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Discordant retention of HIV-infected mothers and children

Evidence for a family-based approach from Southern Mozambique

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Abstract

It is often assumed that children and their caregivers either stay in care together or discontinue together, but data is lacking on caregiver–child retention concordance. We sought to describe the pattern of care among a cohort of human immunodeficiency virus (HIV) infected children and mothers enrolled in care at the Manhica District Hospital (MDH).

This was a retrospective review of routine HIV clinical data collected under a larger prospective HIV cohort study at MDH. Children enrolling HIV care from January 2013 to November 2016 were identified and matched to their mother's HIV clinical data. Retention in care for mothers and children was assessed at 24 months after the child's enrolment. Multinomial logistic regression was performed to evaluate variables associated with retention discordance.

For the 351 mother–child pairs included in the study, only 39% of mothers had concordant care status at baseline (23% already active in care, 16% initiated care concurrently with their children). At 24-months follow up, a total of 108 (31%) mother–child pairs were concordantly retained in care, 88 (26%) pairs were concordantly lost to follow up (LTFU), and 149 (43%) had discordant retention. Pairs with concurrent registration had a higher probability of being concordantly retained in care. Children who presented with advanced clinical or immunological stage had increased probability of being concordantly LTFU.

High rates of LTFU as well as high proportions of discordant retention among mother–child pairs were found. Prioritization of a family-based care model that has the potential to improve retention for children and caregivers is recommended.

Abbreviations: aRRR = adjusted relative risk ratio (RRR) coefficient, ART = antiretroviral therapy, CASG = community antiretroviral therapy support groups, CDC = Center for Disease Control, CISM = Centro de Investigação em Saúde de Manhica, DSDM = differentiated service delivery models, EID = Early Infant Diagnosis, ePTS = electronic HIV patient tracking systems, HDSS = Health and Demographic Surveillance System, HIV = human immunodeficiency virus, IeDEA-SA = International Epidemiological Databases to Evaluate AIDS in Southern Africa, LTFU = lost to follow up, MDH = Manhica District Hospital, MoH = Mozambique Ministry of Health, PMTCT = prevention of mother to child transmission, UNAIDS = The Joint United Nations Programme on HIV and AIDS, WHO = world health organization.

Keywords: ART, children, family, HIV, lost to follow up (LTFU), retention

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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1. Introduction

Mozambique is a high burden human immunodeficiency virus (HIV) country with an estimated adult prevalence of 13.2%.^[1] A massive national effort has been undertaken to address the epidemic with an Acceleration Plan that dramatically increased the number of patients receiving antiretroviral therapy (ART) from approximately 300,000 patients in 2012 to 1,212,562 at the end of 2018.^[2,3] Key guideline updates to expand access to ART included implementation of Option B+ calling for lifelong ART for all pregnant and lactating women in 2013, universal ART for all HIV-infected children under the age of 5 years in 2015, and phased implementation of test and treat for all ages in 2016.^[3] Mozambique has committed to achieve the Joint United Nations Programme on HIV and AIDS (UNAIDS) 90–90–90 targets by 2020, which call for 90% of people living with HIV being diagnosed, 90% of patients managed with ART, and of those, 90% virally suppressed.^[4] However, significant challenges remain.

As of the end of 2018, the country reported results of 73%/55%/32% for the adult cascade, and 50%/50%/73% for the pediatric cascade with extrapolated data on virologic suppression due to limited national access to viral load monitoring. Case identification and linkage to care still need improvement to reach the 2020 goals, but ART retention presents a particular challenge, with recent reported 12-month ART retention of 68% and 70% in adults and children, respectively.^[3]

The barriers to pediatric ART retention in Southern Africa have been considered in recent reviews which included multiple patient level attributes such as age and immunosuppression, caregiver factors including disclosure and knowledge, institutional factors including understaffing and inefficient patient flows, and systemic factors including care integration and monitoring systems.^[5,6] The Mozambique Ministry of Health (MoH) has implemented a number of interventions and differentiated service delivery models (DSDM) to address known barriers to ART retention such as expedited clinical appointments, 3-month drug distribution, and community ART support groups (CASG), but children, particularly at younger ages, are often not eligible to participate.^[7]

The family-based care model, another DSDM that is being implemented by the MoH in which adult and pediatric services are provided together in a single setting, could be instrumental, particularly when there is discordance in caregiver–child ART retention within families.^[7] The extent to which this discordance occurs has not been well-described in the literature and is not captured by routine programmatic data available in Mozambique. This study aimed to address this knowledge gap by describing enrolment patterns and retention discordance from a group of mothers and their children who were followed in a facility with no systematic family-based care model in place.

