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Effectiveness of linkage to care interventions following HIV Self-testing: a systematic review and meta-analysis

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Effectiveness of linkage to care interventions following HIV Self-testing: a systematic review and meta-analysis

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Abstract

Introduction: Early identification of persons living with HIV (PLWH) is crucial to institute timely treatment to prevent HIV-related morbidity and mortality. The convenience, flexibility, and confidentiality of HIV self-testing enhance the acceptability of HIV testing and early detection of PLWH. However, persons who test positive after a self-test are more likely to present late for treatment. This review seeks to evaluate the effectiveness of interventions to improve linkage to care after self-testing.

Methods and analysis: We will search PubMed, Embase, Web of Science, Cochrane Library, PsychInfo, Global Health Library, ClinicalTrials.gov, Current Controlled Trials for all randomized and non-randomized studies published from 1 January 2000 to 31 June 2021 without language restriction. Two review authors will independently screen and select articles (based on the eligibility criteria for this review), extract data, and assess the risk of bias in included studies. Study-specific estimates will be converted to log risk ratios and weighted by the inverse of the variance of the log risk ratio before pooling into a fixed-effect model. The Cochrane's Q χ^2 test and the I^2 statistic will be used to assess and quantify heterogeneity in the included studies, respectively. The Egger's test and funnel plots will be used to assess publication bias. Sensitivity analysis will be conducted using leave-one-out to assess the impact of outliers on the overall summary intervention effect.

Ethics and dissemination

No ethical clearance is need for the current study as it will be based on already published articles. We will publish the findings of this study in international peer-reviewed journals and present them in conferences.

Strengths and limitations of this study

1. This study will permit a systematic assessment of interventions to improve linkage to HIV care among HIV self-testers.
2. Combining studies in a meta-analysis increases the power of our study.
3. We anticipate heterogeneity in study design and participants characteristics in respect trials as a limitation to the study.

Background

The Human Immunodeficiency Virus (HIV) pandemic remains a significant public health concern [1]. In 2019, approximately 38 million people living with the virus worldwide, 70% (24.7 million) of whom resided in Sub-Saharan Africa (SSA) [2]. Globally, 20% of people living with HIV (PLWH) are unaware of their HIV infection status [3].

HIV self-testing is a strategy where people can take an HIV test and ascertain the results on their own, usually in their homes or other private locations [4]. HIV self-testing is essential in reaching PLWH with limited access to conventional health facility-based testing services and increases coverage of essential HIV services [5,6]. The convenience, flexibility, privacy and confidentiality offered by self-testing facilitates its acceptability among HIV infected individuals [7,8]. Various studies have documented a higher preference for self-testing among the general population in SSA [7,9, 10].

HIV status confirmation by health professionals after self-testing, antiretroviral therapy (ART), and retention in care (follow-up) are essential care interventions for PLWH [11]. Although ART coverage in SSA has increased significantly over the past two decades, about 10.3 million PLWH remain untreated with ART [12]. Even those who seek treatment usually do it too late [13 – 15]. Linking self-testing to care is vital in the fight against HIV and overall viral suppression among PLWH [11]. The linkage to care after self-testing for HIV constitutes an essential strategy of achieving the global Sustainable Development Goal (SDG) 3.3 target of ending the HIV/AIDS epidemic by the year 2030 [16]. In the pursuit of achieving the SDG target, governments have implemented various interventions in SSA to address the delay in linkage to care. These include non-cash financial incentives and transport reimbursement, health system interventions such as integration of HIV services into routine care, patient convenience and accessibility comprising home-based initiation of ART after HIV self-test, and behaviour interventions and peer support (i.e. assisted partner services, care facilitation, mobile phone appointment reminders, and health education) [11, 17–20].

Notwithstanding its proven importance in facilitating early initiation to ART, viral load suppression and better prognosis of HIV/AIDS, linkage to care continues to be problematic in SSA as approximately 54% of people who tested positive for HIV are not linked to ART [21,22]. Most

people got to know of their positive status after self-test also start ART very late and at advanced stages of infection [23, 24]. Delay in the linkage to care results in delayed ART initiation, quicker disease progression, and subsequently increased mortality [25, 26].

Evidence from a recent systematic review revealed that men, who are generally less likely to go in for an HIV test than women, are more likely to accept test for HIV using a self-test approach than traditional clinic-based approaches [27]. Key groups such as female sex workers and men who have sex with men (MSM) bear a high burden of HIV infection and face stigma in accessing health care services can benefit from HIV self-testing services [28, 29].

With increasing and almost conclusive evidence regarding the potential of self-testing approaches to increase the number of persons knowing the HIV status on time, the effectiveness of interventions intended to link these self-testers to care remain largely systematically undocumented. This systematic review and meta-analysis aims to evaluate the effectiveness of interventions to improve linkage to HIV care after self-testing. The findings could provide detailed scientific evidence on strategies needed to improve policy and practice regarding effective linkage of self-testing and comprehensive HIV care.

Objective

To evaluate the effectiveness of interventions to improve linkage to HIV care after self-testing.

Review question

What is the effectiveness of interventions to improve linkage to HIV care after self-testing among person ≥ 15 years old?

Methods

Criteria for considering studies into the review

Inclusion criteria

1. Interventional studies (randomized and non-randomized controlled trials) that evaluated the effectiveness of interventions to improve linkage to HIV care after self-testing for HIV
2. Age limit: We will consider studies done among participants of at least 15 years of age.

3. For duplicate studies, only those with the most recent findings or larger sample size will be considered.
4. Studies published from 1 January 2000 to 31 June 2021.

Exclusion criteria

1. Editorials, commentaries, review articles, and case series.
2. Studies with insufficient data to summarise data on effectiveness of interventions to improve linkage to HIV care after self-testing.

Information sources

Search strategy for identifying relevant studies

We will search PubMed, Embase, Web of Science, Cochrane Library, PsychInfo, Global Health Library, ClinicalTrials.gov, and Current Controlled Trials for relevant studies published from 1 January 2000 to 31 June 2021. We will use key text and medical subject headings that capture keywords like HIV self-testing, HIV home testing, and linkage or enrolment to HIV care. We will apply a validated geographic search filter for Africa to improve the precision of our search [30]. Table 1 shows the search strategy for Medline, which will be adapted to search other databases. We will supplement database searches by searching ResearchGate and Google Scholar for grey literature. The reference list of any available relevant review or eligible full-text articles will be perused to identify studies missed during our search.

