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The magnitude of loss to follow-up of HIV-exposed infants along the prevention of mother-to-child HIV transmission continuum of care: a systematic review and meta-analysis

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Introduction: Although prevention of mother-to-child HIV transmission (PMTCT) programs are widely implemented, many children do not benefit from them because of loss to follow-up (LTFU). We conducted a systematic review to determine the magnitude of infant/baby LTFU along the PMTCT cascade.

Methods: Eligible publications reported infant LTFU outcomes from standard care PMTCT programs (not intervention studies) at any stage of the cascade. Literature searches were conducted in Medline, Embase, Web of Knowledge, CINAHL Plus, and Maternity and Infant Care. Extracted data included setting, methods of follow-up, PMTCT regimens, and proportion and timing of LTFU. For programs in sub-Saharan Africa, random-effects meta-analysis was done using Stata v10. Because of heterogeneity, predictive intervals (PrIs; approximate 95% confidence intervals of a future study based on extent of observed heterogeneity) were computed.

Results: A total of 826 papers were identified; 25 publications were eligible. Studies were published from 2001 to 2012 and were mostly from sub-Saharan Africa (three were from India, one from UK and one from Ireland). There was extensive heterogeneity in findings. Eight studies reported on LTFU of pregnant HIV-positive women between antenatal care (ANC) registration and delivery, which ranged from 10.9 to 68.1%, pooled proportion 49.08% [95% confidence interval (CI) 39.6–60.9%], and PrI 22.0–100%. Fourteen studies reported LTFU of infants within 3 months of delivery, range 4.8–75%, pooled proportion 33.9% (27.6–41.5), and PrI 15.4–74.2. Children were also lost after HIV testing; this was reported in five studies, pooled estimate 45.5% (35.9–57.6), PrI 18.7–100%. Programs that actively tracked defaulters had better retention outcomes.

Conclusion: There is unacceptable infant LTFU from PMTCT programs. Countries should incorporate defaulter-tracking as standard to improve retention.

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Background

There have been significant developments in knowledge of interventions that can save lives of HIV-exposed infants. Current WHO guidelines recommend HIV testing of HIV-exposed infants at 4–6 weeks [1] postnatally (early infant diagnosis, EID), and immediate antiretroviral therapy (ART) initiation for those testing positive. As early cessation of breastfeeding is associated with poor health outcomes for HIV-exposed babies [2–6], current guidelines support continued breastfeeding in conjunction with extended infant prophylaxis with nevirapine (WHO option A) [7], and re-testing of the exposed baby at least 6 weeks after cessation of breastfeeding [1]. Also, included within the guidelines are recommendations for infant feeding in the context of HIV [5], which stress that carers need to be educated about the importance of exclusive breastfeeding in the first 6 months of life. All these guidelines necessitate continued follow-up of exposed babies to ensure their full participation in the postnatal care cascade. Yet despite advances in knowledge of effective interventions to save lives of HIV-exposed infants, many infants do not access the full package of services because of loss to follow-up (LTFU) [8–11]. There is literature on LTFU of infants in research settings, and also in real-life program settings. We conducted a systematic review in order to determine the magnitude of LTFU of HIV-exposed infants from real-life (nonresearch intervention) PMTCT programs, and to describe program characteristics associated with lower rates of infant LTFU in order to inform future program and policy development.

Methods

Publications were eligible for inclusion if they reported on LTFU of HIV-exposed infants/children from usual care programs rather than from research studies/programs. Medline, Embase, Web of Knowledge, CINAHL Plus, and Maternity and Infant Care were searched.

Search strategy

The research question was split into three components: children/infants, HIV exposure, and retention/LTFU. For each component, text and Medical Subject Heading (MeSH) searches were performed. The text search terms for the children/infants component were as follows: Child* OR infant* OR newborn OR baby OR babies. The terms for HIV exposure were as follows: "HIV exposed or HIV positive adj3 mother*" OR "HIV infected adj3 mother*" OR "born adj3 HIV positive wom#n" OR "born adj3 HIV infected wom#n" OR PMTCT OR "prevention of mother to child transmission". The terms for retention/LTFU were as follows: "continuum of care" OR retention OR attrition OR "patient dropout" OR "los? to follow up" OR LTFU OR LFU OR "lost follow up" OR "Early infant diagnosis" OR EID. Results from the three components were narrowed to include only publications that featured all three components. The search process was iterative: pilot searches were conducted and checks for suitability of search terms were conducted. Refinements were made and the final search was conducted on 06 August 2012.