2. Methods

2.1. Setting

The study was conducted in Manhiça District, a rural area located 80 km north of the capital Maputo, which has 14 health centers, 1 rural hospital, and 1 referral district hospital, Manhiça District Hospital (MDH). HIV services including prevention of mother to child transmission (PMTCT) services and ART are offered free of charge at all sites. Patients can be tracked within sites using a unique numeric identifier which is used in charts,

paper registers, and in MoH electronic HIV patient tracking systems (ePTS).^[8] A Health and Demographic Surveillance System (HDSS) run by the *Centro de Investigação em Saúde de Manhiça* (CISM) has been in place in Manhiça since 1996, facilitating confirmation of vital status and socio-economic status, among others.^[9]

2.2. Design

This is a descriptive analysis nested under the International Epidemiological Databases to Evaluate AIDS in Southern Africa (IeDEA-SA) Platform at CISM, an observational cohort which was prospectively collecting data for all HIV-exposed and infected children as well as their mothers registered at MDH.^[10] For the purposes of this study, we assumed that mothers were the caregivers of each child. Children less than 15 years of age who enrolled in HIV care from January 2013 to November 2016 were included and their clinical data were abstracted. Mothers' identifiers were retrieved from their children's clinical records and their data was matched to their children's clinical data and then retrospectively evaluated.

2.3. National HIV policies

Because universal ART eligibility for children became national health policy in 2015 in the middle of the study period, the analysis includes both pre-ART and ART patients. Similarly, during the time period of the study, adult ART eligibility depended on clinical stage and immune status, so both pre-ART and ART patients were included. For patients on ART, DSDMs including CASGs and spaced appointments were available for stable adults, but children newly initiating ART were required to have monthly consultations for at least 12 months. For both children and adults not in CASGs, ART dispensing was done on a monthly basis regardless of the frequency of clinical consultations.

2.4. Definitions

The study entry point was the child's enrolment in care, and for children, we determined their health care status at 24 months after enrolment. For mothers, care status was defined at the child's enrolment (baseline) and after 24 months. We defined mothers as having registered in care at MDH if her unique identifier was found in the IeDEA database, ePTS, paper registers, or the child's chart. When mothers enrolled in care at MDH within 30 days before or after the child, they were considered concurrent enrolments. At baseline, children whose mothers were confirmed to be enrolled in other facilities, were HIV-negative, or who had died were excluded.

The baseline and 24-month patient outcomes were retained in care, died, transferred out, and lost to follow-up (LTFU), defined as clinic default >180 days. Electronic patient databases from all health facilities in the district were used in an attempt to verify care status for patients who were LTFU from MDH. Deaths were recorded both from MDH data sources and the HDSS database. The retention of mother–child pairs at 24 months was classified as

- i) concordant retention: both mother and child retained in care;
- ii) concordant LTFU: both mother and child LTFU; and
- iii) discordant: one of both retained in care while the other is LTFU.

Patients who were transferred and/or died during the follow-up period were grouped together with those retained, since these events precluded the possibility of continued retention at MDH, and we were not able to verify ongoing care at facilities outside of the district. Mothers without documentation of enrolment at another clinic at baseline who never registered at MDH were considered LTFU.

Mothers' sociodemographic data was extracted from the HDSS database. Economic status was classified by wealth quintiles, with 1 to 3 defined as low, and 4 to 5 as high.^[11] Children's baseline immunosuppression was defined using age-adjusted Center for Disease Control (CDC) classifications.^[12]

2.5. Statistical analysis

Analyses were conducted using Stata software (version 14.0) (StataCorp LP, College Station, TX). Chi-squared test for categorical variables and the one-way ANOVA test for continuous variables were used to test for associations between baseline clinical and demographic variables and care status of the mother at baseline. Multinomial logistic regression was performed to evaluate variables associated with retention discordance, with relative risk ratio (RRR) coefficients calculated. Variables with a *P* value less than .2 in unadjusted analysis were included in the multivariable analysis, which was adjusted for age and sex. *P* value less than .05 was taken to indicate a significant difference.

2.6. Ethical considerations

This study is nested under the CISM IeDEA-SA protocol (327/CNBS/11), which was approved by the National Bioethics Committee of Mozambique. Written consent was obtained from all caregivers.

