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Linking women who test HIV-positive in pregnancy-related services to long-term HIV care and treatment services: a systematic review

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Abstract

OBJECTIVES To quantify attrition between women testing HIV-positive in pregnancy-related services and accessing long-term HIV care and treatment services in low- or middle-income countries and to explore the reasons underlying client drop-out by synthesising current literature on this topic.
METHODS A systematic search in Medline, EMBASE, Global Health and the International Bibliography of the Social Sciences of literature published 2000–2010. Only studies meeting pre-defined quality criteria were included.
RESULTS Of 2543 articles retrieved, 20 met the inclusion criteria. Sixteen (80%) drew on data from sub-Saharan Africa. The pathway between testing HIV-positive in pregnancy-related services and accessing long-term HIV-related services is complex, and attrition was usually high. There was a failure to initiate highly active antiretroviral therapy (HAART) among 38–88% of known-eligible women. Providing 'family-focused care', and integrating CD4 testing and HAART provision into prevention of mother-to-child HIV transmission services appear promising for increasing women's uptake of HIV-related services. Individual-level factors that need to be addressed include financial constraints and fear of stigma.
CONCLUSIONS Too few women negotiate the many steps between testing HIV-positive in pregnancy-related services and accessing HIV-related services for themselves. Recent efforts to stem patient drop-out, such as the MTCT-Plus Initiative, hold promise. Addressing barriers and enabling factors both within health facilities and at the levels of the individual woman, her family and society will be essential to improve the uptake of services.

keywords antiretroviral therapy, female, patient dropouts, developing countries, HIV infections

Introduction

For more than a decade, effective antiretroviral (ARV) treatment has been available for the prevention of mother-to-child transmission of HIV (PMTCT), and highly active ARV therapy (HAART) for lifelong treatment is becoming increasingly accessible worldwide (UNAIDS 2010). Many studies have demonstrated the effectiveness of HAART during pregnancy and breastfeeding to reduce vertical transmission when compared with no intervention and with short-course PMTCT regimens (Thomas *et al.* 2008; Kilewo *et al.* 2009; Shapiro *et al.* 2009; de Vincenzi and Study Kesho Bora Group 2009; Kouanda *et al.* 2010, The Kesho Bora Study Group 2011). Even where it is impossible to initiate HAART during pregnancy, mother-to-child HIV transmission can be reduced by promoting rapid uptake of HAART following delivery (Taha *et al.* 2009).

Improved access to PMTCT services has decreased vertical HIV transmission, but parallel attention to women's access to HIV care and treatment for themselves has often been lacking. Initiating HAART during pregnancy can result in significant health benefits for women including a stronger immune system, decreased risk of HIV-related morbidity and reduced maternal mortality (Rabkin *et al.* 2004; Black *et al.* 2009). Survival of HIV-exposed infants is also higher among those whose mothers

are on HAART and/or co-trimoxazole preventive therapy (Newell *et al.* 2004; Mermin *et al.* 2008).

The PMTCT 'cascade' is the sequence of steps required for delivery of effective PMTCT interventions; it typically includes: attendance at antenatal care (ANC), HIV counselling, HIV testing, the provision of prophylactic ARVs, safe delivery, safe infant feeding, infant follow-up and HIV testing, and family planning. Attention to women's linkage into long-term HIV care and treatment services, assessment for eligibility for HAART and initiation of HAART if required is also essential but more rarely a priority within such 'cascades'.

This study aimed to quantify attrition along the pathway between women testing HIV-positive in pregnancy-related services and accessing long-term HIV care and treatment services in low- or middle-income countries[1] (LMIC) and to explore the reasons underlying client drop-out by synthesising current literature on this topic.

Methodology

We conducted a systematic search of literature published in English, French, Portuguese or Spanish between 1st January 2000 and 31st December 2010. Medline, EMBASE, Global Health and the International Bibliography of the Social Sciences were searched using the strategy outlined in Box 1. Experts in the field were consulted, and one PhD thesis was also included.

Articles were included in the review if the studies were carried out in a LMIC and contained information specific to access to long-term HIV care and treatment services among women who test HIV-positive in the context of pregnancy. Studies could be observational or descriptive. No publications were excluded on the basis of study design; rather they were assessed for 'fatal flaws' as defined in Appendix 1.

Two researchers (LF, TK) independently assessed a randomly selected 10% of all abstracts that were retrieved by the search and a randomly selected 10% of the articles selected for full-text review to determine the articles for the inclusion in the final review. There was adequate concordance between those included at each stage; 98% agreement, kappa 0.97 on titles/abstracts and 90% agreement, kappa 0.62 on full-text articles. Results were compared and disagreements resolved by consensus before the eligible articles were reviewed by a single researcher (LF). Reference lists for the articles included in the review were hand-searched for additional relevant publications.

[1]This is based on the World Bank's list of low- and middle-income economies.

