

Systematic Review

Linkage to HIV care after home-based HIV counselling and testing in sub-Saharan Africa: a systematic review

Eugene Ruzagira^{1,2}, Kathy Baisley¹, Anatoli Kamali^{2,3}, Samuel Biraro⁴ and Heiner Grosskurth¹ for the Working Group on Linkage to HIV Care^a

¹ London School of Hygiene and Tropical Medicine, London, UK

² MRC/UVRI Uganda Research Unit on AIDS, Entebbe, Uganda

³ International AIDS Vaccine Initiative, New York, NY, USA

⁴ ICAP at Columbia University, New York, NY, USA

Abstract

BACKGROUND Home-based HIV counselling and testing (HBHCT) has the potential to increase HIV testing uptake in sub-Saharan Africa (SSA), but data on linkage to HIV care after HBHCT are scarce. We conducted a systematic review of linkage to care after HBHCT in SSA.

METHODS Five databases were searched for studies published between 1st January 2000 and 19th August 2016 that reported on linkage to care among adults newly identified with HIV infection through HBHCT. Eligible studies were reviewed, assessed for risk of bias and findings summarised using the PRISMA guidelines.

RESULTS A total of 14 studies from six countries met the eligibility criteria; nine used specific strategies (point-of-care CD4 count testing, follow-up counselling, provision of transport funds to clinic and counsellor facilitation of HIV clinic visit) in addition to routine referral to facilitate linkage to care. Time intervals for ascertaining linkage ranged from 1 week to 12 months post-HBHCT. Linkage ranged from 8.2% [95% confidence interval (CI), 6.8–9.8%] to 99.1% (95% CI, 96.9–99.9%). Linkage was generally lower (<33%) if HBHCT was followed by referral only, and higher (>80%) if additional strategies were used. Only one study assessed linkage by means of a randomised trial. Five studies had data on cotrimoxazole (CTX) prophylaxis and 12 on ART eligibility and initiation. CTX uptake among those eligible ranged from 0% to 100%. The proportion of persons eligible for ART ranged from 16.5% (95% CI, 12.1–21.8) to 77.8% (95% CI, 40.0–97.2). ART initiation among those eligible ranged from 14.3% (95% CI, 0.36–57.9%) to 94.9% (95% CI, 91.3–97.4%). Additional linkage strategies, whilst seeming to increase linkage, were not associated with higher uptake of CTX and/or ART. Most of the studies were susceptible to risk of outcome ascertainment bias. A pooled analysis was not performed because of heterogeneity across studies with regard to design, setting and the key variable definitions.

CONCLUSION Only few studies from SSA investigated linkage to care among adults newly diagnosed with HIV through HBHCT. Linkage was often low after routine referral but higher if additional interventions were used to facilitate it. The effectiveness of linkage strategies should be confirmed through randomised controlled trials.

keywords HIV/AIDS, home-based HIV counselling and testing, linkage to care, Uganda

Introduction

Access to antiretroviral therapy (ART) in sub-Saharan Africa (SSA) has expanded considerably, but AIDS-related mortality remains high [1]. A major cause of this

mortality is the late presentation of patients for treatment [2]. Early ART initiation is dependent on early HIV diagnosis, and prompt linkage to and retention in care [3]. HIV counselling and testing (HCT) is essential in expanding HIV prevention and treatment services [4]. However, HCT uptake in SSA remains low [5]. For instance, the proportion of HIV-positive adults in SSA who are aware

^aSee Appendix for the Working Group on Linkage to HIV Care.

of their HIV status has been estimated to be only 60% [6]. In order to expand access to HIV testing in settings with generalised HIV epidemics, WHO recommends community-based HCT with linkage to prevention, care and treatment services, in addition to facility-based HCT [7].

In the community-based HCT model, services are delivered through mobile, workplace-, school- and home-based approaches thus removing structural, logistical and social barriers to HCT [8]. Community-based HCT may also be delivered as part of multidisease campaigns that involve intensive community mobilisation lasting 1–2 weeks followed by mobile HIV testing, often coupled with other preventive medical services (campaign HCT) [9].

Under the home-based HIV counselling and testing (HBHCT) approach, HCT services are conducted by trained HCT service providers in the client's home [10]. HBHCT may be provided to everyone in a community through a door-to-door approach or to household members of known tuberculosis (TB) or HIV-positive patients [4, 10]. According to WHO, there were at least 39 HBHCT programmes in 10 SSA countries by early 2011 [10]. A systematic review published the following year found 21 studies that had reported on the uptake of HBHCT in SSA [11]. As then, several studies have reported successful implementation of HBHCT in rural [12–24] and urban [19, 23] populations in SSA. HBHCT is highly acceptable and has the potential to substantially increase HIV testing uptake in SSA [11]. It is cost effective at reaching previously untested persons compared with other HCT models in settings with high HIV prevalence [25, 26], promotes equitable access of services [27] and may help to promote HCT among couples [28] and prevention of mother-to-child HIV transmission [29]. Importantly, HBHCT facilitates early HIV diagnosis and therefore provides an opportunity for early linkage to care [29]. These attributes highlight the potential of HBHCT as an effective platform for HIV prevention and population-based test-and-treat strategies.

