The HIV Care Continuum: Measuring Latent Enablers and Assessing Pathways to Viral Load Suppression in Resource-Limited Settings

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Abstract

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The HIV care continuum captures the proportion of people who engage in various steps of the treatment cascade from the time of HIV diagnosis to the achievement of viral load suppression. Viral load suppression is the ultimate goal of HIV treatment as it is the best way to mitigate the spread of HIV and contain the epidemic. The best pathway to viral load suppression is not always clear. There are several factors that aid or hinder HIV patients from engaging in every step of the care continuum until they achieve and sustain viral load suppression. This dissertation aims to measure the underlying enablers of engagement in HIV care, relate them to potential barriers, and assess the effect of each enabler and barrier on future engagement in care and viral load suppression using data collected from people living with HIV (PLHIV) in Eswatini.

Firstly, a systematic review was conducted to summarize the methodologies used to measure and analyze barriers and enablers of engagement in HIV care. A search of all peer-reviewed articles published in English globally since 1996 yielded a final selection of 228 articles. The vast majority of the studies were qualitative and descriptive, and there was a scarcity of quantitative studies utilizing predictive methods that can measure the effect of a barrier or enabler on future engagement in care.

Secondly, an empirical analysis was conducted to assess the dimensionality (factor structure) of enablers of engagement in care using a sample largely representative of HIV patients in care in Eswatini. This analysis demonstrated the use of psychometric techniques that can capture underlying latent enablers. These techniques are useful for standardizing the measurements of enablers across studies and programs and can be used to predict future engagement in care. This analysis found financial and access enablers to be the most prominent underlying factors supporting engagement in care in Eswatini, suggesting that these should be an important consideration when designing interventions to retain HIV patients in care in resource-limited settings similar to Eswatini.

Thirdly, in an additional empirical analysis, the latent enablers previously identified were used to select potential barriers and assess their effect on linkage to care, retention in care, and viral load suppression. The analysis also involved an assessment of the mediational pathway from the potential barriers to care to viral load suppression that goes through retention in care. Only perceived HIV stigma was related to any step of the care continuum, with low perceived stigma being marginally associated with less viral load suppression. Retention in care did not mediate the relationship between perceived stigma and viral load suppression.

More psychometric studies are needed to standardize the measurement of underlying factors affecting engagement in HIV care. This dissertation demonstrated their utility by measuring latent enablers of engagement in care, assessing the downstream effects of the latent enablers and corresponding barriers, and assessing the mechanisms by which the barriers affect viral load suppression.

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Chapter 1: Introduction

1.1 Background

Antiretroviral therapy (ART) is a life-saving treatment that prevents the onset of acquired immunodeficiency syndrome (AIDS) among HIV positive persons. However, ART is efficacious only for patients who have access to it and who take it consistently throughout their lifetime. Recent estimates show that 81% of HIV positive persons globally are aware of their infection, 67% of those aware of their infection are on treatment, and 59% of those on treatment are virally suppressed.[1] These estimates reflect progress towards the UNAIDS 90-90-90 targets for 2020[2,3] (updated to 95-95-95 targets for 2030[4]). They are related to the HIV care continuum (also known as the treatment cascade), which outlines the stages of HIV care that HIV patients should go through from initial diagnosis to viral load suppression and measures the proportion of people engaged at each stage with all HIV patients as the denominator. To illustrate the relationship between the 90-90-90 targets and the HIV care continuum, it is useful to note that fulfilling the last "90" goal results in 73% of all HIV positive people being virally suppressed. In Eastern and Southern Africa, the region with the highest burden of HIV in the world (see Figure 1.1), the 95-95-95 estimate was 87-72-65 in 2019; Figure 1.2 shows the care continuum for the region and its relation to the treatment cascade. Understanding the structural and psychosocial reasons behind the differential linkage and retention behavior of people living with HIV (PLHIV) and how that behavior changes across time and predicts viral load suppression is essential for HIV prevention, treatment, and care efforts.

Eswatini (formerly named Swaziland) is a land-locked kingdom in Southern Africa with a population of just over a million people.[5] Given that an estimated 210,000 people are living with HIV in Eswatini, the kingdom has the highest adult HIV prevalence (27.4%) and incidence (1.36 %) in the world according to 2017 estimates,[6,7] which is a substantial decline from 2011 prevalence and incidence estimates of 32%[8] and 2.4%[9] respectively. Heterosexual sex is the primary mode of HIV transmission.[10] The epidemic in Eswatini is possibly driven by gender inequalities, which are characterized by gender-based violence, transactional sex, intergenerational sex, and multi-concurrent partnerships among men, which places a disproportional burden of the epidemic on women.[8,9,11,12] The national scale-up of HIV programs by the Ministry of Health (MoH) in conjunction with implementing partners and other stakeholders has had a tremendous effect on the trajectory of the epidemic, resulting in a 50% decline of HIV infections between 2010 and 2017 and a 28% decrease in HIV-related deaths.[13] Eswatini has made tremendous progress in curtailing the epidemic within its borders, with its UNAIDS 95-95-95 indicators lying at 87-89-91 in 2017.[7] This warrants the investigation of the drivers of linkage and retention in care among PLHIV in order to sustain this progress and to identify lessons that other countries in the region and others with generalized epidemics can draw from.

An in-depth understanding of the engagement of PLHIV with the HIV care continuum requires rigorous assessments of the structural and psychosocial barriers and enablers of linkage and retention in care, which act on the individual, community, and health systems levels. Previous assessments have mostly been descriptive and qualitative,[14-22] and although these studies helped to identify the range of reasons behind HIV patients' engagement or non-engagement in care (linkage and retention), quantification of the dimensionality (factor structure)

of the underlying abstract or unobservable (latent) factors that influence the observed engagement in care is still relatively lagging. Additionally, studies have not assessed how the factors relate to each other at the different time points indicative of the different steps in the HIV care continuum. The differing effects that these latent enablers of linkage and retention have on viral load suppression have also not been assessed. Psychometric (measurement) methods are needed to quantify the attitudes and perceptions behind the health-seeking behaviors of HIV patients and to lay the framework for scale development.

Barriers and enablers of linkage and retention in care may influence viral load suppression by changing ART adherence behavior. Mediational assessments of the pathway from barriers and enablers of linkage and retention in care to viral load suppression via retention in care (as a measure of ART adherence) are limited in the literature and have mostly been conducted in specialized populations or without direct measures of linkage or retention.[23-27] There has also not been an assessment of how factors that enable linkage affect retention, which in turn leads to viral load suppression. Overall, there have not been consistent measures of the reasons reflecting why PLHIV have differential engagement in different steps of the HIV care continuum, and the pathway from linkage to viral load suppression other than mathematical modeling,[28] nor have the psychosocial enablers of linkage and retention on this pathway been assessed using psychometric methods.

The psychometric methods used in this dissertation will lay the foundation for scale development. A "linkage and retention scale" can be used to predict a patient's likelihood of linking and being retained in care after HIV diagnosis and aid standardized quantification of the latent barriers and enablers of linkage and retention based on individual, community and health systems-level variables. By identifying constructs underlying HIV patients' health-seeking

behaviors in line with the 95-95-95 goals, additional studies can investigate the effect of potential interventions and targeted interventions can be implemented to help patients link to care faster upon HIV diagnosis, stay in care and adhere to medication, and achieve viral load suppression. Identification of underlying barriers and enablers of linkage and retention in care will also aid providers in decision-making for differentiated services for HIV positive patients based on their unique needs and health profiles in line with World Health Organization (WHO) differentiated service guidelines.[29,30] Thus, the scale can also be used to propose a differentiated service delivery model that works for each patient upon HIV diagnosis or at different stages of the care continuum.

1. 2 Dissertation Overview

Using data from Link4Health (a cluster-randomized trial assessing the effectiveness of a combination intervention in improving linkage and retention in care among adults in Eswatini [2013-2014][31,32]), this dissertation assesses the dimensionality of enablers of linkage and retention in HIV care in Eswatini in order to capture the underlying latent constructs and assess how they relate to each other and to observed variables at different time points. It also assesses the pathways to viral load suppression and explores the role of retention in care (as a measure of ART adherence) as a mediator of the relationship between barriers to retention in care and viral load suppression.

This dissertation is comprised of five chapters. Following this introductory chapter, Chapter 2 gives an overview of the measurement and analytic approaches to barriers and enablers of engagement in the HIV care continuum. In the format of a systematic review, 228 articles are summarized qualitatively, and a description of the literature assessing the reasons for

differential engagement of PLHIV in the HIV care continuum is given. Chapter 3 assesses the dimensionality of the enablers of engagement in the HIV care continuum. Using psychometric methods, the factor structure of the latent enablers at different time points of the continuum is measured among a population largely representative of HIV patients in care in Eswatini (from the Link4Health study). The longitudinal effects of the enablers on future engagement in care and viral load suppression are also assessed. Chapter 4 also uses data from the Link4Health study and selects a set of variables hypothesized to be the opposite of the enablers identified in Chapter 3 as potential barriers to engagement in care. The effects of these potential barriers measured at baseline on actual engagement (linkage to care at 1 month, retention in care at 12 months, and viral load suppression at 12 months) are investigated. Chapter 4 also assesses the potential mediating effects of retention in care on the pathway from potential barriers to engagement in care to viral load suppression. Finally, Chapter 5 gives an overview of the findings from Chapters 2-4 and discusses the public health implications and future directions.

This dissertation provides the first comprehensive assessment of the methodology used to measure and analyze barriers and enablers of engagement along the multiple steps of the HIV care continuum among HIV patients globally. It also presents the first psychometric assessments of enablers to initial linkage to care among HIV patients and is the only psychometric assessment of enablers to engagement in care using individual-level study data among HIV patients in sub-Saharan Africa. Finally, this dissertation provides the first assessment of the effects of baseline potential barriers to care (assessed at the time of HIV diagnosis) on all future steps of the HIV care continuum and the first mediational assessments of the pathway from the barriers to viral load suppression that goes through retention in care in a generalized epidemic.

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1. 4 Tables and Figures

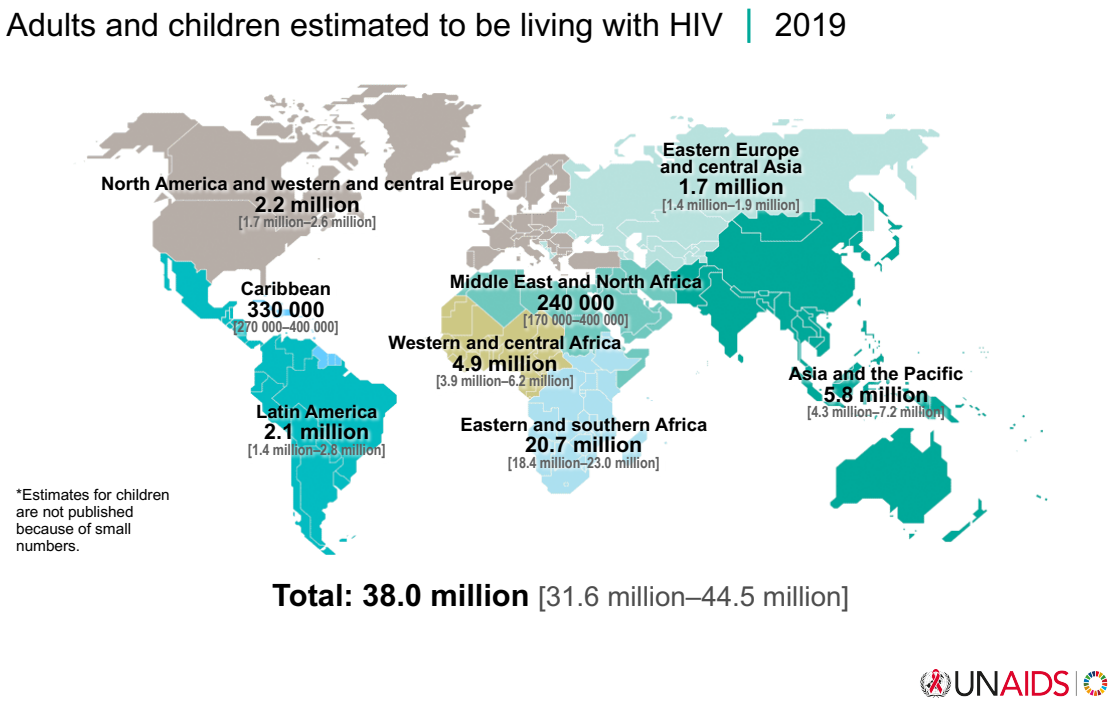

Figure 1.1: UNAIDS estimates for adults and children living with HIV in 2019. Eastern and Southern Africa bears the biggest burden of the epidemic. (UNAIDS, 2020)

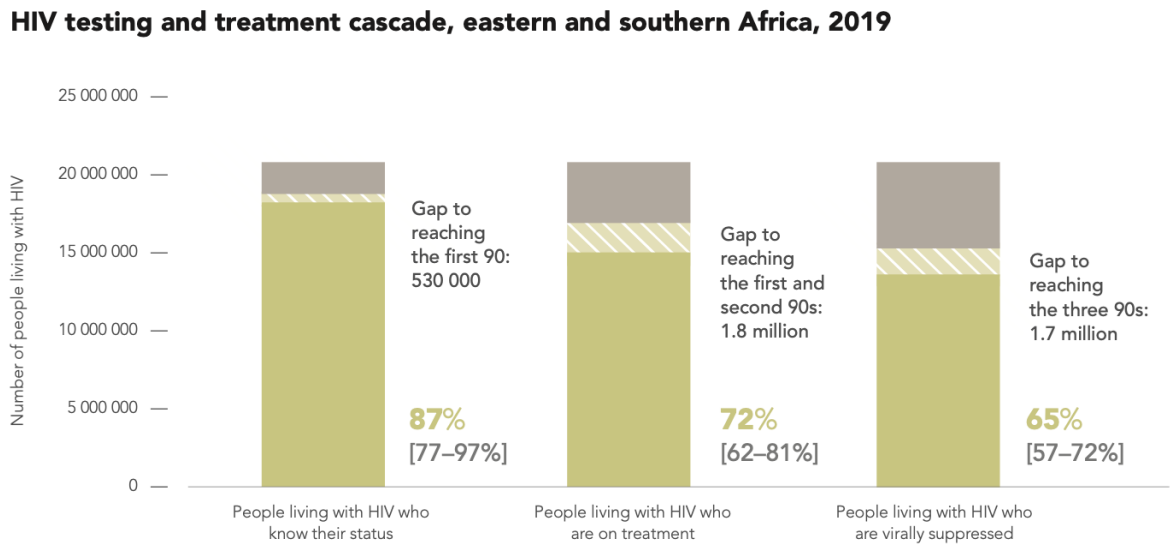

Figure 1.2: HIV testing and treatment cascade for Eastern and Southern Africa in 2019. The gaps to reaching the UNAIDS 90-90-90 targets are also indicated. (UNAIDS, 2020)

Chapter 2: Approaches to the Measurement of Barriers and Enablers of Engagement in The HIV Care Continuum: A Systematic Review

2.1 Abstract

Background: Many HIV patients do not sufficiently navigate all the steps of the HIV care continuum to achieve and maintain viral load suppression. Previous systematic reviews have identified barriers and enablers of engagement in HIV care. However, these reviews have been confined to a single step of the care continuum, have only studied specific populations, or have been restricted to a single country or region of the world. It is also important to systematically assess the methodologies by which the barriers and enablers have been measured in order to identify ways to build on different approaches and capture barriers that are more latent (unobservable). The objective of this systematic review is to summarize the approaches to the measurement and analysis of barriers and enablers of engagement in the HIV care continuum and compare the type of barriers and enablers identified by different approaches.

Methods: An electronic search was conducted in Pubmed, PsychINFO, and Scopus for peer-reviewed articles published in English from January 1996 to January 2020. Only studies measuring barriers or enablers of linkage to care, retention in care, medication initiation or adherence, or viral load suppression directly from HIV patients were included. There were no geographic or population-specific criteria for inclusion. Studies were categorized by the methods used to measure barriers and/or enablers of engagement in care and analytic methods used to

assess their effect on actual engagement and viral load suppression as follows: qualitative, descriptive, studies assessing association or causation, psychometric, and mixed methods studies.

Results: Of the 1,465 articles retrieved, 288 met the inclusion criteria after the final screening stage and were assessed further. Of these, 126 (55%) were qualitative, 63 (28%) descriptive, 16 (7%) assessing association or causation, 16 (7%) mixed methods, and 7 (3%) were psychometric studies. Three-quarters of the studies were conducted in low- and middle-income countries, and more than half assessed barriers and enablers of HIV medication initiation or adherence. Only 10 (4.4%) studies longitudinally assessed the effect of a barrier or enabler of engagement on actual engagement in a future step of the HIV care continuum. Most studies were of clinical cohorts (n=102, 45%). Qualitative and descriptive studies typically identified an exhaustive range of individual, interpersonal, community, health system, and structural factors that affect engagement in care, with qualitative studies being more likely to capture factors related to perceptions and attitudes and descriptive studies capturing factors related to issues involving taking HIV drugs because of their focus on medication adherence. Studies assessing association or causation quantified the association between factors identified descriptively and actual engagement in care. Psychometric studies grouped the barriers and enablers into domains by conducting exploratory or confirmatory factor analysis; hence they usually resulted in a smaller list of broad factors and allowed for the measurement of latent barriers and enablers. Mixed methods studies merged qualitative approaches with one or more quantitative approaches in the same population. They hence allowed for a broader understanding of the inter-relatedness of the different factors at different levels of complexity. Longitudinal assessments of the effects of

barriers and/or enablers on future engagement were largely done in studies assessing association or causation and psychometric studies only.

Conclusion: Qualitative and descriptive studies have primarily been used to assess the barriers and enablers of engagement in the HIV care continuum. More studies assessing association or causation, psychometric, and mixed-methods studies are needed to build on the range of factors identified by qualitative and descriptive studies by quantifying the effect of the factors on actual engagement, standardizing the tools used to measure the barriers and enablers, and predicting future engagement of HIV patients in care. These tools would make comparisons across studies more systematic and help implementers and policymakers capture the underlying reasons behind the differential engagement in care among HIV patients in order to design appropriate interventions and project the direction of future engagement.

2.2 Introduction

UNAIDS set ambitious goals in 2014 to end the AIDS epidemic by 2030 by having 90% of all HIV positive people know their status, 90% of those knowing their status be on sustained antiretroviral therapy (ART) and 90% of those on ART be virally suppressed by 2020.[1,2] These goals were upgraded to 95-95-95 for 2030.[3] A few countries had achieved the 90-90-90 goals by the end of 2019, and some had even surpassed the 95-95-95 targets.[4] Despite these gains, the global 95-95-95 progress currently lies at 81-67-59,[4] meaning that most countries are still lagging.

Understanding the reasons why some HIV patients actively engage in their care while others do not is important for program planning and development of interventions that promote

and sustain the regular care of HIV patients. Retaining HIV patients in care keeps them on the pathway to viral load suppression, which would ultimately bring the HIV epidemic under control.[1-3] Closely linked to the 95-95-95 targets is the HIV care continuum or treatment cascade, which tracks the sequential movement of HIV positive patients from HIV diagnosis to viral load suppression and measures the proportion of patients engaged in care at each step.[5] The psychosocial and structural reasons for non-engagement in HIV care are often intertwined with a complex interaction of multi-level (individual, community, and health systems) and dynamic factors.

A few systematic reviews and meta-analyses have assessed barriers and enablers of some aspects of the HIV care continuum in different populations. [6-15] These reviews have mostly focused on one step of the care continuum, primarily ART initiation or adherence,[6,7,10,11,13-15] or have focused on a single population such as pregnant and postpartum women,[6,8,11,13] Black women,[9] or female sex workers (FSWs),[12] or focused on a single country or region of the world.[7-9,12,13,15] Additional reviews have focused on a single set of barriers and enablers.[16-18] Previous reviews have identified barriers and enablers such as transportation costs and other financial constraints, ability to take time off work and other life commitments, distance to the health facility, stigma and fear of disclosure, health facility logistics, interactions with healthcare providers (including perceived staff competence), quality of care, medication side effects, psychosocial support (including motivation from family or community members), mental health, overall health (which influences risk perception), health education, nutrition, substance use, and mobility to be major factors that determine HIV patients' engagement in care. [6-15] These reviews have helped to summarize the range of reasons why HIV patients may or may not engage in care. However, there is a need to identify underlying latent reasons that represent broader factors

amenable to intervention and to assess if the factors identified differ by methods used to measure them. It is also important to assess the ability of these factors to predict actual engagement in care or viral load suppression in order to allow for a broader understanding of the barriers and enablers across all steps of the care continuum.

Studies investigating the factors that affect engagement in care have used a wide range of methodologies to measure the barriers and enablers. No systematic reviews have been conducted to synthesize the measurement and analytic approaches to barriers and enablers of engagement in the HIV care continuum. Comparing the factors identified by different measurement approaches can help investigators determine if different methodologies capture different barriers and enablers (that is, if some methodologies are more suited to capture some types of barriers and enablers than others), and assess ways to build on different methodologies to quantify these factors more accurately. This assessment of measurement approaches, together with analytic approaches, can aid the development of standardized tools that measure reproducible constructs and can help investigators determine the effect of each barrier or enabler on actual engagement in a future step of the care continuum. Interventions that can mitigate the barriers and enhance the enablers can then be studied further, and this can, in turn, help policymakers and implementers develop interventions that are most effective for different populations and contexts to mitigate barriers or enhance enablers and predict the future engagement behavior of HIV patients.

This systematic review aims to summarize the methodologies used to measure and analyze barriers and enablers of linkage to care, retention in care, ART initiation or adherence and viral load suppression, and to compare the types of barriers and enablers identified by different approaches in peer-reviewed literature published globally between 1996 and 2020.

2.3 Methods

Search Strategy

All procedures were conducted according to Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines.[19-22] The literature review was conducted by searching PubMed, PsychINFO, and Scopus for peer-reviewed articles published in English from January 1996 to January 2020. The year 1996 was chosen because it coincides with the time when highly active antiretroviral therapy (HAART) was first introduced to HIV patients[23-25] and shown to be efficacious in reducing AIDS-related hospital admission and mortality.[26-29] An assessment of the reasons why HIV patients may or may not link to care and be retained on treatment until they are virally suppressed only makes sense if they have access to HIV medication, and this access began in 1996, albeit only for a small proportion of HIV infected people in the world at first. In consultation with a librarian, a combination of the following keywords and exploded Medical Subject Headings (MeSH) terms was used and modified accordingly for the assessment of barriers and enablers of engagement in HIV care (the full search terms are attached in Appendix A):

(score OR index OR scale OR tool OR construct OR measurement OR assessment) AND (barriers OR facilitators OR enablers) AND (linkage OR retention OR continuum OR retained OR linked OR initiated) AND (care OR cascade OR continuum) AND (HIV OR "HIV infection" [MeSH Term] OR "antiretroviral treatment" or AIDS).