3. Results

3.1. Study population and baseline status

During the study period, a total of 394 children were enrolled in HIV care at the MDH as part of the IeDEA cohort. Of these, 43 (11%) were excluded based on their mothers' status. For the 351 mother-child pairs included in this study, only 39% of mothers had concordant care status with their children at MDH at baseline (23% already registered and in care, 16% enrolled concurrently with their children) (Fig. 1).

3.2. Baseline patient characteristics

The median age of the included children was 3.0 years (IQR 1.0–8.0), and 175 (50%) were female. Only 15% had advanced clinical stage (world health organization (WHO) III or IV) and 24% had severe immune suppression. The majority of children (83%) were eligible to initiate ART at the time of enrolment. For included mothers, the median age was 30.2 years (IQR 25.0–36.1), and 65% had low socio-economic status. Clinical and demographic variables according to baseline maternal care status are shown in Table 1. There were significant differences in the child's age, sex, and the year of the child's enrolment according to maternal baseline care status. Children whose mothers were not registered were older compared to children from the other groups (*P* = .02). The proportion of mothers registered but LTFU at enrolment decreased by 1.6 fold (36% (56/154) to 22% (19/85)) from 2013 to 2015, while the proportion of mothers registered and in care increased by 2.1 fold (13% (20/154) to 28% (24/85)) during the same time period (*P* = .001). However, these temporal trends were not statistically significant (*P* = .31, data not shown).

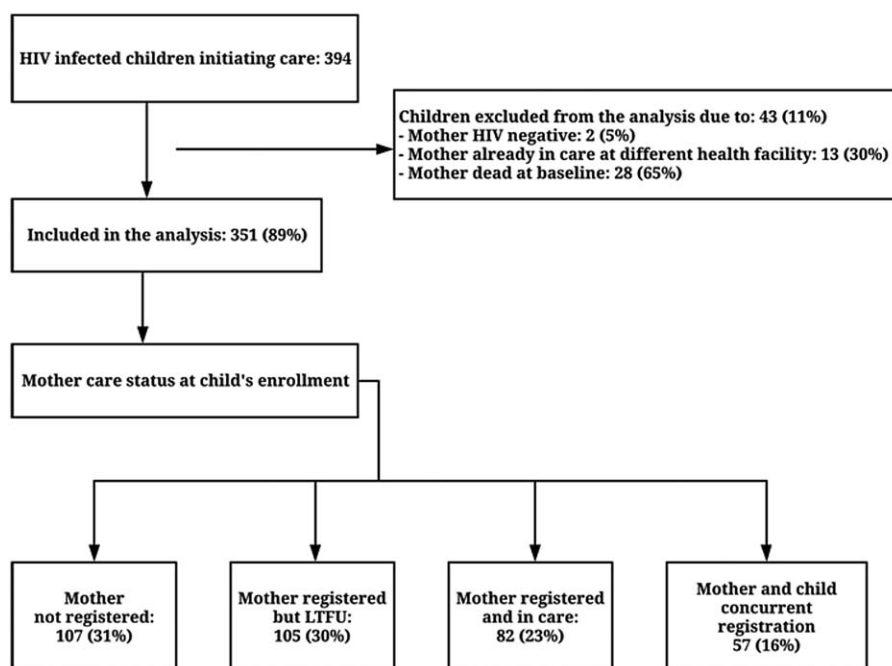


Figure 1. Study enrolment and baseline care status of mothers. LTFU: lost to follow up.

Table 1
Sociodemographic and clinical characteristics of children and mothers at child's enrolment according to the mother's HIV care status, number (percentages).