Box 1 Search strategy for the literature search

Search terms
(HIV or AIDS).ti.
(pregnan* or antenatal or ANC or MCH or maternity).mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, bt, ps, rs, nm, ui]
(diagnos* or test*).mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, bt, ps, rs, nm, ui]
1 and 2 and 3
Limit 4 to (English or French or Portuguese or Spanish)
Limit 5 to yr = '2000–2010'

Where sufficient data existed, client attrition along the pathway between HIV testing in ANC and initiating HAART if required was quantified, and extrapolations were made to estimate the overall number of missed opportunities for starting HAART. Piot-Fransen models were created for the three studies with the largest sample sizes that included data on the steps needed to access treatment, the proportion of women who accessed HAART and the potential effect of fully functional systems of linkages from HIV testing in pregnancy-related services to HAART services.

Results

Results of the systematic search

The search yielded 2543 unique articles. All abstracts were reviewed, and 93 were selected for full-text review, 18 of which met the inclusion criteria. One was excluded as it duplicated reporting in another article, (Tonwe-Gold *et al.* 2007) so 17 were retained. Three additional publications were found from the hand-searches and expert consultations. Twenty publications were included in the final review (Figure 1; Tables 1–3).

Of the 20 publications, 12 (60%) presented quantitative results, while three (15%) presented qualitative findings, one was a mixed methods study (5%) and four (20%) were programme reviews or evaluations, policy analyses or commentaries. Sixteen (80%) of these publications drew on data from sub-Saharan Africa, including four from South Africa.

Patient cascades between testing HIV-positive in ANC and accessing HAART

Thirteen publications showed attrition rates along the pathway to HAART services among women testing HIV-positive in pregnancy-related services. The findings are summarised in Tables 1 and 2 and divided into observational studies (n = 7), and studies that report data following some form of intervention (n = 6). The steps

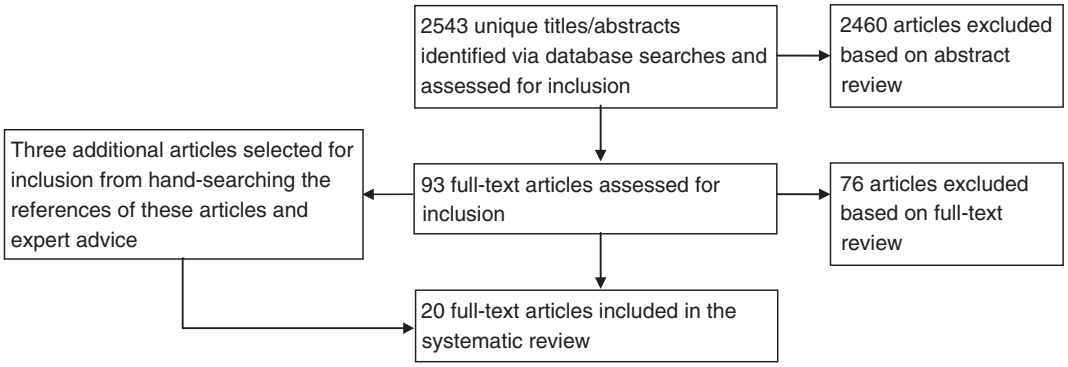

Figure 1 Results of search strategy.

reported along the cascade, PMTCT regimens used and timeframes varied by study.

Overall attrition

Pooling the data presented in Tables 1 and 2 for studies with sufficient data (Chen, Kranzer, Stinson, Balira, Chi, Killam, Mandala, Muchedzi) revealed many missed opportunities for initiating HAART. If all 27 001 HIV-positive women in these studies had been assessed for HAART eligibility and the same study-specific proportion found to be eligible as was found among the women who underwent CD4 count testing, an estimated 7376 women would have been identified as immediately HAART-eligible. Yet, only 1338 women initiated HAART, constituting 43% of those known to be eligible and, based on these extrapolations, only 18% of those who might have required it.

Points of attrition along the cascade

The individual studies document failure to initiate HAART among 38%–88% of known-eligible women. However, the points of attrition along the pathway to assessment and initiation of HAART varied. In the Tanzanian study, 38% of women failed to register at the HIV clinic after an HIV diagnosis in ANC (Balira 2010).

Across most studies, at least 70% of women who registered at the HIV clinic reportedly had blood taken for a CD4 count; studies in Botswana and Zambia are notable exceptions with CD4 count uptake of 59% and 17%, respectively (Mandala *et al.* 2009; Chen *et al.* 2010). The studies that documented the proportion of women returning for their CD4 count results found attrition of 30–33% at this point of the cascade (Chi *et al.* 2007; Mandala *et al.* 2009; Horwood *et al.* 2010).

In one South African study, the proportion of individuals who attended a blood-draw for a CD4 count within 6 months of diagnosis was 84.1% for those tested through STI services, 81.3% for women tested in ANC, 68.9% for those tested in tuberculosis services and 53.5% for people tested through voluntary counselling and testing (Kranzer *et al.* 2010).