Study records

Data management

Citations retrieved from database searches will be imported into EndNote X9 to remove duplicate citations. We will then export the unduplicated citations (containing the article title and abstract) to Rayyan QCRI for screening [31]. Data from eligible full-text articles will be extracted using a secure pre-designed Google Form. Using a web-based electronic questionnaire facilitates monitoring of the data extraction process in real-time, thereby improving the quality of the data extraction process.

Study screening

Two review authors will independently screen citations retrieved from database searches based on title and abstract. The full-text articles of potentially eligible citations will be downloaded, and two authors will then assess them for final inclusion in the review (based on the eligibility criteria for this review). Disagreements between review authors during the screening stage will be resolved through discussions. A third author will only be called upon for arbitration if disagreements between authors persist.

Data item and extraction

We will extract data on the surname of the first author, article publication year, country where the study was conducted, WHO region of the country of study, female proportion, mean or median age in years, trial design, characteristics of study participants, description of intervention and comparison sample size, effect size (e.g., odds ratio or risk ratio), and standard error (or confidence intervals).

Where possible, data from multinational studies will be disaggregated and presented according to the country in which the study was conducted.

Assessment of methodological quality and risk of bias

The updated Cochrane's risk of bias assessment tool for randomized controlled trial – RoB 2.0 will be used to assess the risk of bias of the included study [32]. This tool was selected as it is more robust, easy to understand, and the recent version was developed to account for potential issues with lack of blinding in these trials. The tool evaluates five major compartments of the original study that includes bias due to: (1) randomization, (2) deviation from the intended intervention, (3) missing outcome data, (4) measurement of the outcome, and (5) selection of the reported results. Each major compartment is assessed using questions with five possible responses: Not Applicable, Yes, Probably Yes, No, Probably No, and No Information. An algorithm that comes with the toolset will be used to guide the author's decision in rating each major section as either low risk of bias, some concerns on the methods, or high risk of bias. A study will be qualified as

having a low risk of bias if all the five major compartments were rated as having low risk of bias. If the study was rated to have some concerns in one more domain with no domain rated as high risk, the study will be rated as having "some concerns". A study will be judged to be at high risk of bias if: (1) at least one domain is assessed to be at high risk of bias or (2) there are multiple domains with some concerns such that it significantly reduces the confidence in the results reported by the authors.

Data synthesis and analysis

The '*metafor'* package of the R programming software will be used for data analysis and visualization. All study-specific effect sizes will be converted to log risk ratios (RR), weighted using the inverse of the variance of the logRR before pooling using a fixed-effect meta-analysis model.

The Cochrane's Q χ^2 test and the I^2 statistic will be used to assess and quantify heterogeneity in the included studies, respectively [33]. I^2 values of 25%, 50%, and 75% will constitute low, moderate, and substantial heterogeneity, respectively [34]. Depending on the number of studies available for meta-analysis, substantial heterogeneity between studies will be investigated through meta-regression or subgroup analysis using the following variables: trial design, female proportion, WHO region, and median age of study population. Egger's test and the symmetry of funnels plots will be used to assess for publication bias [35]. A p-value < 0.1 on Egger's test will be considered statistically significant.

We will conduct a leave-one-out sensitivity analysis to identify the effect of outliers on the overall summary estimate.

Presentation and reporting of results

This review will be published following the PRISMA guidelines. The process of study selection will be displayed with the help of a flow chart. A summary of the included trials, average treatment effect, and risk of bias will be presented using tables, forest plots, and funnel plots, respectively.

Protocol amendment

We do not intend to modify the current protocol. Any modification of the protocol will be clearly described in the final report.

Patient and public involvement

Patients and/or the public were not directly involved in this study.

Ethics and dissemination

No ethical clearance is need for the current study as it will be based on already published articles. We will publish the findings of this study in international peer-reviewed journals and present them in conferences.

Declarations

Contributors: LEB conceived the study. LEB and VNA: designed the study and drafted the protocol. HA, RKD, PM: critically revised the protocol for methodological and intellectual content. All authors read and approved the final version of the manuscript prior to submission. VNA is the guarantor of the review.

Competing interest: None.

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Data sharing statement: No additional data are available.

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Table 1: Search strategy for Medline

SN	Search Items	Hits
1.	HIV/	
2.	HIV-1/	
3.	HIV-2/	
4.	HIV infection/	
5.	(HIV or HIV infect* or HIV patient or HIV 1 or HIV 2 or HIV 1 infect* or HIV 2 infect* or human immunodeficiency virus or human immunodeficiency virus 1 or human immunodeficiency virus 1 infect* or human immunodeficiency virus 2 or human immunodeficiency virus 2 infect* or human immunodeficiency virus infect*).ab,ti.	
6.	Acquired Immunodeficiency Syndrome/	
7.	(Acquired immune deficiency syndrome or acquired immunodeficiency syndrome or AIDS).ab,ti.	
8.	1 or 2 or 3 or 4 or 5 or 6 or 7	
9.	"Referral and Consultation"/	
10.	Health Services Accessibility/	
11.	"Quality of Health Care"/	
12.	Quality Indicators, Health Care/	
13.	"Standard of Care"/	
14.	(care adj3 (link* or enrol* or consult* or access* or engag* or connect* or enter or enters or entered or entering or entry or entrance or initiat* or integrat* or attend* or quality or diagnosis)).ab,ti.	
15.	"Continuity of Patient Care"/	
16.	(care adj3 (continuum or cascade*)).ab,ti.	
17.	"treatment cascade*".ab,ti.	
18.	9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17	
19.	8 AND 18	
20.	Search HIV test* OR home test* OR self-test* OR “HIV self-test*” OR “unsupervised self-testing” OR “supervised self-test*”	
21.	19 AND 20	
22.	Date limit: 1 January 2000 to 31 June 2021, with no language restrictions	

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol

Section and topic	Item No	Checklist item	Page #
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	NA
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	NA
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	9
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	9
Support:			
Sources	5a	Indicate sources of financial or other support for the review	9
Sponsor	5b	Provide name for the review funder and/or sponsor	NA
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	NA
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	4-5
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	5
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	5-6
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	6
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	6, Table 1
Study records:			
Data	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	6

management			
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	6-7
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	7
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	7
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	7
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	7-8
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	8
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	8
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	8
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	8
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	8
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	NA

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Abstract

Introduction: Early identification of persons living with HIV (PLWH) is crucial to institute timely treatment to prevent HIV-related morbidity and mortality. The convenience, flexibility, and confidentiality of HIV self-testing enhance the acceptability of HIV testing and early detection of PLWH. However, persons who test positive after a self-test are more likely to present late for treatment. This review seeks to evaluate the effectiveness of interventions to improve linkage to care and prevention after self-testing.

