to be HIV infected in HIV care and treatment. In addition, it collected data on the co-enrollment of infected family members linking them to the index women, thus offering the unique opportunity to provide insights into an overlooked but potentially valuable aspect of ART program design.

Loss to follow-up is a major concern facing ART programs in countries across sub-Saharan Africa. Failure to retain patients on ART threatens the benefit to individuals of ART as well as reducing the potential population benefits of treatment as prevention[21]; for HIV-infected women, retention on ART is essential for their own health and due to their importance as caregivers for their children and households.[18] In our study, the overall levels of LTF seemed somewhat lower than those observed in other cohorts from similar

TABLE 3. HR With 95% CI for the Association Between Co-enrollment of HIV-Infected Family Members at the Same Site and Death or LTF of Index Women After Initiating ART*

	Death				Loss to Follow-up			
	Panel A		Panel B		Panel A		Panel B	
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
No HIV-infected partner/child co-enrolled	1.0	Ref			1.0	Ref	1.0	Ref
HIV-infected partner co-enrolled	0.88	0.58 to 1.31			0.41	0.29 to 0.56		
HIV-infected child co-enrolled	1.00	0.57 to 1.73			0.26	0.14 to 0.46		
Any HIV-infected family member (either partner or child) co-enrolled	0.83	0.57 to 1.22			0.31	0.23 to 0.43		
No HIV-infected partner/child co-enrolled	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref
HIV-infected partner co-enrolled only	0.79	0.51 to 1.23	0.72	0.33 to 1.59	0.25	0.11 to 0.56	0.36	0.24 to 0.55
HIV-infected child co-enrolled only	0.77	0.37 to 1.59	0.86	0.53 to 1.39	0.42	0.30 to 0.60	0.23	0.09 to 0.63
Both HIV-infected partner and child co-enrolled	1.27	0.57 to 2.85	0.54	0.16 to 1.85	0.42	0.18 to 0.95	0.40	0.16 to 0.97
Age (continuous)	1.00	0.99 to 1.00	1.00	0.99 to 1.01	0.95	0.92 to 0.97	0.95	0.92 to 0.98
Nadir $CD4^+$ cell count								
>200	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref
101–200	0.96	0.57 to 1.62	1.11	0.66 to 1.89	0.62	0.46 to 0.83	0.55	0.41 to 0.76
51–100	2.68	1.53 to 4.69	2.59	1.48 to 4.54	0.41	0.25 to 0.68	0.39	023 to 0.66
<50	4.72	2.74 to 8.15	4.23	2.44 to 7.32	0.46	0.26 to 0.82	0.50	0.28 to 0.89
WHO stage I/II	1.0	Ref	1.0	Ref	1.0	Ref	1.0	Ref
WHO stage III	2.35	1.63 to 3.39	1.92	1.27 to 2.91	0.71	0.55 to 0.92	0.67	0.48 to 0.94
WHO stage IV	4.56	2.61 to 7.96	4.31	2.36 to 7.87	0.67	0.41 to 1.10	0.71	0.38 to 1.32

*For each outcome, panel A shows associations between the variable of interest and index women's outcomes adjusted only for site of enrollment; panel B shows associations adjusted for site of enrollment, age, nadir $CD4^+$ cell count, and WHO staging at ART initiation. Throughout, co-enrollment of HIV-infected partners or children is treated as a time-varying covariate.

TABLE 4. Analysis of Associations Between Co-enrollment of Any HIV-Infected Family Member (Partners and/or Children) at Same Site, and LTF Among Index Women Initiating ART, Restricted to Subgroups of Index Women*