In Zambia, uptake of HIV-related services was compared where women were referred from ANC to a separate HAART clinic (control arm) with uptake where HAART was initiated within ANC (intervention arm). Eighty-five per cent of women underwent initial evaluation for HAART eligibility in both study arms, but the proportion of eligible women who initiated HAART was low in both arms at 14% and 33% in control and intervention arms, respectively (Killam *et al.* 2010). Data from sites in 14 countries showed that only 1.4% of HIV-positive pregnant women had received HAART; the proportion of HAART-eligible women was not reported (Ginsburg *et al.* 2007). In contrast, the study in Ivory Coast showed exceptionally high uptake of CD4 count testing (100%) and HAART (95%) (Tonwe-Gold *et al.* 2009).

Figure 2 shows Piot-Fransen models for the three selected studies: two observational studies in South Africa and Zambia, and the intervention arm of Killam *et al.*'s study in Zambia. These studies all revealed high levels of patient attrition, including the intervention arm of Killam *et al.*'s evaluation (Figure 2c) where specific efforts were made to promote uptake of HAART following HIV testing in ANC.

Factors underlying client attrition along the pathway to HAART

Some articles in this review provided insufficient quantitative data to be included in Tables 1 or 2 but gave useful insights into factors affecting attrition along the pathway to HAART. These are outlined in Table 3. Then, factors underlying client attrition along the pathway that have

Table 1 Patient cascades for pregnant women from testing HIV-positive to initiating HAART – Observational studies

Country, author, year of publication	Study design	CD4 for HAART eligibility	HIV-positive	Referred to HIV clinic for HAART assessment	Registered at HIV clinic	Initial screening or CD4 test performed	Returned for results of CD4 test	Eligible for HAART	Started HAART	Should have started HAART (Estimate†)	% of those estimated HAART-eligible who started HAART	Comments
			a	b (% = b/a)	c (% = c/b)	d (% = d/a)‡	e (% = e/d)	f (% = f/d)	g (% = g/f)§	h (a × %f)	i (g/h)	
Kenya (Otieno *et al.* 2010)	Cross-sectional survey	<350	116	116 (100%)	86 (74%)				33			Based on self-reported data. Almost half the initial study population was LTFU. Study population had been part of a PMTCT study that included intensive and prolonged involvement with providers
South Africa (Kranzer *et al.* 2010)	Retrospective cohort	<200	150			125 (83%)		18 (14%)	13 (72%)	21	62%	Based on routinely collected health facility records. Would have missed women who chose to attend a different HIV clinic but the nearest alternative was 10 km away

Table 1 (*Continued*)

Country, author, year of publication	Study design	CD4 for HAART eligibility	HIV-positive	Referred to HIV clinic for HAART assessment	Registered at HIV clinic	Initial screening or CD4 test performed	Returned for results of CD4 test	Eligible for HAART	Started HAART	Should have started HAART (Estimate†)	% of those estimated HAART-eligible who started HAART	Comments
			a	b (% = b/a)	c (% = c/b)	d (% = d/a)‡	e (% = e/d)	f (% = f/d)	g (% = g/f)§	h (a × %f)	i (g/h)	
South Africa (Stinson *et al.* 2010)	Retrospective cohort	<200	3498			3405 (97%)		516 (15%)	262¶ (51%)	525	50%	As only four sites were used to represent three service delivery models, differences between the facilities rather than between the models might explain some of the findings
South Africa (Geddes *et al.*, 2008)	Retrospective cohort	<200	338			262 (78%)			130			Relied on routinely collected health facility data. 11% LTFU
South Africa (Horwood *et al.* 2010)	Cross-sectional study	<200	312			244 (78%)	171 (70%)		27			Based on self-report by women
Tanzania (Balira 2010)	Prospective cohort	<200††	244	199 (82%)	123 (62%)	78 (63%)		18 (23%)	10 (56%)	56	18%	Based on self-reported data. 20% LTFU by final follow-up

Table 1 (*Continued*)

Country, author, year of publication	Study design	CD4 for HAART eligibility	HIV-positive a	Referred to HIV clinic for HAART assessment b (% = b/a)	Registered at HIV clinic c (% = c/b)	Initial screening or CD4 test performed d (% = d/a)‡	Returned for results of CD4 test e (% = e/d)	Eligible for HAART f (% = f/d)	Started HAART g (% = g/f)§	Should have started HAART (Estimate†) h (a × %f)	% of those estimated HAART-eligible who started HAART i (g/h)	Comments
Zambia (Mandala *et al.* 2009)	Retrospective cohort	<350	14 815			2528 (17%)	1680 (67%)	796 (31%)	581 (73%)	4593	13%	Based on routinely collected health facility data. No data on age or WHO clinical staging

HAART, Highly active antiretroviral therapy; LTFU, lost to follow-up; PMTCT, prevention of mother-to-child HIV transmission.
†Estimated number of women who should have started HAART = % women eligible for HAART among those had a CD4 result × total HIV-positive women in the study.
‡Where c is available, % = d/c (Balira)
§Where f is unavailable, no % is given (Otieno, Geddes, Horwood)
¶In Stinson's study, the number of women who started HAART refers to the women who started HAART during pregnancy. Another 61 started HAART within 2 years post-partum, half of them within 7.5 months of delivery.
††Clients were also deemed eligible for HAART if CD4 < 350 and WHO Stage III, or if WHO Stage IV irrespective of CD4 count.