Despite these advantages, few data are available on linkage to care after HBHCT particularly among newly identified HIV-positive persons or on the effectiveness of strategies to increase linkage after HCT [30]. In the absence of interventions to facilitate linkage to care, individuals that test HIV positive through HBHCT may find it more challenging to enter care compared with those identified in facility-based HCT [31]. This is because HBHCT is more likely to reach socio-economically disadvantaged populations that have difficulty accessing healthcare services compared with facility-based HCT [32]. In order to identify effective linkage strategies, data

are specifically required on linkage to care soon after HBHCT. The reasons for this include the current WHO recommendation to initiate ART among all HIV-positive adults regardless of WHO clinical stage and at any CD4 count [33]; increasing use of HBHCT in Africa; and growing importance of early treatment for improved clinical outcomes [34–36] and HIV prevention [37]. A recent systematic review on linkage to care following community- and facility-based HCT [9] included 10 HBHCT studies but did not distinguish linkage outcomes between HBHCT and campaign HCT, between newly and previously diagnosed HIV-positive individuals, or between children/adolescents and adults. Individuals who previously tested HIV-positive and have not yet linked to care are likely to differ from newly identified patients with regard to barriers that may prevent service uptake [12]. Similarly linkage to care among children/adolescents may be influenced by factors that are unique to this population [38, 39].

The specific objectives of our review were to estimate the proportion of individuals in SSA linking to care within 12 months among those who were newly diagnosed with HIV; the proportion initiating daily cotrimoxazole (CTX) prophylaxis (i.e. the people who initiated daily CTX prophylaxis among those who linked to care and were eligible for CTX); and the proportion initiating ART (i.e. the people who initiated ART among those who linked to care and were eligible for ART); and to summarise data on the strategies that have been used to increase linkage to care after HBHCT.

Methods

Search strategy

We searched five databases (Medline, Embase, Global Health, Web of Science, and Africa-Wide information) for studies published between 1st January 2000 (time at which roll-out of ART programmes began in SSA [11]) and 19th August 2016. The following key terms were used as follows: (HIV diagnosis OR HIV voluntary counselling and testing OR HIV testing and counselling OR HIV counselling and testing) AND (home based OR mobile OR community OR household OR door-to-door OR survey) AND (linkage OR access OR uptake OR enrolment OR non-enrolment OR retention OR loss to follow-up OR loss to care OR care OR treatment OR pre-antiretroviral therapy) AND (Africa OR individual names of countries in SSA). No language restriction was applied to the literature search. Identified articles were exported using Endnote reference management software and duplicate articles removed. Two authors (ER and SB)

independently screened titles and abstracts of articles to identify eligible publications, discussed inconsistencies and reached a consensus on their eligibility. Studies were eligible if they were conducted in SSA, and had original data on linkage to care among adults (≥ 18 years) newly identified with HIV infection through HBHCT, defined as HCT services offered in an individual's home. Studies whose study populations included persons < 18 years were eligible, but only data for participants aged ≥ 18 years were utilised to estimate linkage and other outcomes. Studies for which the required information was not published but might have been collected were identified and the corresponding authors approached with requests for additional data. Where two or more eligible articles reported on similar or overlapping populations, the article with the most complete data was included. Review articles were excluded, but their bibliographies as well as those of the identified articles were manually checked to identify any additional studies. Conference abstracts were excluded. All potentially eligible papers were then subjected to full-text screening.

Data extraction and synthesis

A data extraction form was used to collect the following information from each eligible article: first author's name, publication year, country and setting where study was conducted, study population, sample size, study design, definition of linkage to care, strategies used to promote and time for evaluation of linkage to care. We also obtained the number of HIV-positive adults who were newly diagnosed, and, among those, the numbers who linked to care (as defined in the respective studies), and were eligible for, and initiated, CTX prophylaxis and ART (based on national guidelines that were in use at the time of the respective studies). Risk of bias in the included studies was assessed using a component approach, similar to the Cochrane Collaboration's [40], and based on three items: selection bias, outcome ascertainment and attrition. The results were summarised using the PRISMA guidelines [41].

We used the reported data to calculate the proportions [and their 95% confidence intervals (CI), using the Clopper–Pearson method] who linked to care, initiated CTX prophylaxis, were eligible for and initiated ART. The denominator for linkage was all newly diagnosed HIV-positive adults (≥ 18 years) who had a potential minimum follow-up period corresponding to the time point when linkage was assessed (i.e. including those who out-migrated, died, or were lost to follow-up, but excluding those who entered the study at a later date so had a shorter potential follow-up period). We did not stratify our linkage

estimates by individual-level factors that may potentially influence referral uptake, such as HIV disease stage or CD4 count at the time of HIV diagnosis, as these data were not available for most of the studies. However, we compared linkage estimates between studies conducted under different CD4 ART eligibility thresholds, that is ≤ 250 cells/ μl vs. ≤ 350 cells/ μl . The denominator for ART eligibility was all individuals who linked within the specified time period, and those for initiation of CTX prophylaxis and ART were all individuals who linked and were eligible for CTX and ART, respectively. We did not perform a meta-analysis because the identified studies varied widely with regard to design, setting, definition of linkage to care, the time points of and method for ascertaining linkage, and with regard to the strategies used to facilitate linkage.

Results

Summary of search results

The search identified 5905 articles of which 61 were subjected to full-text screening (Figure 1). Of those screened, 21 were eligible for detailed review; two were excluded on the basis of reporting on overlapping study populations [20, 42]. Of the remaining 19 articles, one [19] had all the required data. Additional data were obtained for 13 [12–14, 18, 21–24, 43–47] of the remaining 18 articles after contacting the respective corresponding authors. Thus, 14 studies were included in the review. A summary description of the included studies is presented in Table 1. The studies were conducted in six countries, that is Uganda [13, 14, 43, 44], South Africa [13, 14, 18, 23, 24, 45], Kenya [12, 19], Malawi [46, 47], Lesotho [22] and Swaziland [21] between 2005 and 2015. Most (92%) studies were based in rural [12–14, 18, 21, 22, 24, 43, 45, 47] or semirural settings [44, 46] settings; two were conducted in both rural and urban [19, 23] populations. The number of newly identified HIV-positive adults varied widely across studies (range: 15–1637).