Study Selection and Eligibility Criteria

Articles were organized in Endnote and uploaded into Covidence software (Veritas Health Innovation, Melbourne, Australia). After removing duplicates, articles were screened by two independent reviewers by title and abstract then full text in sequence. Discrepancies were discussed between the reviewers and were resolved at each screening stage. The inter-rater reliability/Cohen's Kappa statistic for title and abstract screening and full-text screening was 0.88/0.68 and 0.83/0.64, respectively, which showed substantial agreement.[30] Articles were eligible for inclusion in the assessment if they met the following criteria:

1. Focused on HIV disease
2. Published in a peer-reviewed journal
3. Published in English
4. Published between 01/01/1996 and 01/31/2020
5. Collected empirical data to assess barriers and/or enablers of linkage to care, retention in care, ART/HAART initiation or adherence (which were usually studied together), or viral load suppression
6. Described a methodology for measuring reasons (barriers and/or enablers) that affect engagement in the different steps of the HIV care continuum (linkage to care, retention in care ART initiation or adherence, or viral load suppression) and corresponding outcomes
7. Directly measured reasons or barriers and enablers of engagement in the HIV care continuum from the patient perspective (or the perspective of caregivers of children)

The first step in the HIV continuum assessed was linkage to care. Reasons for HIV testing were not included because they involve assessments on both HIV positive and negative people, and this review was focused on barriers and enablers of engagement in care after HIV diagnosis.

Data Extraction

After screening by two reviewers, data were extracted by a single reviewer using a standard extraction form (see Tables 2.1 and Appendix B). The first extraction category was "author and year" based on details from the publishing journal. The next was the "country" where the study was conducted, and several times it included multiple countries. Countries were categorized into "low and middle income" or "high income" based on the World Bank country classification scheme by the economy as of June 2020.[31] When a multi-site study included both low-and middle-income and high-income countries, this was indicated in the extraction sheet. The "primary research question" indicated the broader objectives of the study from which the barriers and/or enablers of care engagement were measured. The specific "barriers and enablers assessment" was indicated, which could have been an assessment of a secondary aim of the study and included the specific step/s of the HIV care continuum under assessment. The "study population" indicated the specific population from which barriers/enablers of care engagement were measured, which included high risk groups commonly studied in HIV research (termed key populations). The study population categories were: general population (not a clinical, specialized, or key population); clinical cohort (a cohort enrolled from a health facility or group of facilities and was not exclusively a key population); several key populations (men who have sex with men [MSM], FSWs, injecting drug users [IDUs]/people who inject drugs [PWID], or

other); men; adolescents/youths and/or children; pregnant and/or postpartum women; mothers and/or caregivers. The "sample size" was specific to the population from which barriers/enablers of care engagement were measured even if the study used a broader sample to answer a different question. The method used to measure the barrier/enablers of engagement in HIV care and the analytic methods used to assess the effect of those enablers on other outcomes was also extracted; together, these two criteria were used to characterize the articles into "study types," which were classified under two broad categories: qualitative and quantitative (consisting of "descriptive," "studies assessing association or causation," or "psychometric" studies).

Study Types

Qualitative Studies were those that reported general themes derived from coding transcripts from participants describing reasons for engagement (or lack of engagement) in the HIV care continuum, using methods such as focus group discussions, semi-structured, structured, or in-depth interviews.

Descriptive Quantitative Studies were those that only reported the proportions of respondents indicating one barrier/enabler or another but did not estimate the association between any barriers/enablers and another outcome.

Quantitative Studies Assessing Association or Causation included any quantitative study (excluding psychometric studies) reporting an association between a barrier/enabler and another outcome, even if the barriers/enablers were initially measured descriptively.

Psychometric Quantitative Studies were those that conducted factor analysis or procedures for scale development using the barriers or enablers of engagement in HIV care.

Mixed Methods Studies combined qualitative and at least one quantitative method.

Barriers or Enablers Measured

As consistent with the inclusion criteria described above, all barriers and enablers were self-reported from HIV patients. The specific ascertainment method of the barriers or enablers could have been through open-ended questionnaires or pre-determined checklists or tools in any of the quantitative study types but was, by design, open-ended in qualitative studies. The specific "barriers or enablers measured" were also extracted in order to compare the type of barriers/enablers across studies. A study was deemed to have conducted a "longitudinal assessment of barriers/enablers" if it assessed the effect of a barrier or enabler on a future step of the HIV care continuum (retention in care, ART initiation or adherence, or viral load suppression).

Assessment of Study Quality

As part of the risk of bias assessment as per PRISMA guidelines, [19-22] "Overall study quality" was assessed using the Agency for Healthcare Research and Quality (AHRQ) tool[32] for quantitative studies and the tool developed by Hawker and colleagues (Appendix D)[33] plus the Critical Appraisal Skills Programme (CASP) Checklist[34] for qualitative studies. Mixed method studies were assessed using both sets of tools. The studies were ranked into "good," "fair," and "poor" categories.

2.4 Results

Study Selection

The keyword search yielded 731 articles in Pubmed, 1,398 in PsychINFO, and 594 in Scopus, totaling 2,723 records. After removing 1,258 duplicate records, 1,465 articles were left for the title and abstract screening. Of these, 1,104 were excluded from further screening because they did not meet the general eligibility criteria, leaving 361 articles for full-text screening. An additional 133 articles were excluded, leaving a final sample of 228 articles for assessment. The PRISMA-adapted flow diagram showing the sequence of inclusion and exclusion of articles is shown in Figure 2.1.

The reasons articles retrieved from the search terms were excluded from further assessment included not meeting the eligibility criteria in the following ways: they were studies of comorbidities that may include HIV but did not specifically measure barriers/enablers of HIV care engagement by itself; were not published in peer-reviewed journals, were conference abstracts, review articles, commentaries or gray literature; measured levels of engagement on different steps of the HIV care continuum but did not assess reasons for the different engagement levels (or only assessed barriers and/or enablers of HIV testing or Pre-Exposure Prophylaxis [PrEP], which includes HIV-negative people); only stated or assessed risk factors or potential barriers and/or enablers of engagement in HIV care without directly measuring them (and describing a methodology for doing so with corresponding outcomes) in the current assessment; measured barriers and/or enablers of engagement in care from other stakeholders involved in the care of HIV patients (such as providers, community members, family members) and not the HIV patients themselves or caregivers of children. The more specific reasons for exclusion at the full-text review stage are shown in Figure 2.1.

Characteristics of Studies Included

The characteristics of the studies included are summarized in Table 2.1, categorized by study type as defined earlier. The individual studies are summarized in Appendix B. Of the 288 studies assessed, 126 (55%) were qualitative, [35-160] 63, (28%) descriptive,[161-223] and an equal proportion were studies assessing association or causation,[224-239] and utilizing mixed methods [240-255] (n=16, 7% each). The smallest category consisted of studies utilizing psychometric methods (n=7, 3%).[256-262]

Overall, most (73%) of the studies were conducted in low- and middle-income countries (LMICs). Most (54%) of the studies assessed barriers and enablers of HIV medication initiation or adherence, while 29% assessed barriers and enablers of more than one step of the HIV care continuum. No studies measured barriers and enablers of viral load suppression alone. Only 10 studies (4%) longitudinally assessed the effect of a barrier or enabler on engagement in a future step of the continuum. A large proportion (45%) of the studies measured barriers and enablers using clinical cohorts, followed by studies done on the general population (14%). The least studied group (among risk groups commonly studied in HIV research) were FSWs (1%), and 6% of studies assessed unique key populations that did not fit into the other categories. The most prevalent study quality was "fair" (47%).

Qualitative Studies

The majority (81%) of the 126 qualitative studies were conducted in LMICs, and qualitative studies had a higher proportion of studies conducted in LMICs than other study types. Among the reviewed qualitative studies, 45% investigated barriers and enablers of ART/HAART

initiation or adherence, while 38% investigated barriers and enablers of multiple steps of the care continuum. Only one of the 126 studies assessed how barriers and enablers affected a future step of the care continuum: participants were interviewed longitudinally and focus group discussions were conducted at various time points to assess multi-level barriers and enablers (those occurring at the individual, facility, community, and structural levels), then patients were asked if they had actually engaged or disengaged from care in relation to these factors in follow-up interviews.[94] Most studies were of clinical cohorts (37%) and the general population (14%). Qualitative studies (which were assessed using different tools than quantitative studies) were primarily of fair (45%) or good (42%) quality, having the highest proportion of good-quality studies compared to other study types. Studies of poor quality often measured barriers and enablers as a smaller part of a larger non-qualitative study. These studies generally did not have a clear description of the sampling strategy used to ensure data saturation; lacked an explanation of how data collection was done and what the questionnaires, instruments or topic guides used in the study were; did not have an adequate description of the rigor of the data analysis process or how categories/themes were derived from the data including respondent validation or triangulation; and did not have a clear presentation of results as per the quality assessment tools. [33,34]

Qualitative studies used open-ended questionnaires to collect data on barriers and enablers of engagement in the HIV care continuum using methodologies common to qualitative studies in general, such as focus group discussions (n = 20), semi-structured interviews (n = 37), in-depth interviews (n = 23), other methods such as digital storytelling and concept mapping (n = 13) or a combination of two or more methods (n = 33). During these interviews or discussions, topic guides were often used to solicit stories and narratives from participants regarding their experience in accessing HIV services and engaging in care. Study investigators then coded

responses from participants and grouped the codes into qualitative themes. The themes provided a range of possible factors that hindered or aided HIV patients from effectively engaging in HIV care.

Qualitative studies deduced the most comprehensive list of barriers and enablers of all study types. For example, because investigators usually approached participants without a preconceived or exhaustive list of potential barriers and enablers but deduced them from participants' narratives, they often obtained more personal and subjective responses (tied to perceptions and feelings) than were derived from other methods, such as fear of the consequences of disclosing HIV status, fatalistic attitudes, emotional concerns, and psychosocial issues. Other common themes were pertaining to stigma concerns, psychosocial support, fears about starting HIV treatment, beliefs concerning the efficacy of ART, denialism or acceptance of HIV status, belief in alternative treatments, quality of interactions with health providers, experiences at HIV clinics and financial concerns. Responses also tended to be more specific, such as the particular nuances of the logistics of a health clinic and quality of care. Even though investigators typically used probes and sometimes theoretical frameworks to guide their research, they usually aimed at reaching data saturation; hence they prompted for more responses and sometimes enrolled more participants until no new themes could be derived. In this way, they collected a wide range of barriers and enablers of engagement in the HIV care continuum.

Descriptive Quantitative Studies

Descriptive studies (n = 63) were also mostly conducted in LMICs (73%). A majority of the studies (70%) assessed barriers and enablers of ART/HAART initiation or adherence (the same instruments were usually used to measure both). The descriptive category of studies had a

low proportion of studies assessing multiple steps of the care continuum (13%). By definition, no descriptive studies longitudinally assessed the effect of a barrier or enabler on a future step of the HIV care continuum. A majority of the studies (62%) included clinical cohorts, and descriptive studies had the biggest proportion of clinical cohorts compared to other study types. No studies were done on FSWs or men. Most studies (44%) were of fair quality. However, descriptive studies had the highest proportion of poor-quality studies compared to other study types (30%). Reasons for poor quality included significant attrition biases (systematic differences in the loss of participants from the study) and reporting biases (systematic differences between reported and unreported findings) that were not sufficiently accounted for as per the quality assessment tools.[32] These studies were often conducted as sub-analyses of larger (and often longitudinal) studies assessing a different primary aim; typically, patients lost to follow up (LTFU) from care would be traced and the proportion of participants who responded to particular questions measuring reasons for engagement or non-engagement in HIV care among those who were successfully traced and were willing to participate were recorded. Therefore, the barriers and enablers were recorded as proportions among participants with available data without sufficiently accounting for missing data.

Descriptive studies usually recorded responses from participants using a pre-determined checklist of barriers and enablers to engagement in care (n = 39, of which 14 used responses to questions on reasons for adherence or non-adherence as part of instruments developed to measure medication adherence but not validated for assessing barriers and enablers of adherence). These possible reasons could have been derived from qualitative or other descriptive studies. The remaining 23 studies categorized reasons from open-ended questionnaires into similar checklists. Such lists were usually limited to one step of the care continuum and often

assessed reasons behind ART/HAART initiation or adherence. Most of the barriers and enablers measured through descriptive studies were thus related to issues involving taking HIV drugs, primarily consisting of reaction to drug side effects, deteriorating or improving health, pill burden, cost of drugs, forgetting to take drugs or using reminders to take drugs, mobility issues, busyness, privacy issues related to taking drugs, HIV clinic logistics, access to HIV clinics, drug stock-outs or availability, health information regarding the efficacy of HIV medications, belief in alternative treatments, nutrition issues and other factors involved in taking medication. The list of barriers and enablers for this particular step of the continuum was very expansive.

Quantitative Studies Assessing Association or Causation

More than half (63%) of the 16 studies assessing association or causation were conducted in high-income countries (HICs), and studies assessing association or causation had the highest proportion of studies from HICs than other study types. As observed in other study types, studies assessing association or causation mostly assessed barriers and enablers of ART/HAART initiation or adherence (69%). There were no studies assessing barriers and enablers of initial linkage to care or viral load suppression alone. Although longitudinal assessments of barriers and enablers were not done in 62% of the studies, 38% of the studies assessed the effect of a barrier or enabler on a future step of the care continuum, the second-highest of any study type. This usually involved measuring the barrier or enabler descriptively, then testing for an association of the factor with a future step of the continuum using multivariable methods and controlling for confounding variables. As observed in other study types, most of the studies were of clinical cohorts (56%), followed by the general population (19%). No studies included FSWs, PWIDs, men, adolescents, youth or children, pregnant or postpartum women, mothers or caregivers, and

other key populations. Half the studies were of fair quality, and studies assessing association or causation had the smallest proportion of poor studies compared to other study types (13%). Studies of poor quality usually suffered from significant selection biases (systematic differences in participation or the loss of participants from the study) that were not sufficiently accounted for, or did not adequately control for confounding as per the quality assessment tools.[32]

Studies assessing association or causation first collected barriers and enablers descriptively, recording the proportion of participants who responded in a certain way using a pre-determined checklist of barriers and enablers to engagement in care (of which 4 of the 16 studies used responses to questions on reasons for adherence or non-adherence as part of instruments developed to measure medication adherence). These barriers/enablers were then tested for an association with a health outcome, usually a step of the care continuum (linkage to care, retention in care, ART/HAART initiation or adherence, or viral load suppression). The list of reasons for engagement or non-engagement in these steps of the continuum was, therefore, similar to that of descriptive studies (mostly related to issues involving taking HIV drugs). However, studies assessing association or causation benefited from having an actual effect measure that could quantify the relationship between the barrier/enabler and the outcome or step of the continuum in question, often involving a longitudinal assessment of the predictive ability of the barrier or enabler. For example, studies assessing association or causation could estimate the hazard of discontinuing HAART medication due to medication side effects.[235] Studies assessing association or causation, therefore, went beyond measuring barriers and enablers to assessing their effect on the engagement in care of HIV patients.

Psychometric Quantitative Studies

Psychometric studies (n=7) were mostly conducted in LMICs (71%). They almost exclusively studied barriers and enablers of ART/HAART initiation or adherence and did so at a higher proportion than other study types (86% versus 70% of descriptive studies for example). They also had the largest proportion of studies conducting longitudinal assessments of barriers and enablers (n = 3, 43%), often by employing structural equation modeling (SEM) techniques to assess the effect of a latent (unobservable) factor on a future step of the HIV care continuum (the factor's predictive validity). None of the psychometric studies assessed multiple steps of the care continuum. There was an equal proportion of studies conducted among clinical cohorts and MSM (29% each). No studies included FSWs, PWIDs, men, caregivers and their children, pregnant or postpartum women, and mothers or caregivers. Most of the studies were of fair quality (86%), and there were no poorly ranked studies.

Studies employing psychometric methods usually assessed the factor structure of a list of reasons for engagement or non-engagement in care (n = 6) or other methods of scale development [validating a previous tool] (n = 1) using pre-determined checklists. Studies employing factor analysis methods conducted either exploratory factor analysis (EFA) [n = 2], EFA and confirmatory factor analysis (CFA) (n = 2), or principal component analysis (PCA) and EFA (n = 2) to capture underlying latent factors that are difficult to measure accurately; they grouped the reported barriers and enablers into dimensions and assessed the validity of the constructs and the reliability of the deduced scales. As such, the number of barriers and enablers derived from these methods were usually fewer than those measured through other methods. Factors identified included intentional ART adherence barriers (tied to the patient's deliberate efforts to avoid medication), unintentional ART adherence barriers (external to the patient's

deliberate efforts to avoid medication), medication and health concerns, medication-related adverse effects, stigma concerns, fear of consequences of taking medication, and perceived lack of need of medication. SEM methods were often employed to assess the relationship between the latent factor and a step of the care continuum. For example, EFA and CFA methods were used to identify a six-factor structure that captured latent barriers measuring underlying patient-reported reasons for disengaging from care, and then Cox regression models were used to investigate the ability of these barriers to predict time to clinic return.[257] Therefore, psychometric methods categorized barriers and enablers into broader factors and measured constructs that are latent and may not be captured well by qualitative and descriptive methods; indeed, they built on lists of barriers and enablers identified from these preceding methods.

Mixed Methods Studies

The majority (75%) of the 16 mixed methods studies were conducted in LMICs. Unlike other study types, mixed methods studies mostly assessed barriers and enablers of various steps of the HIV care continuum (44%). None of them conducted longitudinal assessments of barriers and enablers. There was an equal proportion of studies conducted among clinical cohorts and the general population (31% each). No studies included FSWs, PWIDs, mothers or caregivers, and other key populations. Half of the studies were of fair quality. Poor ranking studies suffered from the methodological flaws of both qualitative and quantitative studies described above.

Mixed methods studies measured barriers and enablers using both qualitative and quantitative methods in sequence (n = 5) or used a convergent approach, where they collected the qualitative and quantitative data simultaneously and merged the results during analysis (n = 11). The qualitative portion of the study measured barriers and enablers to care using themes derived

from open-ended questions, while the quantitative portion either used pre-determined checklists (n = 10) or measured the proportion of barriers and enablers derived from the qualitative themes (n = 6). Mixed methods provided a fuller picture of how the barriers and enablers work together to affect care engagement in the same population. For example, qualitative methods were sometimes first used to measure the range of possible barriers or enablers of care engagement and grouped into themes, then descriptive methods were used to report the proportions of patients reporting each barrier or enabler from the derived themes, and then multivariable methods were used to assess the association between the barrier or enabler on a health outcome. On the other hand, quantitative assessments were sometimes done first, then qualitative methods used to further understand patients' experiences with regards to those limiting or enabling factors. The list of barriers and enablers tended to be expansive as it encompassed factors identified using both qualitative and quantitative methods. This list included factors related to personal and subjective responses (tied to perceptions and feelings), such as fear of the consequences of disclosing HIV status, fatalistic attitudes, emotional concerns, and psychosocial issues; and factors involving taking HIV drugs such as reaction to drug side effects, pill burden, cost of drugs, and drug stock-outs or availability.

2.5 Discussion

This systematic review appears to be the first to summarize the methodology of measuring and analyzing barriers and enablers of engagement in the HIV care continuum and to assess the different barriers and enablers captured by different methodologies. It also appears to be the only systematic review to include articles assessing barriers and enablers of multiple steps of the care continuum (starting from linkage to care) across all populations of HIV-infected

people globally. The majority of the 228 articles identified were qualitative or descriptive (making up 83% of the studies combined), and predictive quantitative methods, which are needed to standardize the measurements of barriers and enablers, measure the effects of the barriers or enablers on health outcomes, and predict future care engagement of HIV patients, are lacking in the literature.

The number of factors identified as barriers and enablers of engagement in care tended to decrease with the increasing predictive ability of the methodology used to measure them. Qualitative and descriptive studies typically identified an exhaustive range of individual, interpersonal, community, health system, and structural factors that affect engagement in care, with qualitative studies usually capturing factors related to perceptions and attitudes and descriptive studies capturing measures related to issues involving taking HIV drugs because of their focus on medication adherence. Studies assessing association or causation identified the factors descriptively then tested for an association between a select number of them and health outcomes, usually a step of the care continuum. Studies employing psychometric methods typically aimed to identify broader factors by grouping the barriers and enablers into domains, achieved by factor analysis methods. These methods allowed investigators to capture factors that are more latent quantitatively. Mixed methods studies had the best opportunity to merge two or more of these approaches in the same population. These studies often collected qualitative data prior to or in-tandem with quantitative data and used the emerging themes to descriptively quantify the proportion of participants reporting each factor. Some of the studies also went further to assess the effect of each factor on an important health outcome, such as a step of the care continuum. Alternatively, some mixed methods studies first assessed the factors from quantitative data and then proceeded with qualitative analysis on a sample of the participants to

get a better understanding of how the participants experience these factors. In general, only psychometric and multivariable approaches allowed for longitudinal assessments of the effect of barriers or enablers on a future step of the continuum.

The specific barriers and enablers of engagement in HIV care identified in this systematic review are largely similar to those found in previous reviews and can be broadly summarized as factors pertaining to transportation costs and other financial constraints, ability to take time off work and other life commitments, distance to the health facility, stigma and fear of disclosure, health facility logistics, interactions with healthcare providers (including perceived staff competence), quality of care, medication side effects, psychosocial support (including motivation from family or community members), mental health, overall health (which influences risk perception), health education, nutrition, substance use, and mobility. [6-15] This review, however, was more inclusive of all these factors than any single review because of its non-restriction to a specific step of the care continuum, specific population, or country or region of the world.