Characteristics	Mother care status at child's enrolment, N (%)				Total N = 351	P
	Mother not registered N = 107	Mother registered but LTFU N = 105	Mother registered and in care N = 82	Mother and child concurrent registration N = 57		
Children						
Age in years: median (IQR)	4.0 (1.9–10.0)	2.4 (1.0–7.7)	3.0 (0.8–9.0)	2.3 (1.0–5.0)	3.0 (1.0–8.0)	.025
Age group (in years)						
0–1	11 (10)	26 (25)	21 (26)	8 (14)	66 (19)	.002
1–5	45 (42)	39 (37)	25 (30)	34 (59)	143 (41)	
5–10	24 (23)	21 (20)	18 (22)	13 (23)	76 (21)	
>10	27 (25)	19 (18)	18 (22)	2 (4)	66 (19)	
Child sex						
Female	43 (40)	51 (49)	48 (59)	34 (60)	176 (50)	.033
Male	64 (60)	54 (51)	34 (41)	23 (40)	175 (50)	
Calendar year of 1st visit						
2013	48 (45)	56 (53)	20 (24)	30 (53)	154 (44)	.001
2014	33 (31)	30 (29)	38 (47)	11 (19)	112 (32)	
2015	26 (24)	19 (18)	24 (29)	16 (28)	85 (24)	
WHO clinical stage [†]						
I/II	85 (80)	88 (86)	75 (91)	46 (84)	294 (85)	.182
III/IV	21 (20)	14 (14)	7 (9)	9 (16)	51 (15)	
Immunosuppression [‡]						
None	40 (44)	32 (34)	29 (43)	27 (48)	128 (41)	.157
Mild to moderate	26 (29)	38 (40)	29 (43)	15 (27)	108 (35)	
Severe	25 (27)	25 (26)	10 (15)	14 (25)	74 (24)	
ART eligibility						
No	24 (22)	17 (16)	15 (18)	4 (7)	60 (17)	.095
Yes	83 (78)	88 (84)	76 (82)	53 (93)	291 (83)	
Mothers						
Mothers' age (in years) at the 1st visit of the child* median (IQR)	29.3 (23.8–33.2)	31.7 (25.8–36.9)	30.6 (25.4–36.2)	28.0 (24.0–33.5)	30.2 (25.0–36.1)	.175
Wealth quintile						
Low	61 (69)	63 (67)	38 (52)	36 (71)	198 (65)	.074
High	27 (31)	31 (33)	35 (48)	15 (29)	108 (35)	
ART eligibility						
No	–	66 (63)	46 (56)	40 (70)	152 (62)	.239
Yes	–	39 (37)	36 (44)	17 (30)	92 (38)	

ART = antiretroviral therapy, IQR = interquartile range, SD = standard deviation, WHO = world health organization. *N = 305.

[†] N = 345.

[‡] N = 310.

^{||} N = 306.

3.3. Care status at 24 months follow up

Of the 107 mothers never enrolled at baseline, 14 (13%) enrolled at some point during the study. For the 105 mothers who had previously enrolled and were LTFU at baseline, 41 (39%) reengaged in care, of whom 28 (68%) were still active at 24 months.

Excluding the 15 deaths and 55 transfers in children and the single death and 34 transfers in mothers, a total of 169 (60%) of children ($P = .04$) and 111 (35%) of mothers ($P < .001$) were retained in care.

The probability of retention in care was 65.3% (59.8–70.3) for children, and 59.9% (53.6–65.8) for those 184 mothers who were on care during the study period. Among children, the incidence rate of an episode of LTFU was 20.9 (95% CI 17.3–25.1) per 100 person-years of follow up and 66% (74/112) of LTFU occurred in the first 6 months after the child's enrolment ($P = .03$).

There was a significant difference in retention discordance according to the mother's status at baseline ($P < .001$), with the

greatest discordance in the group with mothers not registered at the baseline (56%) and best in the pairs that enrolled together (19%). In total, 149 (43%) of mother–child pairs had retention discordance at 24 months (Table 2). Of these discordant pairs, the mother was the LTFU patient in 75% of cases, and the child in 25%.

3.4. Factors associated with maternal-child care concordance at 24 months

Concordance was divided into concordant retention and concordant LTFU, and each was then analyzed relative to discordance. Unadjusted and adjusted analysis of independent risk factors for concordant retention and concordant LTFU are shown in Tables 3 and 4. For concordant retention versus discordance, pairs where, at baseline, the mothers were either enrolled but LTFU, active in care, and concurrently enrolled with the child had significant increased probability of being retained

Table 2
Retention concordance for children and their mothers at 24 mo, number (percentages).

	Mother care status at child's enrolment (baseline), N (%)				Total N = 351	P
	Mother not registered N = 107	Mother registered but LTFU N = 105	Mother registered and in care N = 82	Mother and child concurrent registration N = 57		
Paired status of care*						
Both retained	8 (8)	22 (22)	42 (53)	36 (63)	108 (31)	<.001
Both LTFU	39 (36)	30 (29)	9 (11)	10 (18)	88 (26)	
Discordant	60 (56)	50 (49)	28 (36)	11 (19)	149 (43)	

LTFU = lost to follow up.