Selection of eligible papers and additional searches

Results from database searches were combined and duplicates removed. Each title and abstract was reviewed to determine eligibility. A paper was rejected if it was obvious from title/abstract review that it was ineligible. When it was less clear, the full paper was reviewed. Next, reference and citation lists of eligible papers and those of other relevant papers were downloaded from the Web of Knowledge database and reviewed for eligibility. Eligibility review was conducted by E.L.S. Each eligible publication was assessed for quality using a checklist that was adapted from the UK National Institute for Health and Clinical Excellence (NICE) methodology checklist for cohort studies [12]. For each study, an overall subjective judgment was made on how well the study findings were protected against bias and confounding.

Data extraction and synthesis

Information captured using a data collection form included place of study, setting (urban or rural), program years, testing strategy (whether opt-in or opt-out), schedule and methods of infant follow-up, prevention of mother-to-child HIV transmission (PMTCT) regimens offered, whether replacement feeding was offered for free during the years studied, and magnitude and timing of LTFU.

Study findings were split into categories relating to timing of LTFU as follows: LTFU of pregnant HIV-positive women between ANC registration and delivery; LTFU of HIV-exposed infants by age 3 months; LTFU of HIV-exposed infants by 12 months of age; LTFU by 18 months of age, and LTFU of infants after determination of HIV status. For studies in sub-Saharan Africa, random-effects meta-analysis using the method of DerSimonian and Laird [13] was conducted for each category/timing of LTFU using Stata v10. Data values were log-transformed before analysis and the results back-transformed to percentages. There was extensive heterogeneity of study findings; therefore, predictive intervals (PrIs; approximate 95% confidence intervals of a future study based on the observed heterogeneity) were computed as recommended good practice in the presence of significant heterogeneity [14]. To investigate the sources of heterogeneity, random-effects meta-regression analysis [15] was done with each of the extracted variables that were suspected to explain the heterogeneity: setting (urban/rural); model for offering HIV testing; mother's PMTCT regimen (single dose nevirapine vs. more

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intensive regimens); and whether replacement feeding was offered for free during program years.

Results

A total of 826 papers from database and reference/citation lists were reviewed (Fig. 1a). Eighteen eligible papers were identified from database searches, and an additional seven were identified after reviewing reference and citation lists, bringing the total of eligible papers from which data were extracted to 25, (Fig. 1b).

Description of eligible papers

Twenty studies were from sub-Saharan Africa: four [16–19] from South Africa, two each from Kenya [20,21], Nigeria [22,23], Mozambique [24,25], Malawi [26,27], Uganda [28,29], and Ethiopia [30,31], one from each of the following: Zimbabwe [32], Cameroon [33], Angola [34], and Tanzania [35]. Three studies were from India [36–38], and one each from United Kingdom and Ireland [39,40]. All were viewed to be either of good (17 studies) or fair (eight studies) quality [12]; as a result, they were all included in result syntheses as applicable. Seven studies were set in rural areas, 14 in urban areas, and three included both urban and rural sites. The PMTCT regimen provided for mothers during the study period was single dose nevirapine for nine studies and was more intensive (dual/triple therapy) for 13 studies (Table 1).

Loss to follow-up of HIV-positive pregnant women

Eight studies reported on LTFU of HIV-positive pregnant women between ANC registration and delivery. Six of these were in sub-Saharan Africa and two from India. The percentage LTFU in these eight studies ranged from 10.9 to 68.1%. The lowest proportion of 10.9% was reported in Maharashtra, India, a private sector PMTCT program in which women who missed their appointments were followed up by letter, phone calls, or home visits [37]. The pooled estimate of LTFU among the six sub-Saharan African countries was 49.08% (95% confidence interval 39.6–60.9%; PrI 22.0–100% (Fig. 2)].

On meta-regression analysis, only the type of PMTCT regimen (whether single dose nevirapine or more intensive regimens) was also associated with LTFU; there was higher LTFU in the sites that offered single dose nevirapine than in those that offered more intensive regimens ($P = 0.006$). However, this did not account for all heterogeneity; there was 92% residual heterogeneity.

Loss to follow-up of infants by age 3 months

Fourteen studies reported on LTFU of infants soon after delivery; the infants typically did not return for HIV testing at 6 weeks. About half of the studies reported this as LTFU at 6 weeks, but some studies reported loss by 8 weeks, or 3 months. In order to synthesize data from all studies that reported LTFU soon after delivery, a cut-off point of 3 months was reported. The percentage LTFU by age 3 months in the 14 studies ranged from 4.1 to 75.0%. The LTFU percentages in the studies in Ireland, UK, and India were 4.1, 26.0, and 19.6, respectively. The pooled estimate among 11 sub-Saharan African countries was 33.9% (27.6–41.5), PrI 15.4–74.2 (Fig. 3).