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2. Combining studies in a meta-analysis increases the power of our study.
3. We anticipate heterogeneity in study design and participants characteristics in respect trials as a limitation to the study.

Background

The Human Immunodeficiency Virus (HIV) pandemic is still a significant public health concern [1]. In 2019, approximately 38 million people living with the virus worldwide, 70% (24.7 million) of whom resided in Sub-Saharan Africa (SSA) [2]. Globally, 20% of people living with HIV (PLWH) are unaware of their HIV infection status [3]. HIV self-testing is a strategy where people can take an HIV test and ascertain the results on their own, usually in their homes or other private locations [4]. HIV self-testing is essential in reaching PLWH with limited access to conventional health facility-based testing services and increases coverage of essential HIV services [5,6]. This far more important for hard-to-reach groups like men, men who have sex with men (MSM), and injecting drug users [7-9]. The convenience, flexibility, privacy and confidentiality offered by self-testing facilitates its acceptability among HIV infected individuals [7,8]. Studies have documented a higher preference for, and effectiveness of self-testing among the general population in SSA [7,9-11].

Although ART coverage in SSA has increased significantly over the past two decades, about 10.3 million PLWH remain untreated with ART [12]. Even those who seek treatment usually do it too late [13 – 15]. Linking self-testers to care and prevention are vital in the fight against HIV. [11]. Indeed, the linkage to care and prevention after self-testing for HIV constitutes an essential strategy of achieving the global Sustainable Development Goal (SDG) 3.3 target of ending the HIV/AIDS epidemic by the year 2030 [16]. In the pursuit of achieving the SDG target, governments have implemented various interventions in SSA to address the delay in linkage to care. These include non-cash financial incentives and transport reimbursement, health system interventions such as integration of HIV services into routine care, patient convenience and accessibility comprising home-based initiation of ART after HIV self-test, and behaviour interventions and peer support (i.e., assisted partner services, care facilitation, mobile phone appointment reminders, and health education) [11, 17–26].

Evidence from a recent systematic review revealed that men, who are less likely to go in for an HIV test than women, are more likely to accept test for HIV using a self-test approach than traditional clinic-based approaches [27]. Key groups such as female sex workers and men who have sex with men (MSM) bear a high burden of HIV infection and face stigma in accessing health care services can benefit from HIV self-testing services [28, 29].

With increasing and almost conclusive evidence regarding the potential of self-testing approaches to increase the number of persons knowing the HIV status on time, the effectiveness of interventions intended to link these self-testers to care remain systematically undocumented. This systematic review and meta-analysis aim to evaluate the effectiveness of interventions to improve linkage to HIV care and prevention after self-testing. The findings could provide detailed scientific evidence on strategies needed to improve policy and practice regarding effective linkage of self-testing and comprehensive HIV care.

Objective

To evaluate the effectiveness of interventions to improve linkage to HIV care and prevention after self-testing compared to standard of care.

Methods

Criteria for considering studies into the review

Inclusion criteria

1. Interventional studies (randomized and non-randomized controlled trials) that evaluated the effectiveness of interventions to improve linkage to HIV care or prevention after self-testing for HIV.
2. Age limit: We will consider studies done among participants of at least 15 years of age.
3. The primary outcomes will be percentage of persons linked to HIV care after testing positive, and the percentage of persons that receive HIV prevention services (most especially, pre-exposure prophylaxis, PrEP) after testing negative.
4. For duplicate studies, only those with the most recent findings or larger sample size will be considered.
5. Studies published from 1 January 2010 to 30 February 2022.

Exclusion criteria

1. Editorials, commentaries, review articles, and case series.
2. Studies with insufficient data to summarise data on effectiveness of interventions to improve linkage to HIV care after self-testing.

Information sources

Search strategy for identifying relevant studies

We will search PubMed, Embase, Web of Science, Cochrane Library, PsychInfo, Global Health Library, ClinicalTrials.gov, and Current Controlled Trials for relevant studies published from 1 January 2000 to 31 July 2022. We will use key text and medical subject headings that capture keywords like HIV self-testing, HIV home testing, and linkage or enrolment to HIV care (Supplementary Table S1).

We will supplement database searches by searching ResearchGate and Google Scholar for grey literature. The reference list of any available relevant review or eligible full-text articles will be perused to identify studies missed during our search.

Study records

Data management

Citations retrieved from database searches will be imported into EndNote X9 to remove duplicate citations. We will then export the unduplicated citations (containing the article title and abstract) to Rayyan QCRI for screening [30]. Data from eligible full-text articles will be extracted using a secure pre-designed Google Form. Using a web-based electronic questionnaire facilitates monitoring of the data extraction process in real-time, thereby improving the quality of the data extraction process.

Study screening

Two review authors will independently screen citations retrieved from database searches based on title and abstract. The full-text articles of potentially eligible citations will be downloaded, and two authors will then assess them for final inclusion in the review (based on the eligibility criteria for this review). Disagreements between review authors during the screening stage will be resolved through discussions. A third author will only be called upon for arbitration if disagreements between authors persist.