* Patients who were transferred and/or died during the follow-up period were grouped together with those retained. Mothers without documentation of enrolment at another clinic at baseline who never registered at HDM were considered LTFU.

together relative to pairs where the mothers were not enrolled at baseline (adjusted relative risk ratio coefficient (aRRR)=3.44, 95% CI 1.12–10.60; aRRR=17.28, 95% CI 5.43–54.97, and aRRR=38.51, 95% CI 10.62–139.64, respectively). No child-level variables had significant associations in the adjusted analysis.

For concordant LTFU versus discordance, pairs where the child, at baseline, had advanced clinical stage or immune suppression had increased probability of being LTFU together relative to children without advanced clinical stage or immune suppression (aRRR=5.37, 95% CI 1.96–14.69 and aRRR=4.06, 95% CI 1.24–13.35, respectively). On the contrary, pairs where the children initiated ART were less likely to have

concordant LTFU (RRR=0.03, 95% CI 0.01–0.18). No maternal-level variables had significant associations in the adjusted analysis.

4. Discussion

To our knowledge, this is the first report describing HIV care retention among mother–children pairs from sub-Saharan Africa. There were very high rates of 24 month LTFU in children (40%) and their mothers (65%), when considered separately. And maternal-child retention discordance was also high (43%) after 24 months. This high rate of discordance was surprising and has

Table 3
Sociodemographic and clinical factors associated with HIV care concordance among child–mother pairs (unadjusted analysis).

Characteristics	Unadjusted analysis (N = 351)					
	RRR* (both retained vs discordant)	95% CI	P	RRR* (both LTFU vs discordant)	95% CI	P
Child's age in years at enrolment	0.99	0.93–1.04	.704	0.98	0.92–1.04	.497
Child's sex						
Female	Ref					
Male	0.86	0.52–1.41	.549	1.01	0.59–1.70	.985
Child's WHO clinical stage at enrolment						
I/II	Ref					
III/IV	0.32	0.13–0.83	.018	1.85	0.96–3.58	.066
Immunosuppression at enrolment						
No	Ref					
Mild to moderate	0.85	0.46–1.57	.598	1.41	0.67–2.98	.369
Severe	1.41	0.69–2.91	.349	2.56	1.10–5.92	.028
ART status						
Not eligible	Ref					
Eligible but not initiated ART	0.43	0.03–5.98	.529	1.05	0.28–3.92	.936
Eligible and initiated ART	2.31	0.46–11.71	.310	0.20	0.07–0.55	.002
Calendar year of enrolment						
2013	Ref					
2014	0.83	0.47–1.47	.519	1.10	0.59–2.06	.760
2015	1.02	0.54–1.92	.947	1.69	0.87–3.26	.119
Mother age at child's enrolment	1.00	0.97–1.04	.810	0.98	0.94–1.02	.375
Mother wealth quintile						
Low	Ref					
High	1.45	0.84–2.48	.179	0.54	0.28–1.04	.065
Mother care status at child enrolment						
Not enrolled	Ref					
Enrolled, but LTFU	3.30	1.35–8.05	.009	0.92	0.50–1.69	.796
Enrolled and in care	11.25	4.67–27.10	<.001	0.49	0.21–1.16	.105
Concurrent enrolment with child	24.55	9.03–66.73	<.001	0.40	0.54–3.60	.487

ART = antiretroviral therapy, LTFU = lost to follow up, RRR = relative risk ratio, WHO = world health organization.

* Reference category: discordant.

Table 4
Sociodemographic and clinical factors associated with HIV care concordance among child–mother pairs (adjusted analysis).

Characteristics	Adjusted analysis (N = 339)					
	RRR* (both retained vs discordant)	95% CI	P	RRR* (both LTFU vs discordant)	95% CI	P
Child's age in years at enrolment						
Child's sex						
Female						
Male						
Child's WHO clinical stage at enrolment						
I/II	Ref					
III/IV	0.40	0.11–1.47	.167	5.37	1.96–14.69	.001
Immunosuppression at enrolment						
No	Ref					
Mild to moderate	1.27	0.57–2.82	.559	2.55	0.88–1.24	.084
Severe	2.65	0.99–7.10	.052	4.06	1.24–13.35	.021
ART status						
Not eligible	Ref					
Eligible but not initiated ART	1.73	0.04–68.28		0.93	0.09–9.07	.947
Eligible and initiated ART	2.44	0.19–32.01	.497	0.03	0.01–0.18	<.001
Calendar year of enrolment						
2013	Ref					
2014	0.79	0.34–1.82	.578	0.82	0.31–2.15	.687
2015	0.51	0.20–1.31	.160	1.68	0.59–4.79	.332
Mother age at child's enrolment						
Mother wealth quintile						
Low	Ref					
High	1.94	0.95–3.97	.070	0.40	0.16–1.02	.055
Mother care status at child enrolment						
Not enrolled	Ref					
Enrolled, but LTFU	3.44	1.12–10.60	.031	0.73	0.28–1.87	.508
Enrolled and in care	17.28	5.43–54.97	<.001	0.32	0.07–1.54	.156
Concurrent enrolment with child	38.51	10.62–139.64	<.001	2.43	0.66–8.97	.183