Table 2 Patient cascades for pregnant women from testing HIV-positive to initiating HAART – Intervention studies

Country, First author, Year of Publication	Study design	Intervention	CD4 for HAART eligibility	HIV-positive a	Referred to HIV clinic for HAART assessment b (% = b/a)	Registered at HIV clinic c (% = c/b)	Initial screening or CD4 test done d (% = d/a)	Returned for results of CD4 test e (% = e/d)	Eligible for HAART f (% = f/d)	Started HAART g (% = g/f)	Should have started HAART (Estimate) h (a × %f)	% of those estimated HAART-eligible who started HAART i (g/h)	Study limitations
Botswana (Chen *et al.* 2010)	Observational retrospective cohort	Concurrent clinical trial providing CD4 testing and rapid HAART initiation for women with a CD4 higher than the national eligibility threshold	<200	688			397 (59%)		62 (16%)	23 (37%)	107	21%	Based on routine hospital data.
Zambia (Killam *et al.* 2010)	Stepped-wedge evaluation	Integration of HAART into ANC services. Control arm shown in top row; intervention shown in bottom row	<250	3046		2589 (85%)			716 (28%)	103 (14%)	853	12%	Cost and human resources implications of such integration not reported
			<250	3753		3193 (85%)			846 (26%)	278 (33%)	976	28%	

Table 2 (*Continued*)

Country, First author, Year of Publication	Study design	Intervention	CD4 for HAART eligibility	HIV-positive a	Referred to HIV clinic for HAART assessment b (% = b/a)	Registered at HIV clinic c (% = c/b)	Initial screening or CD4 test done d (% = d/a)	Returned for results of CD4 test e (% = e/d)	Eligible for HAART f (% = f/d)	Started HAART g (% = g/f)	Should have started HAART (Estimate) h (a × %f)	% of those estimated HAART-eligible who started HAART i (g/h)	Study limitations
Zambia (Chi *et al.* 2007)	Evaluation	Scripted talk on the benefits of CD4 testing and long-term HIV care; encouragement to enrol into long-term care and treatment; and escort by CHWs to the on-site HIV facility for immediate attention	<200†	680	433 (64%)		302 (70%)	206 (68%)	72 (24%)	33 (46%)	163	20%	Based on routine clinic data
Ivory Coast (Tonwe-Gold *et al.* 2009)	Description of programme outcomes	MTCT + initiative: family-focused care and treatment with regular clinical and lab assessments	<200‡			605	605 (100%)		259 (43%)	246 (95%)			No information on the no. of women who declined programme enrolment.

Table 2 (*Continued*)

Country, First author, Year of Publication	Study design	Intervention	CD4 for HAART eligibility	HIV-positive	Referred to HIV clinic for HAART assessment	Registered at HIV clinic	Initial screening or CD4 test done	Returned for results of CD4 test	Eligible for HAART	Started HAART	Should have started HAART (Estimate)	% of those estimated HAART-eligible who started HAART	Study limitations
				a	b (% = b/a)	c (% = c/b)	d (% = d/a)	e (% = e/d)	f (% = f/d)	g (% = g/f)	h (a × %f)	i (g/h)	
Zimbabwe (Muchedzi *et al.* 2010)	Cross-sectional survey	Peer counsellors to provide additional support including home tracing in the case of missed appointments	<350	147¶		95 (65%)	77 (81%)		43 (56%)	35 (81%)	82	43%	Based on self-report. 23% LTFU
Multi-country (Ginsburg *et al.* 2007)	Review of programmatic indicators	NGO-supported PMTCT programme	Varied by country	98 304						1388			Based on routine programme monitoring data; incomplete reporting

HAART, Highly active antiretroviral therapy; LTFU, lost to follow-up; ANC, antenatal care; CHWs, community health workers; PMTCT, prevention of mother-to-child HIV transmission.
†Clients were also deemed eligible for HAART if CD4 < 350 and WHO Stage III, or if WHO.
‡These data were collected between August 2003 and August 2005. Until Dec 2004, the criteria for initiating HAART were CD4 < 350/mm^3 and WHO Stage 4, 3 or 2, or CD4 < 200 mm^3. From January 2005 patients with Stage 2 and CD4 < 350 mm^3 were not eligible for HAART.
§Where a is unavailable, %=d/c (Tonwe-Gold).
¶201 women were diagnosed with HIV and eligible for this study but, before the follow-up time, 46 were lost-to-follow-up (41 had moved out of the study area and five had relocated to other countries) and eight had died. Only the remaining 147 have been included here as the surviving others may have registered at a different HIV clinic.