Data item and extraction

We will extract data on the surname of the first author, article publication year, country where the

study was conducted, WHO region of the country of study, female proportion, mean or median age in years, trial design, characteristics of study participants, description of intervention and comparison, and sample size. To assess effectiveness of interventions to linkage to HIV care among self-testers, we will extract data on the number of persons tested HIV positive following (i) HIV self-testing and were linked to HIV care; (ii) HIV self-testing but were not linked to HIV care; (iii) a controlled testing approach and were linked to HIV care; and (iv) a controlled testing approach and were not linked to HIV care. To assess effectiveness of interventions to linkage to PrEP, we will extract data on the number of persons who tested HIV negative following (i) HIV self-testing and were offered PrEP; (ii) HIV self-testing but were not were not offered PrEP; (iii) a controlled testing approach and were were offered PrEP; and (iv) a controlled testing approach and were not were offered PrEP. Where information on the stratum-specific frequency is not reported, we will extract information on the effect size (e.g., odds ratio or risk ratio) and their corresponding standard errors (or confidence intervals) comparing the primary outcomes in the intervention and control groups. Where possible, data from multinational studies will be disaggregated and presented according to the country in which the study was conducted.

Assessment of methodological quality and risk of bias

The updated Cochrane's risk of bias assessment tool for randomized controlled trial – RoB 2.0 will be used to assess the risk of bias of the included study [31]. This tool was selected because it is more robust, easy to understand, and the recent version was developed to account for potential issues with lack of blinding in these trials. The tool evaluates five major compartments of the original study that includes bias due to: (1) randomization, (2) deviation from the intended intervention, (3) missing outcome data, (4) measurement of the outcome, and (5) selection of the reported results. Each major compartment is assessed using questions with five possible responses: Not Applicable, Yes, Probably Yes, No, Probably No, and No Information. An algorithm that comes with the toolset will be used to guide the author's decision in rating each major section as either low risk of bias, some concerns on the methods, or high risk of bias. A study will be qualified as having a low risk of bias if all the five major compartments were rated as having low risk of

bias. If the study was rated to have some concerns in one more domain with no domain rated as high risk, the study will be rated as having "some concerns". A study will be judged to be at high risk of bias if: (1) at least one domain is assessed to be at high risk of bias or (2) there are multiple domains with some concerns such that it significantly reduces the confidence in the results reported by the authors.

Data synthesis and analysis

The '*metafor'* package of the R programming software will be used for data analysis and visualization. All study-specific effect sizes will be converted to log risk ratios (RR), weighted using the inverse of the variance of the logRR before pooling using a fixed-effect meta-analysis model.

The Cochrane's Q χ^2 test and the I^2 statistic will be used to assess and quantify heterogeneity in the included studies, respectively [32]. I^2 values of 25%, 50%, and 75% will constitute low, moderate, and substantial heterogeneity, respectively [33]. Depending on the number of studies available for meta-analysis, substantial heterogeneity between studies will be investigated through meta-regression or subgroup analysis using the following variables: trial design, female proportion, WHO region, and median age of study population. Egger's test and the symmetry of funnels plots will be used to assess for publication bias [34]. A p-value < 0.1 on Egger's test will be considered statistically significant.

We will conduct a leave-one-out sensitivity analysis to identify the effect of outliers on the overall summary estimate.

Presentation and reporting of results

This review will be published following the PRISMA guidelines. The process of study selection will be displayed with the help of a flow chart. A summary of the included trials, average treatment effect, and risk of bias will be presented using tables, forest plots, and funnel plots, respectively.

Protocol amendment

We do not intend to modify the current protocol. Any modification of the protocol will be clearly described in the final report.

Patient and public involvement

Patients and/or the public were not directly involved in this study.

Ethics and dissemination

No ethical clearance is need for the current study as it will be based on already published articles. We will publish the findings of this study in international peer-reviewed journals and present them in conferences.

Discussion

HIV self-testing is a promising approach, most especially in putting hard to reach populations on treatment on time. This is fundamental in breaking the transmission chain, as well as allowing persons to live longer. The gains expected from HIV self-testing will not be achieved if these persons fail either to link to care or to prevention. Understanding the effectiveness of these interventions, as well as the reported barriers and facilitators to linkage to care and prevention, will allow for health policies that will improve testing and linkage to care rates. The focus in the recent literature has been on linking persons who self-test positive to care. This review has an added value, as it seeks to identify interventions that link persons who test negative to prevention interventions, and most especially pre-exposure prophylaxis (PrEP) and other behavioural change interventions.

Declarations

Contributors: LEB conceived the study. LEB and VNA: designed the study and drafted the protocol. HA, RKD, PM: critically revised the protocol for methodological and intellectual content. All authors read and approved the final version of the manuscript prior to submission. VNA is the guarantor of the review.

Competing interest: None.

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Data sharing statement: No additional data are available.

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Table S1: Search strategy for MEDLINE via OVID SP®

SN	Search terms
1.	exp HIV/
2.	HIV?1.mp.
3.	Exp HIV?2.mp.
4.	exp HIV infection$/
5.	human immun?deficiency virus.mp.
6.	exp Acquired Immunodeficiency Syndrome/ or AIDS.mp.
7.	Or/1-6
8.	self?test$.mp.
9.	test$ adj3 and (home* or remote or personal).mp.
10.	(option$ adj1 test$).mp.
11.	(alternative adj3 test$).mp.
12.	(dried blood spot adj3 (home* or remote or personal or self*)).ti,ab.
13.	((home$ or self$ or mail$) adj3 (collection$ or sampl$ or test$ or kit$)).ti,ab.
14.	Or/8-13
15.	"Referral and Consultation"/
16.	Health Services Accessibility/
17.	((continuity or quality or standard or link$ or cascade) adj3 care)).mp.
18.	Or/15-17
19.	exp clinical trial/ or (trial or randomized or randomised).ti. or randomly.ab. or randomi?ed.ab. or placebo.ab. or controlled clinical trial.pt.
20.	7 and 14 and 18 and 19
21	exp animals/ not humans.sh.
22.	20 not 21
23.	exp case reports/ or Cohort Studies/ or cohort$.mp. or cross-sectional stud$.mp. or cross?sectional stud$.mp. or case-control stud$.mp. or case control stud$.mp.
24.	22 not 23
25.	(exp adolescence/ or exp adolescent/ or exp child/ or exp childhood disease/ or exp infant disease/ or (adolescen* or babies or baby or boy? or boyfriend or boyhood or child or child* or child*3 or children* or girl? or infant* or juvenil* or juvenile* or kid? or minors or minors* or neonat* or neonat* or newborn* or new-born* or paediatric* or peadiatric* or pediatric* or perinat* or preschool* or puber* or pubescen* or school or school child* or school* or schoolchild* or schoolchild* or teen* or toddler? or underage? or under-age? or youth*).ti,ab,kf,hw.) not ((exp child/ or exp infant/ or exp adolescent/) and exp adult/)
26.	24 not 25
27.	limit 26 to (english language or french language and yr="2010 -Current")