Summary of study objectives and populations

The included studies aimed to assess acceptability of HBHCT [18, 19, 21–24, 46, 47], and HIV prevalence [19], linkage to care [12–14, 18, 19, 21–24, 43–45], uptake of ART [13, 14, 18, 24, 44, 47], and viral suppression [13, 14, 18], in the context of HBHCT. Two studies compared HBHCT and mobile HCT with regard to uptake and cost of HCT, HIV positivity rates and linkage to care [21, 22]. Three observational studies [13, 18, 44] and one randomised trial [14] were designed to evaluate the effect of specific interventions on linkage to HIV

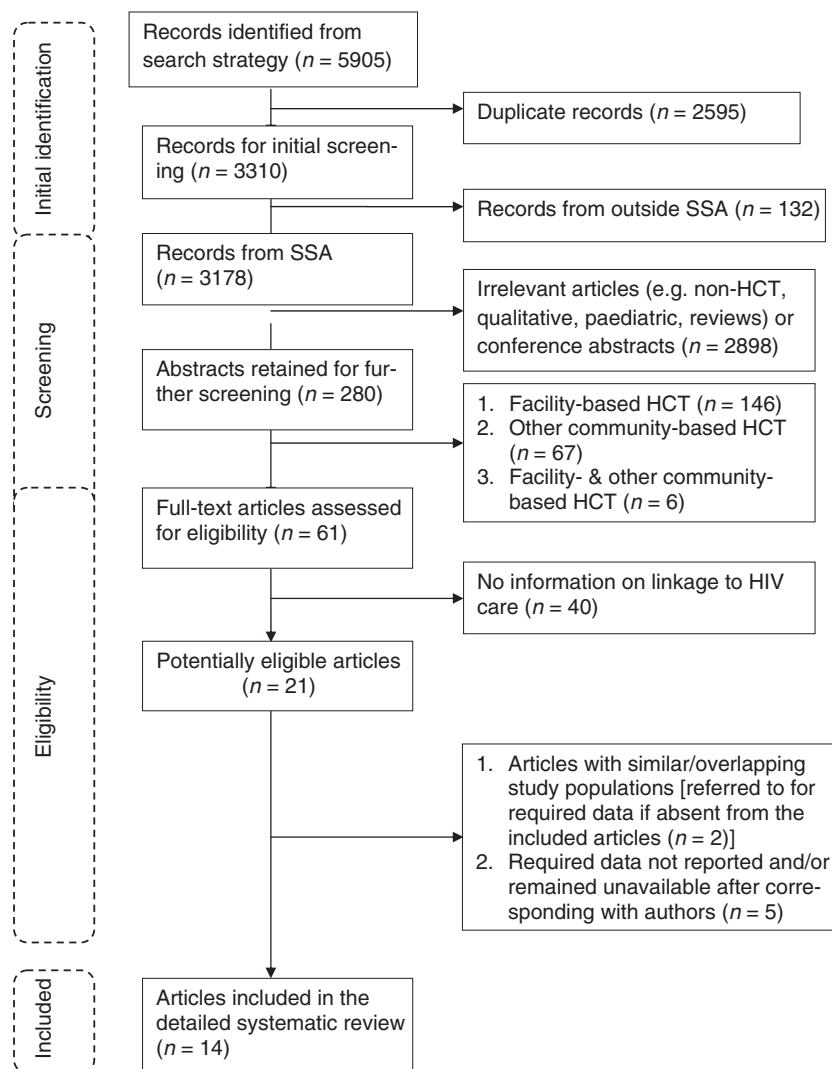


Figure 1 Systematic search flow diagram.

care, uptake of ART and other outcomes. Except for one study in which HBHCT was provided to household contacts of TB index patients [23], all the other studies used the door-to-door HBHCT approach. Study participants mostly comprised individuals aged ≥ 13 years. However, two studies also recruited children (< 13 years) [19, 21]. With the exception of two studies that recruited newly identified HIV-positive individuals [22, 23], participants in other studies were a mixture of previously and newly identified HIV-positive patients.

Risk of bias

Only two [13, 18] studies had a low risk of bias for all assessed items (Table 2). Risk of selection bias was low

($\geq 80\%$ HBHCT coverage) in four studies [13, 18, 19, 44]. Risk of attrition bias was low ($\geq 80\%$ participant retention) in eight [13, 14, 18, 23, 24, 44–46] of 10 studies in which participants were followed. Self-reported linkage to care was confirmed by tracking referrals and review of records at the referral clinic in only two studies [43, 45]. In the first study [43], no information was reported on the proportion of participants for whom clinic records were not found. In the second study [45], clinic records were found for only 71% of the tracked referrals, and self-reported data were used to ascertain linkage for the rest of the participants. Self-reported linkage to care was confirmed by review of documentation issued to patients by HIV clinics (e.g. clinic cards) in three studies [13, 14, 18]; linkage was not verified with