Table 3 Studies in the review with insufficient data for creating a patient cascade

Author, year of Publication	Study setting	Study design	Comments
Abrams *et al.* (2007)	Review using data from 13 countries in sub-Saharan African and Southeast Asia	Review of rationales for linking PMTCT and HIV treatment services, focusing on PMTCT as a gateway to family-based HIV care and treatment.	Looked at why it is important to strengthen links between PMTCT and long-term care and treatment Promotion of family-centred care as an approach for achieving this
Chinkonde *et al.* (2009)	2 UNC-supported PMTCT programmes, Lilongwe, Malawi	Qualitative interviews and focus group discussions with women who had attended the PMTCT programme and their husbands	Sought to understand high levels of attrition from the PMTCT programme Major barriers to retention in the programme included: fear of involuntary HIV disclosure and negative community reactions; unequal gender relations; long walking distances; and lack of support from husbands Facilitator: social support
Duff *et al.* (2010)	PMTCT + programme in a regional hospital, Uganda	Qualitative descriptive exploratory study: qualitative interviews and a focus group discussion with HIV-positive mothers	Greatest barrier to accessing HAART: economic concerns, especially transport costs to clinics Other barriers: stigma, non-disclosure to sexual partners, long waiting times at clinics, and suboptimal provider–patient interactions
Gruskin *et al.* (2008)		Policy analysis	Analysis of the implications of WHO's guidance on provider-initiated HIV testing and counselling (PITC) for the health and human rights of pregnant women Potential of PITC as a gateway to long-term care and treatment services is highlighted Attention to the implementation processes needed to ensure the success of the guidance
Levy (2009)	Lilongwe, Malawi	Qualitative interviews and focus group discussions with women living with HIV participating in the PMTCT programme and key informant interviews with staff working in the PMTCT programme and health system	Identified a disjuncture between women's expectations of PMTCT and the services received Main problems: Marginalisation of the woman's health in favour of the infant's health Lack of attention to the social determinants of health Health system weaknesses
Nakanjako *et al.* (2009)	Resource-limited settings	Review of strategies to optimize treatment outcomes in resource-limited settings	Highlighted eight strategies for optimising HIV treatment outcomes, including strengthening the links between HIV diagnosis and long-term care and treatment services

Table 3 (*Continued*)

Author, year of Publication	Study setting	Study design	Comments
Pfeiffer *et al.* (2010)	Public sector health facilities, Mozambique	Case study	Comparison of sites pre- and post-integration of HIV clinics into primary health care Difficult to tease out the effect of integration as the intervention also included retraining health workers; strengthening laboratory, testing and referral linkages; and improving district-level health management

HAART, Highly active antiretroviral therapy; PITC, Provider-initiated HIV testing and counselling; PMTCT, Prevention of mother-to-child HIV transmission; UNC, University of North Carolina.

emerged from all the studies reviewed are presented, separated into health systems factors, health worker-related factors and individual-level factors.

Health systems-related factors

Lack of continuity of care, gaps in the referral process and the need to strengthen linkages between PMTCT and HAART services were noted across a wide range of settings (Levy 2009; Nakanjako *et al.* 2009; Otieno *et al.* 2010). A case study in Mozambique found that enrolment in HIV services increased from 30% to 75% after their integration into the facilities that provided ANC/PMTCT (Pfeiffer *et al.* 2010).

In South Africa, Stinson compared the PMTCT cascade across three models of health services delivery: 'integrated services' whereby a weekly HAART service was provided within ANC; 'proximal services' where women were referred from ANC to HAART services in a separate building on the same premises; and 'distal services' whereby women were referred from ANC to HAART services at a separate facility within 5 km (Stinson *et al.* 2010). The cascade is presented in aggregate in Table 1 because no significant association was found between the model of care and the proportion of women starting HAART during pregnancy. The authors noted that providing HAART services on-site only once a week in the 'integrated' model may have been insufficient to affect HAART initiation during pregnancy (Stinson *et al.* 2010).

In Killam's study in Zambia, the proportion of women who enrolled for HIV care both before delivery and within 60 days of HIV diagnosis was 25% and 44% in the control (non-integrated) and intervention (integrated) arms, respectively (AdjOR 2.06, 95% CI: 1.27–3.34). The proportion of women who initiated HAART before delivery and within 60 days of diagnosis was 14% and 33%, respectively (AdjOR 2.01, 95% CI: 1.37–2.95). The authors postulated that this might have been due to clients' relative comfort in the PMTCT setting as well as providers' increased ownership of, and commitment to, this task. They acknowledged that further work is required to elucidate the reasons underlying the persistently high client drop-out (Killam *et al.* 2010).

The co-location of HAART services within ANC in the Killam study did not lead to HAART initiation earlier in pregnancy. Elsewhere, the length of treatment adherence preparation that was required before a woman could be started on HAART was noted as a potential factor influencing women's ability to start HAART during pregnancy (Chen *et al.* 2010; Stinson *et al.* 2010).