The lowest LTFU percentages were reported in Ireland and Malawi. In Ireland, there was a system for follow-up of HIV-exposed infants, which was enhanced by having a single center for the coordination of care of HIV-exposed infants. However, although the study in Malawi [26] reported low LTFU rates at 6 weeks, by the 6-month postnatal visit 41% of infants had been lost; the babies were initiated on cotrimoxazole prophylaxis, but were lost from further evaluation. In that study all PMTCT services were centrally provided at the hospital during the reported period. This is one example in which centralization of PMTCT services may not have worked well: authors reported that women may have increasingly found it more difficult to come back to the hospital because of long distances in an area where there was no public transport (women had to either walk or use bicycles) and would, therefore, have benefited from decentralized services at local clinics. The program in Cameroon [33] tracked clients using mobile phones; 90% of clients had mobile phones. This tracking may have improved their LTFU rates as they had comparatively lower LTFU rates than other sites of 17%. There was also good tracking of defaulters in the UK study in London [39], which reported a LTFU of 26%. Of note, the majority of infants lost to follow-up in that program were born to African mothers, 89% compared with 71% of those who completed follow-up.

Both Mozambican studies reported LTFU rates of about 75%, in a setting in which there was lack of confidential counseling for women in crowded postnatal wards. The authors reported that this environment may have resulted in HIV-positive women feeling uncomfortable, thereby lessening their chances of returning to the hospital for the baby's EID. In addition, authors reported that the provision of EID services occurred in a different building from the one where referral was made possibly resulting in women getting lost between referral and follow-up. Related to this, in one of the studies from Ethiopia [30] some infants who had defaulted from EID had been to a healthcare center for pentavalent vaccination at 6 weeks: 86% of infants were brought for pentavalent vaccine compared with 52% for EID.

In meta-regression analysis, none of the variables extracted from the studies explained the heterogeneity in LTFU findings by age 3 months.

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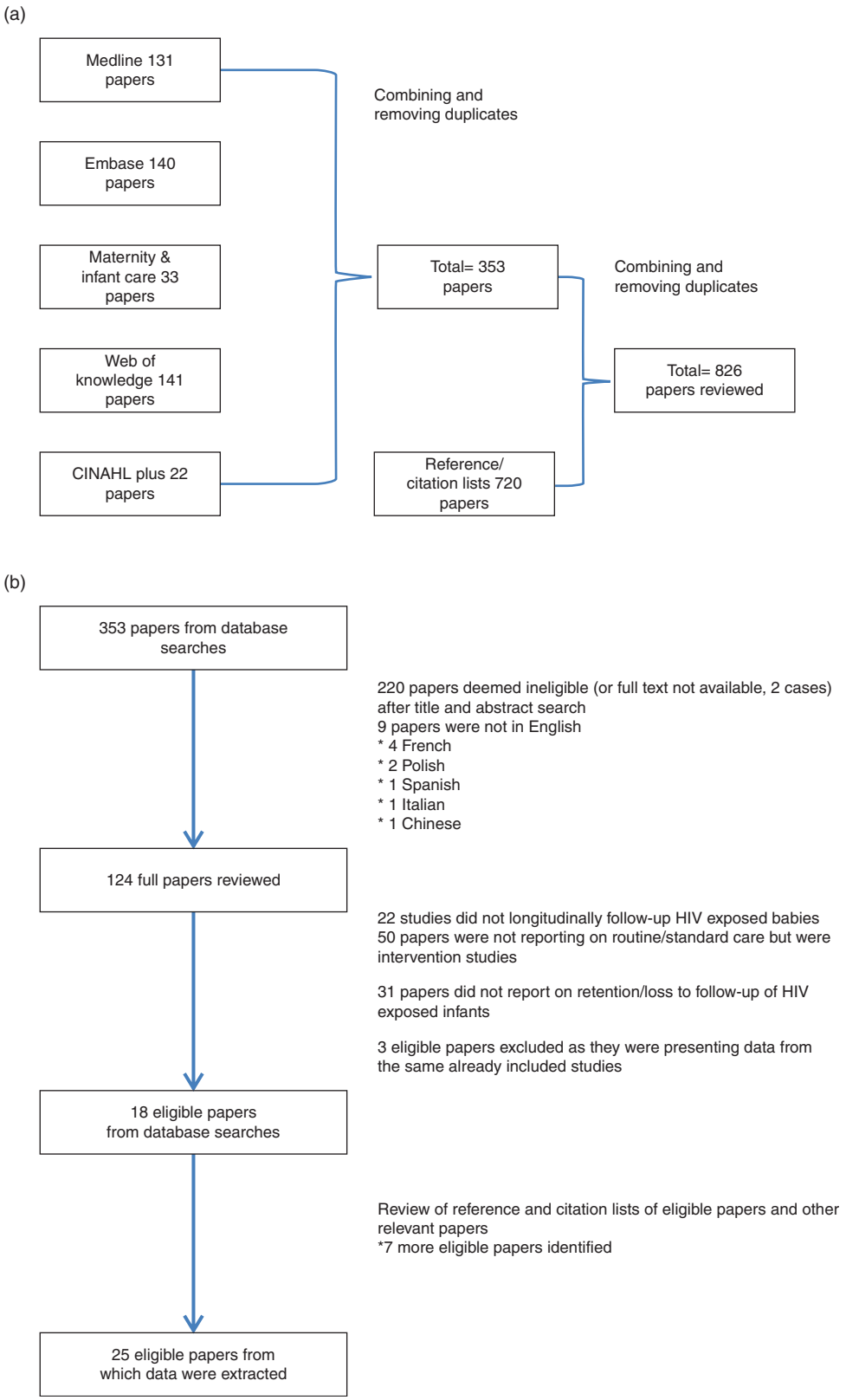