Table 1 Description of studies included in the systematic review

Author, year	Country, setting	Study period	Study design	Age eligibility (years)	HIV care provider	CD4 ART eligibility threshold (cells/ μ l)	Linkage to care definition	Linkage assessment time (months)	Linkage strategies	Number in analysis (Number of HIV-positive persons in study) [†]	Linked n (%), 95% CI	Initiated CTX [‡] n (%), 95% CI	Eligible for ART [§] n (%), 95% CI	Initiated ART n (%), 95% CI
Genbergs, 2015 [12]	Kenya, rural	2009–2011	Retrospective population-based cohort study of HBHCT among participants enrolled in a clinical care programme	≥ 13	Public clinic	≤ 50	Registration at clinic	3	Referral only	1329 (3482)	109 (8.2, 6.8–9.8)	Not reported	41 (37.6, 28.5–47.4)	23 (56.1, 39.7–71.5)
Dalal, 2013 [19]	Kenya, rural & urban	2008	Prospective population-based cohort study of HBHCT among participants enrolled in a disease surveillance programme	All ages [¶]	Public clinic	≤ 50	Registration at clinic	1	Referral only	1637 (2739)	414 (25.3, 23.2–27.5)	375/414 (90.6, 87.3–93.2)	120 (29.0, 24.7–33.6)	39 (33.0, 24.2–41.7)
Wringe, 2012 [47]	Malawi, rural	2008–2010	Retrospective population-based cohort study of HBHCT among participants enrolled in a demographic surveillance programme	≥ 15	Research clinic	≤ 50	Screening for ART eligibility	12	Referral only	431 (473)	126 (29.2, 24.9–33.8)	Not reported	67 (53.2, 44.1–62.1)	63 (94.0, 85.4–98.3)
Parker, 2015 [21]	Swaziland, rural	2013	Prospective population-based intervention of HBHCT vs. mobile HCT	≥ 18 months	Public clinic	≤ 350	Registration at clinic	6	Referral only	142 (170)	45 (31.7, 24.1–40.0)	Not reported	17 (37.8, 23.8–53.5)	9 (52.9, 27.8–77.0)
Velen, 2016 [23]	South Africa, rural & urban	2013–2014	Prospective cohort study of HBHCT among household contacts of TB index patients enrolled in a TB contact tracing trial	≥ 14	Public clinic	≤ 50	Registration at clinic	3	Referral only	25 (26)	8 (32.0, 14.9–53.5)	Not reported	Not reported	Not reported

E. Ruzagira *et al.* **Linkage to HIV counselling and testing in SSA**

Table 1 (Continued)

Author, year	Country, setting	Study period	Study design	Age eligibility (years)	HIV care provider	CD4 ART eligibility threshold (cells/ μ l)	Linkage to care definition	Linkage assessment time (months)	Linkage strategies	Number in analysis (Number of HIV-positive persons in study) [†]	Linked <i>n</i> (%), 95% CI	Initiated CTX [‡] <i>n</i> (%), 95% CI	Eligible for ART [§] <i>n</i> (%), 95% CI	Initiated ART <i>n</i> (%), 95% CI
Iwuiji, 2016 [24]	South Africa, rural	2012–2014	Community-based cluster randomised trial of immediate ART initiation <i>vs.</i> ART initiation according to national guidelines following HBHCT	≥ 16	Public & research clinics	Any CD4 count (intervention arm) ≤ 350 (standard-of-care arm)	Registration at clinic	12	Referral & follow-up counselling ^{††}	358 (2569)	162 (45.3), 40.0–50.6)	Not reported	101 (71.6), 63.4–78.9) ^{††}	81 (80.2), 71.1–87.5)
Naik, 2015 [45]	South Africa, rural	2009–2011	Prospective population-based cohort of participants offered HBHCT as a standard-of-care service & in the context of a trial of HBHCT <i>vs.</i> facility-based HCT.	≥ 14	Public clinic	≤ 200	Obtaining a CD4 count	3	Referral & at least 3 follow-up counselling visits ^{§§}	410 (492)	248 (60.5), 55.6–65.3)	Not reported	41 (16.5), 12.1–21.8)	33 (80.5), 65.1–91.2)
Labhardt, 2014 [22]	Lesotho, rural	2011	Community-based cluster randomised trial of HBHCT <i>vs.</i> mobile HCT	All ages	Public clinic	≤ 350	Registration at clinic	1	Referral & POC CD4 count testing	37 (39)	9 (24.3), 11.8–41.2)	Not reported	7 (77.8), 40.0–97.2)	1 (14.3), 0.36–57.9)
Becker, 2014 [46]	Malawi, peri-urban	2009	Population-based uncontrolled intervention study of couple HBHCT & couple family planning services	15–49 (female); ≥ 15 (male)	Public clinic	≤ 250	Registration at clinic	1 week	Referral & provision of funds for transport to clinic to participants who disclosed their HIV status to their partners ^{¶¶}	15 (46)	8 (53.3), 26.6–78.7)	Not reported	Not reported	Not reported

E. Ruzagira *et al.* Linkage to HIV counselling and testing in SSA

Table 1 (Continued)

Author, year	Country, setting	Study period	Study design	Age eligibility (years)	HIV care provider	CD4 ART eligibility threshold (cells/ μ l)	Linkage to care definition	Linkage assessment time (months)	Linkage strategies	Number in analysis (Number of HIV-positive persons in study) [†]	Linked <i>n</i> (%), 95% CI	Initiated CTX [‡] <i>n</i> (%), 95% CI	Eligible for ART [§] <i>n</i> (%), 95% CI	Initiated ART <i>n</i> (%), 95% CI
Nakigizi, 2011 [43]	Uganda, rural	2005–2008	Retrospective population-based cohort of participants receiving HBHCT or other community-based HCT in an HIV surveillance programme	15–49	Research clinic	≤ 50	Registration at clinic	6	Referral & follow-up counselling ^{†††}	1137 (1451)	781 (68.7), 65.9–71.4	781/781 (100.0)	237 (30.3), 27.1–33.7	225 (94.9), 91.3–97.4
Tumwebaze, 2012 [44]	Uganda, rural & peri-urban	2010–2011	Population-based uncontrolled intervention study of HBHCT & a combination of linkage strategies	≥ 18	Public clinic	≤ 50	Registration at clinic	3	Referral, CD4 count laboratory testing (results returned to participant a week later), & follow-up counselling (1, 2 & 3 months)	77 (152)	63 (81.8), 71.4–89.7	63/63 (100.0)	13 (20.6), 11.5–32.7	8 (61.5), 31.6–86.1
Barnabas, 2014 [13]	South Africa & Uganda, rural	2011–2013	Population-based uncontrolled intervention study of HBHCT & a combination of linkage strategies	≥ 18	Public clinic	≤ 50	Registration at clinic	12	Referral, POC CD4 count testing, follow-up counselling (1, 3, 6, 9, & 12 months), & viral load testing (0 & 6 months)	229 (635)	227 (99.1), 96.9–99.9	212 (16.7), 2.1–48.4 SA; 86/110 (78.2, 69.3–85.5) UG	74 (32.6), 26.5–39.1	59 (79.7), 68.8–88.2
van Rooyen, 2013 [18]	South Africa, rural	2011–2012	Population-based uncontrolled intervention study of HBHCT & a combination of linkage strategies	≥ 18	Public clinic	≤ 200 ; ≤ 350 (from August 2011)	Registration at clinic	6	Referral, POC CD4 count testing, & follow-up counselling (1, 3, & 6 months)	73 (201)	70 (95.9), 88.5–99.1	Not reported	35 (50.0), 37.8–62.2	19 (54.3), 36.6–71.2