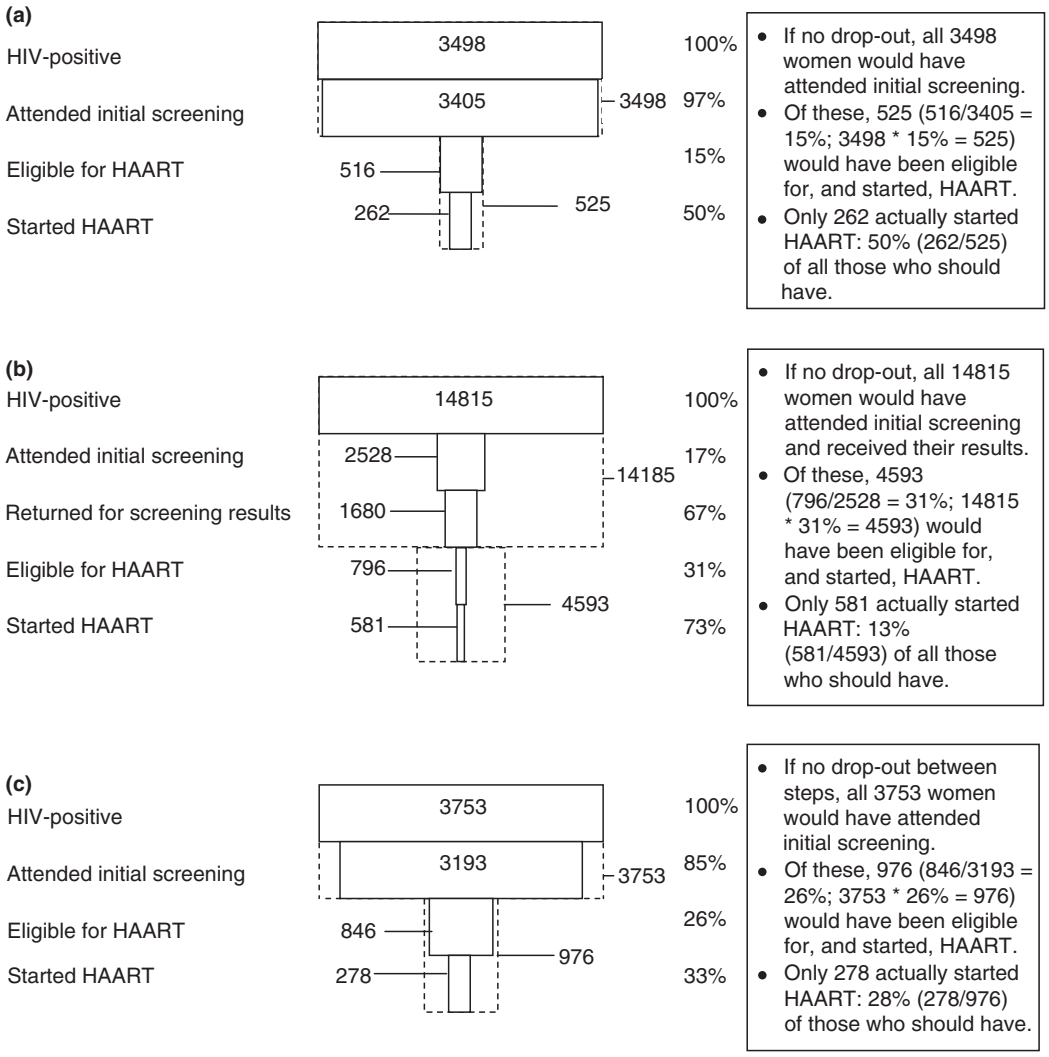

Figure 2 Piot-Fransen models illustrating patient cascades from HIV testing in pregnancy-related services to highly active antiretroviral therapy (HAART) services. (a) Piot-Fransen model for data from the Stinson *et al.* 2010 observational study in South Africa. (b) Piot-Fransen model for data from the Mandala *et al.* 2009 observational study in Zambia. (c) Piot-Fransen model for data from the intervention arm of the Killam *et al.* 2010 study in Zambia. The boxes with solid lines show the actual number of women who completed each step along this pathway. On the right-hand side are the proportions of women completing each step in the cascade. The dotted lines show an ideal patient cascade, i.e. with no patient drop-out, which is explained in the boxes on the right-hand side.

None of the studies in which HIV care and treatment services were initiated within ANC included data on client loss during transition from ANC to the site of long-term HIV care and treatment services.

Whether blood was drawn in ANC or the HIV clinic affected the proportion of women who had a CD4 count performed. Aggregating the studies in Tables 1 and 2 where the CD4 blood-draw was performed within ANC, 10 433 of 11 902 (88%) women had blood taken for a CD4 count compared with 379 of 827 (46%) in the studies where blood was drawn at the HIV clinic ($P < 0.001$). There was no difference between these two groups in the proportion of HAART-eligible women who started HAART ($P = 0.691$). None of the studies in this review used point-of-care CD4 tests.

Mandala *et al.* (2009) suggested that low uptake of CD4 count testing in their study might have been due to health workers not always drawing blood for CD4 counts

every day, limited sensitisation of providers and clients on the importance of CD4 count testing, repeated adjustment of the patient pathway and high levels of stigma. In Zambia, only two of the factors studied were independently associated with women having a CD4 count performed: ability to have blood drawn for the CD4 count on the day of diagnosis and urban location (Mandala *et al.* 2009).