This systematic review highlights the scarcity in the literature of studies using certain methodologies or assessing specific groups of people or steps of the care continuum. Only seven of the 228 studies assessed used psychometric methods. Psychometric methods allow the standardization and validation of tools that can be used in future studies and in program settings and are an important step in scale development.[263,264] Validated tools would make comparisons across studies easier and can be used to systematically quantify the reported reasons why HIV patients engage or disengage from care and predict future engagement. Longitudinal assessments of the effects of barriers or enablers on future steps of the care continuum are largely absent in the literature. There is also a scarcity of studies assessing multiple steps of the care continuum and none assessing barriers and enablers of viral load suppression alone based on the criteria for

this review. Only a quarter of studies were from HICs. Even though these countries are mostly in the Western and Central Europe and North America regions of the world, which comprises 6% of PLHIV in the world, the region's 95-95-95 progress lies at 88-81-67,[4] hence there is a need to continue to investigate barriers and enablers of engagement in care in these regions. Finally, there is a scarcity of studies among children, adolescents and youth (and their caregivers), men, MSM, FSWs, PWID, and other key populations. Given that 62% of all new HIV infections globally were among key populations and their partners in 2019 and that one in four infections in sub-Saharan Africa were among adolescent girls and young women,[4] it is vital to understand the factors that affect engagement in care in these populations in order to improve HIV-related morbidity and mortality, and ultimately achieve community viral load suppression to mitigate the spread of HIV.

This review had several limitations. It only assessed articles written in English, which could have excluded studies written in other languages with no English translation that would have otherwise met the inclusion criteria. It also did not include non-peer-reviewed articles, conference abstracts, review articles, commentaries, or gray literature, but exclusion of this type of literature was necessary for a clear and rigorous assessment of the methodology used in the studies. This systematic review did not include an assessment of the measurement and analytic approaches of barriers and enablers of HIV testing, which is the first step in the HIV care continuum. This limits the potential to add to the literature an understanding of factors that influence the decision or opportunity to test for HIV, which includes both HIV positive and negative persons at a broader community level (and may have downstream effects on other steps of the continuum); this review only assesses factors unique to HIV patients that influence their engagement in care after HIV diagnosis. Finally, the classification of study types was based on a

combination of measurement and analytic methods, which is not the usual classification of studies but was necessary for the comparison of different approaches as per the objectives of the study.

This review had several strengths. It appears to be the first to systematically summarize the methodology of studies measuring barriers and enablers of engagement in the HIV care continuum. It also appears to be the only systematic review to summarize articles assessing barriers and enablers of the linkage, retention, ART initiation and adherence, and viral load suppression steps of the HIV care continuum together across all populations of PLHIV globally. It is one of the few systematic reviews not restricted to specific populations or regions of the world. Other than a meta-analysis assessing barriers to ART adherence,[14] it is the only systematic review that specifically had measurements of barriers or enablers collected directly from patients and not merely assessed as risk factors (that is, variables not measured as barriers and enablers but later assessed as such) as an eligibility criteria, assuring a more accurate measurement of the intended constructs.

In conclusion, this systematic review established that qualitative and descriptive studies can be used to identify the range of barriers and enablers of engagement in the HIV care continuum. However, more studies assessing association or causation, psychometric, and mixed-methods studies are needed to measure more latent constructs in a standardized way, quantify the effect of each factor on actual care engagement and predict future engagement.

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2.7 Tables and Figures

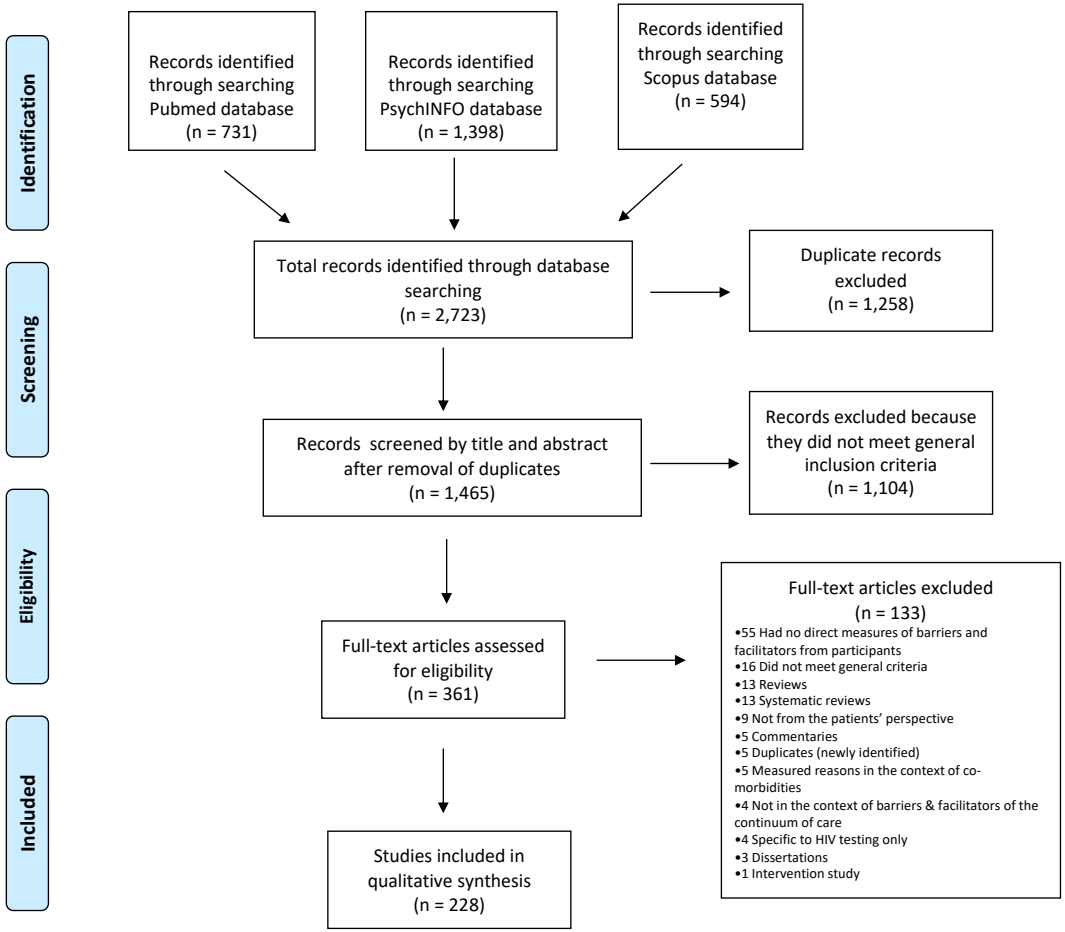

Figure 2.1: PRISMA Flow Diagram for Systematic Review

Table 2.1: Characteristics of Studies Included by Measurement Approach for Barriers/Enablers of Engagement in the HIV Care Continuum

	Qualitative Analysis [n=126 , 55.3%]		Quantitative (Descriptive) [n=63, 27.6 %]		Quantitative (Assessing Association or Causation) [n=16 , 7.0 %]		Quantitative {Psychometric (Factor Analysis or Scale Development)} [n=7, 3.1 %]		Mixed Methods (Qualitative and Quantitative) [n=16, 7.0 %]		Total (n = 228)	
Characteristic	**Number of Studies**	**% of Studies**	**Number of Studies**	**% of Studies**	**Number of Studies**	**% of Studies**	**Number of Studies**	**% of Studies**	**Number of Studies**	**% of Studies**	**Number of Studies**	**% of Studies**
Type of Country/Countries												
Low and Middle Income	102	81.0	46	73.0	6	37.5	1	14.3	12	75.0	167	73.2
High Income	23	18.3	16	25.4	10	62.5	5	71.4	4	25.0	58	25.4
Mixture of High and Middle/Low Income Countries	1	0.8	1	1.6	0	0.0	1	14.3	0	0.0	3	1.3
Step/s in the Care Continuum for Which Barrier/Enablers Were Measured												
Linkage to Care	5	4.0	3	4.8	0	0.0	0	0.0	0	0.0	8	3.5
Retention in Care	16	12.7	8	12.7	2	12.5	1	14.3	4	25.0	31	13.6
ART/HAART Initiation or Adherence	57	45.2	44	69.8	11	68.8	6	85.7	5	31.3	123	53.9
Viral Load Suppression	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Multiple Steps	48	38.1	8	12.7	3	18.8	0	0.0	7	43.8	66	28.9
Longitudinal Assessment of Barriers and Enablers												
Done	1	0.8	0	0.0	6	37.5	3	42.9	0	0.0	10	4.4
Not Done	125	99.2	63	100.0	10	62.5	4	57.1	16	100.0	218	95.6
Population in Which Barriers and Enablers were Assessed												
General Population	17	13.5	5	7.9	3	18.8	1	14.3	5	31.3	31	13.6
Clinical Cohort	47	37.3	39	61.9	9	56.3	2	28.6	5	31.3	102	44.7
Key Population (MSM) or gay and bisexual	5	4.0	2	3.2	1	6.3	2	28.6	1	6.3	11	4.8

	Qualitative Analysis [n=126 , 55.3%]		Quantitative (Descriptive) [n=63, 27.6 %]		Quantitative (Assessing Association or Causation) [n=16 , 7.0 %]		Quantitative {Psychometric (Factor Analysis or Scale Development)} [n=7, 3.1 %]		Mixed Methods (Qualitative and Quantitative) [n=16, 7.0 %]		Total (n = 228)	
men and/or transgender men or women												
Key Population (FSW)	3	2.4	0	0.0	0	0.0	0	0.0	0	0.0	3	1.3
Key Population (IDUs/PWID)	10	7.9	3	4.8	0	0.0	0	0.0	0	0.0	13	5.7
Key Population (Other e.g. people with alcohol abuse/dependence problems, prisoners, young adults, other women, refugees, persons living with disabilities, people in discordant relationships, mobile populations)	9	7.1	3	4.8	0	0.0	1	14.3		0.0	13	5.7
Men	6	4.8	0	0.0	0	0.0	0	0.0	1	6.3	7	3.1
Adolescents/Youths and/or Children	4	3.2	1	1.6	0	0.0	1	14.3	1	6.3	7	3.1
Caregivers and Children/Adolescents	5	4.0	1	1.6	3	18.8	0	0.0	1	6.3	10	4.4
Pregnant and/or Postpartum Women	14	11.1	7	11.1	0	0.0	0	0.0	2	12.5	23	10.1
Mothers and/or Caregivers	6	4.8	2	3.2	0	0.0	0	0.0	0	0.0	8	3.5
Quality of Studies*												
Good	53	42.1	16	25.4	6	37.5	1	14.3	5	31.3	81	35.5
Fair	57	45.2	28	44.4	8	50.0	6	85.7	8	50.0	107	46.9
Poor	16	12.7	19	30.2	2	12.5	0	0.0	3	18.8	40	17.5

ART = Antiretroviral Therapy
HAART = Highly Active Antiretroviral Therapy
MSM = Men who have Sex with Men
FSW = Female Sex Workers

IDUs = Injecting Drug Users
PWID = People Who Inject Drugs
*Study quality was assessed using the Agency for Healthcare Research and Quality (AHRQ) tool[32] for quantitative studies and the tool developed by Hawker and colleagues (Appendix D)[33] plus the Critical Appraisal Skills Programme (CASP) Checklist[34] for qualitative studies. Mixed method studies were assessed using both sets of tools.

Chapter 3: Latent Enablers of Engagement in the HIV Care Continuum in Eswatini

3.1 Abstract

Background: Although most people living with HIV (PLHIV) remain in care until they achieve viral load suppression, a substantial proportion are not able to make the initial linkage step, and others are unable to stay in care or adhere to medications. The barriers to and enablers of linkage and retention in care have primarily been assessed qualitatively and descriptively. Drawing from the Link4Health two-arm trial conducted in Eswatini, this study employs psychometric methods to assess the reasons behind different levels of engagement in care among PLHIV in Eswatini and how these reasons predict future engagement and viral load suppression.

Methods: Link4Health was conducted in Eswatini (2013-2014) to assess the effectiveness of a combination intervention strategy (CIS) in improving linkage and retention in HIV care among newly diagnosed HIV positive adults compared to standard of care (SOC). This analysis included Link4Health participants who linked to care within 1 month of HIV diagnosis (n=1,931), and an additional analysis was done on those who were on ART for at least 4 months (n=1,120). At both the 1- and 12-month visits, participants were asked to list reasons why they linked to care in general and at a specific clinic, and at the 12-month visit, why they had stayed in care. Confirmatory factor analysis (CFA) and structural equation modeling (SEM) techniques were used to assess the factor structure of enabling factors for linkage and retention in care, and to

assess the relationship between the latent enablers and observed measures of retention and viral load suppression.

Results: According to the CFAs, the best-fitting models were: a one-factor structure for the range of enablers for linking to care in general at 1 month in the SOC arm ("Instructed/Easy Access"), a two-factor structure for enablers for linking to care in general at 12 months in the CIS arm ("Instructed" and "Easy Access/Financial Reasons"), a two-factor structure for enablers for linking to care at a specific clinic at 1 month in the CIS arm ("Stigma Mitigation/Psychosocial Support" and "Good Clinical Services"), and a one-factor structure for enablers for linking to care in general at 12 months among participants on ART for at least 4 months in the CIS arm ("Instructed/Easy Access"). The "Instructed/Easy Access" factor predicted future retention in care at 12 months in both the SOC and CIS arms, but it did not predict viral load suppression. None of the hypothesized factor models for linkage to care at a specific clinic at 12 months or retention in care at 12 months were of good fit.

Conclusion: Financial and access reasons appear to be the predominant enablers of linkage to care in general, while psychosocial reasons such as stigma mitigation and having psychosocial support and good clinical services matter more for linkage at a specific clinic.

3.2 Introduction

The HIV care continuum describes the sequential stages of HIV medical care that people living with HIV (PLHIV) need to navigate from initial diagnosis to sustained viral load suppression.[1] This model is the foundation for the UNAIDS 95-95-95 goals (upgraded from 90-90-90), which aim to end AIDS by 2030 by having 95% of all HIV positive people know their status, 95% of those knowing their status be on sustained ART and 95% of those on ART be virally suppressed.[2-4] Achieving these goals is contingent upon having effective systems to facilitate linkage and retention in care across the clinical continuum.[2-4] While high achievement of the 'first' UNAIDS goal – 95% of those HIV positive knowing their status – likely requires intervention mechanisms outside of the traditional clinical context, improving achievement of the second and third UNAIDS goals will likely be heavily based on clinical interventions. Prompt initiation on ART has been implemented at the policy level based on a combination of increased community-based testing and changes to a 'treat all' approach to initiate all HIV positive patients on ART as soon as possible,[5-7] but the downstream implications have been heterogeneous.[6-14] For example, some implementers have reported increased attrition and non-adherence following shifts to 'treat all' from a CD4 threshold-based criterion for ART initiation.[6,13,14] Thus, while ART adherence is critical, identifying actionable ways of improving adherence or at least identifying individuals at risk for non-adherence remains understudied. Since ART adherence is critical to achieving viral load suppression and sustained health for HIV positive patients,[15] it is important to understand the underlying reasons behind whether or not PLHIV link to care in a timely manner and are retained in care (the steps that precede ART adherence), adhere to ART, and are virally suppressed (the consequence of ART adherence) in order to curtail the HIV epidemic.

Several barriers and enablers of linkage and retention in HIV care have been identified in the literature, and they include factors such as transportation costs and other financial constraints, ability to take time off work and other life commitments, distance to the health facility, stigma and fear of disclosure, health facility logistics, interactions with healthcare providers (including perceived staff competence), quality of care, medication side effects, psychosocial support (including motivation from family or community members), mental health, overall health (which influences risk perception), health education, nutrition, substance use, and mobility. [16-24] However, these barriers and enablers have mostly been assessed qualitatively and descriptively.[16-24] Although these approaches are useful for understanding the range of potential barriers and enablers of linkage and retention (from emerging themes), understanding the underlying constructs behind these themes and how these barriers and enablers relate to each other at different stages of the HIV care continuum will require a step beyond qualitative and descriptive analysis. Many barriers and enablers are latent (not easily observable) and can best be captured by methods that can classify them into dimensions that can be measured quantitatively. Factor analysis is one such approach as it allows researchers to assess the factor structure of the reasons behind differential engagement in care of HIV patients.

Psychometric (measurement) methods have been used to analyze barriers and enablers of retention and ART adherence in a few studies, [25-31] but most were limited to assessments of barriers and enablers of ART adherence by using adherence-specific scales,[25,27-31] with one assessing factors associated with retention.[26] Additional studies used existing scales to assess the effect of hypothesized barriers or enablers on ART adherence or retention in care without directly measuring the barriers or enablers from patients.[32-37] Thus, all previous studies assessed only one step of the care continuum, i.e., retention in care or ART adherence. None have

assessed barriers or enablers to initial engagement to care (linkage). Only three did a longitudinal assessment of the impact of the barriers to retention or adherence on future outcomes of retention or viral load suppression.[25-27] Only one included countries in sub-Saharan Africa, using program data from three East African countries, and this study was prone to selection bias as it only used available routine data.[26] In order to obtain valid findings that are relevant to generalized epidemic settings, it is important to assess enablers of engagement in care (that is, linkage and retention), using individual-level data from a cohort representative of people in care in a high-burden country.

This study aims to assess the factor structure of enablers of linkage and retention in HIV care in Eswatini by:

1. Conducting confirmatory factor analysis (CFA) to capture the underlying latent (unobservable) constructs that enable linkage and retention in care at 1 month and 12 months
2. Assessing how the latent constructs are related to observed variables expected to measure the same constructs (potential barriers to linkage and retention in care)
3. Assessing how the latent constructs are independently related to downstream outcomes of measured retention in care and viral load suppression

This analysis will capture latent enablers of engagement in care and assess their effect on future engagement at different time points in the HIV care continuum, which is important for helping HIV patients stay in care and curtailing the HIV epidemic.

3.3 Methods

Study Population, Design and Setting

This analysis included participants of the Link4Health study, which has been described elsewhere.[38,39] Briefly, Link4Health was a cluster-randomized implementation science trial conducted in Eswatini from August 2013 to November 2014 to assess the effectiveness of a combination intervention strategy (CIS) in improving linkage and retention in care among newly diagnosed HIV positive adults compared to standard of care (SOC). Link4Health employed a package of interventions comprised of five evidence-based components: point-of-care CD4+ count testing, accelerated ART initiation, SMS appointment reminders, basic healthcare and educational packages, and non-cash financial incentives (mobile phone credit). [38,39] This study was primarily designed to assess the effect of the CIS intervention on linkage to care within 1 month of HIV diagnosis and retention in care within 12 months of HIV diagnosis at the individual participant level. Participants in the CIS arm were more likely to achieve the primary outcome than those in the SOC arm (relative risk [RR] 1.52, 95% CI 1.29-1.96, p=0.002), and more likely to be retained in care at 12 months regardless of time to linkage (RR 1.48, 95% CI 1.18-1.86, p=0.002), but there was no difference in linkage (separate from retention at 12 months), mean time to linkage and viral suppression among those on ART for at least 6 months.[38]

The study unit of randomization was a public secondary-level HIV clinic paired with its largest affiliated public primary-level HIV clinic.[38,39] There were a total of 11 existing secondary-level HIV clinics in the country at the time of the study, and 10 of these were selected as study units based on clinic patient volume.[38,39] Study units were pair-matched by supporting implementation partner, clinic location (rural vs. urban), and clinic size (based on expected

monthly enrollment of adult HIV patients per facility).[38,39] One of each pair of the matched study units was randomly assigned to the CIS arm, with the other being assigned to the SOC arm.[38,39] A cluster design was chosen to ensure service delivery was not disrupted, allow for a better fit with routine operations of the clinics, and ease the implementation of the study for the clinic staff. [38,39] The study staff and clinic providers at each study unit were not blinded to the study arm assignment of their site. [38,39] Participant eligibility criteria included having received a positive HIV test, being at least 18 years of age, willing to receive HIV care at a selected clinic, and consenting to study procedures.[38,39]

All participants completed a baseline questionnaire and had relevant clinical medical records abstracted covering visits up to 14 months after study enrollment. Participants were also given follow-up questionnaires at 1 and 12 months after study enrollment. All data were collected in English or SiSwati. The survey included open-ended questions about why participants linked or were retained in care in general and at a specific clinic at each time point, and the study staff fit the participant responses into a pre-determined list of possible responses. Specifically, participant reasons for linking to care in general and at a specific clinic at 1 month were collected in response to the following questions: "Why did you go to the ART clinic after testing positive?," and "Why did you go to that specific ART clinic?" respectively. Participants were asked again at 12 months to list reasons for linking to care in general, linking to care at a specific clinic, and retaining in care based on the following questions: "Why did you go to an HIV care clinic during the last 12 months?," "Why did you go to that specific ART clinic?," and "Why do you continue to get HIV care at that clinic?" respectively. The specific questions asked to measure each reason for linking and retaining in care are summarized in Appendix C. The current analysis is limited to participants who linked to care within 1 month of the study, and an

additional analysis was performed on participants who were on ART for at least 4 months (regardless of time to linkage) during the study period to allow for an assessment of the effects of enablers of engagement in care on viral load suppression (Figure 3.1).

All participants provided written consent to participate in the study, and the study was approved by the Institutional Review Boards (IRBs) at Columbia University and the Swaziland Science and Ethics Committee.

Measures

Linkage and Retention in Care and Viral Load Suppression

Linkage to care in the Link4Health study was defined as a participant having made at least one visit to any clinic within the assigned study unit, having had an HIV chronic care file opened, and having had a clinical assessment. Retention in care was defined as a participant being alive and having made a clinic visit at least once 90 days before the end of the 12-month study period, as verified by clinic records. Viral load suppression was defined as a participant having HIV-1 RNA < 1,000 copies/mL 12 months after HIV diagnosis and was assessed as a binary variable. Implausible viral load measures were coded as missing. For variables that had "don't know" and "refused" responses, these responses were also coded as missing. Sensitivity analyses imputing missing values for viral load were conducted as described below.

Items Used in Confirmatory Factor Analysis

Using follow-up questionnaires, study staff asked participants to list reasons why they had accessed care in general and at a specific clinic (at 1 and 12 months) and had been retained in care (at 12 months). Participants were allowed to list more than one reason, and the

interviewer could prompt for more reasons. The study staff then selected all applicable reasons on the pre-determined checklist based on the responses from each participant. Table 3.1 shows the instrument used to code participant responses to questions assessing reasons for linking to care in general at both 1 month and 12 months. Table 3.2 shows the instrument used to code participant responses to questions assessing reasons for linking to care at a specific clinic at both 1 month and 12 months, which was also the same instrument used for reasons for retaining in care at 12 months. Reasons (henceforth called items) were measured on a binary scale.

