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Service delivery models for enhancing linkage to and retention in HIV care services for adolescent girls and young women and adolescent boys and young men: a protocol for an overview of systematic reviews

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ABSTRACT

Introduction Recent advances in the HIV care continuum have shown that an individual diagnosed with HIV should be initiated on antiretroviral therapy as soon as possible regardless of the CD4 count levels and retained in HIV care services. Studies have reported large losses in the HIV continuum of care, before and after the era of universal test and treat. Several systematic reviews have reported on the strategies for improving linkage to and retention in HIV treatment and care. The purpose of this overview of systematic reviews is to identify HIV care interventions or service delivery models (SDMs) and synthesise evidence on the effects of these to link adolescent girls and young women (AGYW) and adolescent boys and young men (ABYM) to care and retain them in care. We also aim to highlight gaps in the evidence on interventions and SDMs to improve linkage and retention in HIV care of AGYW and ABYM.

Methods and analysis An electronic search of four online databases: PubMed, Cochrane Database of Systematic Reviews, Cumulative Index to Nursing and Allied Health Literature (CINAHL) and Web of Science will be performed to identify systematic reviews on the effects of linkage to and retention in HIV care interventions or SDMs for AGYW aged 15–24 years and ABYM aged 15–35 years. Our findings on the effects of interventions and SDMs will be interpreted considering the intervention and or SDMs' effectiveness by the time period, setting and population of interest. Two or more authors will independently screen articles for inclusion using *a priori* criteria.

Ethics and dissemination Ethics approval is not required for this study as only published secondary data will be used. Our findings will be disseminated through peer-reviewed publication, conference abstracts and through presentations to stakeholders and other community fora. The findings from this overview of systematic reviews will inform mixed-methods operations research on HIV intervention programming and delivery of HIV care services for AGYW and ABYM in South Africa.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ In the times of universal test and treat, it is important to identify and consolidate the evidence-based interventions to improve linkage to and retention in HIV care services for young people.
⇒ We will use validated guidelines and assessment tools for search methods, data extraction, methodological quality and reporting of included studies.
⇒ We will include all systematic reviews of randomised controlled trials, non-randomised controlled trials, controlled before and after studies, interrupted time series studies and other mixed-methods studies.
⇒ We will include only published systematic reviews and reviews written in English, which is a potential limitation of this review.

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BACKGROUND

HIV/AIDS remains one of the most serious public health challenges, with 38.4 million people living with HIV (PLHIV) and 650 000 deaths attributed to AIDS globally in 2021.[1] There were over 28.7 million people accessing antiretroviral therapy (ART) in 2021, which is 75% of all PLHIV.[1] Advances in the HIV care continuum now recommend that an individual diagnosed with HIV be initiated on ART as soon as possible regardless of their CD4 count levels and retained in HIV care services.[2] Early ART initiation is associated with improved viral suppression, improved chances of having undetectable viral load, reduced risk of disease progression and death and improved quality of life.[3 4]

Having an undetectable viral load leads to reduced transmission at population level as PLHIV with an undetectable viral load is less likely to transmit the virus.[5–7] Immediate ART initiation is dependent on successful linkage to HIV care services; however, gaps in successful linkage to care continue to prevail. For example, in 2021 globally, 85% of those living with HIV knew their HIV status, 88% of those who knew their HIV status were accessing ART and among those on ART, and among these, 92% were virally suppressed.[1] Once initiated on ART, retention in HIV care is also important.

Poor retention in HIV care services increases the risk of suboptimal ART adherence, which increases the risk of drug resistance and treatment failure .[8] Although most PLHIV know their HIV status, retention in HIV care services is a challenge. For example, in South Africa, only 70% of those who knew their HIV status were on ART in 2017.[9] Bisnauth *et al* found that mobility, such as moving house or relocation, ART side effects or pill burden and time constraints were some of the most common reasons reported for disengagement from care or loss to follow-up by PLHIV.[10] Retention in HIV care for ART services for vulnerable populations, such as adolescents, is particularly challenging and has been noted as a global priority for action.[11–13] Previous studies also confirmed that retention in care, treatment adherence and treatment outcomes for adolescents in southern Africa are worse, compared with other age groups.[13–16]