On the basis of the observations in their study hospital in Botswana, Chen *et al.* (2010) proposed potential reasons for failure to undergo CD4 testing including a shortage of reagents; lack of access to transportation for specimens and test results; inability to perform the test before delivery and insufficient/lost specimens; and failure to initiate HAART such as delay in receipt of CD4 count results and lack of referral to the ART clinic. In other settings, women highlighted shortages of staff and supplies as well as cost of services as barriers to accessing services (Levy 2009; Otieno *et al.* 2010).

Health worker-related factors

As the interface between the health system and the client, health workers played a critical role in influencing women's care-seeking decisions. Negative provider–client interactions impeded uptake of services in Uganda (Duff *et al.* 2010). In Malawi, health workers' exclusive focus on the biomedical aspects of HIV and their failure to address social factors that might affect care-seeking, such as poverty and food insecurity, were highlighted as shortcomings (Levy 2009). In the same study, although women described accessing HIV-related services for their own health, providers sometimes failed to refer asymptomatic women to the HIV clinic and focused their attention on their infants' health (Levy 2009). The lack of sensitisation for providers and clients on the value of timely HAART initiation has also been noted as contributing to patient attrition (Mandala *et al.* 2009). Reflecting the power inequality between health provider and client, women's often unquestioning acceptance of providers' attitudes towards their health can affect their experiences of health services (Gruskin *et al.* 2008).

Individual-level factors

Women's fears regarding confidentiality, transport costs to access services, general dislike of health facilities, not feeling ready and low knowledge of HIV and HAART have also been cited as barriers to access (Duff *et al.* 2010; Otieno *et al.* 2010). The perceived stigma of being seen attending the clinic, being given food support that was only given to people with HIV and being visited at home contributed to the visibility of infection and potential involuntary disclosure, and therefore constituted reasons for non-attendance at services in a study in Malawi (Chinkonde *et al.* 2009).

Non-disclosure of HIV status to a woman's sexual partner contributed towards non-enrolment in HIV-related services in one study (Duff *et al.* 2010) but not in another (Otieno *et al.* 2010). The only study to examine the HIV status of women's sexual partners found no association with women's uptake of HIV-related services (Otieno *et al.* 2010).

Promising practices for addressing client attrition along the pathway to HAART

Perhaps the most promising model of service provision reported to date is the MTCT-Plus Initiative, which involves 'family-focused care', which aims to enrol not only the pregnant woman diagnosed with HIV into HIV care and treatment services but also her HIV-infected family members (Abrams *et al.* 2007; Tonwe-Gold *et al.* 2009). In a study in Ivory Coast, this approach resulted in all the 605 pregnant women who registered at the HIV clinic receiving their CD4 count result, and 95% of the 259 HAART-eligible women starting HAART (Tonwe-Gold *et al.* 2009). Although the study did not report attrition levels between HIV diagnosis and registering at the HIV clinic, these subsequent results were very impressive. The authors concluded that screening for HAART eligibility and initiation of HAART within pregnancy-related services were crucial for linking HIV-positive women into these services (Tonwe-Gold *et al.* 2009).

Other efforts to reduce attrition along the pathway to HIV care and treatment included the use of escorts for women between ANC and HAART services; pregnant women bypassing queues in HAART services; and regular meetings between staff from PMTCT and HAART services to track patients and discuss their needs (Abrams *et al.* 2007; Chi *et al.* 2007).

Discussion

The fragmentation of health services, with pregnancy-related services being managed separately from HIV care, for example, emerged as a major barrier to successful linkage into long-term HIV care and treatment services. Several initiatives designed to stem patient drop-out between HIV testing in pregnancy-related services and long-term HIV care and treatment services appear promising, but the plethora of barriers to accessing services means that single service change is likely to only partially solve the problem.

The rubric of 'integration' continues to be used to encompass a wide range of service delivery models. Specificity regarding which services are made available, when and by whom will be critical to understanding the effectiveness of different models of 'integrated' service delivery. Where staffing and infrastructure allow, it would seem most beneficial to ensure the daily availability within PMTCT services of assessment for HAART-eligibility and initiation of HAART. It will be important to ensure a smooth transition to the HIV clinic for women who initiate HIV-related services within pregnancy-related services, whenever this is performed. In addition, it would be useful for health workers to highlight within counselling sessions the benefits of HAART among women with a low CD4 count both for the woman's own health and for PMTCT. Point-of-care CD4 testing is increasingly being introduced and has considerable potential for improving retention in care at this stage of the cascade (Mtapuri-Zinyowera *et al.* 2010; Jani *et al.* 2011).

The provision of HAART within ANC has previously been shown to improve uptake and reduce time to treatment initiation (van der Merwe *et al.* 2006). It was therefore surprising that integration of HAART did not lead to earlier uptake of HAART during pregnancy in the studies led by Killam in Zambia and Stinson in South Africa. Further details of the study contexts, such as treatment preparation processes, might have helped to explain these differences.