Fig. 1. Literature search results and selection of eligible papers. (a) Results of literature searches. (b) Selection of eligible papers.

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Table 1. Description of eligible studies.

Author	City and country	Program years	Setting	Testing strategy	Mother's PMTCT regimen	Infant follow-up schedule	LTFU outcome/s reported	LTFU *n*/*N* (%)
Sam *et al.* [39]	London, United Kingdom	1992–2001	Urban	Not reported	Not reported	Infant follow-up visits, including HIV testing	Infants LTFU before determination of HIV status by 3 months	27/104 (26.0)
Ferguson *et al.* [40]	Ireland	1999–2008	-	Opt-out	HAART or triple therapy	All exposed infants referred to one clinic for management	Infants LTFU before 3 months of age	40/964 (4.1)
Ahoua *et al.* [28]	Arua, Uganda	2000–2005	Rural	Opt-in	HAART or dual therapy	Infant follow-up at 1,6,10 and 14 weeks, then every 3 months until HIV test at 18 months	1) HIV-positive women LTFU between ANC registration and delivery	520/1037 (50.1)
							2) Infants LTFU at 18 months	303/567 (53.4)
Sherman *et al.* [19]	Johannesburg, South Africa	2001–2001	Urban	Not reported	Single dose nevirapine	Infant follow-up; HIV testing using ELISA at 12 months	Infants who did not return for testing at 12 months	57/67 (85.1)
Perez *et al.* [32]	Buhera Zimbabwe	2001–2003	Semi-rural	Opt-in	Single dose nevirapine	Monthly for growth monitoring; baby tested at 15 months	LTFU of HIV-positive women between ANC registration and delivery	167/326 (51.2)
Doherty *et al.* [17]	Nine provinces, South Africa	2002	Rural and urban	Opt-in (mostly)	Single dose nevirapine	HIV test using rapid tests at 12 months; re-testing at 18 months if positive	Infants who did not return for HIV testing at 12 months	958/1907 (50.2)
Manzi *et al.* [26]	Thyolo District Malawi	2002–2003	Rural	Opt-out	Single dose nevirapine	Follow-up according to EPI schedule up to 18 months. HIV test at 18 months	1) HIV-positive women LTFU between ANC registration and delivery	440/646 (68.1)
							2) Infants LTFU by 6-week postnatal visit	10/206 (4.9)
Moses *et al.* [27]	Lilongwe Malawi	2002–2006	Urban	Opt-in until 2005	Single dose nevirapine	EID using DNA PCR at 6 weeks	Infants who did not return for HIV testing at 6 weeks	2070/3160 (65.5)
Oladokun *et al.* [23]	Ibadan Nigeria	2002–2007	Urban	Opt-in since 2005	Single dose nevirapine until 2005	HIV test at 18 months using PCR	1) Babies who did not return for HIV testing at 18 months	63/303 (20.8)
							2) Babies whose HIV test results were not collected	88/207 (42.5)
Panditrao *et al.* [37]	Maharashtra India	2002–2008	Urban and rural	Not reported	Dual therapy	EID using DNA PCR	1) HIV-positive women LTFU between ANC registration and delivery	80/733 (10.9)
							2) Infants who did not return for EID	151/770 (19.6)
Black *et al.* [16]	Johannesburg South Africa	2004–2007	Urban	Not reported	HAART	EID using DNA PCR at 6 weeks	Infants who did not return for HIV testing at 6 weeks	191/493 (38.7)
Geddes *et al.* [18]	Durban, South Africa	2004-2007	Urban	Opt-out since 2006	HAART or dual/triple therapy	EID at HIV clinic; HIV-positive infants followed at same clinic	Infants who did not return for HIV testing at 6 weeks	128/699 (18.3)
Goswami and Chakravorty [36]	Kolkata India	2004–2007	Urban	Opt-in	Single dose nevirapine	Follow-up in pediatric clinic of hospital; HIV test using ELISA at 18 months	1) HIV-positive women LTFU between ANC registration and delivery	113/248 (45.6)
							2) Babies who did not return for testing at 18 months	36/95 (37.9)
Nuwagaba-Biribonwoha *et al.* [35]	Lake region, Tanzania	2006–2007	-	Not reported	Single dose nevirapine	EID using DNA PCR.	1) Infants whose EID HIV PCR results were not collected after testing (both positive and negative infants)	199/441 (45.1)
							2) HIV-positive infants whose EID results were not collected after testing	24/75 (32)
Azcoaga-Lorenzo *et al.* [20]	Busia District Kenya	2006–2008	Rural	Opt-out	HAART or dual therapy	HIV test at 6 weeks; if negative re-test 6 weeks after stoppage of breastfeeding	1) HIV-positive women LTFU between ANC registration and delivery	632/1668 (37.9)
							2) Infants LTFU before determination of HIV status at 6 weeks	148 (19.3)
Hassan *et al.* [21]	Kilifi, Kenya	2006-2008	Rural	Opt-out	Not reported	Infant follow-up for 18 months; HIV testing as follows: PCR at 6 weeks, rapid test at 12 and 18 months if breastfeeding	1) Infants lost before determination of HIV status at 18 months	119/180 (66.1)
							2) Infants whose HIV test results were not collected	46/102 (45.1)