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol

Section and topic	Item No	Checklist item	Page #
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	NA
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	NA
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	9
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	9
Support:			
Sources	5a	Indicate sources of financial or other support for the review	9
Sponsor	5b	Provide name for the review funder and/or sponsor	NA
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	NA
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	4-5
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	5
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	5-6
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	6
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	6, Table 1
Study records:			
Data	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	6

management			
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	6-7
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	7
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	7
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	7
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	7-8
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	8
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	8
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	8
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	8
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	8
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	NA

BMJ Open

Effectiveness of linkage to care and prevention interventions following HIV Self-testing: a global systematic review and meta-analysis protocol

Journal:	*BMJ Open*
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Primary Subject Heading:	HIV/AIDS
Secondary Subject Heading:	Epidemiology
Keywords:	HIV & AIDS < INFECTIOUS DISEASES, EPIDEMIOLOGY, STATISTICS & RESEARCH METHODS

Effectiveness of linkage to care and prevention interventions following HIV Self-testing: a global systematic review and meta-analysis protocol

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Abstract

Introduction: Early identification of persons living with HIV (PLWH) is crucial to institute timely treatment to prevent HIV-related morbidity and mortality. The convenience, flexibility, and confidentiality of HIV self-testing enhance the acceptability of HIV testing and early detection of PLWH. However, persons who test positive after a self-test are more likely to present late for treatment. This review seeks to evaluate the effectiveness of interventions to improve linkage to care and prevention after self-testing.

Methods and analysis: We will search PubMed, Embase, Web of Science, Cochrane Library, PsychInfo, Global Health Library, ClinicalTrials.gov, Current Controlled Trials for all randomized and non-randomized studies published from 1 January 2010 to 31 July 2022 without language restriction. Two review authors will independently screen and select articles (based on the eligibility criteria for this review), extract data, and assess the risk of bias in included studies. Study-specific estimates will be converted to log risk ratios and weighted by the inverse of the variance of the log risk ratio before pooling into a fixed-effect model. The Cochrane's Q χ^2 test and the I^2 statistic will be used to assess and quantify heterogeneity in the included studies, respectively. The Egger's test and funnel plots will be used to assess publication bias. Sensitivity analysis will be conducted using leave-one-out analysis to assess the impact of outliers on the overall summary intervention effect.

Ethics and dissemination

No ethical clearance is need for the current study as it will be based on already published articles. We will publish the findings of this study in international peer-reviewed journals and present them at conferences.

Strengths and limitations of this study

1. This study will permit a systematic assessment of interventions to improve linkage to HIV care and prevention interventions among HIV self-testers.
2. Combining studies in a meta-analysis increases the power of our study, preventing chance findings and type II error.
3. We anticipate heterogeneity in study design and participants characteristics in respect trials as a limitation to the study.

Background

The Human Immunodeficiency Virus (HIV) pandemic is still a significant public health concern [1]. In 2019, approximately 38 million people were living with the virus worldwide, 70% (24.7 million) of whom resided in Sub-Saharan Africa (SSA) [2]. Globally, 20% of people living with HIV (PLWH) are unaware of their status [3]. HIV self-testing is a strategy where people can take an HIV test and ascertain the results on their own, usually in their homes or other private locations [4]. HIV self-testing is essential in reaching PLWH with limited access to conventional health facility-based testing services and increases coverage of essential HIV services [5,6]. This is particularly important for hard-to-reach groups like men, men who have sex with men (MSM), and injecting drug users [7-9]. The convenience, flexibility, privacy and confidentiality offered by self-testing facilitates its acceptability among HIV infected individuals [7,8]. Studies have documented a higher preference for, and effectiveness of, self-testing among the general population in SSA [7,9-11].

Although ART coverage in SSA has increased significantly over the past two decades, about 10.3 million PLWH remain untreated with ART [12]. Even those who seek treatment usually do it too late [13 – 15]. Linking self-testers to care and prevention are vital in the fight against HIV [11]. Indeed, the linkage to care and prevention after self-testing for HIV constitutes an essential strategy of achieving the global Sustainable Development Goal (SDG) 3.3 target of ending the HIV/AIDS epidemic by the year 2030 [16]. In the pursuit of achieving the SDG target, governments have implemented various interventions in SSA to address the delay in linkage to care. These include non-cash financial incentives and transport reimbursement, health system interventions such as integration of HIV services into routine care, patient convenience and accessibility comprising home-based initiation of ART after HIV self-test, and behavioral interventions and peer support (i.e., assisted partner services, care facilitation, mobile phone appointment reminders, and health education) [11, 17–26].

Evidence from a recent systematic review revealed that men, who are less likely to go in for an HIV test than women, are more likely to accept test for HIV using a self-test approach than traditional clinic-based approaches [27]. Key groups such as female sex workers and MSM who bear a high burden of HIV infection and face stigma in accessing health care services can benefit from HIV self-testing services [28, 29].

With increasing and almost conclusive evidence regarding the potential of self-testing approaches to increase the timely awareness of HIV status, the effectiveness of interventions to improve linkage self-testers to care remain systematically undocumented. This systematic review and meta-analysis aim to evaluate the effectiveness of interventions to improve linkage to HIV care and prevention after self-testing. The findings could provide detailed scientific evidence on strategies needed to improve policy and practice regarding effective linkage of self-testing and comprehensive HIV care.

Objective

To evaluate the effectiveness of interventions to improve linkage to HIV care and prevention after self-testing compared to standard of care.

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Criteria for considering studies into the review

Inclusion criteria

1. Interventional studies (randomized and non-randomized controlled trials) that evaluated the effectiveness of interventions to improve linkage to HIV care or prevention after self-testing for HIV.
2. Age limit: We will consider studies done among participants of at least 15 years of age. We chose 15 years as threshold because most studies on HIV include individuals within the sexual reproductive age group (i.e., 15-49 years).
3. The primary outcomes will be percentage of persons linked to HIV care after testing positive, and the percentage of persons that receive HIV prevention services (most especially, pre-exposure prophylaxis, PrEP) after testing negative.
4. For duplicate studies, only those with the most recent findings or larger sample size will be considered.
5. Studies published from 1 January 2010 to 31 July 2022.