E. Ruzagira *et al.* **Linkage to HIV counselling and testing in SSA**

Table 1 (Continued)

Author, year	Country, setting	Study period	Study design	Age eligibility (years)	HIV care provider	CD4 ART eligibility threshold (cells/ μ l)	Linkage to care definition	Linkage assessment time (months)	Linkage strategies	Number in analysis (Number of HIV-positive persons in study) [†]	Linked <i>n</i> (%), 95% CI	Initiated CTX [‡] <i>n</i> (%), 95% CI	Eligible for ART [§] <i>n</i> (%), 95% CI	Initiated ART <i>n</i> (%), 95% CI
Barnabas, 2016 [14]	South Africa & Uganda, rural	2013–2015	Household randomised controlled trial of referral only vs. referral plus other linkage strategies after HIV diagnosis through HBHCT or mobile HCT (6 linkage strategies) ^{†††}	≥ 16	Public clinic	≤ 350 ; ≤ 500 (from January 2015)	Registration at clinic	9	Referral only	82 (226)	70 (85.4), 75.8–92.2)	216 (33.0), 4.3–77.7) SA; 20/25 (80.0), 59.3–93.2) UG	37 (52.9), 40.6–64.9)	28 (75.7), 58.8–88.2)
									Referral & POC CD4 count testing	81 (213)	73 (90.1), 81.5–95.6)	114 (25.0), 0.63–80.6) SA; 37/38 (97.4), 86.2–99.9) UG	43 (58.9), 46.8–70.3)	25 (58.1), 42.1–73.0)
									Referral & counsellor clinic linkage facilitation	104 (231)	102 (98.1), 93.2–99.8)	113 (33.3), 0.84–90.6) SA; 18/21 (85.7), 63.7–97.0) UG	51 (50.0), 39.9–60.1)	39 (76.5), 62.5–87.2)
									Referral, POC CD4 count testing, & counsellor clinic linkage facilitation	72 (206)	69 (95.8), 88.3–99.1)	0/3 (0.0), SA; 23/27 (85.2), 66.3–95.8) UG	43 (62.3), 49.8–73.7)	23 (53.5), 37.7–68.8)
									Referral & follow-up counselling (1, 3, & 6 months)	87 (229)	80 (92.0), 84.1–96.7)	0/12 (0.0), SA; 30/30 (100.0) UG	41 (51.3), 39.8–62.6)	31 (75.6), 59.7–87.6)
									Referral, POC CD4 count testing & follow-up counselling (1, 3, & 6 months)	85 (220)	81 (95.3), 88.4–98.7)	1/5 (20.0), 0.51–71.6) SA; 28/28 (100.0) UG	46 (56.8), 45.3–67.8)	36 (78.3), 63.6–89.1)

[†]Only adults (≥ 18 years) newly diagnosed with HIV through HBHCT were included in the analysis.
[‡]Uptake of CTX prophylaxis is shown separately for South Africa (SA) and Uganda (UG) because eligibility criteria are different in each country.
[§]Based on locally recommended CD4 count eligibility threshold during the study period.
[¶]Children aged <13 years were offered HBHCT if their biological mothers were HIV-positive or deceased.
^{**}Follow-up counselling was offered to individuals who did not link to care within 3 months of referral; number and timing of follow-up visits were not specified.
^{††}Information on ART eligibility and initiation was not available for persons who linked to the public health facilities. Hence, the denominator used for ART eligibility (*n* = 141) is the number of persons who linked to the research clinics.
^{†††}Timing of follow-up visits was not specified.
^{¶¶}The number of participants who disclosed their HIV status to their partners was not reported.
^{††††}Number and timing of follow-up visits were not specified.
^{†††††}Results for linkage to care and other outcomes are presented separately for each of the six linkage strategies.