The hypothesized factorial models for the CFAs were obtained from themes identified in qualitative and descriptive studies and from an exploratory factor analysis (EFA) performed using data collected from a related study in Mozambique (Engage4Health[40,41]) conducted during the same period. The Engage4Health study was used to identify potential enablers of engagement in care in the Link4Health study because it assessed a similar broader research question in a country that also has a generalized epidemic and is in the same region as Eswatini. The EFA outcomes obtained from the Engage4Health analysis are depicted by the grouping of items into specific factors and illustrated graphically in figures as described below. The correlations (factor loadings) between the items in the Engage4Health EFA (depicting reasons for linking or retaining in care) that were similar to those in the Link4Health study and the latent factors they represented are summarized in Appendix D. The hypothesized factors included in the current analysis were limited to those that could be extracted from available items in the Link4Health study. After the factors were selected from the Engage4Health EFA and from previous qualitative and descriptive studies, an appropriate label was given for each factor based on the construct it was hypothesized to capture. For the assessment of reasons for linking to care in general at both 1 month and 12 months, two and four-factor models were hypothesized (from the

EFA and previous studies respectively, though the "Instructed" factor was unique to the current study). The two-factor model consisted of the following factors and the corresponding number of items as illustrated in Figure 3.2: "Instructed" (2 items); "Access/Financial Reasons" (2 items). The four-factor model consisted of the following factors and the corresponding number of items as illustrated in Figure 3.3: "Instructed" (2 items); "Access/Financial Reasons" (3 items); "Family/Community Motivation" (2 items); "Risk Perception" (2 items). For the assessment of reasons for linkage to care at a specific clinic at 1 month and 12 months and retention in care at a specific clinic at 12 months, four and five-factor models were hypothesized (from the EFA and previous studies respectively, though the "Instructed" factor was unique to the current study). The four-factor model consisted of the following factors and the corresponding number of items as illustrated in Figure 3.4: "Instructed" (2 items); "Access/Financial Reasons" (4 items); "Good Clinical Services" (6 items); "Stigma Mitigation/Psychosocial Support" (2 items). The five-factor model consisted of the following factors and the corresponding number of items, as illustrated in Figure 3.5: "Instructed" (2 items); "Access/Financial Reasons" (4 items); "Good Clinical Services" (6 items); "Stigma Mitigation/Psychosocial Support" (4 items); good "Staff Competence" (3 items).

Potential Barriers to Engagement in Care

As part of the construct validity assessment in the CFAs, latent factors identified in the CFAs were assessed for an association with observed variables that were expected to measure similar constructs and were considered potential barriers to linkage and retention in care. These included perceived stigma at baseline, perceived psychosocial support at baseline, a summative combination of perceived stigma and psychosocial support variables as described below (in order

to compare to the combined "Stigma Mitigation/Psychosocial Support" latent enabler), perceived staff competence at baseline (binary), travel time to the health facility at baseline (binary, split by 30 minutes or more vs. less than 30 minutes), and employment status at baseline (binary, unemployed vs. employed). Perceived stigma was measured as a summative score from a set of questions from the baseline questionnaire. Specifically, participants ranked their stigma concerns on a 4-point Likert scale from "strongly agree" to "strongly disagree," and a summative score was created from the following questions: "you feel others may be concerned they could 'catch' your illness through contact like a handshake or eating food you make"; "you feel others will avoid you because you are HIV-positive"; "you feel you need to keep your HIV status a secret"; "due to your being HIV positive, you have a sense of being unequal in your relationships with others." Participants were also asked how concerned they were that other people would find out they were HIV positive, with responses ranging from very concerned, a little concerned, to not at all concerned, and responses were added to the summative score. Perceived stigma was also dichotomized by the median value from the summative score. Perceived psychosocial support was measured as a summative score from a set of questions from the baseline questionnaire. Specifically, participants ranked their perceived availability of support and social capital on a 3-point scale and from an additional question: "Would you like your family members to give you more, the same or less emotional support" (a response of "more" was considered "low" support) and "How many close friends do you have these days? These are people you feel at ease with, can talk to about private matters, or call on for help." (a response of "less than two" was considered "low" support). [42] The responses to these two questions were summed up, and a binary measure was created using the median value as the cut-off point. Perceived staff competency was estimated from the following question asked at baseline as a binary measure:

"health care workers in ART clinics are not knowledgeable about HIV," and responses were categorized as yes/no.

Variables Used in the Analysis of the Relationship Between Latent Enablers of Engagement in Care and Retention in Care and Viral Load Suppression

Factors identified in the CFA were used as primary exposures of interest in an assessment of their relationship to downstream measures of engagement in care (retention in care and viral load suppression). Retention in care and viral load suppression were measured in the manner described above. In addition, several variables hypothesized as potential confounders of the relationship between enablers of linkage to care and retention in care, and enablers of linkage to care and viral load suppression a priori were controlled for in the regression-based models. These include gender (binary), age (four categories: 18-24, 25-39, 40-49, >50), education (binary, split by none/primary vs. secondary or higher), employment status (binary, split by unemployed vs. employed) and marital status (four categories: widowed/divorced, married, not married to current partner, single).

Statistical Analysis

Univariate statistics (chi-square tests for the categorical variables) were used to assess the distribution of the variables among the participants linked to care and participants on ART for at least 4 months by intervention arm. CFAs were performed in both the full dataset and in strata of different intervention arms.

CFAs were used to assess the factor structure of enablers of linkage to care at 1 and 12 months and retention in care at 12 months. The CFAs were fit using weighted least squares with

mean and variance adjustment (WLSMV) on a tetrachoric correlation matrix, which is the default matrix for binary data.[43] The direction, magnitude, and statistical significance of factor loadings ≥ 0.3 (the lowest acceptable correlation coefficient[44,45]) were assessed. No rotations were employed, and cross-loadings were not allowed since CFA is dependent on a priori theory, and item residual covariance was fixed at 0. The following indices were used to assess model fit: Comparative Fit Index (CFI) and Tucker-Lewis Index (TLI) [≥ 0.9 considered acceptable and ≥ 0.95 good fit] and Root Mean Square Error of Approximation (RMSEA) [≤0.08 considered acceptable and ≤0.05 good fit].[46,47] Chi-square tests were used to compare nested models (i.e., fewer vs. more factors).[48] When the models did not converge, individual items with factor loadings < 0.3 or with minimal variation of responses in the levels of the items were removed one at a time, and the CFAs were repeated to re-specify the models, but theoretical justification took precedence. Construct validity was assessed using factor loadings and the correlation between latent factors and observed factors expected to be closely related to the latent factors (i.e., the potential barriers of retention in care described above). Internal reliability was assessed by variance explained from the CFAs and ordinal coefficient alpha, which is more suitable for categorical variables than Cronbach's Alpha (with ≥ 0.7 cut-off point considered acceptable reliability).[49-53]

The relationship between different factors identified in the CFAs as enablers of linkage to care was assessed across different time points (1 month and 12 months). An assessment was also done for the relationship between enablers of linkage at 1 month and 12 months and observed retention in care and viral load suppression at 12 months. Structural equation models (SEMs) were used for regression-based estimates with binary outcomes (retention in care or viral load suppression), resulting in a probit coefficient that can be interpreted in the same way as a linear

regression coefficient for both observed and latent factors.[43,48] Variables hypothesized to be potential confounders of the relationship between enablers of linkage to care and retention in care, and enablers of linkage to care and viral load suppression as described above were fit into the adjusted models. The same model fit indices described in the CFA were employed to assess SEM goodness of fit.

Missing viral load suppression and clinical staff competency values were imputed by multiple imputations using multiple imputations with Markov Chain Monte Carlo (MCMC) equations methodology[54-57] assuming that, conditioned on measured variables, data were missing at random. Imputations averaged across 20 datasets had sufficient relative efficiency. Results from the multiple imputation-adjusted sample were compared to a complete case sample to assess the robustness of study findings.

Sample size and power calculations were done using Monte Carlo simulations in Mplus (version 8) [58,59] for the CFAs and to conduct SEMs. Monte Carlo studies draw large samples from data generated from hypothesized populations that have hypothesized parameter values, estimate a model from each sample, then average parameter estimates and standard errors across the several samples.[58] It is estimated that a sample of 265 with no missing data (or 315 with missing data) is sufficient to give a power estimate of 0.8 for non-normally distributed data when conducting CFA, and there is a consensus that 5 to 10 subjects per item gives sufficient power to conduct a CFA.[49] The CFA at 1 month was done on the 1,931 participants who linked to care within 1 month of the study, while the CFA at 12 months was done on the 1,185 participants who were retained in care and the last CFA was done among 1,120 participants on ART for at least 4 months.[38] Given that the maximum number of items on any of the questionnaires used was 20, all CFAs were sufficiently powered.

Descriptive assessments were done using SAS 9.4 software, and CFAs and SEMs were done using Mplus software (version 8).

3.4 Results

Participant Characteristics

As previously described,[38] 2,197 participants were enrolled in the Link4Health study, and of these, 1,931 were linked to care within 1 month, including 1,013 in the CIS arm, and 918 in the SOC arm. Of the 1,120 participants on ART for at least 4 months, 592 were in the CIS arm while 528 were in the SOC arm. Figure 3.1 shows a population flow chart depicting the selection of the analytic cohorts. Table 3.3 below shows the characteristics of participants who were linked to care within 1 month stratified by intervention arm. Over half the participants were female (59%), and most (55%) were aged 25-39. Just over half (54%) had secondary or higher education. More than half (53%) were unemployed. Most (45%) had a partner they were not married to while 37% were married. About 72% of participants with viral load data were virally suppressed, while 23% were missing viral load suppression data. About 61% were retained in care at the 12-month survey. The participants who were on ART for at least 4 months were similar to those who linked to care within 1 month (Tables 3.3 and 3.4). Notable differences included a smaller proportion of those virally suppressed (68%) and a greater proportion retained in care (79%) among participants on ART for at least 4 months. Almost all (98%) of these participants had been linked to care within 1 month.

Confirmatory Factor Analysis and Structural Equation Modeling

Overall, the theoretical models were not supported in the collapsed form of the dataset (i.e., when the two intervention arms were combined). However, after stratification by intervention arm, one stratum of intervention arm had a model with a good or acceptable fit for each assessment of reasons for linkage to care as described below.

Factor Structure of Enablers of Linking to Care in General at 1 Month

In the SOC arm, the two-factor model exhibiting hypothesized latent variables "Instructed" and "Access/Financial Reasons" for participants linking to care in general at 1 month showed good fit indices. The standardized correlation coefficient between the factors was >1, however, which suggested an unstable model and that the factor items likely formed a single factor. The two models were compared using the chi-square test; findings showed no statistically significant differences (chi-square = 3.272 for the two-factor model and 4.769 for the one-factor model—a chi-square difference of at least 3.84 would signify a significant difference at an alpha level of 5% and one degree of freedom), suggesting that the one-factor model fit the data well (CFI /TLI = 0.982/0.945, RMSEA = 0.039). This implies that participants were instructed to go to health facilities that were the most accessible to them, which coincided with mitigating financial burdens, possibly related to transportation costs, and these factors worked together to enable participants in the SOC arm to link to care within 1 month. The one-factor model labeled "Instructed/Easy Access," and corresponding loadings of each item to the latent variable is shown in Figure 3.6. Item 2 ("study staff told me to") had the highest correlation with the latent factor (factor loading = 0.696), while the rest of the items had moderate correlations with the

latent factor (factor loadings = 0.547-0.621). This model had an ordinal alpha value of 0.571, which suggested low internal reliability (or consistency).

To assess the robustness of the hypothesized latent variables, the association between latent and observed variables expected to measure the same constructs was examined. The "Instructed/Easy Access" latent factor was not associated with reported travel time to health facility but was associated with employment status—participants who linked to care because of being instructed, having easy access and for financial reasons were more likely to be unemployed than those who linked to care for other reasons (standardized correlation coefficient 0.320, p-value < 0.001) [Table 3.5]. The moderate factor loadings and the moderate association between the latent factor and observed variables expected to be closely related to the latent factors suggest acceptable construct validity.

At the 1-month visit, half of the participants in the SOC arm reported linking to care because "healthcare worker told me to," while only 4% reported "care and treatment are free" (Table 3.6). About 48% of the variability in the response "study staff told me to" (item 2) can be explained by the latent factor (R-square = 0.484), but very little of the variability in the rest of the items can be explained by latent factor (R-square = 0.300-0.385).

The "Instructed/Easy Access" latent factor significantly predicted future retention in care (Figure 3.6). That is, participants in the SOC arm who reported linking to care because of instruction, easy access to the health facility and financial reasons were more likely to be retained in care 12 months later than those who linked to care for other reasons, adjusting for gender, age, education, employment status, and marital status (standardized regression coefficient 0.300, p-value < 0.001).

None of the CFA models for the CIS arm for linkage to care in general at 1 month were of good fit.

Factor Structure of Enablers of Linking to Care in General at 12 Month

The two-factor model in the CIS arm exhibiting hypothesized latent variables "Instructed" and "Easy access/Financial Reasons" for participants linking to care in general at 12 months exhibited a good fit (CFI/TLI = 0.998/0.989, RMSEA = 0.042). Figure 3.7 shows the two-factor model and corresponding loadings of each item to the latent variables. Item 1 ("health care worker told me to") had the highest correlation with the "Instructed" latent factor (factor loading = 0.990), and the rest of the items also had high correlations with the latent factor (factor loadings = 0.701-0.823). The correlation between the two latent factors was very high (0.994). Ordinal alpha could not be used to assess reliability for this model because each latent factor was derived from only two items, but the R-square values (Table 3.7) for items making up the "Instructed" latent factor were very high (0.678-0.980), and those of items making up the "Easy Access/Financial Reasons" latent variable were moderate (0.492-0.500), suggesting acceptable reliability overall.[49,50]

The latent factor exhibiting "Easy Access/Financial Reasons" for linking to care was not associated with reported travel time to health facility but was associated with employment status—participants who linked to care because of having easy access and for financial reasons were more likely to be unemployed than those who linked to care for other reasons (standardized correlation coefficient 0.174, p-value 0.025) [Table 3.5]. The combination of high factor loadings and correlation with one of the observed variables measuring similar constructs suggest acceptable construct validity.

None of the participants in the CIS arm reported a noticeably higher proportion of reasons of linking to care in general at 12 months than others, but only 2.4% of participants reported "care and treatment are free" as an enabler of linkage to care linked to care (Table 3.7).

None of the latent factors in this model predicted retention in care. None of the CFA models for the SOC arm for linkage to care in general at 12 months were of good fit.

Factor Structure of Enablers of Linking to Care at a Specific Clinic at 1 Month

Initially, the four-factor model in the CIS arm for linkage to care at a specific clinic at 1 month would not converge, likely because many items did not have sufficient variation. The model was re-specified, removing one item at a time that had little variation, but the hypothesized theoretical structure of which items would load on specific latent variables was not altered. Eventually, two factors remained: "Stigma Mitigation/Psychosocial Support" exhibited by items 7 and 8 and "Good Clinical Services" exhibited by items 12, 13, 14, 15, and 16 (Figure 3.8). This two-factor model had good fit indices (CFI/TLI = 1.000/1.012, RMSEA = 0.000). For the "Stigma Mitigation/Psychosocial Support" factor, item 8 ("clinic is far away; HIV status is kept confidential there") had a high correlation with the latent factor (factor loading = 0.694), and the remaining item 7 had a modest correlation with the latent factor (factor loading = 0.483) [Figure 3.8]. For the "Good Clinical Services" factor, item 16 ("lab tests are available") had a high correlation with the latent factor (factor loading = 0.745), but the rest of the items had moderate correlations with the latent factor (factor loadings =0.374-0.504). The correlation between the two latent factors was very high (0.947). The "Good Clinical Services" latent factor had an ordinal alpha value of 0.556, which suggests low reliability. Ordinal alpha could not be used to assess reliability for the "Stigma Mitigation/Psychosocial Support" factor because it was

only derived from two items; the R-square values (Table 3.8) for items making up this latent factor were low (0.233 and 0.482).

The latent factor exhibiting “Stigma Mitigation/Psychosocial Support” as a reason for linking to care was correlated with the binary baseline measure of perceived stigma, with participants who linked to care at a specific clinic at 1 month because of sufficient stigma mitigation and psychosocial support being less likely to have reported low perceived stigma at baseline than those who linked to care for other reasons (standardized correlation coefficient -0.500, p-value 0.022) [Table 3.5]. The latent factor did not exhibit any association with perceived psychosocial support or a combination of perceived stigma and perceived psychosocial support variables. The combination of moderate factor loadings and correlation with one of the observed variables expected to measure a similar construct suggests moderate construct validity. The latent factor exhibiting “Good Clinical Services” was not correlated with perceived staff competence.

Very few participants reported linking to care at a specific clinic for any of the items exhibiting “Stigma Mitigation/Psychosocial Support” or “Good Clinical Services” latent factors (Table 3.8). The variability in the items that could be explained by latent factors was very little to moderate (R-square = 0.140-0.554).

None of the latent factors in this model predicted future retention in care. None of the hypothesized CFA models for linkage to care at a specific clinic at 1 month in the SOC arm were of good fit.

Factor Structure of Enablers of Linking to Care in General at 12 Months Among Participants on ART for at Least 4 Months

Among participants on ART for at least 4 months, the two-factor model in the CIS arm exhibiting latent variables "Instructed" and "Easy access/Financial Reasons" for participants linking to care in general at 12 months showed good fit indices. The standardized correlation coefficient between the factors was >1, however, which suggested an unstable model and that the factor items likely formed a single factor. The two models were compared using the chi-square test; findings showed no statistically significant differences (chi-square = 0.626 for the two-factor model and 0.601 for the one-factor model—a chi-square difference of at least 3.84 would signify a significant difference at an alpha level of 5% and one degree of freedom), suggesting that the one-factor model fit the data well (CFI/TLI = 1.000/1.006, RMSEA = 0.000). As explained earlier, this implies that participants were instructed to go to health facilities that were the most accessible to them, which coincided with mitigating financial burdens, possibly related to transport costs, and these factors worked together to enable participants in the CIS arm to link to care within 1 month. The one-factor model labeled "Instructed/Easy Access," and corresponding loadings of each item to the latent variable is shown in Figure 3.9. Item 1 ("health care worker told me to") had the highest correlation with the latent factor (factor loading = 0.972), followed by item 2 ("study staff told me to") [(factor loading = 0.887]; the rest of the items also had high correlations with the latent factor (factor loadings = 0.605 and 0.772). This model had an ordinal alpha value of 0.571, which suggested low internal reliability (or consistency).

The "Instructed/Easy Access" latent factor was not associated with reported travel time to the health facility, nor was it associated with employment status (Table 3.5). The high factor

loadings and the lack of an association between the latent factor and observed variables expected to be closely related to the latent factors suggest moderate construct validity.

At the 12 month visit, a small proportion of the CIS participants who were on ART for at least 4 months linked to care because of the items exhibiting the "Instructed/Easy Access" latent variable (Table 3.9); in fact, only 2% of participants reported "care and treatment are free" as an enabler of linkage to care. The items most explained by the latent factor are items 1 and 2 (R-square = 0.994 and 0.786 respectively), and the rest were moderately explained by the latent factor (R-square = 0.366 and 0.597).

The "Instructed/Easy Access" latent factor significantly predicted retention in care (Figure 3.9). That is, participants who linked to care in the previous 12 months because of instruction, easy access to the health facility and financial reasons were more likely to be retained in care at 12 months than those who linked to care for other reasons, adjusting for gender, age, education, employment status, and marital status (standardized regression coefficient 0.396, p-value < 0.001). The "Instructed/Easy Access" latent variable did not predict viral load suppression at 12 months in both the complete case and imputed analyses (the imputed results are shown in Figure 3.9).

None of the CFA models for the SOC arm for linkage to care in general at 12 months among participants on ART for at least 4 months were of good fit.

Factor Structure of Enablers of Linkage to Care at a Specific Clinic at 12 months and Retention in Care at 12 Months

None of the CFA models hypothesized for assessing underlying reasons for linkage to care at a specific clinic at 12 months or retention in care at 12 months exhibited good or

acceptable fit indices even after model re-specification; hence they could not be compared with other enablers of linkage to care.

3.5 Discussion

In this analysis of latent enablers of linkage and retention in HIV care in Eswatini, several factors, including financial and access reasons were the most prominent factors in predicting the outcomes in the HIV care continuum. The current study used psychometric methods to assess the enablers of linkage and retention in care and how they relate to observed measures across the HIV care continuum. It appears to be the first study to use such methods to assess factors associated with initial linkage to care and one of the first studies to use psychometric methods in a sub-Saharan African population with a generalized epidemic. The enablers that emerged were: "Instructed/Easy Access" for linking to care in general (at 1 month for SOC arm participants and at 12 months for CIS arm participants on ART for at least 4 months); "Instructed" and "Easy Access/Financial Reasons" for linking to care in general at 12 months for CIS arm participants; and "Stigma Mitigation/Psychosocial Support" and "Good Clinical Services" for linking to care at a specific clinic at 1 month for CIS arm participants. Smaller models with fewer factors were of a better fit than bigger models. However, the emerging underlying factors were the same for both the CIS and SOC arms for the same set of questions (though at different time points). There was no instance where both arms had a stable model for the same set of questions asked at the same time to allow for close comparison.