Exclusion criteria

1. Editorials, commentaries, review articles, and case series.

2. Studies with insufficient information to summarize data on effectiveness of interventions to improve linkage to HIV care after self-testing.

Information sources

Search strategy for identifying relevant studies

We will search PubMed, Embase, Web of Science, Cochrane Library, PsychInfo, Global Health Library, ClinicalTrials.gov, and Current Controlled Trials for relevant studies published from 1 January 2010 to 31 July 2022. We will use key text and medical subject headings that capture keywords like HIV self-testing, HIV home testing, and linkage or enrolment to HIV care (Supplementary Table S1-S8).

We will supplement database searches by searching ResearchGate and Google Scholar for grey literature. The reference list of any available relevant review or eligible full-text articles will be perused to identify studies missed during our search.

Study records

Data management

Citations retrieved from database searches will be imported into EndNote X9 to remove duplicate citations. We will then export the unduplicated citations (containing the article title and abstract) to Rayyan QCRI for screening [30]. Data from eligible full-text articles will be extracted using a secure pre-designed Google Form. Using a web-based electronic questionnaire facilitates monitoring of the data extraction process in real-time, thereby improving the quality of the data extraction process.

Study screening

Two review authors will independently screen citations retrieved from database searches based on title and abstract. The full-text articles of potentially eligible citations will be downloaded, and two authors will then assess them for final inclusion in the review (based on the eligibility criteria for this review). Disagreements between review authors during the screening stage will be resolved through discussions. A third author will only be called upon for arbitration if disagreements between authors persist.

Data item and extraction

We will extract data on the surname of the first author, article publication year, country where the study was conducted, WHO region of the country of study, female proportion, mean or median age in years, trial design, characteristics of study participants, description of intervention and comparison, and sample size. To assess effectiveness of interventions to linkage to HIV care among self-testers, we will extract data on the number of persons tested HIV positive following (i) HIV self-testing and were linked to HIV care; (ii) HIV self-testing but were not linked to HIV care; (iii) a controlled testing approach and were linked to HIV care; and (iv) a controlled testing approach and were not linked to HIV care.

To assess effectiveness of interventions to linkage to PrEP, we will extract data on the number of persons who tested HIV negative following (i) HIV self-testing and were offered PrEP; (ii) HIV self-testing but were not offered PrEP; (iii) a controlled testing approach and were offered PrEP; and (iv) a controlled testing approach and were not offered PrEP. Where information on the stratum-specific frequency is not reported, we will extract information on the effect size (e.g., odds ratio or risk ratio) and their corresponding standard errors (or confidence intervals) comparing the primary outcomes in the intervention and control groups. Where possible, data from multinational studies will be disaggregated and presented according to the country in which the study was conducted.

Assessment of methodological quality and risk of bias

The updated Cochrane's risk of bias assessment tool for randomized controlled trial – RoB 2.0 will be used to assess the risk of bias of the included study [31]. This tool was selected because it is more robust, easy to understand, and the recent version was developed to account for potential issues with lack of blinding in these trials. The tool evaluates five major compartments of the original study that includes bias due to: (1) randomization, (2) deviation from the intended intervention, (3) missing outcome data, (4) measurement of the outcome, and (5) selection of the reported results. Each major compartment is assessed using questions with five possible responses:

Not Applicable, Yes, Probably Yes, No, Probably No, and No Information. An algorithm that comes with the toolset will be used to guide the author's decision in rating each major section as either low risk of bias, some concerns on the methods, or high risk of bias. A study will be qualified as having a low risk of bias if all the five major compartments were rated as having low risk of bias. If the study was rated to have some concerns in one or more domain, with no domain rated as high risk, the study will be rated as having "some concerns". A study will be judged to be at high risk of bias if: (1) at least one domain is assessed to be at high risk of bias or (2) there are multiple domains with some concerns such that it significantly reduces the confidence in the results reported by the authors.

Data synthesis and analysis

The '*metafor'* package of the R programming software will be used for data analysis and visualization. All study-specific effect sizes will be converted to log risk ratios (RR), weighted using the inverse of the variance of the logRR before pooling using a fixed-effect meta-analysis model.

The Cochrane's Q χ^2 test and the I^2 statistic will be used to assess and quantify heterogeneity in the included studies, respectively [32]. I^2 values of 25%, 50%, and 75% will constitute low, moderate, and substantial degree of heterogeneity, respectively [33]. Depending on the number of studies available for meta-analysis, substantial heterogeneity between studies will be investigated through meta-regression or subgroup analysis using the following variables: trial design, female proportion, WHO region, and median age of study population. Egger's test and the symmetry of funnel plots will be used to assess for publication bias [34]. A p-value < 0.1 on Egger's test will be considered statistically significant.

We will conduct a leave-one-out sensitivity analysis to identify the effect of outliers on the overall summary estimate.

Presentation and reporting of results

This review will be published following the PRISMA guidelines. The process of study selection will be displayed with the help of a flow chart. A summary of the included trials, average treatment effect, and risk of bias will be presented using tables, forest plots, and funnel plots, respectively.

Protocol amendment

We do not intend to modify the current protocol. However, any modification of the protocol will be clearly described in the final report.

Patient and public involvement

Patients and/or the public were not directly involved in this study.

Ethics and dissemination

No ethical clearance is needed for the current study as it will be based on already published articles. We will publish the findings of this study in international peer-reviewed journals and present them in conferences.

Discussion

HIV self-testing is a promising approach, most especially in putting hard to reach populations on treatment on time. This is fundamental in breaking the transmission chain, and allowing persons to live longer. The gains expected from HIV self-testing will not be achieved if these persons fail either to link to care or to prevention. Understanding the effectiveness of these interventions, and the reported barriers and facilitators to linkage to care and prevention, will allow for health policies that will improve testing and linkage to care rates. The focus in the recent literature has been on linking persons who self-test positive to care. This review has an added value, as it seeks to identify interventions that link persons who test negative to prevention interventions, and most especially pre-exposure prophylaxis (PrEP) and other behavioral change interventions.