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Table 1 (*continued*)

Author	City and country	Program years	Setting	Testing strategy	Mother's PMTCT regimen	Infant follow-up schedule	LTFU outcome/s reported	LTFU *n*/*N* (%)
Seth *et al.* [38]	New Delhi, India	2006–2010	Urban	Not reported	Single dose nevirapine	All exposed infants followed up until 18 months. HIV-positive infants are put on HAART and followed further	LTFU of babies before determination of HIV status at 18 months	47/162 (29.0)
Cook *et al.* [25]	Zambézia Province, Mozambique	2007–2008	Rural	Opt-out	HAART or dual therapy	Infants referred to 'child at risk' clinics. EID using PCR test	Infants who did not come back for EID	333/443 (75.2)
Anoje *et al.* [22]	South-South region, Nigeria	2007–2009	Rural and urban	Not reported	HAART or dual therapy	EID at 6 weeks; if negative, re-test 6 weeks after cessation of breast feeding	HIV-positive infants LTFU after testing (EID, not enrolled in ART program)	85/125 (68)
Namukwaya *et al.* [29]	Kampala, Uganda	2007–2009	Urban	Not reported	HAART or dual therapy	Infant testing by PCR at 6 weeks	1) HIV-positive women LTFU between ANC registration and delivery	3134/7941 (39.5)
							2) Infants who did not return for HIV testing by 3 months	2442/4807 (50.8)
Lussiana *et al.* [34]	Luanda, Angola	2007–2011	Urban	Not reported	HAART	Monthly follow-up. HIV test at 9, 12, and18 months using rapid tests	1) LTFU of HIV-positive women between ANC registration and delivery	164/382 (42.9)
							2) Infants not returning for hospital evaluations after delivery	42/218 (19.3)
Shargie *et al.* [31]	Addis Ababa, Ethiopia	2008–2009	Urban	Not reported	HAART or dual/triple therapy	EID at 6 weeks; follow-up for cotrimoxazole prophylaxis	LTFU of infants during follow-up period after EID	36/118 (30.5)
Nlend *et al.* [33]	Yaonde, Cameroon	2008–2010	Urban	Opt-out	HAART or dual therapy	EID at 6 weeks; done at referral center	Infants who did not return for HIV testing at 6–8 weeks	103/587 (17.5)
Mirkuzie *et al.* [30]	Addis Ababa Ethiopia	2009	Urban	Not reported	HAART or dual/triple therapy	HIV test at 6 weeks; monthly follow-up until 6 months, then every 3 months until 18 months	Infants who did not return for HIV testing at 6 weeks	106/221 (48.0)
Ciampa *et al.* [24]	Zambézia Province Mozambique	2009–2010	Rural	Opt-out	HAART or dual therapy	HIV testing using PCR at 1 month	Infants who did not return for HIV testing by age 3 months	247/332 (74.4)

EID, early infant diagnosis; LTFU, loss to follow-up; PMTCT, prevention of mother-to-child HIV transmission.