To increase the linkage to and retention in HIV care services, differentiated care models exist such as HIV testing and point of care CD4 testing modalities, where CD4 count results are obtained near real time at a place of treatment and ART adherence clubs and support groups. However, these models are mainly focused on the general population while adolescent girls and young women (AGYW) and adolescent boys and young men (ABYM) require special attention as access and uptake of health services is typically lower among young people.[17 18] Several studies have reported substantial loss-to-follow-up between HIV diagnosis and receiving CD4 count results or between CD4 testing and ART initiation.[19–22] While universal test and treat (UTT) sought to address these losses, delays in initiating ART and loss to follow-up continue to be reported.[23 24] This leads to late ART initiation and poorer health outcomes among PLHIV. Consequently, AIDS-related deaths are decreasing at a slower rate, but this varies by region and population as well as by linkage to care programming.[17 18]

AGYW (15–24 years) are a critical population in HIV care. Although the number of new infections are declining in the general population, new infections among AGYW are decreasing at a slower rate than the general population globally and even slower in sub-Saharan Africa, with some parts remaining stagnant.[1 17 18] The slow decrease of new infections among AGYW has prompted a global reaction for AGYW-focused interventions to reduce the HIV infection rates and facilitate their access to HIV treatment and care services. Globally, adolescent girls form the majority (56%) of PLHIV, a number higher than in adolescent boys (44%).[25 26] AIDS-related deaths among adolescent girls aged 15–19 years are declining at a slower rate compared with other age groups.[1] Additionally, access to HIV care services and uptake of ART treatment, in particular, is often reported to be lower among adolescents compared with older age groups.[25 26] There is an increasing need to improve the care pathway from HIV diagnosis to linkage to and retention in HIV care services for adolescents, including AGYW, as several studies highlight substantial losses in the continuum of care from HIV testing to ART initiation.[27 28]

While AGYW are disproportionately affected by HIV, heterosexual men remain a critical population in HIV prevention. An estimated 75% of men living with HIV (aged 15 years and older) in eastern and southern Africa knew their HIV status, compared with 83% of women living with HIV of the same age in 2017.[29] In 2017, an estimated 300 000 men in sub-Saharan Africa died of AIDS-related complications compared with 270 000 women. This observation may be explained by differences in treatment coverage between men and women. Men are less likely than women to test for HIV, engage in care in a timely way and remain in care .[30–32]

In South Africa, in 2018, 93% of women living with HIV were aware of their status compared with 88% of HIV-positive men.[1] Recently, there has been an increase in HIV prevalence among ABYM.[33] In 2017, HIV prevalence among South African adolescent girls (15–19 years) and young women (20–24 years) was 5.8% and 15.6%, respectively.[26] HIV prevalence among men, in 2017, was 4.7% (15–19 years), 4.8% (20–24 years), 12.4% (25–29 years) and 18.4% (30–24 years). Furthermore, HIV incidence was 0.49% among South African men aged 15–24 years compared with 1.51% among women of the same age.[34]

Several systematic reviews and meta-analyses of interventions or service delivery models (SDMs) to improve linkage to and retention in HIV care services have been conducted indicating varying effects to promote linkage to and retention in HIV care for PLHIV.[13 35 36] We identified one overview of systematic reviews. Mbuagbaw *et al* conducted an overview of systematic reviews focusing on treatment initiation, adherence to ART and retention in care for vulnerable populations, but their overview did not explore the results of reviews among adolescent and young populations.[37] Our proposed overview of systematic reviews will specifically focus on AGYW and ABYM, as the infection rates are increasing and death rates are declining slower among these subpopulations. AGYW and ABYM are a vulnerable group which recently emerged as a priority in the global fight against HIV/AIDS. Compared with older populations, adolescents and young people experience different barriers to HIV treatment, such as less autonomy and more limited access to resources and less independence.[38] The overview of systematic reviews we propose will fill in this gap and provide evidence synthesis specific to interventions or SDMs for linking

and retaining adolescents and young people in HIV care services.