These findings suggest that the CIS intervention, which was designed to support linkage and retention, compared to SOC, affected participants' reasons for linking to care differently from those who did not receive the intervention. Models with a good fit emerged more often in

the CIS arm than the SOC arm, and when the same underlying factors were detected for both arms, the latent factors in the CIS arm had higher factor loadings. The SOC arm only had a good-fitting model at the earlier time point for reasons for linking to care in general, while the CIS arm had good-fitting models for linking to care at later time points, other than linking to care at a specific clinic, suggesting that it took time for the intervention components to aid the continued engagement of participants in a consistent way. Particularly, the financial incentives component of the CIS package was administered at different time points throughout the Link4Health study and was designed to aid retention than initial linkage, which is also supported by the fact that the CIS intervention had an effect on retention in care (regardless of time to linkage) but not on linkage to care in the Link4Health study as described earlier.[38] This time effect could also explain why the SOC arm had lower factor loadings than the CIS arm for the same questions asked at different times (indicative of linkage to care at 1 month for the SOC arm, since the CIS arm had no constructs emerging at 1 month, and continued engagement in care at 12 months in the CIS arm)—participants may not have a good perception of what the enablers of engagement in care are immediately after their HIV diagnosis, but this perception could develop into a stronger construct over time. The CIS arm also had a larger number of people who linked and were retained in care than SOC arm, so the CIS arm may have a sample size advantage, although the SOC arm had more variation in the CFA items than the CIS arm. Participants in the CIS arm could have also given reasons for engaging in care that they deemed more acceptable to the interviewer, given that they were not blinded to the fact that they were given a package of interventions aimed to help them link or be retained in care. Reasons for linking to care at a specific clinic could have been tied to intervention components that affected participant perception of "Good Clinical Services." Particularly, the point-of-care CD4+ count testing,

accelerated ART initiation, SMS appointment reminders components of the CIS package, which were administered close to the time of HIV diagnosis, could have affected participants' perception of the quality of clinical services and aided linkage to care at a specific clinic.[38] However, since the CIS package as a whole did not have an effect on linkage to care as described earlier,[38] it is difficult to determine which components were more effective than others, but psychometric methods can pick up underlying constructs which consistently enable particular patients to link to care in this case (enablers that are more recognizable), and these may be tied to some components of the package intervention intended to aid all patients to link to care.

Access and financial factors emerged as important enablers of linkage to care in general at different time points, while "Stigma Mitigation/Psychosocial Support" and "Good Clinical Services" emerged as important factors to linkage to care at a specific clinic. These results were similar to a psychometric analysis of East African PLHIV for whom poverty/transport costs, quality of care at the clinic, and fear of HIV disclosure were important barriers to re-engagement in HIV care.[26] The East African study was, however, subject to considerable selection bias as it only assessed patients with available follow-up data from clinics participating in the specific HIV programs; the similar findings nonetheless support the possibility that these factors may be strong barriers (and corresponding enablers) in the sub-Saharan African context.[19,60] An ecological study, including 59 countries assessing enablers of increased ART coverage, found social/financial protection and anti-discrimination to be factors associated with improved ART coverage of PLHIV.[61] The ecological study, however, only included countries with complete data (which subjects it to significant bias) and had a limited sample size. Also, since it was an ecological study, causal inferences cannot be drawn from it. Stigma was also found to be a significant barrier to ART adherence in a US population of HIV patients.[27] A study from a

European survey of men who have sex with men (MSM) also found fear of consequences that included HIV disclosure and lack of accessibility to be important factors associated with not taking ART.[29] None of the factors which emerged in this analysis were found in a factor analysis of Australian mostly gay men assessing reasons for not taking ART, [28] a study of German HIV patients assessing barriers to ART adherence,[30] nor a study assessing barriers to HAART adherence in a population of HIV positive adolescents in the US.[31] A comparison with studies assessing barriers of engagement, however, assumes that the enablers to engagement are perfect opposites to barriers, but this can only be assessed with certainty in the same study. Also, many of these studies assessed factors affecting ART adherence, which is very different from linkage. Still, since some of the questions assessing reasons for linkage in the current study were asked at the 12-month follow-up period, linkage and retention at 12 months may have meant the same thing to some Link4Health participants since the questions did not emphasize initial linkage only. Finally, six of the previous seven psychometric studies were all based in high-income countries with concentrated epidemics, hence there may be cultural and contextual factors that may be different from the setting of the current study, which is characterized of a generalized epidemic in a low-income country. Some of the cultural and contextual factors in Eswatini compared to high-income countries may make the definitions of constructs depicting access and financial factors not directly comparable, and HIV stigma may mean different things in a high prevalence setting like Eswatini with a generalized epidemic compared to settings with concentrated epidemics.

The current study found that access and financial factors predicted future retention in care, while mitigation of stigma concerns/good psychosocial support and good clinical services did not predict future retention. Access and financial concerns have also been found to be related

to future engagement, retention, or ART adherence in previous studies.[26,61] However, unlike the current study, most studies have also found stigma concerns to be important predictors of future engagement or ART adherence.[27,29,34-37,61] These studies, however, used different measures of stigma, some using validated scales,[34-37,61] and others not.[27,29] Similarly, previous studies have found factors defining good clinical services to be predictive of future retention or ART adherence.[26,29,32]However, a US study of PLHIV found that trust in the health care system was not associated with subsequent linkage, retention, and ART adherence, and trust in physicians was not associated with linkage or ART adherence, though it was associated with retention in care.[32] A study done on a US population of PLHIV with a history of alcohol abuse or dependence found that psychosocial support was not predictive of ART adherence or viral suppression.[25] In the current study, access, or financial factors also did not predict viral suppression.

The one-factor models, indicating instruction and access/financial enablers in the current study, were the only ones predictive of future retention in care. Combining the instruction reasons with those indicating access/financial reasons may produce a more stable construct than defining them separately. It is reasonable to assume that health care workers and study staff instructed participants to link to the health facility that was nearest to them, hence the most accessible. Accessibility, therefore, emerges as the most important factor in ensuring future retention. This factor, however, did not predict viral load suppression, suggesting that accessibility is not sufficient in itself to ensure that HIV patients consistently take medications. Other psychosocial enablers are needed to work in-tandem with accessibility to ensure viral load suppression among HIV patients, which is essential for curtailing the HIV epidemic at a population level.

This study had several limitations. The assessment was done using data from a study not primarily designed for psychometric assessments. The data were collected from a "checklist" questionnaire at the discretion of the interviewer who selected all applicable reasons from responses from each participant, which limits the number of possible responses; that is, each participant could have selected more responses if they were completing the questionnaire themselves. Interviewers could have been more prone to consistently record access and financial enablers, which can be expected to be at the forefront of residents of resource-limited settings. These considerations, together with the fact that response options were dichotomous, which is not ideal for factor analysis,[49] reduced the variability of the items and resulted in a poor endorsement for many of them. Ideally, non-continuous psychometric data are of better quality when collected from Likert scale-type questions,[49] and if participants select the options themselves. Several items thus had to be removed from the factor analysis to allow the models to converge. Removing items from the CFAs limits the generalizability of the findings as model re-specification was largely determined by the quality of the data as opposed to low association with the latent factors and renders some of the analyses more exploratory than confirmatory (though all analyses were based on CFAs). Also, some of the factors were only derived from two items, which is not ideal for factor analysis and makes assessments of reliability difficult.[49] Ordinal alpha calculation is dependent on the number of items and the average of their correlations, and it cannot be performed on a two-item factor since the average correlation of two items is their actual correlation.[53] Reliability measures were generally low, primarily due to the modest correlations between the items and latent factors. Additionally, some factors did not have an association with observed factors expected to be measuring similar constructs, which compromised their validity. However, some of the observed factors used to assess construct

validity may be different constructs from the latent constructs (or may only capture part of the latent construct), such as the stigma mitigation/psychosocial support one, which was associated with perceived stigma at baseline but not perceived psychosocial support. Indeed, the direction of association with perceived stigma was opposite of the expected one—participants who reported stigma mitigation as an enabler of linkage at a specific clinic at 1 month in the CIS arm were less likely to have reported high perceived stigma at baseline compared to those who linked to care for other reasons. Perceived stigma is likely to change as more time passes from initial HIV diagnosis. Furthermore, this study only assesses data from patients already linked to care, who are more likely to link to care and be retained in care than the general population, assuming barriers to engagement in care would be the opposite of the enablers, but this cannot be established in this analysis. Lastly, this study was done before WHO's "treat all" guidelines,[62] thus, some outcomes may only be applicable to patients who were eligible for ART (those with CD4+ count <350 cells/μL).

This study had several strengths. It appears to be the first study to use psychometric methods to assess factors associated with initial linkage to care among HIV positive patients, which is important for capturing latent enablers of engagement in care and assessing their effect on future engagement at different time points in the HIV care continuum. It also appears to be the only study assessing enablers of engagement in care (as opposed to barriers alone) using psychometric methods while using individual participant data. It is one of two studies to use data from an African country for the proposed methods, and the only one not using an ecological design (which is prone to the ecological fallacy) or using program data from several African countries (which is prone to selection bias). Lastly, given that it uses data from 10 of the 11-existing secondary-level HIV clinics (pair matched with the largest affiliated public primary-

level HIV clinics) in Eswatini at the time of the Link4Health study, this current study has grounds for generalizability to PLHIV in Eswatini formally enrolled in care only, and possibly to similar settings with generalized HIV epidemics.

In conclusion, this study established that psychometric methods can be used to assess the reasons behind the differential engagement of HIV patients at different levels of the HIV care continuum. Financial and access reasons emerged as the most prominent factors and should be important considerations when designing interventions to improve linkage and retention of HIV patients in care. Interventions to improve engagement in care for HIV patients in resource-limited settings similar to Eswatini should thus continue to focus on reducing transport difficulties and clinic costs using approaches such as decentralization of care, task-shifting, community-based care and integration of services to minimize patient visits.[19,60]

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62. World Health Organization. *Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection: Recommendations for a Public Health Approach—Second Edition.* Geneva, Switzerland: WHO;2016.

3.7 Tables and Figures

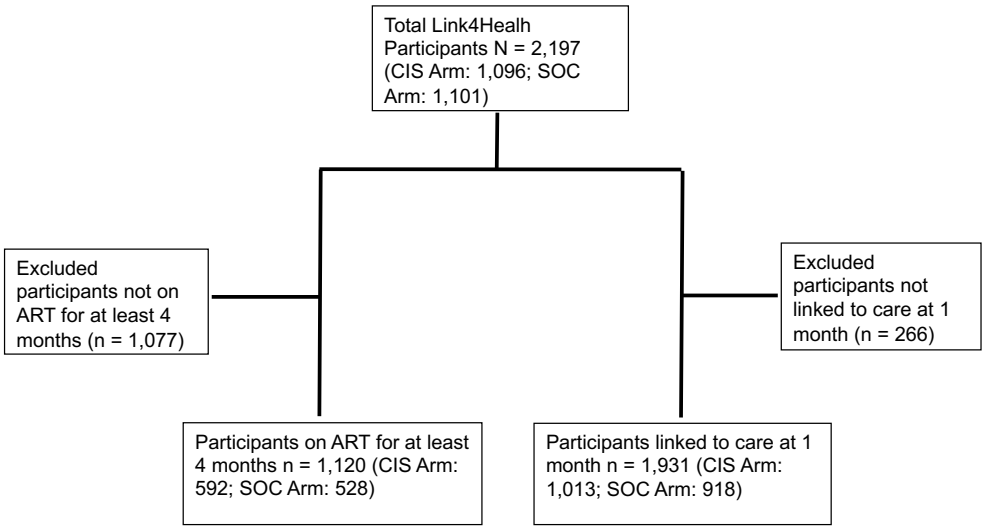

Figure 3.1: Population flow chart of Link4Health participants depicting selection of analytic cohorts. The two analytic cohorts are not mutually exclusive but were analyzed separately.

Table 3.1: Reasons for Linking to Care in General at 1-Month and 12-Month Follow-Up

Item Number	Item
L1	Health care worker told me to
L2	Study staff told me to
L3	Clinic was convenient/close
L4	Had to come to the clinic anyway for something else
L5	Care and treatment are free
L6	My spouse/partner told me to go
L7	Other family/friend/community member told me to go
L8	I was sick and wanted to get care
L9	I knew it would be good for me
L10	Other

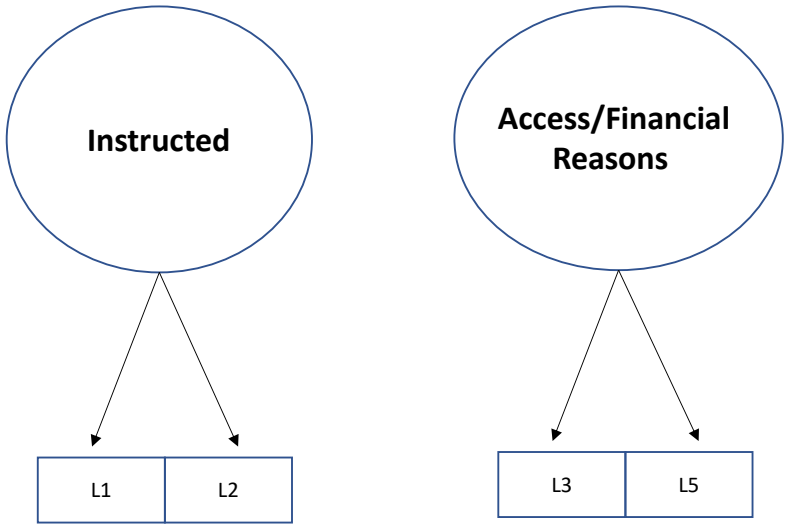

Figure 3.2: Hypothesized 2-factor model for linkage to care in general at 1 and 12 months. Circles indicate latent (unobserved) constructs while squares indicate observed variables. L = Linkage to care items.

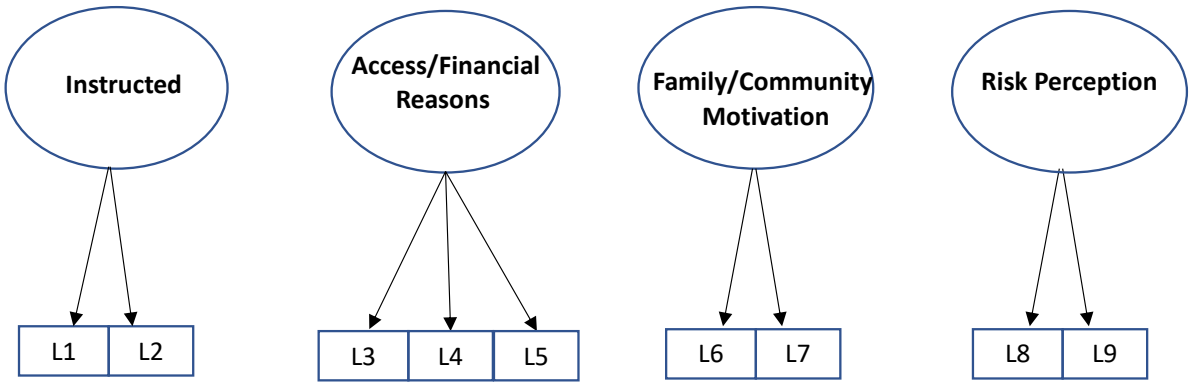

Figure 3.3: Hypothesized 4-factor model for linkage to care in general at 1 and 12 months. Circles indicate latent (unobserved) constructs while squares indicate observed variables. L = Linkage to care items.

Table 3.2: Reasons for Linking to Care at a Specific Clinic at 1-Month and 12-Month Follow-Up and Retention in Care at 12 Months

Item Number	Item
L1	Clinic is convenient/close
L2	Transportation is easy/cheap
L3	Services are affordable/free
L4	Short clinic waiting time
L5	Starting ART is easy/quick
L6	Treatment supporter is not required
L7	I have a friend/family member who goes there
L8	Clinic is far away; HIV status is kept confidential there
L9	Health care worker told me to
L10	Study staff told me to
L11	It is where I go for all services
L12	Staff are respectful; nice
L13	Care is good
L14	There is a doctor there
L15	Medications are available
L16	Lab tests are available
L17	Offers services I need (eg. food)
L18	Support groups
L19	Offers Peer Educators
L20	Other

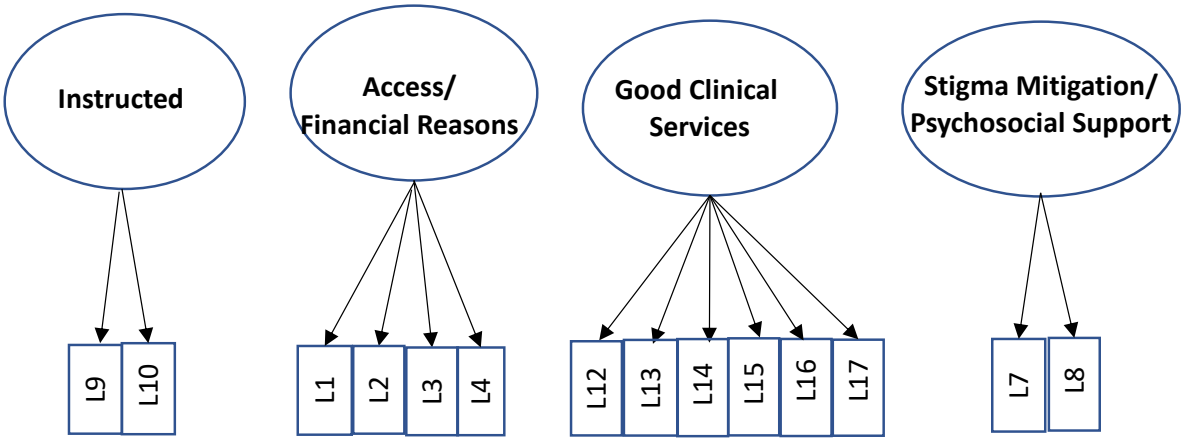

Figure 3.4: Hypothesized 4-factor model for linkage to care at a specific clinic at 1 and 12 months and retention in care at 12 months. Circles indicate latent (unobserved) constructs while squares indicate observed variables. L = Linkage to care items.

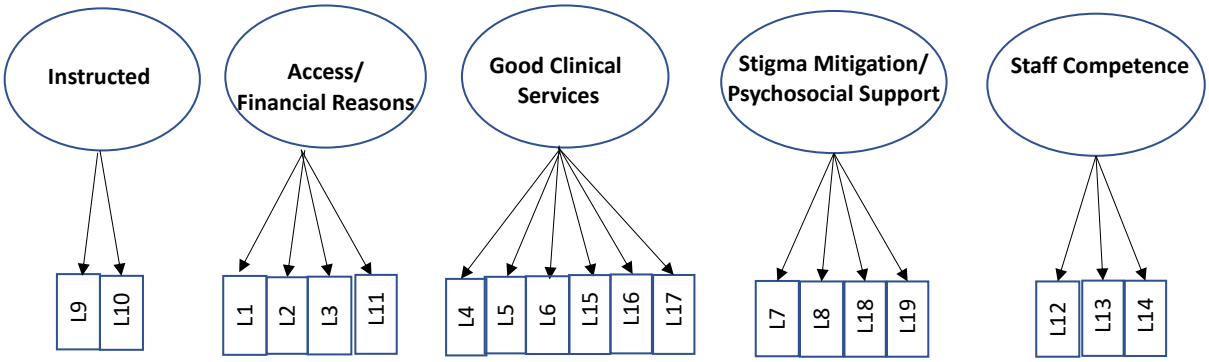

Figure 3.5: Hypothesized 5-factor model for linkage to care at a specific clinic at 1 and 12 months and retention in care at 12 months. Circles indicate latent (unobserved) constructs while squares indicate observed variables. L = Linkage to care items.

Table 3.3: Demographic and Clinical Characteristics: Link4Health Study Participants Linked to Care at 1 Month

	CIS (N= 1,013)		SOC (N= 918)		Total (N=1,931)		P-Value
Characteristic	**Number**	**%**	**Number**	**(%)**	**Number**	**(%)**	
Gender							
Female	609	60.1	522	56.9	1131	58.6	0.1469
Male	404	39.9	396	43.1	800	41.4	
Age Category							
18-24	193	19.1	183	19.9	376	19.5	0.4767
25-39	562	55.5	504	54.9	1066	55.2	
40-49	147	14.5	147	16.0	294	15.2	
>50	111	11.0	84	9.2	195	10.1	
Education							
None/Primary	446	44.0	432	47.1	878	45.6	0.2006
Secondary or Higher	563	55.8	485	52.9	1048	54.4	
Missing	4	0.4	1	0.1	5	0.3**	
Employment Status							
Employed	434	42.8	467	50.9	901	46.7	0.0004
Unemployed	579	57.2	451	49.1	1030	53.3	
Marital Status							
Widowed/Divorced*	24	2.4	34	3.7	58	3.0	0.3727
Married*	374	36.9	346	37.7	720	37.3	
Not Married to Current Partner*	459	45.3	409	44.6	868	45.0	
Single*	153	15.1	128	13.9	281	14.6	
Missing**	3	0.3	1	0.1	4	0.2	
Viral Load Suppression							
Suppressed*	560	69.3	519	76.2	1079	72.5	0.003
Not Suppressed*	248	30.7	162	23.8	410	27.5	
Missing**	205	20.2	237	25.8	442	22.9	
Retained in Care							
Yes	708	69.9	477	52.0	1185	61.4	<.0001
No	305	30.1	441	48.0	746	38.6	
Perceived Stigma (Baseline) [#]							
Yes*	580	57.4	386	42.1	966	50.1	<.0001
No*	430	42.6	532	58.0	962	49.9	
Missing**	3	0.3	0	0.0	3	0.2	

Perceived Psychosocial Support (Baseline) [#]							
Yes*	515	51.0	648	70.6	1163	60.3	<.0001
No*	495	49.0	270	29.4	765	39.7	
Missing**	3	0.3	0	0.0	3	0.2	
Perceived Clinical Staff Competence							
Yes*	777	90.1	767	94.8	1544	92.4	0.0003
No*	85	9.9	42	5.2	127	7.6	
Missing**	151	14.9	109	11.9	260	13.5	
Travel Time to the Health Facility							
30 Minutes or More*	56	5.6	172	18.8	228	11.9	<.0001
Less Than 30 Minutes*	945	94.4	745	81.2	1690	88.1	
Missing**	12	1.2	1	0.1	13	0.7	

*Among complete cases
**Proportion of total sample
[#]A composite score was created from several questions and split by the median

Table 3.4: Demographic and Clinical Characteristics: Link4Health Study Participants on ART for at Least 4 Months