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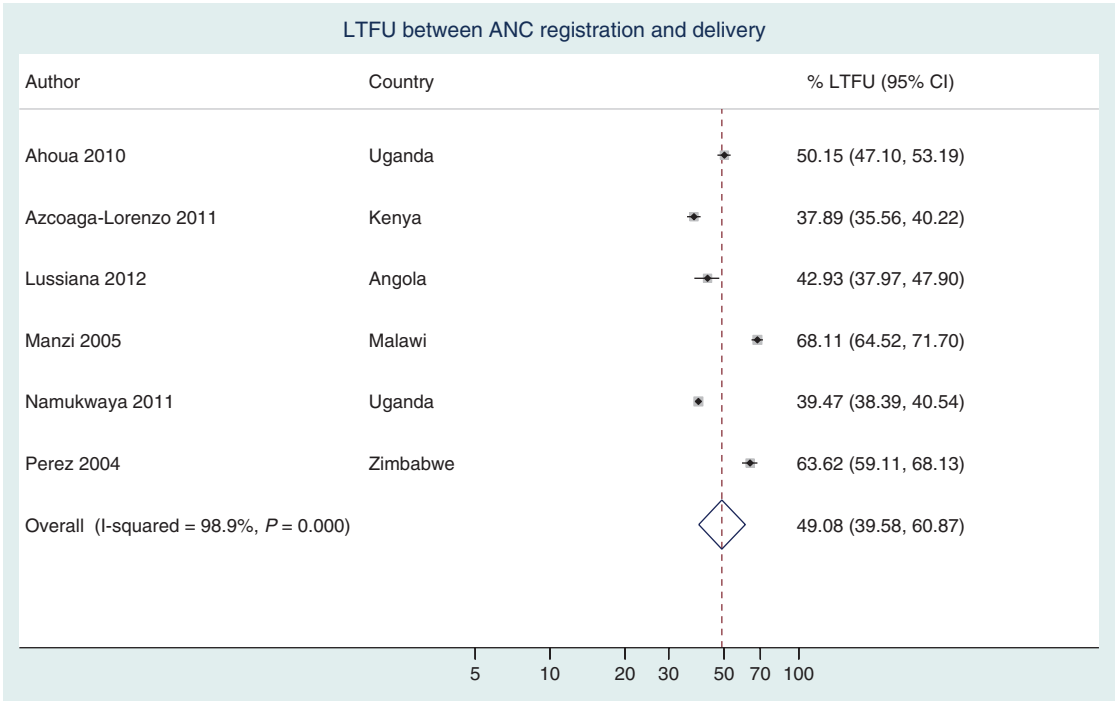

Fig. 2. Loss to follow-up of HIV-positive pregnant women between ANC registration and delivery. CI, confidence interval; LTFU, loss to follow-up.