To better use existing evidence, an examination of a broader scope of interventions and SDMs to promote linkage to and retention in HIV care services for AGYW and ABYM is needed. This study will conduct an overview of systematic reviews to find, assess and synthesise/summarise all published peer-reviewed systematic reviews and meta-analyses of studies that examined the effects of interventions or SDMs to improve linkage to and retention in HIV care services among AGYW and ABYM. The interventions or SDMs will be classified into health facility based, community based, school based and various hybrid combinations of aforementioned groups of models. The proposed overview of reviews will seek to answer the question: Which interventions, strategies or SDMs for linking AGYW and ABYM to HIV care and improving their retention in care are effective?

Objectives

1. To identify interventions and SDMs that are effective at linking AGYW and ABYM to HIV care services and retaining them in HIV care.
2. To synthesise the evidence on the effects of interventions and SDMs to link AGYW and ABYM to HIV care services and retain them in HIV care.
3. To highlight gaps in the evidence on interventions and SDMs to improve linkage and retention in HIV care of AGYW and ABYM.

METHODS

This study proposes a narrative overview of systematic reviews of interventions and SDMs to link AGYW and ABYM to HIV care services and retain them in HIV care.

Protocol and registration

Methods for this overview have been developed based on the criteria for conducting overviews of reviews in the *Cochrane Handbook of Systematic Reviews of Interventions*. This protocol has been registered on the International prospective register of systematic reviews. Ethics approval is not required for this review as we will analyse published literature only.

Eligibility criteria

Setting

The overview will include systematic reviews that include studies conducted anywhere in the world.

Study design

Due to the relatively large body of evidence from individual experimental studies in the field of HIV care and treatment and the large number of reviews of this evidence, the current overview aims to review published, peer-reviewed systematic reviews of original studies with at least one included study. Systematic reviews that include any of the following types of studies that involve interventions or programmes or SDMs to improve linkage to and retention in care will be eligible for inclusion in the overview: randomised controlled trials, non-randomised controlled trials, controlled before and after studies, interrupted time series studies and other mixed-methods studies. This study will exclude abstracts that do not have full-text articles available, non-systematic reviews and other overviews.

We will not limit publication dates or location of studies to capture all relevant systematic reviews published covering all the HIV/AIDS treatment and management guideline strategies. The international guidelines for HIV treatment and management have changed over the years where initially, only advanced AIDS clinical stages were used as criteria to initiate treatment. Following this, guidelines were updated and CD4 count, and viral load levels were revised to allow treatment initiation much earlier in the disease progression. Recently, the UTT strategy is being implemented. Therefore, our overview of systematic reviews will capture evidence covering the period of these varying HIV treatment policies.

Systematic reviews will be defined according to Higgins as follows: a systematic review includes, (a) a clearly stated set of objectives with an explicit, reproducible methodology, (b) a systematic search that attempts to identify all studies that would meet the eligibility criteria, (c) an assessment of the validity of the findings of the included studies (eg, assessment of risk of bias and confidence in cumulative estimates) and (d) systematic presentation, and synthesis, of the characteristics and findings of the included studies.[39] We will, therefore, consider a review to be a systematic review if it includes the following:

- Clearly stated objectives and eligibility criteria of studies.
- A systematic search that attempts to identify all studies that would meet the eligibility criteria.
- Assessed the risk of bias of included studies.

Population

The WHO definition of AGYW includes adolescent girls aged 10–19 years old and young women aged 20–24 years old; while the definition of ABYM includes adolescent boys aged 10–19 years old and young men include men aged 15–35 years old. For the purposes of this overview, AGYW are defined as adolescent girls aged 15–19 years and young women aged 20–24 years old; and ABYM are defined as adolescent boys aged 15–19 years and young men aged 15–35 years old. We have defined and distinguished the ages of young women and men to able to capture interventions and SDMs that specifically address these age groups rather than the general youth or young adults as they may be treated similar to adults in some clinical settings. Thus, this overview will include studies that comprise of AGYW and ABYM diagnosed with HIV. In cases where the systematic review includes both paediatric and older adult populations, it will only be included if the data can be disaggregated by age for the population of interest in this overview. As interventions and models may differ for different groups, and relevant outcomes

may be different by age, we will consider categorising the evidence based on the following groupings:

For AGYW, the groupings will be 1= (10–14 years), 2= (11–18 years), 3= (15–19 years) 4= (15–24 years), 5= (19–24 years) and ABYM, 1= (15–19 years), 2= (20–24 years), 3= (25–30 years), 4= (31–35 years), 5= (15–24), 6= (25–35 years).