	CIS (N= 592)		SOC (N= 528)		Total (N=1,120)		P-Value
Characteristic	**Number**	**%**	**Number**	**(%)**	**Number**	**(%)**	
Gender							
Female	318	53.7	280	53.0	598.0	53.4	0.8183
Male	274	46.3	248	47.0	522.0	46.6	
Age Category							
18-24	75	12.7	85	16.1	160	14.3	0.2375
25-39	346	58.5	292	53.3	638	57.0	
40-49	94	15.9	93	17.6	187	16.7	
>50	77	13.0	58	11.0	135	12.1	
Education							
None/Primary*	271	45.9	256	48.6	527	47.1	0.3627
Secondary or Higher*	320	54.2	271	51.4	591	52.9	
Missing**	1	0.2	1	0.2	2	0.2	
Employment Status							
Employed	254	42.9	280	53.0	534	47.7	0.0007
Unemployed	338	57.1	248	47.0	586	52.3	
Marital Status							
Widowed/Divorced	18	3.0	27	5.1	45	4.0	0.3911
Married	238	40.2	201	38.1	439	39.2	
Not Married to Current Partner	244	41.2	220	41.7	464	41.4	
Single	89	15.0	79	15.0	168	15.0	
Viral Load Suppression							
Suppressed*	258	62.8	284	74.4	542	68.4	0.0005
Not Suppressed*	153	37.2	98	25.7	251	31.7	
Missing**	181	30.6	146	27.7	327	29.2	
Linked to Care Within 1 Month							
Yes	584	98.7	512	97.0	1096	97.8	0.0528
No	8	1.4	16	3.0	24	2.1	
Retained in Care							
Yes	502	84.8	383	72.5	885	79.0	<.0001
No	90	15.2	145	27.5	235	21.0	
Perceived Stigma (Baseline) [#]							

Yes	353	59.6	215	40.7	568	50.7	<.0001
No	239	40.4	313	59.3	552	49.3	
Perceived Psychosocial Support (Baseline) [#]							
Yes	280	47.3	153	29.0	433	38.7	<.0001
No	312	52.7	375	71.0	687	61.3	
Perceived Clinical Staff Competence							
Yes*	456	90.5	452	96.8	908	93.5	<.0001
No*	48	9.5	15	3.2	63	6.5	
Missing**	88	14.9	61	11.6	149	13.3	
Travel Time to the Health Facility							
30 Minutes or More*	30	5.1	87	16.5	117	10.5	<.0001
Less Than 30 Minutes*	555	94.9	440	83.5	995	89.5	
Missing**	7	1.2	1	0.2	8	0.7	

*Among complete cases
**Proportion of total sample
[#]A composite score was created from several questions and split by the median

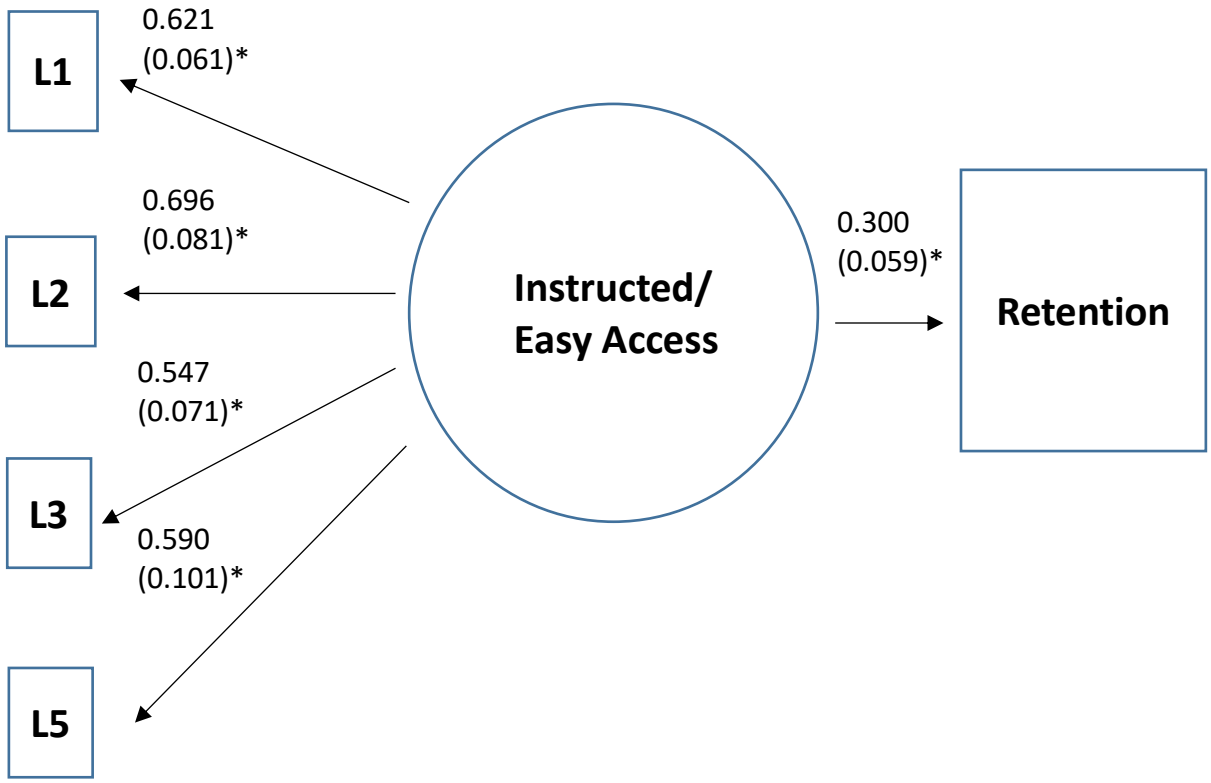

Figure 3.6: CFA and SEM Measurement Model for Linkage to Care in General at 1 Month in SOC Arm and Association with Retention in Care at 12 Months (adjusting for gender, age, education, employment status and marital status). Circles indicate latent (unobserved) constructs while squares indicate observed variables. L = Linkage to care items. Values are standardized regression coefficients with corresponding standard errors in parenthesis. The asterisk (*) indicates a significant association at P< 0.05.

Table 3.5: Standardized Correlations Between Latent and Observed Variables: Link4Health Study Participants

Latent Factor and Corresponding Observed/Measured Variable	Estimate	P-Value
Linkage to Care in General at 1 Month in SOC Arm		
"Instructed /Easy Access" Latent Factor versus Measured Travel Time to Health Facility	0.115	0.095
"Instructed /Easy Access" Latent Factor versus Measured Employment Status	0.320	<0.001*
Linkage to Care in General at 12 Months in CIS Arm		
"Instructed" Latent Factor versus Measured Travel Time to Health Facility	-0.113	0.367
"Easy Access/Financial Reasons Latent Factor versus Measured Employment Status	0.174	0.025*
Linkage to Care at a Specific Clinic at 1 Months in CIS Arm		
"Stigma Mitigation/ Psychosocial Support" Latent Factor versus Measured Perceived Stigma at Baseline	-0.500	0.022*
"Stigma Mitigation/ Psychosocial Support" Latent Factor versus Measured Perceived Psychosocial Support at Baseline	-0.150	0.452
"Stigma Mitigation/ Psychosocial Support" Latent Factor versus Measured Perceived Stigma and Perceived Psychosocial Support at Baseline	-0.415	0.060
"Good Clinical Services" Factor Latent Factor versus Measured Perceived Staff Competence	0.190	0.344
Linkage to Care in General at 12 Month in CIS Arm Among Participants on ART for at Least 12 Months		
"Instructed /Easy Access" Latent Factor versus Measured Travel Time to Health Facility	-0.015	0.876
"Instructed /Easy Access" Factor Latent Factor versus Measured Employment	0.000	0.999

*Significant association

Table 3.6: Frequency of Responses to Questions About Linking to Care in General at 1 Month in SOC Arm

Item	Response to question: Why did you go to the ART clinic after testing positive?	Yes		No		R-Square
		n	%	n	%	
L1	Health care worker told me to	465	50.7	453	49.3	0.385
L2	Study staff told me to	100	10.9	818	89.1	0.484
L3	Clinic was convenient/close	167	18.2	751	81.8	0.300
L5	Care and treatment are free	37	4.0	881	96.0	0.348

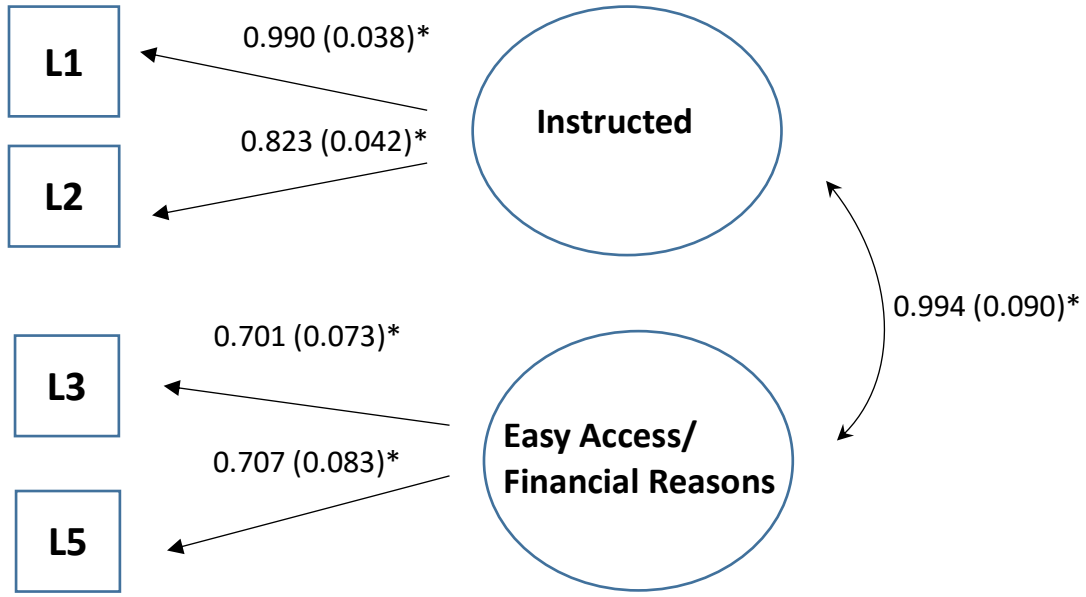

Figure 3.7: CFA Measurement Model for Linkage to Care in General at 12 Months in CIS Arm. Circles indicate latent (unobserved) constructs while squares indicate observed variables. L = Linkage to care items. Values are standardized regression coefficients with corresponding standard errors in parenthesis. The asterisk (*) indicates a significant association at P< 0.05.

Table 3.7: Frequency of Responses to Questions About Linkage to Care in General at 12 Month in CIS Arm

Item	Response to question: Why did you go to an HIV care clinic during the last 12 months?	Yes		No		R-Square
		n	%	n	%	
L1	Health care worker told me to	160	15.8	853	84.2	0.980
L2	Study staff told me to	93	9.2	920	90.8	0.678
L3	Clinic was convenient/close	143	14.1	870	85.9	0.492
L5	Care and treatment are free	24	2.4	989	97.6	0.500

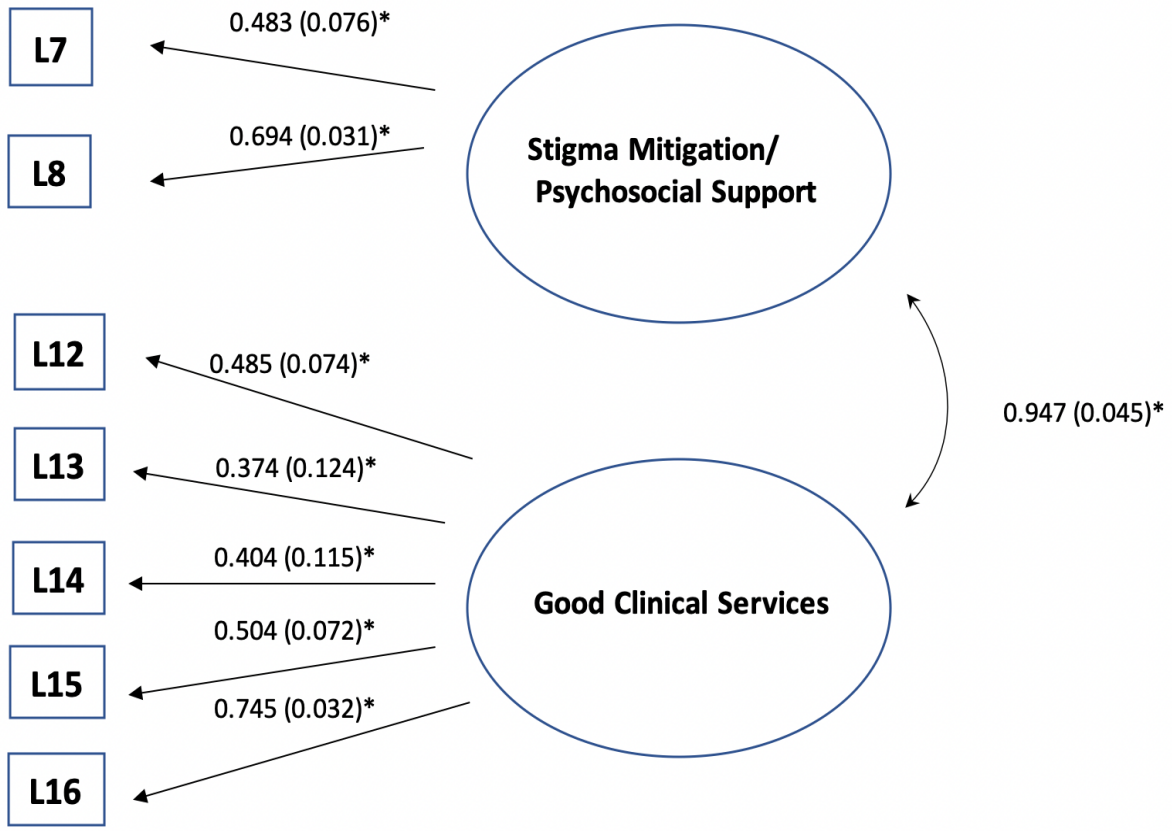

Figure 3.8: CFA Measurement Model for Linkage to Care at a Specific Clinic at 1 Months in CIS Arm. Circles indicate latent (unobserved) constructs while squares indicate observed variables. L = Linkage to care items. Values are standardized regression coefficients with corresponding standard errors in parenthesis. The asterisk (*) indicates a significant association at P< 0.05.

Table 3.8: Frequency of Responses to Questions About Linkage to Care at a Specific Clinic at 1 Month in CIS Arm

Item	Response to question: Why did you go to that specific ART clinic?	Yes		No		R-Square
		n	%	n	%	
L7	I have a friend/family member who goes there	12	1.2	1001	98.8	0.233
L8	Clinic is far away; HIV status is kept confidential there	6	0.6	1007	99.4	0.482
L12	Staff are respectful; nice	13	1.3	1000	98.7	0.236
L13	Care is good	39	3.8	974	96.2	0.140
L14	There is a doctor there	31	3.1	982	96.9	0.163
L15	Medications are available	11	1.1	1002	98.9	0.254
L16	Lab tests are available	5	0.5	1008	99.5	0.554

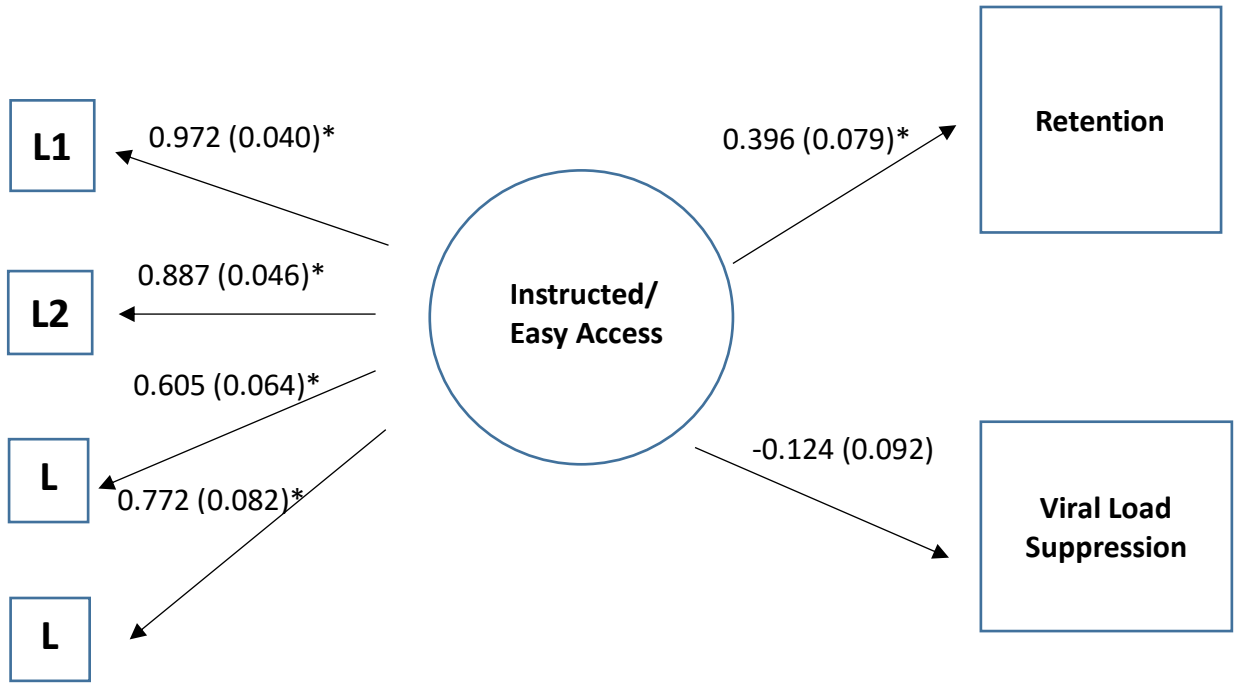

Figure 3.9: CFA and SEM Measurement Model for Linkage to Care in General at 12 Months in CIS Arm Among Participants on ART for at Least 12 Months and Association with Retention in Care at 12 Months and Viral Load Suppression at 12 Months (adjusting for gender, age, education, employment status and marital status and imputing missing viral load values). Circles indicate latent (unobserved) constructs while squares indicate observed variables. L = Linkage to care items. Values are standardized regression coefficients with corresponding standard errors in parenthesis. The asterisk (*) indicates a significant association at P< 0.05.

Table 3.9: Frequency of Responses to Questions About Linkage to Care in General at 12 Months in CIS Arm Among Participants on ART for at Least 4 Months

Item	Response to question: Why did you go to an HIV care clinic during the last 12 months?	Yes		No		R-Square
		n	%	n	%	
L1	Health care worker told me to	98	16.8	486	83.2	0.944
L2	Study staff told me to	61	10.4	523	89.6	0.786
L3	Clinic was convenient/close	89	15.2	495	84.8	0.366
L5	Care and treatment are free	14	2.4	570	97.6	0.597

Chapter 4: Effects of Barriers to Care on Engagement Along the HIV Care Continuum: Assessing Pathways to Viral Load Suppression in Eswatini

4.1 Abstract

Background: Antiretroviral therapy (ART) adherence is essential to slow disease progression among HIV patients. In many resource-limited settings, patients obtain ART primarily from health facilities hence retention in HIV care, defined as attendance at regular, scheduled appointments, can be used to approximate ART adherence. Many barriers to retention in care and other steps of the HIV care continuum have been identified, but longitudinal assessments of the effects of these barriers on different steps of the continuum are scarce in the literature. Mediational assessments of the role of retention in care on the pathway from barriers to retention in care to viral load suppression are also limited, and none have been done in the setting of a generalized epidemic. Drawing from the Link4Health trial conducted in Eswatini, a study of linkage and retention in care, this analysis assessed the effects of several potential barriers to care on linkage to care, retention in care, and viral load suppression. This analysis also examined the role of retention in care as a potential mediator of the association between potential barriers to retention in care and viral load suppression.

Methods: Link4Health (2013-2014) was a two-arm cluster-randomized trial assessing the effect of a combination intervention package on linkage and retention in HIV care among newly

diagnosed HIV-infected adults in Eswatini. Assessments of the effect of potential barriers to engagement in care (linkage and retention in care) on subsequent linkage, retention in care, and viral load suppression were done among participants who were on ART for at least 4 months (n =1,120). In multivariable analyses, random-intercept regression models were employed in multi-level log-Poisson models with robust standard errors to assess the effect of potential barriers to engagement in care measured at baseline on: linkage to care at 1 month, retention in care at 12 months, and viral load suppression at 12 months. The effects of different measures of retention in care (capturing consistency of engagement and study retention) on viral load suppression were also examined. To assess potential mediation, the change in the effect estimate capturing the relationship between a potential barrier to retention in care and viral load suppression after adjusting for retention in care was examined.

Results: Low perceived stigma at baseline was minimally associated with a lower likelihood of viral load suppression at 12 months (crude RR = 0.96, 95% CI [0.93-0.99]), but this effect approached the null after adjusting for intervention arm, age, gender, education, marital status and employment status (adjusted RR = 0.97, 95% CI [0.93-1.00]). Perceived stigma was not associated with linkage or retention in care. Perceived psychosocial support, perceived clinic staff competence, travel time to health facility, and patient employment status were not associated with linkage, retention in care, or viral load suppression. No measures of retention in care were associated with viral load suppression, and there was no evidence that retention in care mediated the association between perceived baseline stigma and viral load suppression.

Conclusion: In this study, potential barriers to engagement in care did not predict future engagement or viral load suppression, although perceived stigma had a minimal effect on viral load suppression; there was no evidence that this effect was mediated by retention in care. Validated measures of potential barriers to engagement in care are needed to capture abstract constructs more accurately and alternative measurements of other potential barriers indicating wealth and access should be explored in future studies.