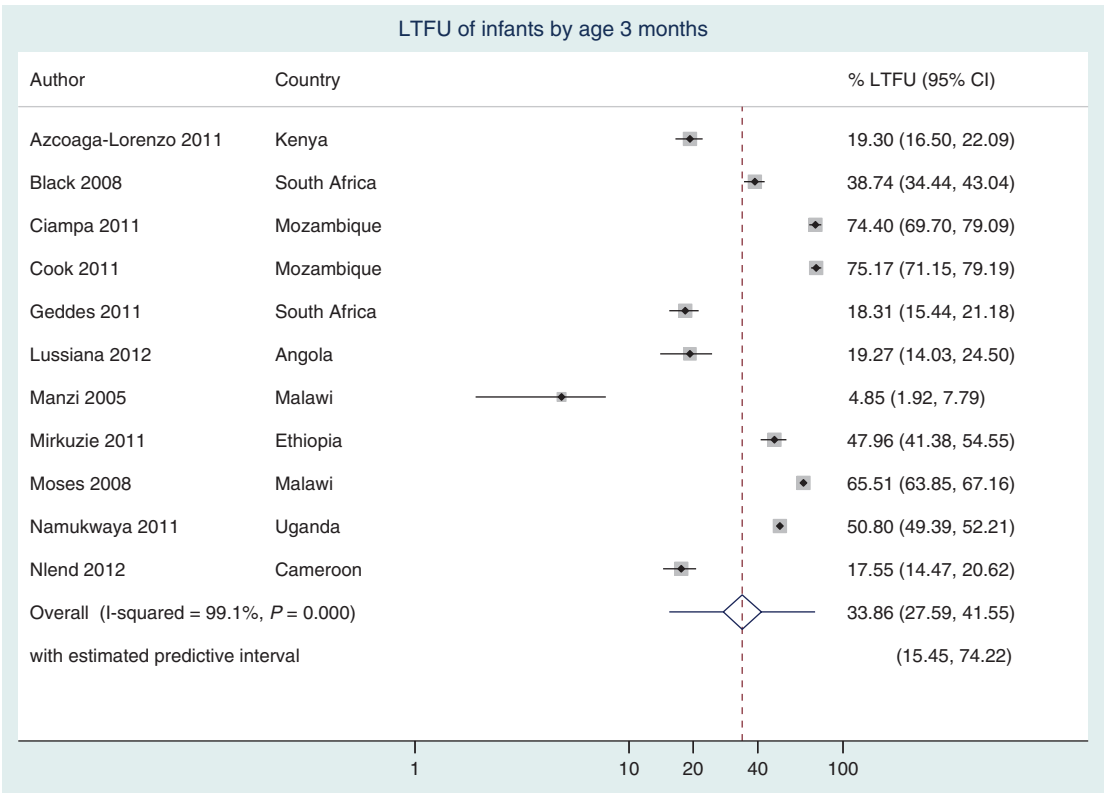

Fig. 3. Loss to follow-up of infants by age 3 months. CI, confidence interval; LTFU, loss to follow-up.

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Loss to follow-up of infants at 12 and 18 months

Two studies (both from South Africa) reported on LTFU of infants after 12 months. The studies reported losses of 85.1 and 50.2%, respectively. Both programs offered single dose nevirapine.

Five programs, three of which offered single dose nevirapine, reported on LTFU of infants by 18 months. Two were from India, with LTFU percentages of 37.9 and 29, and one each from Uganda (53.4%), Kenya (66.1%), and Nigeria (20.8%).

Loss to follow-up of infants after HIV testing

Five studies (all from Sub-Saharan Africa) reported on LTFU of infants following HIV testing, mostly EID by PCR: infants were lost during the recommended follow-up period after receipt of HIV results at about 45 days (one study) [31], did not enrol into ART programs after testing HIV positive in the EID program (one study) [22], or did not return to collect HIV test results after EID (two studies) [21,35]. The percentage LTFU after testing ranged from 30.5 to 68.0%, pooled estimate, 45.5% (35.9–57.6), and PrI 18.7–100%.

Again the benefit of active follow-up of defaulters was apparent in the study in Tanzania [35], where the program actively tracked HIV-positive infants who had not returned to collect results. As a result, a lower percentage LTFU of 32% among HIV-positive infants was observed compared with 48% among the HIV-negative infants.

Discussion

This systematic review revealed that there is an unacceptable LTFU of HIV-exposed infants at several points in the PMTCT care cascade in the programs reported here. There was significant heterogeneity in the study findings; pooled estimates were reported together with PrIs to indicate the uncertainty in the estimates. An estimated 49% of HIV-positive pregnant women in Sub-Saharan Africa are lost between ANC registration and delivery, whereas about 34% of infants are lost to follow-up by 3 months. A further 45% of infants are lost after HIV testing.

Of importance, the retention in a program is not necessarily equivalent to retention in the healthcare system; those women who have self-transferred out of a program to another facility should not be regarded as lost to follow-up. In this review, a third of programs either actively sought but did not find evidence of women self-transferring to other neighboring health sites or provided the only PMTCT services in the communities in which they operated. Four studies [16,24,25,39] acknowledged the possibility of migration being misclassified as LTFU and the rest of the studies did not discuss this kind of LTFU.

If a woman is LTFU before delivery, she may not take her intrapartum antiretroviral prophylaxis and her baby is unlikely to be initiated on the necessary prophylaxis after delivery, and may not be registered for regular follow-up in the PMTCT program. For the mother, LTFU can result in delayed evaluation for disease progression and initiation of life-saving ART. In this systematic review, we found that programs that had an effective system for tracking defaulters had better retention outcomes suggesting that programmers should consider incorporating interventions to actively track women who have missed their appointments. It is important that tracking methods be appropriate for the setting. For example, the program in Uganda [29] had a high LTFU of 40% despite having a telephone tracking system because only 50% of clients had telephone contacts. Tracking requires resources, and depending on the setting and methods used can be expensive. Clearly, data on the relative costs and benefits of introducing such follow-up activities are required. There are other interventions that have been found to improve retention, for example, provision of confidential counseling space postpartum and direct accompaniment of mothers to the centers where continued care will be accessed from [24,41]. However, some have not been assessed as part of routine care, so the extent to which they would translate is unclear. Our search strategy was not designed to find all interventions that improve retention; we described nonresearch interventions that were found to be effective in programs that reported infant LTFU.