Declarations

Contributors: LEB conceived the study. LEB and VNA: designed the study and drafted the protocol. HA, RKD, PM: critically revised the protocol for methodological and intellectual

content. All authors read and approved the final version of the manuscript prior to submission. VNA is the guarantor of the review.

Competing interest: None.

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Data sharing statement: No additional data are available.

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Table S1: Search strategy for MEDLINE via OVID SP®

SN	Search terms
1.	exp HIV/
2.	HIV?1.mp.
3.	Exp HIV?2.mp.
4.	exp HIV infection$/
5.	human immun?deficiency virus.mp.
6.	exp Acquired Immunodeficiency Syndrome/ or AIDS.mp.
7.	Or/1-6
8.	self?test$.mp.
9.	test$ adj3 and (home* or remote or personal).mp.
10.	(option$ adj1 test$).mp.
11.	(alternative adj3 test$).mp.
12.	(dried blood spot adj3 (home* or remote or personal or self*)).ti,ab.
13.	((home$ or self$ or mail$) adj3 (collection$ or sampl$ or test$ or kit$)).ti,ab.
14.	Or/8-13
15.	"Referral and Consultation"/
16.	Health Services Accessibility/
17.	((continuity or quality or standard or link$ or cascade) adj3 care)).mp.
18.	Or/15-17
19.	exp clinical trial/ or (trial or randomized or randomised).ti. or randomly.ab. or randomi?ed.ab. or placebo.ab. or controlled clinical trial.pt.
20.	7 and 14 and 18 and 19
21	exp animals/ not humans.sh.
22.	20 not 21
23.	exp case reports/ or Cohort Studies/ or cohort$.mp. or cross-sectional stud$.mp. or cross?sectional stud$.mp. or case-control stud$.mp. or case control stud$.mp.
24.	22 not 23
25.	(exp adolescence/ or exp adolescent/ or exp child/ or exp childhood disease/ or exp infant disease/ or (adolescen* or babies or baby or boy? or boyfriend or boyhood or child or child* or child*3 or children* or girl? or infant* or juvenil* or juvenile* or kid? or minors or minors* or neonat* or neonat* or newborn* or new-born* or paediatric* or peadiatric* or pediatric* or perinat* or preschool* or puber* or pubescen* or school or school child* or school* or schoolchild* or schoolchild* or teen* or toddler? or underage? or under-age? or youth*).ti,ab,kf,hw.) not ((exp child/ or exp infant/ or exp adolescent/) and exp adult/)
26.	24 not 25
27.	limit 26 to (english language or french language and yr="2010 -Current")

Table S2: Search strategy for EMBASE via OVID SP®

SN	Search terms
1.	exp HIV/
2.	HIV?1.mp.
3.	Exp HIV?2.mp.
4.	exp HIV infection$/
5.	human immun?deficiency virus.mp.
6.	exp Acquired Immunodeficiency Syndrome/ or AIDS.mp.
7.	Or/1-6
8.	self?test$.mp.
9.	test$ adj3 and (home* or remote or personal).mp.
10.	(option$ adj1 test$).mp.
11.	(alternative adj3 test$).mp.
12.	(dried blood spot adj3 (home* or remote or personal or self*)).ti,ab.
13.	((home$ or self$ or mail$) adj3 (collection$ or sampl$ or test$ or kit$)).ti,ab.
14.	Or/8-13
15.	"Referral and Consultation"/
16.	Health Services Accessibility/
17.	((continuity or quality or standard or link$ or cascade) adj3 care)).mp.
18.	Or/15-17
19.	exp clinical trial/ or (trial or randomized or randomised).ti. or randomly.ab. or randomi?ed.ab. or placebo.ab. or controlled clinical trial.pt.
20.	7 and 14 and 18 and 19
21	exp animals/ not humans.sh.
22.	20 not 21
23.	exp case reports/ or Cohort Studies/ or cohort$.mp. or cross-sectional stud$.mp. or cross?sectional stud$.mp. or case-control stud$.mp. or case control stud$.mp.
24.	22 not 23
25.	(exp adolescence/ or exp adolescent/ or exp child/ or exp childhood disease/ or exp infant disease/ or (adolescen* or babies or baby or boy? or boyfriend or boyhood or child or child* or child*3 or children* or girl? or infant* or juvenil* or juvenile* or kid? or minors or minors* or neonat* or neonat* or newborn* or new-born* or paediatric* or peadiatric* or pediatric* or perinat* or preschool* or puber* or pubescen* or school or school child* or school* or schoolchild* or schoolchild* or teen* or toddler? or underage? or under-age? or youth*).ti,ab,kf,hw.) not ((exp child/ or exp infant/ or exp adolescent/) and exp adult/)
26.	24 not 25
27.	limit 26 to (english language or french language and yr="2010 -Current")

Table S3: Search strategy for Global Health Library via OVID SP®

SN	Search terms
1.	exp HIV/
2.	HIV?1.mp.
3.	Exp HIV?2.mp.
4.	exp HIV infection$/
5.	human immun?deficiency virus.mp.
6.	exp Acquired Immunodeficiency Syndrome/ or AIDS.mp.
7.	Or/1-6
8.	self?test$.mp.
9.	test$ adj3 and (home* or remote or personal).mp.
10.	(option$ adj1 test$).mp.
11.	(alternative adj3 test$).mp.
12.	(dried blood spot adj3 (home* or remote or personal or self*)).ti,ab.
13.	((home$ or self$ or mail$) adj3 (collection$ or sampl$ or test$ or kit$)).ti,ab.
14.	Or/8-13
15.	"Referral and Consultation"/
16.	Health Services Accessibility/
17.	((continuity or quality or standard or link$ or cascade) adj3 care)).mp.
18.	Or/15-17
19.	exp clinical trial/ or (trial or randomized or randomised).ti. or randomly.ab. or randomi?ed.ab. or placebo.ab. or controlled clinical trial.pt.
20.	7 and 14 and 18 and 19
21	exp animals/ not humans.sh.
22.	20 not 21
23.	exp case reports/ or Cohort Studies/ or cohort$.mp. or cross-sectional stud$.mp. or cross?sectional stud$.mp. or case-control stud$.mp. or case control stud$.mp.
24.	22 not 23
25.	(exp adolescence/ or exp adolescent/ or exp child/ or exp childhood disease/ or exp infant disease/ or (adolescen* or babies or baby or boy? or boyfriend or boyhood or child or child* or child*3 or children* or girl? or infant* or juvenil* or juvenile* or kid? or minors or minors* or neonat* or neonat* or newborn* or new-born* or paediatric* or peadiatric* or pediatric* or perinat* or preschool* or puber* or pubescen* or school or school child* or school* or schoolchild* or schoolchild* or teen* or toddler? or underage? or under-age? or youth*).ti,ab,kf,hw.) not ((exp child/ or exp infant/ or exp adolescent/) and exp adult/)
26.	24 not 25
27.	limit 26 to (english language or french language and yr="2010 -Current")