	No. Index Women in Strata	Percent of Index Women in Strata With Any Co-enrolled Family Member, %	Stratum-Specific HR for Loss to Follow-up for Co-enrollment of HIV-Infected Family Member	
			HR	95% CI
Age 15–29, yrs	1744	30	0.36	0.25 to 0.51
Age ≥30, yrs	1133	31	0.26	0.15 to 0.46
Married/cohabiting	1891	38	0.38	0.27 to 0.53
Not married/cohabiting	689	17	0.15	0.06 to 0.37
Nadir CD4 cell count				
>200	812	30	0.47	0.28 to 0.78
101–200	1161	32	0.24	0.14 to 0.42
51–100	284	29	0.36	0.10 to 1.26
<50	184	32	0.13	0.02 to 1.00
Primaparous	416	21	0.27	0.11 to 0.61
Multiparous	2461	32	0.34	0.25 to 0.47
Country/site				
South Africa				
Soweto	253	25	0.60	0.17 to 2.08
Durban	220	28	0.19	0.02 to 1.48
Cape Town	135	5	0.73	0.27 to 2.00
Uganda	215	57	0.70	0.10 to 4.96
Mulago				
Nsambya	233	44	0.95	0.23 to 3.81
Mozambique	70	36	0.24	0.01 to 4.47
Cameroon	595	18	0.12	0.02 to 0.86
Rwanda	131	53	0.23	0.07 to 0.68
Kenya				
Kisumu	201	39	0.14	0.03 to 0.62
Eldoret	179	41	0.45	0.25 to 0.79
Cote d'Ivoire	374	22	0.92	0.26 to 3.25
Zambia	271	30	0.34	0.16 to 0.74

*Other than the estimates for age groups, all HRs are age adjusted; in addition, HRs for age group, marital/cohabiting status, $CD4^+$ count, and parity are adjusted for site of care.

settings,[22] but despite this, we demonstrated that women's risk of LTF decreased by approximately 50% when an HIV-infected family member was co-enrolled. This association was consistent across subgroups of age, parity, partner status, and site. The strength and consistency of this finding highlights the central role that family and social support can play in shaping health-seeking behaviors among HIV-infected individuals. The results also point to family-level factors as a potentially important avenue for interventions to promote retention. Although not all patients initiating ART have an HIV-infected family member who may be enrolled into care, the findings demonstrate the need for models of HIV care that encourage family-focused approaches, when appropriate.[7]

This study has several strengths. It enrolled a large number of patients and their family members from diverse settings in 8 sub-Saharan African countries, facilitating the generalizability of findings. The key association noted was largely consistent across programs in different countries, as well as across clinical and demographic subgroups. However, this analysis is subject to several limitations. The index patients were all women who were enrolled from PMTCT programs and such individuals may differ from other HIV-infected adults, and in particular, further work is needed to examine whether similar findings would be observed among men. In addition, we used only a relatively crude surrogate measure of engagement in family-focused care, specifically, whether another HIV-infected family member was enrolled within the same program. This measure does not allow exploration of the specific aspects of co-enrollment that may influence retention outcomes—such as disclosure, social support, patient-level economic savings, or other issues. Nonetheless, these data point to the need for further research to understand the ways in which co-enrollment in HIV services operates to improve outcomes.

The findings from our study are particularly salient given the 2013 WHO guidelines, which recommend the universal initiation of ART in all HIV-infected pregnant and breastfeeding women (option B+)[23] as well as more recent attention to understanding optimal models for service delivery.[24] This is likely to result in a dramatic increase in the numbers of HIV-infected pregnant women on ART in many parts of Africa. Early data from option B+ programs raise concerns regarding the retention in pregnant and postpartum women on ART under the option B+ strategy.[25] Our data

suggest that models of service delivery that seek to engage HIV-infected children and/or partners in care may lead to better retention outcomes for women on ART. Such an approach should be pursued to enhance retention of patients on ART, including women engaged in option B+.

In summary, this study demonstrates that HIV-infected women on ART who have other HIV-infected family members co-enrolled into care may be less likely to be lost to follow-up from treatment programs. Based on these data, interventions that build on women's family contexts and that recognize HIV as a condition that often involves multiple family members warrant further consideration in both research and policies to promote retention in ART services across sub-Saharan Africa.