4.2 Introduction

The devastating effects of HIV have largely been mitigated by the development and scale-up of antiretroviral therapy (ART), which prevents the onset of acquired immunodeficiency syndrome (AIDS) among HIV positive persons. However, ART is only effective if there is a high level of patient adherence to the treatment.[1] High ART adherence is a pre-requisite for viral load suppression among people living with HIV (PLHIV). UNAIDS estimates indicate that in order to curtail the HIV epidemic, the level of viral load suppression among all PLHIV needs to be at least 73%.[2,3] This estimation is in line with the 95-95-95 goals (upgraded from 90-90-90) set by UNAIDS to end AIDS by 2030 by having 95% of HIV positive persons know their status, 95% of those knowing their status be on treatment, and 95% of those on treatment be virally suppressed.[2-4]

From an implementation science perspective, it is important to determine which interventions will promote better engagement in care, which in turn may improve viral load suppression. Delivery of such interventions would be easier if there were similar barriers across different steps of the HIV care continuum, which tracks the sequential movement of HIV

positive patients from HIV diagnosis to viral load suppression and measures the proportion of patients engaged in care at each step.[5]

Several barriers and enablers to engagement in HIV care (linkage and retention in care) have been established in previous studies.[6-14] These studies suggest structural, psychosocial, and medical reasons why HIV patients drop out of care at each step of the continuum, which act on the individual, community, and health systems level. The reasons include transportation costs and other financial constraints, ability to take time off work and other life commitments, distance to the health facility, stigma and fear of disclosure, health facility logistics, interactions with healthcare providers (including perceived staff competence), quality of care, medication side effects, psychosocial support (including motivation from family or community members), mental health, overall health (which influences risk perception), health education, nutrition, substance use, and mobility.[6-14]

It is also important to assess whether and how barriers to engagement in care affect viral load suppression. Specifically, barriers to engagement in care may impact ART initiation or adherence, which in turn impacts viral load suppression. Where biological measures of drug levels in the body are not available, an imperfect, yet widely available measure of clinical engagement in care can be used to assess how consistently HIV patients engage with the health care system and do not drop out of care (retention in care), as a proxy for ART adherence, in settings where medication is only available through the clinic.[15]

Identifying potential barriers to engagement in care across the sequential steps of the HIV care continuum can help in determining pathways to viral load suppression (see Figure 4.1). Further, establishing if the potential barriers to engagement in care lead to actual disengagement from care (characterized by poor retention in care), and whether this disengagement reduces viral

load suppression can be done through mediation assessments. The average causal effect of potential barriers to engagement in care on viral load suppression is unlikely to be fully mediated by retention in care for two reasons: first, there are other direct pathways that operate through structural and psychosocial factors, and second, retention in care is not a perfect measure of ART adherence hence the intended construct may not be fully captured. Figure 4.1 shows these hypothesized pathways using perceived stigma as an example of a potential barrier.

Longitudinal assessments of the barriers and enablers of engagement in care that affect different steps of the HIV care continuum, as well as mediational assessments of the mechanistic pathways by which barriers and enablers of retention in care contribute to viral load suppression are scarce in the literature.[16-25] No assessments have been done on populations with generalized epidemics, and the one study that included countries in sub-Saharan Africa was ecological and did not use individual-level data.[24] This warrants further investigation of the role of potential barriers to engagement in care in affecting future engagement and viral load suppression in resource-limited settings with generalized epidemics such as Eswatini.

This analysis aims to assess the effects of potential barriers to engagement in care on different steps of the HIV care continuum. Specifically, it aims to assess whether specific potential barriers to engagement in care are related to viral load suppression and whether one pathway linking potential barriers to engagement in care to viral load suppression involves changes in retention in care after initial engagement. The specific potential barriers to engagement in care investigated were selected from a previous assessment of latent enablers of engagement in care, presumed to be opposite of the barriers, using the same dataset (unpublished data). These potential barriers are perceived stigma, perceived psychosocial support, perceived

clinic staff competence, travel time to health facility, and patient employment status. This analysis investigates the following hypotheses:

1. Participants who reported low perceived stigma, high perceived psychosocial support, high perceived clinic staff competence, short travel time to the health facility or were employed at baseline were more likely to be linked to care at 1 month, retained in care at 12 months and virally suppressed at 12 months
2. Any relationship between a potential barrier to engagement in care and viral load suppression is partially, but not wholly, mediated by retention in care

4.3 Methods

Study Population, Design and Setting

This analysis utilized data from participants of the Link4Health trial, which has been described elsewhere. [26,27] Briefly, Link4Health was a two-arm cluster-randomized implementation science trial assessing the effectiveness of a combination intervention strategy (CIS) in improving linkage and retention in care among newly diagnosed HIV positive adults compared to standard of care (SOC). It was conducted in Eswatini from August 2013 to November 2014. The Link4Health study employed a package of five evidence-based components: point-of-care CD4+ count testing, accelerated ART initiation, SMS appointment reminders, basic healthcare and educational packages, and non-cash financial incentives (mobile phone credit). [26,27] The primary aim was to assess the effect of the intervention on the combined outcome of linkage to care within 1 month of HIV diagnosis and retention in care within 12 months of HIV diagnosis at the individual participant level. Participants in the CIS arm were

more likely to achieve the primary outcome than those in the SOC arm (relative risk [RR] 1.52, 95% CI 1.29-1.96, p=0.002), and more likely to be retained in care at 12 months regardless of time to linkage (RR 1.48, 95% CI 1.18-1.86, p=0.002), but there was no difference in linkage (separate from retention at 12 months), mean time to linkage and viral suppression among those on ART for at least 6 months.[26]

In the Link4Health study, the study unit of randomization was a public secondary-level HIV clinic paired with its largest affiliated public primary-level HIV clinic.[26,27] There were a total of 11 existing secondary-level HIV clinics in the country at the time of the study, and 10 of these were selected as study units based on clinic patient volume.[26,27] Study units were pair-matched by supporting implementation partner, clinic location (rural vs. urban), and clinic size (based on expected monthly enrollment of adult HIV patients per facility).[26,27] One of each pair of the matched study units was randomly assigned to the CIS arm, with the other being assigned to the SOC arm.[26,27] A cluster design was chosen to ensure service delivery was not disrupted, allow for a better fit with routine operations of the clinics, and ease the implementation of the study for the clinic staff. [26,27] The study staff and clinic providers at each study unit were not blinded to the study arm assignment of their site.[26,27] Participant eligibility criteria included having received a positive HIV test, being at least 18 years of age, willing to receive HIV care at a selected clinic, and consenting to study procedures.[26,27]

Link4Health participants were administered a questionnaire at baseline and had relevant medical and clinical data abstracted up to 14 months after study enrollment. Participants were also administered follow-up questionnaires at 1 and 12 months after study enrollment. All data were collected in English or SiSwati. The survey included demographic and clinical questions, including questions about potential barriers to engagement in care, as will be described below.

Viral load was measured from collected from dried blood samples obtained at the 12-month follow-up interview. The current analysis is limited to participants who were on ART for at least 4 months during the study period. This is because HIV patients can usually achieve viral load suppression anywhere from 12 to 24 weeks of consistent ART intake.[28]

Written consent was obtained from all Link4Health participants, and the study was approved by the Institutional Review Boards (IRBs) at Columbia University and the Swaziland Science and Ethics Committee.

Measures

Exposures

The exposures for both Hypotheses 1 and 2 were hypothesized barriers to engagement in care: perceived stigma, perceived psychosocial support, perceived staff competence, travel time to the health facility, and employment status. HIV stigma refers to the attribute of having an HIV-positive status being viewed negatively by a culture or society and a negative social meaning being attached to the HIV positive individual.[29] Perceived stigma was measured as a summative score from a set of questions from the baseline questionnaire, and again at the 12-month follow-up. Specifically, participants ranked their stigma concerns on a 4-point Likert scale from "strongly agree" to "strongly disagree," and a summative score was created from the following questions: "you feel others may be concerned they could 'catch' your illness through contact like a handshake or eating food you make"; "you feel others will avoid you because you are HIV-positive"; "you feel you need to keep your HIV status a secret"; "due to your being HIV positive, you have a sense of being unequal in your relationships with others." Participants were also asked at these two time points how concerned they were that other people would find out

they were HIV positive, with responses ranging from very concerned, a little concerned to not at all concerned, and responses were added to the summative score. Perceived stigma was also dichotomized by the median value of the summative score. Perceived psychosocial support was measured as a summative score from a set of questions from the baseline questionnaire, and again at 12-month follow-up . Specifically, participants ranked their perceived availability of support and social capital on a 3-point scale using the following question: "Would you like your family members to give you more, the same or less emotional support" (a response of "more" was considered "low" support). Participants were also asked: "How many close friends do you have these days? These are people you feel at ease with, can talk to about private matters, or call on for help." (a response of "less than two" was considered "low" support). [30] The responses to these two questions were summed, and a binary measure was created using the median value as the cut-off point. The travel time to health facility was estimated based on the reported travel time from home to the health facility at baseline, and a binary measure was created where 30 minutes or more was considered a "long time" and less than 30 minutes a "short time." Perceived clinic staff competence was estimated from the following question asked at baseline as a binary measure: "health care workers in ART clinics are not knowledgeable about HIV," and responses were categorized as yes/no. Employment status was measured as a binary variable at baseline (unemployed vs. employed).

Mediator

The mediator of interest for Hypothesis 2 (which was also one of the outcomes for Hypothesis 1) was retention in care. Retention in care was defined in three ways:

1) Participant being alive and having made a clinic visit at least once 90 days prior to the end of the study period (retained in care) [yes/no]
2) Participant having made all follow-up ART visits no longer than five days after each scheduled date (consistently engaged in care) [yes/no]. Participants were required to come to the HIV clinic monthly for the first 6 months, and if stable, every 3 months thereafter.
3) A combination of 1) and 2) with the following four levels of an ordinal variable:
    i. Retained and consistent
    ii. Not retained but consistent
    iii. Retained but not consistent
    iv. Not retained and not consistent

Following inspection of the distribution of viral load suppression across the 4 categories of definition 3 and observing no difference, this measure was dichotomized into "not retained and not consistent" (category iv) vs all other consistency and retention measures (categories i-iii) in order to set the lowest level as the reference and allow for a broader definition of retention in care that captures both not being lost to follow-up (LTFU) and consistently meeting clinic appointments.

Outcomes

The outcomes assessed for Hypothesis 1 were: i) linkage to care at 1 month, ii) retention in care at 12 months, iii) viral load suppression at 12 months, among all participants on ART for at least 4 months. The outcome for Hypothesis 2 was viral load suppression at 12 months.

Linkage to care in the Link4Health study was defined as a participant having made at least one visit to any clinic within the assigned study unit, having had an HIV chronic care file opened, and having had a clinical assessment. Retention in care was originally defined as a participant being alive and having made a clinic visit at least once 90 days before the end of the study period and was also redefined in the manner explained above (for the definition of the mediator). Viral load suppression was defined as a participant's blood sample having HIV-1 RNA < 1,000 copies/mL 12 months after HIV diagnosis and was assessed as a binary variable in this analysis. Implausible viral load measures were coded as missing. In sensitivity analyses, missing viral load measures were imputed in several ways, as described below.

Potential Confounders

Each analysis controlled for the intervention arm, as well as several variables hypothesized *a priori* to contribute to confounding of the relationship between each potential barrier to engagement in care and linkage, retention in care, and viral load suppression (Hypothesis 1). These hypothesized confounders included gender (binary), age (four categories: 18-24, 25-39, 40-49, >50), education (binary, none/primary vs. secondary or higher), employment status (binary, unemployed vs. employed) and marital status (four categories: widowed/divorced, married, not married to current partner, single). The same variables were hypothesized to confound the relationship between potential barriers to care and retention in care, potential barriers to care and viral load suppression, and retention in care and viral load suppression in Hypothesis 2.

Statistical Analysis

Univariate statistics (chi-square tests for the categorical variables) were used to assess the distribution of the exposures, outcomes, and confounders by intervention arm. All potential barriers were coded such that higher scores indicated positive traits that were hypothesized to results in better engagement in care (that is, less perceived stigma , more perceived psychosocial support, high perceived staff competence, employment and short travel time to the health facility was hypothesized to result in better linkage to care, retention in care, and viral load suppression). To assess the relationship between any two variables, multivariable random-intercept regression models were employed in multi-level log-Poisson models with robust standard errors. These were used to obtain relative risk regression estimates, to account for clustering within units, and to control for confounding variables. The intervention arm was also adjusted for in all analyses.

In order to select the appropriate measurement of retention in care to use for analyses testing Hypotheses 1 and 2, the association between the different measures of retention in care described above and viral load suppression was first conducted.

Traditional mediational assessment methods proposed by Baron and Kenny,[31] and shown pictorially in Figure 4.2 were used for the assessment in Hypothesis 2. A potential mediator has to, on adjustment, reduce the magnitude of the effect estimate of the exposure on the outcome. An assessment for the total effect between barriers to retention in care and viral load suppression is reflected by path c; the effect barriers to retention in care on retention is path a; the effect of retention in care on viral load suppression is path b; the indirect effect of barriers to retention in care on viral load suppression that goes through retention in care is path ab; and the direct effect of barriers of retention in care on viral load suppression is path c' [see Figure 4.2]. These assessments hold under the following assumptions: no unmeasured confounding of the

association between the exposure and outcome; no unmeasured confounding of the association between the mediator and the outcome; and no interaction between the exposure and the mediator. SAS 9.4 software was used for all analyses.

Missing Data

Several participants were LTFU at each stage of the treatment cascade in the Link4Health Study. Viral load data were missing for 29% of participants on ART for at least 4 months. Preliminary assessments ruled out missing completely at random (MCAR) as the mechanism for this missingness; consequently, viral load data were assumed to be missing at random (MAR), meaning they were not systematically different from partial cases (participants without complete follow-up data) conditional on measured covariates. Multiple imputations (with MAR assumption) were conducted on viral load suppression using multivariable imputation by the fully conditional specification (FCS)/chained equations (MICE) methods for the dichotomous viral load measure.[32] Several variables were tested for their ability to predict missingness and viral load suppression and were used to impute values for viral load suppression. A maximum of 10 datasets were imputed sufficient to achieve a relative efficiency of at least 99% for each imputed variable, and the estimates were summarized across the different datasets to provide standard errors that account for uncertainty due to missing values.[32,33] The imputed results were compared to results from analyses with complete cases (participants with complete follow-up data) in sensitivity analyses. To assess the robustness of the findings and the possibility that instead of being MAR, the data were missing not at random [MNAR], sensitivity analyses were also conducted with single imputations assuming all participants with unknown viral load data were not virally suppressed (worst-case MNAR assumption).

For the perceived clinic staff competence variable, the missing data mechanism was assessed to determine if the missing data were related to the outcomes of interest (under MCAR assumption), and the analysis with partial cases was compared to that with complete cases in sensitivity analyses. Additional sensitivity analyses were conducted with single imputations to determine the extent of the bias by comparing worst-case assumptions and best-case assumptions (under MNAR assumption). The multivariable analyses conducted for the rest of the potential barriers to care measured at baseline are based on complete case analyses.

4.4 Results

Participant Characteristics

A total of 1,120 Link4Health participants (592 in CIS and 528 in SOC) were recorded as being on ART for at least 4 months and consequently included in this analysis (Table 4.1). About half the participants were female (53%), and most (57%) were aged 25-39. About half (53%) had secondary or higher education, and most (41%) had a partner they were not married to while 39% were married. About 68% of those with viral load data were virally suppressed, while 29% were missing viral load data. Participants with missing viral load data did not significantly differ from those with available data on demographic variables such as age, education, marital status and employment status (data not shown). Most participants (98%) were linked to care within 1 month, while about 79% were retained in care at the 12-month survey (not [LTFU]). About 40% were consistently engaged in care (that is, they made all follow-up ART visits no longer than five days after each scheduled date). The median number of visits was 9 (interquartile range [IQR] 6-10) over 12 months of follow-up. About half (51%) had perceived

stigma related to their HIV status at baseline, but this number increased to 59% among those with available data at the end of the survey, though it was still half of the overall population. About 39% had perceived psychosocial support at baseline, but this number increased to 49% among those with available data at the end of the survey, though it was still 42% of the overall population. About 94% of participants with available data believed the clinic staff were competent at baseline, though this was 81% of the overall population. About 11% of participants reported that it took them 30 minutes or more to get to the health facility. About half (52%) of participants were unemployed.

Effect of Retention in Care on Viral Load Suppression

The association between different measures of retention in care and viral load suppression using viral load data from multiple imputations for participants who had missing data is shown in Table 4.2. Retention in care was not significantly associated with viral load suppression, regardless of whether it was measured as being retained in care (not being LTFU), being consistently engaged in care (making all follow-up ART visits no longer than five days after each scheduled date), or a combination of both (being retained in care and/or being consistently engaged in care). The third definition of retention was thus used in subsequent analyses. Adjusting for the intervention arm did not significantly alter the results (Table 4.2). There was no significant difference between complete case analyses (see Appendix E.i) and analyses from multiple and worst-case single imputed viral load measures (see Appendix E.ii) in sensitivity analyses.

Effect of Potential Barriers to Care Engagement on Linkage to Care, Retention in Care, and Viral Load Suppression

The association between potential barriers to engagement in care and all steps of the HIV care continuum (linkage to care, retention in care, and viral load suppression) using viral load data from multiple imputations for participants who had missing data is shown in Table 4.3 (to test Hypothesis 1). The perceived stigma at baseline was the only potential barrier tested that was associated with any step of the HIV care continuum. In the crude analysis, every unit decrease in perceived stigma was associated with a 4% decrease in the likelihood of being virally suppressed at 12 months (crude risk ratio [cRR] = 0.96, 95% CI [0.93-0.99]); which can also be interpreted as every 10 unit decrease in perceived stigma was associated with a 31% decrease in the likelihood of being virally suppressed at 12 months. This means that participants with less perceived stigma at baseline were less likely to be virally suppressed at 12 months. The confidence intervals for this association, however, slightly expanded after adjusting for intervention arm, age, gender, education, marital status, and employment status (adjusted RR [aRR] = 0.97, 95% CI [0.93-1.00]). The binary measure of perceived stigma at baseline (split by the median) was not associated with viral load suppression or any other step of the HIV care continuum (data not shown). Perceived psychosocial support, perceived clinic staff competence, employment status, and travel time to the health facility did not predict future linkage to care, retention in care, or viral load suppression. Adjusting for potential confounders did not significantly alter the results. Sensitivity analyses showed that complete case analyses (see Appendix F.i) were similar to analyses with multiple and worst-case imputed viral load measures (see Appendix F.ii), and imputing missing values for perceived staff competence with extreme values (all “yes” or “no”) did not alter the results (see Appendix G.i and Appendix G.ii).

Mediation Analysis

Since perceived stigma at baseline (continuous form) was the only potential barrier identified in main effects analysis as associated with viral load suppression, the mediation Hypothesis 2 was explored for this barrier only. Adjusting for retention in care did not significantly reduce the association between perceived baseline stigma and viral load suppression at 12 months follow-up, as shown in Table 4.4 (i.e., path c' in Figure 4.2 could not be established). For the following measures of retention in care—being retained in the study, being consistently engaged in care, and a combination of study retention and consistency of engagement in care—the following risk ratios were observed in the mediation assessment: aRR = 0.96, 95% CI (0.93-1.00), aRR = 0.96, 95% CI (0.92-1.00), and aRR = 0.96, 95% CI (0.93-1.00) respectively. Given that all measures of retention in care were also not associated with viral load suppression (i.e., path b in Figure 4.2 could not be established), and that perceived stigma was not related to retention in care (i.e., path a in Figure 4.2 could not be established) the requirements for mediation were not met.

4.5 Discussion

This study appears to be the first to assess the effects of potential barriers to engagement in care on different steps of the HIV care continuum and also to explore the potential mediating role of retention in care on the pathway from the barriers to retention in care to viral load suppression in a generalized epidemic. Only perceived stigma at baseline showed a potential relationship with any step of the HIV care continuum, being marginally associated with viral load suppression in the crude analysis. However, the magnitude of this association was small and in the opposite direction that was hypothesized, with individuals reporting low perceived stigma

having a slightly lower likelihood of achieving viral load suppression. After adjusting for confounding, this association could not be adequately separated from a finding of no effect, and an alternative operationalization of the exposure as a binary measure yielded null results. Taking these findings together, the data do not suggest a meaningful relationship between perceived stigma as measured and viral load suppression, but a potential relationship could exist with more accurate measures that should be explored further. No other potential barriers were associated with any step of the HIV care continuum in this population. There was no evidence that the relationship between perceived stigma and viral load suppression was mediated by retention in care. In this analysis, consistent care-seeking behavior (consistently meeting clinic appointments) did not have a different effect on viral load suppression from merely not being lost to care.

Given that the CIS intervention had no effect on linkage to care or viral load suppression in the Link4Health study, but had an effect on retention in care,[26] the findings of the current analysis are mostly consistent with the possibility that the intervention components that could have been intended to mitigate some of the barriers to engagement in care (such as financial incentives mitigating the unemployment and long travel time to health facility barriers and point-of-care CD4+ count testing and accelerated ART initiation also mitigating the long travel time to health facility barrier) were not effective enough in themselves to aid linkage to care and enhance viral load suppression, though an effect with retention in care would have been expected. None of the intervention components, however, could have sufficiently mitigated perceived stigma, which had a minimal relationship with viral load suppression. It must be noted, however, that the intervention arm was controlled for in the current analysis, and crude assessments did not significantly differ from adjusted analyses.

This analysis does not provide any evidence that perceived stigma as measured acts in the hypothesized direction on reducing viral load suppression. HIV patients who had less perceived stigma were as or slightly less likely to be virally suppressed. Since participants had to obtain their medication from the health facility, it is reasonable to expect that those who are more concerned about stigma would visit the health facility less in order to avoid being noticed by other people and would subsequently take less medication and have low viral suppression. On the other hand, it is possible that participants reporting more perceived stigma may see taking medication as a way of hiding their HIV status through symptom improvement, which would be more consistent with the direction of the current findings. Since the study did not use validated measures of stigma, it is possible that the construct intended may not have been measured accurately. Additionally, since questions were asked at baseline, it is likely that self-reported perceived stigma on the date of HIV diagnosis may not accurately reflect actualized stigma and that perceptions of stigma may lessen or at least change over time. It is important to note, however, that 12-month follow-up measures of perceived stigma were not associated with viral load suppression at 12 months, and there was a very small correlation between baseline and 12-month follow-up perceived stigma measures (data not shown). Measures at the 12-month follow-up time are, however, subject to selection bias as they only capture participants retained in the study.

Among the 10 studies that longitudinally assessed the effect of barriers to engagement in care on steps of the HIV care continuum, only one found perceived stigma to be associated with viral load suppression. HIV-related stigma was found to be an important predictor of viral load suppression among African-American women participating in a stigma-reduction intervention, but non-ART adherence was not a significant mediator.[19] The direction of the association was

opposite that found in the current study, with women reporting higher levels of HIV-related stigma being less likely to be virally suppressed.[19] Unlike the current study, perceived stigma has also been found to be related to ART adherence[16,25] and adherence to clinic visits[23] in studies done with US populations. These studies, however, used validated scales to measure perceived stigma, unlike the current study, which measured stigma through a combination of questions derived from sub-scales of stigma measures that had not been validated as used. These other studies are also all based in the US, which is a high-income country with a concentrated HIV epidemic, making it difficult to compare it with a study done in Eswatini, a low-income country with a generalized epidemic. Additionally, HIV stigma may be less pronounced in a high prevalence setting like Eswatini compared to the US, but the two countries can only be compared directly if stigma is measured using the same scale.