Interventions

This overview will include systematic reviews of studies evaluating interventions or SDMs to improve linkage to and retention in HIV care. These interventions or SDMs might include services promoting ART initiation, facilitating CD4 count testing at point of care or promoting UTT strategies. They might include community-based, school-based or health facility-based interventions and hybrid models with more than one service delivery points (SDPs). It will include reviews that include studies conducted in any setting and delivered by any provider (eg, healthcare providers, educators (within and outside of school settings) or lay providers).

Comparison

This overview will include reviews of studies in which the interventions or SDMs to promote linkage to and retention in HIV care are compared with any alternative intervention or no intervention or a standard of care package.

Outcomes

This overview will only include systematic reviews that identify linkage to and retention in HIV care as prespecified outcomes. Linkage to HIV care is defined as successful linkage to HIV care services within 3 months of HIV-positive diagnosis.[36 40 41] However, according to the UTT strategy, a shorter period between testing HIV positive and initiating ART is necessary to indicate successful initiation onto ART, which can be immediately or within 2 weeks of diagnosis. Therefore, we will include all reviews with the definitions covering the period before and including the period when UTT strategy was introduced. For the purposes of this study, 'linkage to HIV care' will be defined as having been linked to HIV care services either by having their CD4 count done (for older reviews) or by having been initiated into ART (for relatively recent reviews) within a specified period after an HIV-positive test result.

Retention in care is defined as remaining in contact with HIV care services, once linked to the services, collecting treatment, based on the frequency of clinic visits (varying from 1 month to 1 year) or the number of viral load tests conducted each year.[42 43] This study defines 'retention in HIV care' as being alive and on ART, collecting repeat treatment, based on the frequency of clinic visits (varying from 2 weeks to 1 year) or the number of viral load tests conducted each year after being linked to HIV care.

Exclusion criteria

We will exclude systematic reviews that:

- Are not in English.
- Include only key populations, for example, men who have sex with men, sex worker, intravenous drug users and transgender people.
- Report adherence without our outcomes of interest in the HIV continuum of care.
- Describe factors affecting barriers/facilitators or associated factors to linkage and retention in HIV care.

Table 1 Developing the search strategy for the overview of systematic reviews

Time period	No filter
Language	The search strategy will not be filtered by language, however, only systematic reviews published in English will be included.
Setting	Any setting
Study design	Systematic reviews or meta-analyses including randomised controlled trials, non-randomised controlled trials, controlled before and after studies, interrupted time series studies and other mixed-methods studies (quantitative, qualitative or mixed).
Search terms	See Table below (search strategy)
No filter	All content related to linkages and service delivery models to HIV care services for AGYW and ABYM for linkage to and retention in HIV care
Databases	PubMed (https://www.ncbi.nlm.nih.gov/pubmed/) Cochrane library (https://www.cochranelibrary.com/) Cumulative Index to Nursing and Allied Health Literature (CINAHL) Web of Science Grey literature (eg, Google Scholar)

ABYM, adolescent boys and young men; AGYW, adolescent girls and young women.

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

This study will not limit the search period by date of publication. We will search five databases: PubMed, Cochrane Database of Systematic Reviews (the Cochrane Library), CINAHL, Web of Science and Google scholar for grey literature. In general, MEDLINE/PubMed and EMBASE index most systematic reviews.[44] EMBASE is a subscription-based database, which we do not have access to. We will search additional regional and subject-specific databases such as CINAHL and Web of Science. The initial search strategy (tables 1 and 2) will be developed for one of the databases, PubMed database, using subject headings and free-text words that describe linkage to HIV care SDMs. Full search strategy for all databases is included in online supplemental file 1. Search strategies for the other databases will be adapted from the initial strategy accordingly to each database's specific requirements. Language will be restricted to English. References will be managed using Endnote X

Table 2 Search strategy for the overview of systematic reviews (PubMed example, full strategy appended)