Table 2 Risk of bias within studies

Author, year	Selection of participants†	Outcome ascertainment‡	Loss to follow-up§
Genberg, 2015 [12]	HBHCT coverage could not be estimated because the size of the target population was not reported. <i>Unclear risk</i>	Clinic-verified data. No information on persons who may have linked to clinics outside the study area. <i>Unclear risk</i>	No participant follow-up
Dalal, 2013 [19]	HBHCT coverage was 82%. <i>Low risk</i>	Self-report for all participants. <i>High risk</i>	48% (881/1839) loss to follow-up. <i>High risk</i> ¶
Wringe, 2012 [47]	HBHCT coverage could not be estimated because the total number of persons in the target population was not reported. <i>Unclear risk</i>	Clinic-verified data. No information on persons who may have linked to clinics outside the study area. <i>Unclear risk</i>	No participant follow-up
Parker, 2015 [21]	HBHCT was conducted in only 26% of households in the target area due to time constraints. It is not clear how these households were selected. <i>High risk</i>	Clinic-verified data. Participants who were referred health facilities outside the study area were excluded from analysis. <i>Unclear risk</i>	No participant follow-up
Velen, 2016 [23]	HBHCT was offered to household contacts of TB patients selected through convenience sampling. <i>High risk</i>	Self-report for all participants. <i>High risk</i>	12% (3/26) loss to follow-up. <i>Low risk</i>
Iwuji, 2016 [24]	HBHCT coverage was 64%. <i>High risk</i>	Clinic-verified data. No information on persons who may have linked to clinics outside the study area. <i>Unclear risk</i>	16% (58/358) loss to follow-up. <i>Low risk</i> ††
Naik, 2015 [45]	HBHCT coverage could not be estimated because the size of the population targeted for testing in the participating communities was not reported. <i>Unclear risk</i>	Self-report & clinic-verified data or self-report only (29% of participants). <i>High risk</i>	18% (79/438) loss to follow-up. <i>Low risk</i> ††
Labhardt, 2014 [22]	HBHCT coverage could not be estimated because the total number of persons in the target population was not reported. <i>Unclear risk</i>	Clinic-verified data. No information on persons who may have linked to clinics outside the study area. <i>Unclear risk</i>	No participant follow-up
Becker, 2014 [46]	HBHCT was offered to all eligible participants in one village and approximately one-third in two other villages (no information on how participants in these two villages were selected). <i>High risk</i>	Self-report for all participants. <i>High risk</i>	2% (1/46) loss to follow-up. <i>Low risk</i>
Nakigozi, 2011 [43]	Annual HIV testing coverage in the cohort is >90%. However, 21% of the persons who tested HIV-positive were excluded from the analysis because they had either refused to learn their HIV results (3%) or received their HIV result less than six months before data-set closure (18%). <i>High risk</i>	Self-report & clinic-verified data. No information on whether self-reported linkage was confirmed with clinic records for all participants. <i>Unclear risk</i>	Loss to follow-up not reported. <i>Unclear risk</i>
Tumwebaze, 2012 [44]	HBHCT coverage was 80%. <i>Low risk</i>	Self-report for all participants. <i>High risk</i>	2% (3/152) loss to follow-up. <i>Low risk</i>

Table 2 (Continued)

Author, year	Selection of participants†	Outcome ascertainment‡	Loss to follow-up§
Barnabas, 2014 [13]	HBHCT coverage was 96%. <i>Low risk</i>	Self-report & review of documentation issued to patient by the HIV clinic. <i>Low risk</i>	10% (62/635) loss to follow-up. <i>Low risk</i>
van Rooyen, 2013 [18]	HBHCT coverage was 91%. <i>Low risk</i>	Self-report & review of documentation issued to patient by the HIV clinic. <i>Low risk</i>	2% (5/201) loss to follow-up. <i>Low risk</i>
Barnabas, 2016 [14]	HBHCT coverage could not be estimated because the size of the population targeted for testing in the participating communities was not reported. <i>Unclear risk</i>	Self-report & review of documentation issued to patient by the HIV clinic. <i>Low risk</i>	3% (40/1325) loss to follow-up. <i>Low risk</i>

†In population-based studies, there was low risk of bias if HBHCT coverage (defined as the number of persons accessing HBHCT of the total resident population) was $\geq 80\%$, high risk if HBHCT coverage was $< 80\%$, and unclear risk if there was no information on coverage. In non-population-based cohort studies, there was low risk if participants were randomly selected, high risk if the selection was non-random and unclear risk if there was insufficient information on participant selection.

‡There was low risk of bias if ascertainment of linkage to care was by both self-report and examination of HIV clinic records or documentation issued to patients by the HIV clinic for $\geq 80\%$ of the participants, high risk if ascertainment was by self-report only and unclear risk if there was insufficient information on ascertainment of linkage outcomes for some study participants.

§There was low risk if retention of HIV-positive persons identified through HBHCT was $\geq 80\%$, high risk if retention was $< 80\%$ and unclear risk if information was not available.

¶Only applicable to HIV-positive individuals who were newly identified through HBHCT.

**Only applicable to newly identified HIV-positive persons who were referred to care at least 12 months before the end of the first phase of the trial that is May 2014.

‡‡Only applicable to HIV-positive individuals who were not engaged in care at baseline.

the HIV clinics. In five studies [12, 21, 22, 24, 47], ascertainment of linkage to care was based on data from HIV clinics in the areas where the studies were conducted; participants who may have linked to HIV clinics outside of the study areas were not tracked. Only self-reported data were used in the rest of the studies [19, 23, 44, 46].

Linkage to HIV care

In all studies, persons who tested HIV positive were referred for care. Additional strategies to facilitate linkage to care were used in nine (64%) [13, 14, 18, 22, 24, 43–46] of the studies (Table 1). These strategies included: provision of funds for transport to the HIV clinic [46]; follow-up counselling [13, 14, 18, 24, 43–45]; lay counsellor facilitation of the initial HIV clinic visits (the counsellor met the HIV-positive participant at the clinic and explained the clinic processes and the benefits of ART) [14]; point-of-care (POC) CD4 count [13, 14, 18, 22] and home-based collection of samples for viral load [13] testing and provision of results. Linkage to care was ascertained within 3 months of HBHCT in 50% of studies [12, 19, 22, 23, 44–46]. Ascertainment of linkage in the remaining studies was carried out >3 to 6 [18, 21, 43] and >6 to 12 [13, 14, 24, 47] months after HBHCT.

Linkage to care ranged from 8.2% (95% CI, 6.8–9.8%) [12] to 85.4% (95% CI, 75.8–92.2%) [14] when only referral was offered, and 24.3% (95% CI, 11.8–41.2%) [22] to 99.1% (95% CI, 96.9–99.9%) [13] when referral plus additional interventions to facilitate linkage were offered (Table 1). In general, linkage to care was lower (<33%) in the studies that offered referral only [12, 19, 21, 23, 47] and higher (>80%) in those that used a combination of additional linkage strategies [13, 14, 18, 44].