Of importance is the observation that even with active tracking of defaulters, there are still unacceptably high levels of LTFU along the PMTCT cascade, suggesting that other barriers need to be overcome. Qualitative studies have found that the following factors affect uptake of PMTCT services: fear of involuntary disclosure of HIV status, fear of stigma, disbelief of mother's HIV result, distance from health facility, fear of HIV-positive result for the baby, cultural norms, cost of transport, and unfriendly healthcare workers [42–49]. These challenges need to be addressed so that programs offer acceptable, culturally sensitive services that will attract all intended beneficiaries.

That cultural norms play a significant part in retention along the PMTCT cascade may be further evidenced by the fact that the majority of infants who were LTFU in the program in London were born of African mothers; their reasons for dropping out of care may be similar to the barriers reported in African settings, where LTFU rates are highest, but may also be due to concerns about immigration status. There is evidence from Cote d'Ivoire that economically disadvantaged women find it more difficult to participate in PMTCT programs [50],

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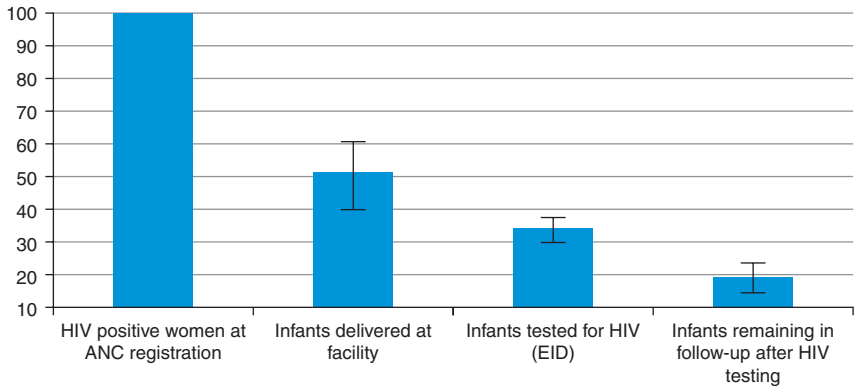

Fig. 4. Simulation of cumulative loss to follow-up of exposed infants along prevention of mother-to-child HIV transmission cascade. EID, early infant diagnosis.

suggesting the need for structural interventions to promote retention.

Another program characteristic that was found to be associated with LTFU was the type of antiretroviral prophylaxis regimen offered; programs that offered single dose nevirapine had higher rates of LTFU than those that offered more intensive regimens. Single dose nevirapine was used in earlier programs than dual/triple prophylaxis, when programs were in the learning stages of how best to provide PMTCT services. In addition, dual/triple therapy necessitates more visits for prescription refills, exposing the woman to more intensive support, which may increase understanding of importance of PMTCT, acceptance of HIV status, and client's connectedness with the healthcare system. The recent introduction of the WHO Option B+ program, in which all HIV-positive pregnant/lactating women are given antiretroviral drugs, which are continued for life may help increase retention rates. Results from the Malawian Option B+ program indicate encouraging retention of 77% after 12 months of the program [51].

WHO has recommended that integrating child health services with PMTCT will likely improve infant retention in care [52]. In one of the Ethiopian programs reviewed here [30], infants who had been lost from the PMTCT program at 6 weeks had in fact been retained within the child health program (as evidenced by receipt of pentavalent vaccine at 6 weeks postnatally). Integration of these two services may have reduced LTFU in the PMTCT program. Importantly, integration should ensure confidentiality is maintained; fear of involuntary disclosure is a recurring theme in qualitative studies exploring barriers to continued attendance of HIV-related care visits. The two programs in Mozambique had very high levels of LTFU of 75%, which the authors partly attributed to lack of confidential counseling space.

If we simulate a cumulative LTFU cascade using data obtained in this systematic review for sub-Saharan African countries, we will see that out of 100 HIV-positive pregnant women who are enrolled into a PMTCT program, only 19 infants are retained in care following HIV testing, (Fig. 4).

The strength of this systematic review is that it synthesizes real-life data from PMTCT programs. It provides a picture of how routine services function. Although studies were observational, they were generally of reasonable quality and did not suffer from significant bias in measurement of LTFU outcomes.

There was significant heterogeneity in the study findings, with very wide PrIs. The main limitation of this review was our inability to fully explore the causes of heterogeneity. Another limitation of the review is that it did not include gray literature, which is likely to have had some reports from routine programs. This is a trade-off that was made by preferring peer-reviewed publications that were considered to have been more rigorously reviewed.

In conclusion, there are unacceptably high levels of LTFU of HIV-exposed infants at important points of the PMTCT cascade. Effective tracking of defaulters reduces LTFU; programmers should initiate effective interventions for tracking defaulting clients. In addition, each PMTCT site should investigate the patient-level factors that limit adherence to visit schedules and address them in a culturally sensitive and appropriate way.

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Conflicts of interest

No conflicts of interest are declared.

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