Set		Search terms
1	HIV	HIV OR human immune-deficiency virus OR human immuno-deficiency virus
2	ART	antiretroviral therapy OR antiretrovirals OR antiretroviral treatment OR Highly Active Antiretroviral Therapy OR ART OR HAART
3	Linkage or retention in care	Linkage OR "Linkage to care" OR "Linkage to HIV care" OR "Referral to care" OR retention OR "retention in HIV care" OR "remaining in HIV care" OR "remaining in care" OR "continuing in care" OR "continuing in HIV care" OR "continuity of patient care" OR Attrition OR dropouts OR "loss to follow-up" OR "lost to care" OR "lost in care" OR initiat* OR start* OR uptake OR "ART initiation" OR modalities
4	Study design	systematic(tiab] OR "systematic review"(tiab] OR meta-analysis [tiab] OR systematic review(pt] OR meta-analysis(pt)
5		Sets 1–4 will be combined with "AND"

ART, antiretroviral therapy.

V.7.[45] The search strategies were first applied on 1 March 2022 and the data collection is expected to conclude on 30 June 2022.

SELECTION OF STUDIES

Search results will be imported into EndNote V.X7 and duplicates will be removed.[45] The remaining abstracts will be imported into Rayyan and two or more authors will independently screen titles and abstracts to identify relevant studies for full-text review. Rayyan is a web tool designed to speed up the process of screening and selecting studies.[46] Abstracts that are relevant, but reviewers have an unclear (unsure) inclusion status and where two authors have disagreed on inclusion will be moved to full-text screening, so that the article can be thoroughly examined for its eligibility status. Two authors will independently screen full-text articles for final inclusion using a standardised eligibility screening form. The outcomes of the independent multiple screening will be discussed and if two authors disagree and consensus cannot be reached, a third author who is not part of the initial screening team will arbitrate. Reviewers will meet regularly to discuss and resolve any discrepancies arising from the screening of abstracts and full-text articles until consensus is reached.

DATA EXTRACTION AND MANAGEMENT

Two or more reviewers will independently perform data extraction for each review and populate a predefined table (online supplemental appendix 1). The predefined table is an excel table developed by the review team to standardise data extraction by the multiple reviewers who will extract the data.

Discrepancies in the data extracted will be resolved by discussion to reach a consensus. If necessary, a third reviewer will be invited to arbitrate.

We will record the following information for each included review: details of the review including the title of the publication, first author's name, year of publication; details of the population included; specific country and settings where the intervention or modalities were implemented; a description and classification of the intervention or SDM (including healthcare provider, implementers of the intervention, lay providers, within or outside of a health facility or school or other details, healthcare context); study designs and a description of the outcome measures. We will also extract number of included participants; median or mean sample size; description of participants (ie, median, or mean ages, average per cent of AGYW and ABYM) and effect measures. We will pilot a data extraction form with two reviewers on three eligible reviews.

We will obtain additional information from the original reports of included studies in the reviews where necessary. These results will be published in appendices in the final manuscript.

ASSESSMENT OF METHODOLOGICAL QUALITY OF INCLUDED REVIEWS

The methodological quality of each included systematic review will be independently assessed by two reviewers using the validated Risk of Bias In Systematic reviews tool.[47] A guidance document will be used to ensure consistency between reviewers.

Every domain will be given a rating of Y='yes', PY='probably yes', PN='probably no', N='no', NI='no information'. Domains that are rated as 'no information' will be removed from the denominator in the overall quality ranking. Discrepancies in the ratings of the methodological reviews will be resolved by consensus between the reviewers and, if necessary, arbitration by another reviewer not part of the original quality assessment team. In addition to the quality assessment, we will report on the tools used for quality of evidence in each specific review and record the quality score or assessment.

DATA SYNTHESIS AND PRESENTATION

This study proposes a narrative overview of systematic reviews of interventions and SDMs to link AGYW and ABYM to HIV care services and retain them in HIV care. The primary outcomes for this study are linkage to and

retention in HIV care, defined by one or more of the following:

For linkage to HIV care service

1. AGYW and ABYM diagnosed with HIV who are initiated on ART after HIV diagnosis or who had a CD4 count performed after HIV diagnosis, or AGYW and ABYM initiated on ART within a specified time period after receiving CD4 count results.