Among seven studies that were conducted in the context of a CD4 ART eligibility threshold of ≤ 250 cells/ μ l [12, 19, 43–47], linkage to care ranged from 8.2% (95% CI, 6.8–9.8%) [12] to 81.8% (95% CI, 71.4–89.7) [44]. Linkage was lower (<30.0%) in the studies that offered referral only [12, 19, 47] and higher (>50%) in those that used at least one additional linkage strategy [43–46].

Among four studies conducted in the context of a CD4 ART eligibility threshold of ≤ 350 cells/ μ l [13, 21–23], linkage to care ranged from 24.3% (95% CI, 11.8–41.2) [22] to 99.1% (95% CI 96.9–99.9) [13]. Linkage was <33% in the two studies that offered referral only [21, 23]. Linkage was also low (24.3%) in one study that used referral and POC CD4 count testing [22], but very high (99.1%) in a study that offered referral, POC CD4 testing and additional linkage strategies [13].

Uptake of CTX prophylaxis and ART

Five studies conducted in Kenya [19], Uganda [43, 44] and Uganda and South Africa [13, 14] had data on initiation of CTX prophylaxis among eligible individuals who linked to care. CTX prophylaxis is only recommended for patients with CD4 count ≤ 200 cells/ μ l, WHO stage 3 or 4 or HIV/TB co-infection in South Africa [48] but is routinely provided to all HIV-positive persons irrespective of CD4 count or WHO disease stage in Uganda [49] and Kenya [50]. Of the studies conducted in Uganda and Kenya, additional interventions to facilitate referral uptake were offered in all except one. CTX uptake in these studies ranged from 78.2% (95% CI, 69.3–85.5%) [13] to 100% [14, 43, 44] (Table 1). CTX uptake was also high [90.6% (95% CI, 87.3–93.2%)] in the study that offered referral only [19]. Interventions to facilitate linkage were offered in the two studies that were conducted in South Africa. Uptake of CTX among patients with CD4 count ≤ 200 cells/ μ l in these studies ranged from 0% [14] to 33.3% (95% CI, 4.3–77.7) [14].

Twelve studies [12–14, 18, 19, 21, 22, 24, 43–45, 47] had data on ART eligibility and ART initiation among patients who linked to care. The proportion of individuals eligible for ART initiation ranged from 16.5% (95% CI, 12.1–21.8) [45] to 77.8% (95% CI, 40.0–97.2) [22] (Table 1). ART uptake among those who linked to care ranged from 33.0% (95% CI, 24.2–41.7%) [19] to 94.0% (95% CI, 85.4–98.3%) [47] in the studies that provided referral only. A similar range, that is 14.3% (95% CI, 0.36–57.9%) [22] to 94.9% (95% CI, 91.3–97.4%) [43] was observed in the studies that provided referral plus additional linkage interventions. ART initiation rates were highest ($\geq 90\%$) in the two studies in which HIV care services were provided through community-based research clinics [43, 47].

Discussion

Home-based HIV counselling and testing is increasingly being used in SSA, and an effectively conducted HBHCT strategy would be a key pre-condition for HIV control programmes that propagate a test-and-treat approach for HIV prevention [45]. The success of such programmes will partly depend on their capacity to achieve high levels of linkage to care following HIV diagnosis [16]. Hence, it is necessary to identify and set up strategies that will effectively link persons identified with HIV through HBHCT to care and treatment. As observed in this review, however, only a few studies have investigated linkage to care among adults newly identified with HIV through HBHCT in SSA. Linkage to care was below

E. Ruzagira *et al.* **Linkage to HIV counselling and testing in SSA**

33% in five of six studies where participants were only referred for care with no further interventions to facilitate referral [12, 19, 21, 23, 47], a figure that is lower than those for client-initiated facility-based HCT (61%) and provider-initiated facility-based HCT (55%) [9]. With the exception of two studies [22, 24], studies that used additional linkage strategies recorded moderate (>50% to <80%) [43, 45, 46] to high ($\geq 80\%$) [13, 14, 18, 44] levels of linkage. These trends remained irrespective of the CD4 ART eligibility threshold at the time of the studies. In general, linkage to care was highest when participants were offered POC CD4 count testing and follow-up counselling [13, 14, 18]. These findings suggest that HBHCT coupled with interventions to facilitate referral uptake may achieve similar or even higher linkage compared to facility-based HCT.

WHO recommends CTX prophylaxis for all adults with WHO stage 3 and 4 HIV disease and/or with a CD4 count ≤ 350 cells/mm³, and regardless of CD4 count in settings where malaria and/or severe bacterial infections are highly prevalent [33]. For this reason, CTX prophylaxis is an essential component of HIV care in many settings in SSA, and its uptake may be used as an indicator of access to HIV care [19, 51]. However, only a small number of studies included in this review had data on the uptake of CTX. In Kenya and Uganda where routine CTX prophylaxis is recommended irrespective of CD4 count or clinical stage [49, 50], uptake was high (>70%) irrespective of whether or not additional interventions were applied. This may be because CTX is widely available, inexpensive and simple to use [52]. In contrast and in spite of facilitated linkage, uptake of CTX prophylaxis among those eligible (based on guidelines that were in use at the time of the studies) in South Africa was low ($\leq 33\%$). The reasons for this are not clear. However, previous studies have found irregular supply and lack of stocks of CTX, lack of awareness among healthcare workers and perceived low priority of CTX prophylaxis due to the absence of a reporting requirement, to be some of the barriers to implementation of CTX prophylaxis policies [53].