ART = antiretroviral therapy, LTFU = lost to follow up, RRR = relative risk ratio, WHO = world health organization.

* Reference category: discordant.

implications for ongoing efforts to improve retention for both adults and children.

ART initiation in children reduced the probability of concordant LTFU. This is not surprising given other studies which have shown the positive impact of ART initiation on pediatric LTFU.^[6,13,14] This study was conducted prior to the implementation of universal ART eligibility for all children regardless of age, and we hypothesize that current concordant LTFU may be lower with the implementation of test and treat approach.^[15]

Previous literature has shown that advanced clinical stage and immune suppression are risk factors for LTFU in both children and adults, and in this study these baseline factors in children were also predictive of concordant LTFU.^[5,6,16] Ongoing efforts to prioritize care for the sickest pediatric patients should take into consideration the fact that their advanced presentation may also compromise the retention of their caregivers.

Mother–child pairs that enrolled in care concurrently were 38 times more likely to have concordant retention in comparison to pairs where the mothers were not enrolled at baseline. The study dataset does not allow for verification of visit timing, but these women and children were the pairs most likely to be seen together during clinical consultations, similar to the family-based care model which is now being offered by the MoH.^[17] Furthermore, 39% of mothers who were LTFU at child enrolment returned to care afterwards. These findings support the growing body of evidence that demonstrates the positive impact of family-based

HIV care on retention, benefiting both pediatric and adult patients.^[5,17,18]

Focused attention on the mother–child pair has been the norm in PMTCT programs and several approaches which have been shown to improve retention are particularly applicable to family-based HIV care. These include the use of peer mentors or community health workers to improve community–clinical linkages, strategies to increase male involvement, a one-stop-model approach where drug dispensing and clinical consultations are integrated, and the use of incentives.^[19–24] Integration of these interventions into existing family-based HIV care approaches maximize improvements in retention.

In this study, the median age at enrolment was 3 years, but with recent advances in Early Infant Diagnosis (EID) programs, the average of infected children enrolling in HIV care has decreased.^[25,26] The dynamics of family retention may be different with infants as compared to older children, and could be assessed in future studies. Another area for additional research would be retention concordance of entire family units, including fathers who were not included in this study. Finally, a comparative study of family versus non-family-based approaches could help to quantify the true impact of family care on retention concordance.

While some limitations of the study have been discussed previously, other methodological limitations should be mentioned. Mothers were assumed to be the primary caregivers for their children, which might not have always been the case,

thereby potentially underestimating true child-caregiver concordant retention. This study used a standard definition of LTFU as defaulting >180 days, but this could have underestimated the true LTFU rate for pediatric patients who often need monthly or bi-monthly consultations.^[27] Because mothers' HIV registration numbers were not routinely recorded in the pediatric charts, various data sources were used to try to triangulate their status, but enrolments, silent transfers, and deaths may have been missed, all of which would overestimate LTFU. In addition, with our methodology, patients who were transferred were considered as retained, as we were not able to verify ongoing care at other health facilities. This may have led to a small over-estimation of retention if they, in fact, did not continue care after transfer. And finally, our estimates of the influence of the mothers' care status at baseline on retention concordance lacked precision due to a small sample size which resulted in large confidence intervals.

5. Conclusion

Urgent action is needed if Mozambique will progress towards the 90/90/90 goals for HIV-infected adults and children. Retention is a particular challenge and this study demonstrated that maternal-child retention discordance is quite common. A family-based care model of service delivery would primarily benefit children who depend on adults for their retention in care, but also holds promise for caregivers with respect to retention and return to care if LTFU. Prioritized expansion of family-based care is recommended.

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Author contributions

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