A review of family-focused approaches to PMTCT underscored their importance for linkage into long-term care and treatment services, highlighting the MTCT-Plus Initiative and the CDC-Uganda Global AIDS Program as salient examples, although no quantitative data were provided on linkage into HIV-related services for the latter programme (Betancourt *et al.* 2010). However, both programmes have relied on high levels of external funding, and their sustainability needs confirmation (Myer *et al.* 2005).

A Cochrane review on integrating PMTCT services with other services found only one study that met its inclusion criteria, highlighting the weakness of the evidence base regarding the potential impact of integration on coverage and uptake of services, quality of care and health outcomes (Tudor Car *et al.* 2011). A systematic review of adult retention in HIV care between testing and treatment in sub-Saharan Africa revealed high patient drop-out across different populations and HIV testing locations and highlighted the need for improved health information systems to allow patient tracking across different service delivery points (Rosen & Fox 2011). The authors noted the difficulty inherent in cross-study comparison because of the lack of standardised terminology, definitions and time intervals, which applies equally to comparisons of the studies in this review (Rosen & Fox 2011).

Moving beyond the calls for increased attention to the health system factors affecting this attrition, addressing the personal and social factors that might constrain women's uptake of these services remains essential. Although disclosure of HIV status to a sexual partner has been shown to promote adherence to PMTCT interventions (Medley *et al.* 2004; Delva *et al.* 2006), this review found no clear-cut evidence of an association between such disclosure and initial uptake of HIV-related services. Despite limited autonomy in household decision-making (Berman *et al.* 1994; Nanda 2002; Vlassoff & Moreno 2002), women's decision-making around accessing long-term care and treatment services for their own HIV infection is an area that remains under-explored in current literature.

Limitations of this review

With the exception of one PhD thesis identified through discussions with experts, this systematic review only captures information on studies published in peer-reviewed academic literature; it may thus fail to capture lessons learned from interventions whose findings have not (yet) been published. Non-abstracted work and publications not listed within the databases searched will also have been excluded. Conference abstracts were not included in the review because of the paucity of detail they often include.

Certain caveats are important because of the assumptions in the extrapolations of data carried out. For example, the number of women requiring HAART would be over-estimated if the women who had blood drawn for a CD4 count were more likely to be symptomatic (and therefore more likely to need HAART) than the women who did not have blood taken for a CD4 count. Despite these limitations, such calculations can give a useful estimate of these missed opportunities.

Conclusion

This review provides strong evidence that, in most settings that have been studied to date in LMICs, relatively few women successfully negotiate the many steps between testing HIV-positive in pregnancy-related services and accessing HIV services for themselves. Improving this will require attention to barriers and enabling factors both within health facilities and at the level of the individual woman and her wider family and society. Box 2 lists health facility-level interventions recommended for improving linkage into HIV care and treatment services from HIV testing in pregnancy-related services.

Additional work is needed to better understand the effectiveness and sustainability of these interventions in varied settings. It is critical that the strengths and weaknesses of existing and new interventions be documented so that lessons learnt can be translated into concrete benefits in terms of access to HIV-related services for the pregnant women who require them.

Box 2 Health facility-level interventions to improve linkage between HIV testing in pregnancy-related services and long-term HIV care and treatment services

- Introduction into post-test counselling of messages on the importance of assessment for and, if eligible, initiation of HAART both for PMTCT and for women's health.
- Point of care CD4 count testing with in-session results available within pregnancy-related services.
- Full integration of HIV care and treatment services into ANC services (where infrastructure and staffing allow) with CD4 count testing and HAART initiation available daily, and women's transition to the HIV clinic weeks/months post-partum.
- Improved linkages between HIV testing in delivery and PNC services to HIV care and treatment services (whether in ANC or a separate HIV clinic).
- Provision of family-focused care, including, at a minimum, the offer of counselling, testing, treatment and psychosocial support for women's partner and children and other household members. Ideally, this would also include: male involvement in PMTCT and pregnancy-related counselling e.g. infant feeding counselling; accessing to reproductive health and family planning services; screening for intimate partner violence; nutrition counselling; attention to mental health issues; and attention to early childhood development.
- Peer support for women newly diagnosed with HIV, including escorts to the HIV clinic if these services are not available within the ANC setting.
- Improved health information systems that enable tracking of patients between hospital departments (and, ideally, across health facilities).
- Institution of communication systems that allow tracing of patients lost to follow-up.
- Incentives to attend the hospital e.g. transport subsidies, food supplements etc.

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Appendix 1

Criteria for considering a study 'fatally flawed'

A study was considered to be fatally flawed if, having read it, we answered 'no' to any one of the following questions

Are the aims and objectives of the research clearly stated?
Is the research design clearly specified and appropriate for the aims and objectives of the research?
Do the researchers provide a clear account of the process by which their findings were produced?
Do the researchers display enough data to support their interpretations and conclusions?
Is the method of analysis appropriate and adequately explicated?

Source: Dixon-Woods ***et al.*** (2006), Medical Research Methodology. ***BMC* 6**, 35.

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