For retention in HIV care services

1. AGYW and ABYM who return for routine HIV care check-up after 1 month, 3 months and/ or 6 months since being initiated on ART.
2. AGYW and ABYM who return monthly or regularly for their ART refill.
3. AGYW and ABYM retained in HIV care after 1 month, 3 months and/or 6 months of an HIV-positive diagnosis.

We will present the summary using tables and figures as 'Overview of reviews table', including the characteristics of included systematic reviews. We will denote systematic reviews that contain overlapping outcomes using appropriate footnotes. We will report outcomes according to the effect measures reported in the included reviews and will describe the results with respect to the following characteristics: setting (country, facility, eg, school or health facility or community), age groups: 15–19 years, 20–24 years for AGYW and same for ABYM with additional 25–30 years and 31–35 years, whether the interventions are biomedical, behavioural or other, details regarding the intervention using the template for intervention description and replication checklist and guide, number of trials included for each comparison.[48] Presentation of results will align with guidelines in the *Cochrane Handbook of Systematic Reviews of Interventions* and the *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA) statement.[39 49] Furthermore, a PRISMA-P reporting checklist was used for this protocol.[50] A PRISMA flow diagram will be used to summarise the process of study selection. Summary tables will be used to present data in a structured format. All descriptive explanations of heterogeneity provided will be reported by the review authors and highlight cases where descriptive explorations of heterogeneity are not provided.

Data will be presented graphically to visually demonstrate the data in terms of quality of evidence, quality of reviews and the effect sizes where provided. In addition, a section on 'implications for policy and practice' summarising the results and evidence base will be presented.

SUBGROUP ANALYSIS

In the descriptive analysis, subgroup analyses based on the subgroups described above will be explored to understand which interventions or SDMs are most effective in linking and retaining AGYW and ABYM to HIV care services and which models are not effective.

POTENTIAL LIMITATIONS

It is possible that relevant studies may be missed despite using robust search strategies of multiple databases because of the language restrictions, the restrictions on study type and type of reviews and the limited use of grey literature. Despite these limitations, this overview of systematic reviews will undoubtedly provide rich and useful information as the selected databases offer a wide scope of fields covering all facets of the review objectives.

ETHICS AND DISSEMINATION

Ethics approval is not required for this study as only published secondary data will be used. Our findings will be disseminated through peer-reviewed publication, conference abstracts and through presentations to public health communities and other community fora.

DISCUSSION

This is a proposed narrative overview of systematic reviews on interventions or service models that aimed to increase or enhance linkage to and retention in HIV care services for AGYW and ABYM. It will identify effective, evidence-based interventions and SDMs to link AGYW and ABYM to care and retain them in HIV care. The findings will inform research into the current SDMs, which may require adaptations. Our findings will be of value to healthcare managers, intervention implementers, service providers and policymakers in HIV care service to improve the current SDMs used to link AGYW and ABYM to HIV care services and retain them in these services. This research will also identify gaps in the evidence, which will inform suggestions for future research priorities.

The results of this overview will help establish an effective SDM for increasing linkage to HIV care services for AGYW and ABYM and may enhance quality of life. The results will also help inform programmes that aim to reduce ongoing HIV transmission and reinfection among AGYW and ABYM living with HIV either through early ART initiation or through immediate identification of HIV-related complications, including early detection of drug resistance or poor adherence. Establishing the effective SDMs for linkage to and retention in HIV care for AGYW and ABYM will help inform the design of future interventions aiming to increase uptake of HIV care services as well as help improve the linkage to care pathways to facilitate linkage and retention in care among AGYW and ABYM living with HIV. The identified effective SDMs for linkage to and retention in HIV care services will be key in reducing HIV transmission and reinfection, thereby reducing the burden of HIV, and improving quality of life and well-being among these subpopulations. Evidence shows that being initiated to ART and retained in HIV care improve health-related quality of life of HIV-positive individuals to equate that of HIV-negative individuals.[51–53]

We acknowledge that some studies not published in English may be missed in this overview. However, we are

hopeful that we will find useful and relevant studies with this language restriction because of the global focus of the overview (ie, through its wider geographical coverage as opposed to a restricted location or region).

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