Consistent with previous findings [11], significant proportions of HIV-positive persons identified through HBHCT were still ineligible for ART (based on national guidelines that were in use at the time of the respective studies). The finding that ART uptake was highest in the studies where services were provided through community-based research clinics may be attributed to such clinics being more accessible and less prone to limitations that characterise many public sector ART care programmes in SSA, including the requirement for several visits to prepare patients for ART [14], crowded, busy

and unwelcoming clinics [54], non-functioning laboratories [54], and inadequate supply or lack of antiretroviral drugs [55]. Additionally, some research clinics are likely to have close and long-standing relationships with communities in which they are located.

Home-based HIV counselling and testing studies with facilitated linkage have been shown to achieve higher ART initiation rates among participants who link to care compared to those without facilitated linkage [9]. However, ART initiation rates were high in some but not all studies with facilitated linkage described in this review. Additionally, some studies without facilitated linkage achieved higher ART initiation rates [47] than those with facilitated linkage [13, 14, 18, 22, 24, 44, 45]. It is likely that clinic-level factors such as those mentioned above as well as individual-level confounding factors such as HIV disease stage may be more important in influencing events after linkage to care. Also, people who link to care in the absence of facilitated linkage may be more motivated to receive care.

This review has some limitations. The review was limited to SSA. Even so, the number of relevant studies found is small and represents only six countries, four of which are in Southern Africa. This may limit the generalisability of the findings. The methods used in the identified studies varied widely, making it impractical to combine findings from individual studies into a pooled analysis. Outcome assessments in most of the included studies were based solely on self-reports or records in HIV clinics within the respective study areas; hence, linkage to care may have been overestimated in the case of self-reports or underestimated if some individuals linked to clinics outside of their communities.

Importantly, most of the studies that included interventions to facilitate linkage to HIV care were observational, determining intervention effects without control groups. A major limitation of observational studies is that it is difficult to account for the effects of confounding factors such as HIV disease stage, fear of stigma, healthcare seeking behaviour and familiarity with the healthcare services. Moreover, in some of the studies, two or more interventions were delivered concurrently, making it difficult to distinguish the effects of each. Randomised trials represent the gold-standard in evaluating an intervention including its likely effect size [56]. It is therefore desirable to confirm the impact and establish the cost-effectiveness of these interventions in randomised controlled trials. Indeed, a number of trials have been designed to investigate the effect of different interventions on linkage to care among persons that test HIV positive through HBHCT [57–61]. Findings from these trials are expected in the near future and may provide more robust data on

the impact of interventions on linkage to care after HBHCT.

Except for one study in which some of the newly identified HIV-positive individuals were offered immediate ART irrespective of CD4 count [24], all the other studies were conducted in the context of old ART eligibility criteria, that is CD4 counts of ≤ 200 cells/ μ l, ≤ 250 cells/ μ l, ≤ 350 cells/ μ l or ≤ 500 cells/ μ l and by implication, prolonged pre-ART care periods. Therefore, the extent to which the findings of this review are relevant to settings in which the new WHO recommendation of immediate ART initiation irrespective of CD4 count [33] has been adopted is not clear. A future review of the evidence on linkage to care after HBHCT under the new treatment guidelines will be needed.

In conclusion, we found that only few published studies investigated linkage to HIV care among adults newly diagnosed with HIV through HBHCT in SSA. In general, HBHCT without additional intervention strategies to increase service uptake achieved inadequate linkage, while HBHCT combined with some kind of additional strategy seemed to achieve higher linkage. There is a need to confirm the impact of the most promising linkage strategies through randomised controlled trials before they can be recommended for large scale adoption. Moreover, it will be important to demonstrate the effectiveness of linkage strategies under the new WHO treat-all policy.

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E. Ruzagira *et al.* **Linkage to HIV counselling and testing in SSA**

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Appendix: Working Group on Linkage to HIV Care

London School of Hygiene & Tropical Medicine, London, UK (Eugene Ruzagira, Heiner Grosskurth, Kathy Baisley, Alison Wringe); MRC/UVRI Uganda Research Unit on AIDS, Entebbe, Uganda (Eugene Ruzagira, Anatoli Kamali); International AIDS Vaccine Initiative, New York, USA (Anatoli Kamali); ICAP at Columbia University, New York, USA (Samuel Biraro); International Clinical Research Center, Department of Global Health, University of Washington, Seattle, USA (Connie Celum, Ruanne V. Barnabas); Human Sciences Research Council, Durban, KwaZulu-Natal, South Africa (Heidi van Rooyen), Department of Health Services, Policy & Practice, Brown University, Providence, USA (Becky L. Genberg), University of Toronto, Dalla Lana School of Public Health, Toronto, Canada (Paula Braitstein); College of Health Sciences, School of Public Health, Moi University, Eldoret, Kenya (Samson Ndege), Rakai Health Sciences Program, Kalisizo, Rakai, Uganda (Gertrude Nakigizi); Médecins Sans Frontières, Geneva, Switzerland & CIBER de Epidemiología y Salud Pública, Universidad Miguel Hernández, Alicante, Spain (Lucy A. Parker); Clinical Research Unit, Medical Services and Diagnostic, Swiss Tropical and Public Health Institute University of Basel, Basel, Switzerland (Niklaus D. Labhardt); Population Reference Bureau, Washington, USA (Reshma Naik); Population, Family and Reproductive Health Department, Johns Hopkins School of Public Health, Baltimore, USA (Stan Becker); Johns Hopkins University School of Medicine, Baltimore, USA (Christopher J. Hoffmann); Africa Centre for Population Health, University of KwaZulu-Natal, Durban, South Africa (Collins C. Iwuji, Joseph Larmarange).

Corresponding Author Eugene Ruzagira, MRC/UVRI Uganda Research Unit on AIDS, P.O Box 49, Entebbe, Uganda.
E-mail: eugene.ruzagira@mrcuganda.org, eruzagira@yahoo.com