REFERENCES

1. UNAIDS. *Global Report: UNAIDS Report on the Global AIDS Epidemic 2013*. Geneva, Switzerland: UNAIDS; 2013.
2. Harries AD, Makombe SD, Schouten EJ, et al. Different delivery models for antiretroviral therapy in sub-Saharan Africa in the context of "universal access". *Trans R Soc Trop Med Hyg.* 2008;102:310–311.
3. Cornell M, Grimsrud A, Fairall L, et al. Temporal changes in programme outcomes among adult patients initiating antiretroviral therapy across South Africa, 2002–2007. *AIDS.* 2010;24:2263–2270.
4. Grimsrud A, Kaplan R, Bekker LG, Myer L. Outcomes of a nurse-managed service for stable HIV-positive patients in a large South African public sector antiretroviral therapy programme. *Trop Med Int Health*. 2014;19(9):1029–1039.
5. Decroo T, Rasschaert F, Telfer B, et al. Community-based antiretroviral therapy programs can overcome barriers to retention of patients and decongest health services in sub-Saharan Africa: a systematic review. *Int Health.* 2013;5:169–179.
6. Woodd SL, Grosskurth H, Levin J, et al. Home-based versus clinic-based care for patients starting antiretroviral therapy with low CD4(+) cell counts: findings from a cluster-randomized trial. *AIDS.* 2014;28:569–576.
7. Abrams EJ, Myer L, Rosenfield A, et al. Prevention of mother-to-child transmission services as a gateway to family-based human immunodeficiency virus care and treatment in resource-limited settings: rationale and international experiences. *Am J Obstet Gynecol.* 2007;197(suppl 3): S101–S106.
8. Martire LM, Schulz R, Helgeson VS, et al. Review and meta-analysis of couple-oriented interventions for chronic illness. *Ann Behav Med.* 2010; 40:325–342.
9. Von Korff M, Gruman J, Schaefer J, et al. Collaborative management of chronic illness. *Ann Intern Med.* 1997;127:1097–1102.
10. Berg CA, Upchurch R. A developmental-contextual model of couples coping with chronic illness across the adult life span. *Psychol Bull.* 2007; 133:920–954.
11. Rochat TJ, Bland R, Coovadia H, et al. Towards a family-centered approach to HIV treatment and care for HIV-exposed children, their mothers and their families in poorly resourced settings. *Future Virol.* 2011;6:687–696.
12. Tolle MA. A package of primary health care services for comprehensive family-centred HIV/AIDS care and treatment programs in low-income settings. *Trop Med Int Health.* 2009;14:663–672.
13. Leeper SC, Montague BT, Friedman JF, et al. Lessons learned from family-centred models of treatment for children living with HIV: current approaches and future directions. *J Int AIDS Soc.* 2010;13(suppl 2):S3.
14. van Kooten Niekerk NK, Knies MM, Howard J, et al. The first 5 years of the family clinic for HIV at Tygerberg Hospital: family demographics, survival of children and early impact of antiretroviral therapy. *J Trop Pediatr.* 2006;52:3–11.
15. Richter L. An introduction to family-centred services for children affected by HIV and AIDS. *J Int AIDS Soc.* 2010;13(suppl 2):S1.
16. Sherr L. Fathers and HIV: considerations for families. *J Int AIDS Soc.* 2010;13(suppl 2):S4.
17. Richter LM, Sherr L, Adato M, et al. Strengthening families to support children affected by HIV and AIDS. *AIDS Care.* 2009;21(suppl 1):3–12.
18. Myer L, Rabkin M, Abrams EJ, et al. Focus on women: linking HIV care and treatment with reproductive health services in the MTCT-Plus Initiative. *Reprod Health Matters.* 2005;13:136–146.
19. Toro PL, Katyal M, Carter RJ, et al. Initiation of antiretroviral therapy among pregnant women in resource-limited countries: CD4+ cell count response and program retention. *AIDS.* 2010;24:515–524.
20. Tonwe-Gold B, Ekouevi DK, Bosse CA, et al. Implementing family-focused HIV care and treatment: the first 2 years' experience of the mother-to-child transmission-plus program in Abidjan, Côte d'Ivoire. *Trop Med Int Health.* 2009;14:204–212.
21. Tanser F, Barnighausen T, Grapsa E, et al. High coverage of ART associated with decline in risk of HIV acquisition in rural KwaZulu-Natal, South Africa. *Science*. 2013;339:966–971.
22. Rosen S, Fox MP. Retention in HIV care between testing and treatment in sub-Saharan Africa: a systematic review. *PLoS Med.* 2011;8:e1001056.
23. World Health Organization. *Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection*. Geneva, Switzerland: World Health Organization; 2013.
24. World Health Organization. *March 2014 Supplement to the 2013 Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection*. Geneva, Switzerland: World Health Organization; 2014.
25. Tenthani L, Haas AD, Tweya H, et al. Retention in care under universal antiretroviral therapy for HIV-infected pregnant and breastfeeding women ("Option B+") in Malawi. *AIDS.* 2014;28:589–598.