Table S4: Search strategy for PsychiInfo via OVID SP®

SN	Search terms
1.	exp HIV/
2.	HIV?1.mp.
3.	Exp HIV?2.mp.
4.	exp HIV infection$/
5.	human immun?deficiency virus.mp.
6.	exp Acquired Immunodeficiency Syndrome/ or AIDS.mp.
7.	Or/1-6
8.	self?test$.mp.
9.	test$ adj3 and (home* or remote or personal).mp.
10.	(option$ adj1 test$).mp.
11.	(alternative adj3 test$).mp.
12.	(dried blood spot adj3 (home* or remote or personal or self*)).ti,ab.
13.	((home$ or self$ or mail$) adj3 (collection$ or sampl$ or test$ or kit$)).ti,ab.
14.	Or/8-13
15.	"Referral and Consultation"/
16.	Health Services Accessibility/
17.	((continuity or quality or standard or link$ or cascade) adj3 care)).mp.
18.	Or/15-17
19.	exp clinical trial/ or (trial or randomized or randomised).ti. or randomly.ab. or randomi?ed.ab. or placebo.ab. or controlled clinical trial.pt.
20.	7 and 14 and 18 and 19
21	exp animals/ not humans.sh.
22.	20 not 21
23.	exp case reports/ or Cohort Studies/ or cohort$.mp. or cross-sectional stud$.mp. or cross?sectional stud$.mp. or case-control stud$.mp. or case control stud$.mp.
24.	22 not 23
25.	(exp adolescence/ or exp adolescent/ or exp child/ or exp childhood disease/ or exp infant disease/ or (adolescen* or babies or baby or boy? or boyfriend or boyhood or child or child* or child*3 or children* or girl? or infant* or juvenil* or juvenile* or kid? or minors or minors* or neonat* or neonat* or newborn* or new-born* or paediatric* or peadiatric* or pediatric* or perinat* or preschool* or puber* or pubescen* or school or school child* or school* or schoolchild* or schoolchild* or teen* or toddler? or underage? or under-age? or youth*).ti,ab,kf,hw.) not ((exp child/ or exp infant/ or exp adolescent/) and exp adult/)
26.	24 not 25
27.	limit 26 to (english language or french language and yr="2010 -Current")

Table S5: Search strategy for ClinicalTrial.gov

SN	Search terms
1.	Hiv or "human immunodeficiency virus" OR "Acquired Immunodeficiency Syndrome" OR AIDS
2.	"self test " OR "self-test" OR "home test" OR "remote test" OR "personal test"

Table S6: Search strategy for Current Controlled Trials

SN	Search terms
1.	Hiv or "human immunodeficiency virus" OR "Acquired Immunodeficiency Syndrome" OR AIDS
2.	"self test " OR "self-test" OR "home test" OR "remote test" OR "personal test"

Table S7: Search strategy for Cochrane Library

SN	Search terms
1.	HIV:tw
2.	("human immunodeficiency virus* " OR "human immuno deficiency virus* " OR "human immuno-deficiency virus* "):tw
3.	("acquired immune deficiency syndrome" OR "acquired immune-deficiency syndrome" OR "acquired immunodeficiency syndrome" OR AIDS):tw
4.	#1 OR #2 OR #3
5.	(self?test*):tw
6.	(test* and (home* or remote or personal)):tw
7.	(option* AND test*):tw
8.	(alternative AND test*):tw
9.	(dried blood spot AND (home* or remote or personal or self*)):ti,ab,kw
10.	((home* or self* or mail*) AND (collection* or sampl* or test* or kit*)):ti,ab,kw
11.	#5 OR #6 OR #7 OR #8 OR #9 OR #10
12.	("Referral and Consultation"):tw
13.	(Health Services Accessibility):tw
14.	((continuity or quality or standard or link* or cascade) AND care):tw
15.	#12 OR #13 OR #14
16.	(trial):pt
17.	#4 AND #11 AND #15 AND #16
18	Limit: Cochrane Library publication date from Jan 2010 to present

Table S8: Search strategy for Web of Science

SN	Search terms
1.	TS=(HIV)
2.	TS=("human immunodeficiency virus* " OR "human immuno deficiency virus* " OR "human immuno-deficiency virus* ")
3.	TS=("acquired immune deficiency syndrome" OR "acquired immune-deficiency syndrome" OR "acquired immunodeficiency syndrome" OR AIDS)
4.	#1 OR #2 OR #3
5.	TS=(self-test* OR self test*)
6.	TS=(test* and (home* or remote or personal))
7.	TS=(option* AND test*)
8.	TS=(alternative AND test*)
9.	TS=(dried blood spot AND (home* or remote or personal or self*))
10.	TS=((home* or self* or mail*) AND (collection* or sampl* or test* or kit*))
11.	#5 OR #6 OR #7 OR #8 OR #9 OR #10
12.	TS=("Referral and Consultation")
13.	TS=(Health Services Accessibility)
14.	TS=((continuity or quality or standard or link* or cascade) AND care)
15.	#12 OR #13 OR #14
16.	TS=(trial)
17.	#4 AND #11 AND #15 AND #16
18	Limit: publication date from Jan 2010 to present

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol

Section and topic	Item No	Checklist item	Page #
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	NA
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	NA
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	9
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	9
Support:			
Sources	5a	Indicate sources of financial or other support for the review	9
Sponsor	5b	Provide name for the review funder and/or sponsor	NA
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	NA
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	4-5
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	5
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	5-6
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	6
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	6, Table 1
Study records:			
Data	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	6

management			
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	6-7
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	7
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	7
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	7
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	7-8
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	8
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	8
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	8
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	8
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	8
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	NA