A few studies done in the US have found ART adherence to be a significant mediator of the relationship between barriers to engagement in care and viral load suppression.[17,18,20,22] Particularly, one study found the effect of depression and substance use on viral load suppression to be partially mediated by self-reported inconsistent ART utilization.[17] Another study done among a population of men who have sex with men (MSM) or drug users found that ART adherence mediated the association between homelessness and viral load suppression.[18] In a study done among HIV positive men and women with alcohol use disorders, self-reported HAART adherence was found to partially mediate the relationship between medication adherence self-efficacy and viral load suppression.[20] Finally, a study assessing the effects of general barriers to ART adherence on viral load suppression found ART adherence to be a partial mediator.[22] All these studies used different measures of ART adherence, and although they were self-reported, these measures are likely to more closely estimate actual adherence than the

retention measures used in the current study. Interestingly, one of the studies found the effects of internalized stigma on suboptimal ART adherence to be mediated by lower clinic visit adherence, [23] suggesting that ART adherence and visit adherence are still constructs whose relationship is not negligible. The specific barriers measured may also have a different effect on viral load suppression and ART adherence than perceived stigma. Some of the studies also utilized key populations, such as MSM or drug users, unlike the general population in Eswatini. As noted earlier, both the experience of PLHIV in the US and the factors that affect engagement in care in the US are likely to be different from those in Eswatini.

This study had several limitations. It did not use validated measures of abstract constructs such as perceived stigma and perceived psychosocial support. However, it used different combinations of the composite variables derived from sub-scales to assess these factors. Of note, the binary and continuous forms of perceived stigma had slightly different effects on viral load suppression—the continuous form, which captured the full range of the data and had a monotonous relationship with the outcome in sensitivity analyses (data not shown), was the significant one. This study also used retention in care to approximate ART adherence, which may not be a sufficient proxy.[15] Patients who pick up drugs consistently do not necessarily ingest the drugs, which could explain why retention in care, measured by different combinations of consistency of engagement in care and study retention, had no effect on viral load suppression. Additionally, this study only assessed participants who were on ART for at least 4 months, hence the findings may not be applicable to HIV patients on ART for a shorter time. Finally, almost a third of participants were missing viral load data, and 13% were missing data on perceived clinic staff competence. Multiple and single imputations were, however, conducted on viral load

suppression and perceived clinic staff competence respectively, and results from complete case analyses did not differ from analyses with imputed data, suggesting that the bias was minimal.

This study had several strengths. It appears to be the only study assessing the effects of potential barriers to engagement in care on different steps of the HIV care continuum in a population with a generalized epidemic. It also appears to be the only study assessing the mediational effects of retention in care on the pathway from the barriers to retention in care to viral load suppression in sub-Saharan Africa using individual-level data. This study also attempted to parse out the effects of consistent care engagement versus merely not dropping out of care on viral load suppression. Finally, given that it uses data from 10 of the 11-existing secondary-level HIV clinics (pair matched with the largest affiliated public primary-level HIV clinics) in Eswatini at the time of the Link4Health study, this current study has grounds for generalizability to PLHIV in Eswatini formally enrolled in care only, and possibly to other resource-limited countries with generalized epidemics.

In conclusion, perceived stigma at baseline only had a minimal effect on viral load suppression after 12 months follow-up and did not affect linkage or retention in care. Perceived psychosocial support, perceived clinic staff competence, employment status, and travel time to the health facility did not have an effect on linkage to care, retention in care, or viral load suppression. In this study, clinic attendance and study retention did not appear to be good proxies for ART adherence, and retention did not mediate the relationship between perceived stigma and viral load suppression. Most barriers to engagement in care are abstract constructs and may be better captured by the use of validated measures. Furthermore, these barriers are not static and could change over the course of an HIV patient's life; thus, continuous measures across the continuum are warranted. Perceived stigma and other barriers may play a more important role in

routine than study settings and should be investigated further. Future studies should also use alternative measurements of other potential barriers indicating wealth, access, and other factors to explore how these factors affect a client's relationship with the health facility, taking into account the characteristics of the specific facility. These could include the particular services patients have to pay for (in settings where services are not free), the range of services provided, the attitude of clinic staff, and other logistical factors that may weigh into a patient's decision to engage with the health care system at the facility level.

4.6 References

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4.7 Tables and Figures

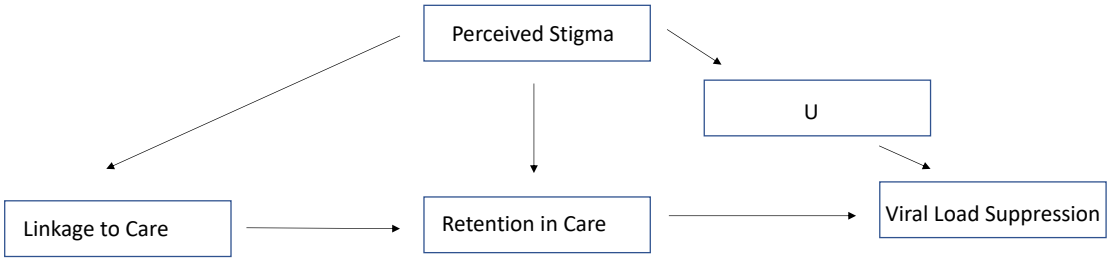

Figure 4.1: The pathways to viral load suppression. Perceived stigma is as an example of a potential barrier to engagement in care and may have an effect on linkage to care, retention in care, or viral load suppression. Also illustrated is the role of retention in care on the pathway from perceived stigma to viral load suppression. U represents other unmeasured psychosocial and structural factors.

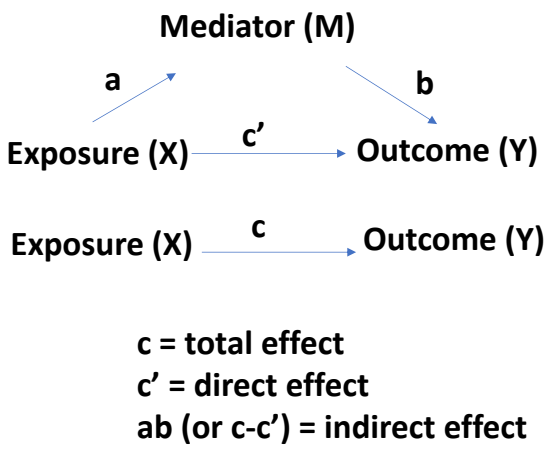

Figure 4.2: Traditional mediation model proposed by Baron and Kenny. The total effect between the exposure and outcome is shown by path c; the effect of the exposure on the mediator is reflected in path a; the effect of the mediator on viral load suppression is path b; the indirect effect of the exposure on the outcome that goes through the mediator is the path ab (or c-c′); and the direct effect of the exposure on the outcome is path c′.

Table 4.1: Demographic and Clinical Characteristics: Link4Health Study Participants on ART for at Least 4 Months: Link4Health Data, Eswatini, 2013-2014

	CIS (N= 592)		SOC (N= 528)		Total (N=1120)		P-Value
Characteristic	**Number**	**%**	**Number**	**(%)**	**Number**	**(%)**	
Gender							
Female	318	53.7	280	53.0	598.0	53.4	0.8183
Male	274	46.3	248	47.0	522.0	46.6	
Age Category							
18-24	75	12.7	85	16.1	160	14.3	0.2375
25-39	346	58.5	292	53.3	638	57.0	
40-49	94	15.9	93	17.6	187	16.7	
>50	77	13.0	58	11.0	135	12.1	
Education							
None/Primary*	271	45.9	256	48.6	527	47.1	0.3627
Secondary or Higher*	320	54.2	271	51.4	591	52.9	
Missing**	1	0.2	1	0.2	2	0.2	
Marital Status							
Widowed/Divorced	18	3.0	27	5.1	45	4.0	0.3911
Married	238	40.2	201	38.1	439	39.2	
Not Married to Current Partner	244	41.2	220	41.7	464	41.4	
Single	89	15.0	79	15.0	168	15.0	
Viral Load Suppression							
Suppressed*	258	62.8	284	74.4	542	68.4	0.0005
Not Suppressed*	153	37.2	98	25.7	251	31.7	
Missing**	181	30.6	146	27.7	327	29.2	
Linked to Care Within 1 Month							
Yes	584	98.7	512	97.0	1096	97.8	0.0528
No	8	1.4	16	3.0	24	2.1	
Retained in Care							
Yes	502	84.8	383	72.5	885	79.0	<.0001
No	90	15.2	145	27.5	235	21.0	
Consistently Engaged in Care							
Yes	240	40.5	202	38.3	442	39.5	0.4352
No	352	59.5	326	61.7	678	60.5	
Consistency and Retention Combined							
Consistent and Retained	189	31.9	142	26.9	331	29.6	<.0001

Consistent but not Retained	51	8.6	60	11.4	111	9.9	
Retained but not Consistent	313	52.9	241	45.6	554	49.5	
Not Retained and not Consistent	39	6.6	85	16.1	124	11.1	
Perceived Stigma (Baseline) [#]							
Yes	353	59.6	215	40.7	568	50.7	<.0001
No	239	40.4	313	59.3	552	49.3	
Perceived Stigma (12-Month Follow-Up) [#]							
Yes*	286	56.2	287	62.7	573	59.3	0.0407
No*	223	43.8	171	37.3	394	40.7	
Missing**	83	14.0	70	13.3	153	13.7	
Perceived Psychosocial Support (Baseline) [#]							
Yes	280	47.3	153	29.0	433	38.7	<.0001
No	312	52.7	375	71.0	687	61.3	
Perceived Psychosocial Support (12-Month Follow-Up) [#]							
Yes*	303	59.5	169	36.9	472	48.8	<.0001
No*	206	40.5	289	63.1	495	51.2	
Missing**	83	14.0	70	13.3	153	13.7	
Perceived Clinical Staff Competence							
Yes*	456	90.5	452	96.8	908	93.5	<.0001
No*	48	9.5	15	3.2	63	6.5	
Missing**					149	13.3	
Travel Time to the Health Facility							
30 Minutes or More*	30	5.1	87	16.5	117	10.5	<.0001
Less Than 30 Minutes*	555	94.9	440	83.5	995	89.5	
Missing**	7	1.2	1	0.2	8	0.7	
Employment Status							
Employed	254	42.9	280	53.0	534	47.7	0.0007
Unemployed	338	57.1	248	47.0	586	52.3	

*Among complete cases
**Proportion of total sample
[#]A composite score was created from several questions and split by the median

Table 4.2: Relative Risk Regression for Effect of Retention in Care on Viral Load Suppression: Link4Health Data, Eswatini, 2013-2014

Retention Measure	Effect on Viral Load Suppression			
	Crude Analysis		Adjusted Analysis[#]	
	RR	95% CI	RR	95% CI
Retained in Care at 12m (not LTFU) [No vs Yes]	1.05	(0.84-1.32)	1.08	(0.85-1.36)
Consistently Engaged in Care (No vs Yes)	0.99	(0.84-1.67)	1.00	(0.84-1.19)
Not Retained and Not Consistent and vs All Other Consistency and Retention Combinations	0.96	(0.70-1.33)	0.99	(0.71-1.38)

[#]Adjusted for intervention arm

Table 4.3: Relative Risk Regression for Effect of Potential Barriers of Care Engagement on Linkage, Retention and Viral Load Suppression: Link4Health Data, Eswatini, 2013-2014

Potential Barrier	Effect on Linkage				Effect on Retention				Effect on Viral Load Suppression			
	Crude Analysis		#Adjusted Analysis		Crude Analysis		#Adjusted Analysis		Crude Analysis		#Adjusted Analysis	
	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
Perceived Stigma [Baseline] (Continuous)	1.00	(0.99-1.01)	1.00	(0.99-1.02)	1.00	(0.99-1.02)	1.00	(0.99-1.03)	0.96*	(0.93-0.99)*	0.97	(0.93-1.00)
Perceived Psychosocial Support [Baseline] (Continuous)	1.00	(0.99-1.01)	1.00	(0.98-1.02)	1.00	(0.99-1.02)	1.00	(0.98-1.03)	1.00	(0.94-1.06)	0.99	(0.93-1.06)
Perceived Clinical Staff Competence (No vs Yes)	1.00	(0.91-1.11)	1.00	(0.82-1.23)	1.07	(0.94-1.21)	1.04	(0.84-1.29)	0.99	(0.64-1.52)	0.95	(0.57-1.60)
Employment Status (Employed vs Unemployed) ##	1.00	(0.95-1.05)	1.00	(0.91-1.10)	0.96	(0.90-1.03)	0.97	(0.87-1.09)	1.01	(0.83-1.22)	1.01	(0.80-1.27)
Travel Time to the Health Facility (30 Minutes or More vs Less Than 30 Minutes)	1.00	(0.93-1.09)	1.00	(0.86-1.18)	1.03	(0.92-1.16)	1.06	(0.89-1.28)	1.15	(0.84-1.58)	1.18	(0.80-1.72)

#Adjusted for intervention arm, age, gender, education, employment, and marital status (except for the Employment Status potential barrier)

##Adjusted for intervention arm, age, gender, education, and marital status

*Significant association

Table 4.4: Mediation Assessment Showing Relative Risk Regression for Effect of Potential Barriers of Care Engagement on Viral Load Suppression Mediated by Retention in Care: Link4Health Data, Swaziland, 2013-2014

Potential Barrier	Effect on Viral Load Suppression				Mediation?
	Crude Analysis		#Adjusted Analysis		
	RR	95% CI	RR	95% CI	
Perceived Stigma [Baseline] (Continuous)	0.96*	(0.93-0.99)*	0.96*	(0.93-1.00)*	No

#Adjusted for retention in care
*Significant association

Chapter 5: Conclusions

5.1 Overview

The goal of this dissertation was to apply novel approaches to the measurement of reasons for the differential engagement of HIV patients in the care continuum and identify pathways to viral load suppression. It specifically aimed to assess the dimensionality (factor structure) of enablers of engagement in the HIV care continuum, to use the identified latent enablers as a guide to identify potential barriers to care in the same population, and assess how both the latent enablers and potential barriers affect future engagement in care and viral load suppression. The mediating role of retention in care on the pathway from potential barriers to engagement in care to viral load suppression was also investigated. A systematic review was also conducted to identify gaps in the literature regarding the measurement and analytic approaches of barriers and enablers of engagement in multiple steps of the HIV care continuum. The findings and implications of each of these results are summarized below.

5.2 Summary of Results

In Chapter 2, a systematic review of the literature on barriers and enablers of engagement in HIV care was assessed, particularly the measurement and analytic methods of these factors. It showed a relative scarcity in the literature of studies using predictive quantitative methods compared to the number of qualitative and descriptive studies. The factors measured in qualitative studies were extensive and presented the range of reasons why HIV patients engage in or disengage from care. Descriptive studies mostly focused on factors affecting antiretroviral therapy (ART) adherence; hence they provided an extensive list of medication-related reasons for ART adherence or non-adherence. Studies assessing association or causation assessed the

effect of reasons for engagement or disengagement from care on health outcomes; they often assessed the effect of these reasons on future engagement in care or viral load suppression. Psychometric studies conducted factor analysis to identify the factor structure of the reported barriers or enablers, and one validated an existing scale used to measure barriers to ART adherence. They hence provided validated tools that can be adapted to measure the same factors in other studies. Additionally, they included assessments of the effect of the factors on future engagement in care and viral load suppression. Mixed methods studies, by design, combined the approaches of both qualitative and quantitative methods and gave a more comprehensive picture of the factors influencing the differential engagement in care among HIV patients.

Chapter 3 was intended to address the gap in the literature of psychometric assessments of the latent factors affecting engagement in HIV care. It utilized reported enablers from a subset of HIV patients participating in a cluster randomized trial (Link4Health study) who had linked to care at 1 month and an additional subset of participants who had been on ART for at least 4 months in Eswatini. Confirmatory factor analysis (CFA) was conducted from hypothesized factor structures built from the systematic review and previous studies and resulted in the identification of several latent factors that enabled Link4Health participants to link to care: a one-factor structure indicative of linking to care in general at 1 month because of easy access and financial reasons (proximity to clinic and free services) for participants in the control arm; a two-factor structure indicative of linking to care in general at 12 months because of being instructed and having both easy access and financial reasons for participants in the intervention arm; a two-factor structure indicative of linking to care at a specific clinic at 1 month because of having both perceived stigma mitigation and psychosocial support, and experiencing good clinical services for participants in the intervention arm; and a one-factor structure indicative of linking to care in

general at 12 months because of easy access and financial reasons for participants on ART for at least 4 months in the intervention arm. The “Instructed/Easy Access” factor predicted future retention in care at 12 months, but it did not predict viral load suppression.

Chapter 4 built on the latent enablers identified in Chapter 3 and assessed variables hypothesized to be opposite of these enablers as potential barriers to engagement in HIV care. Only perceived stigma at baseline showed a potential relationship with any step of the HIV care continuum, with low perceived stigma being marginally associated with less viral load suppression. However, there was no mediational effect identified in the pathway from perceived stigma to viral load suppression that went through retention in care. Measuring retention in care as consistently meeting clinic appointments or merely being retained in the study did not have a differential effect on viral load suppression.

5.2 Strengths and Limitations

This dissertation had several limitations. The systematic review in Chapter 2 only assessed articles written in English and could have missed articles without an English translation that would have otherwise met the inclusion criteria. However, the outcomes from studies of the same type done in the same region of the world with a common study population were very similar; hence it is unlikely that studies published in other languages would have substantially changed the overall results from the review. The review also did not include non-peer-reviewed literature, but this was essential for the assessment of methodological rigor. Chapter 3 used Link4Health data that were not primarily designed for psychometric analysis and required elimination of some responses with poor representation, which compromised the generalizability of the findings. The reliability of the scales was also generally low. The analysis also included

participants already linked to care and could only assess enablers of linkage and the effects of linking to care for specific reasons compared to other reasons on future engagement in care and viral load suppression. However, it reflects real-world settings where data are only available for patients engaged in care and proposes methods to make inferences to patients lost to follow-up (LTFU) or not consistently engaged (by identifying potential barriers to engagement in care).

Chapter 4 used data from Link4Health participants who had been on ART for at least 4 months, and this could limit the generalizability of the findings to HIV patients on treatment for a shorter time. The study also did not use validated measures of latent potential barriers to engagement in care, and these barriers could have changed over time. The study also used retention in care as a proxy for ART adherence, which could have been an imperfect measure given that it had no association with viral load suppression. Additionally, there were substantial missing viral load data, but results from multiple imputations did not differ from those with complete cases in sensitivity analyses. Finally, the Link4Health study was conducted before WHO's "treat all" guidelines,[1] thus, some outcomes may only be applicable to patients who were eligible for ART (those with CD4+ count <350 cells/μL).

This dissertation had several strengths. It presents the first systematic review of the measurement and analytic approaches to barriers and enablers of engagement in the HIV care continuum in Chapter 2. It is also the first to summarize barriers and enablers of engagement in multiple steps of the continuum encompassing all populations at risk of HIV infection across all regions of the world. The review includes strict selection criteria such as the direct measurement of barriers and enablers of engagement in care from the patients, as opposed to potential risk factors or the providers' and other stakeholders' perspectives. This criterion ensured that the intended constructs were measured more accurately and that the same constructs were measured

across the studies. The psychometric assessment in Chapter 3 was the first to use these measurement techniques to assess reasons for initial linkage to care and was the first to use individual-level data to assess enablers of engagement in care in sub-Saharan Africa. The CFA approach was chosen because it is based on an a priori theory about the relationship between observed and latent constructs, in contrast to exploratory factor analysis, which assumes no a priori theory about the dimensionality of the underlying constructs.[2] CFA was also chosen instead of principal component analysis (PCA), which is used to find optimal ways of combining variables into a smaller number of subsets (data reduction) without assuming latent underlying constructs.[2] Since this dissertation was based on the premise that there are underlying latent constructs that enable HIV patients to engage in HIV care, PCA would have simply reduced the number of variables used to assess reasons for engagement in care without revealing domains amenable to intervention that are otherwise unobservable based on variables that measure different aspects of the same construct, nor would it have allowed for the quantification of the relationship between the latent variables and observed variables, which is an essential procedure for scale development. The results of the psychometric assessments were also largely representative of HIV patients in care in Eswatini, given that it uses data from 10 of the 11-existing secondary-level HIV clinics (pair matched with the largest affiliated public primary-level HIV clinics) and may be applicable to other resource-limited settings with generalized epidemics. Chapter 4 presented the first assessment of potential barriers to care on multiple steps of the HIV care continuum (from linkage to care) in a generalized epidemic. It was also the first individual-level assessment of the mediational effects of retention in care on the pathway from potential barriers to care to viral load suppression in a generalized epidemic. The results are also

largely generalizable to HIV patients in care in Eswatini and possibly other resource-limited settings with similar epidemics.

5.3 Implications and Future Directions

This dissertation's findings have several implications for HIV programming and future studies concerning the barriers and enablers of engagement in the HIV care continuum.

The systematic review in Chapter 2 showed that the barriers and enablers of engagement in care have been extensively studied in qualitative and descriptive studies. These studies, in general, all have similar findings, hence additional studies of the same kind may not add substantially to the literature. Research funds should be directed to predictive quantitative and mixed methods studies that utilize the findings from these qualitative and descriptive studies to measure the latent underlying factors and measure them as broad constructs that can be replicated in other studies and used to design interventions. Predictive methods will also allow the assessment of how the factors change over time and the effect they have (if any) on actual engagement in care in the future and viral load suppression. Psychometric studies would also provide a standardized way to measure these factors in programmatic settings and make comparisons across studies more systematic.

Psychometric assessments for the measurement of enablers of engagement in care were assessed in Chapter 3. CFAs identified financial, and access factors as the most prominent underlying enablers of engagement in HIV care in general in Eswatini, and they may be applicable to other resource-limited settings. These may be a result of reduced transportation costs and direct costs of receiving care at the clinic where applicable. Several approaches to mitigate these barriers, such as decentralization of care, task-shifting, community-based care, and

integration of services to minimize patient visits[3,4] are already underway and should be scaled up. Decentralization of care makes HIV services available at more primary-level health facilities and provides more opportunities for HIV patients to engage in care as it removes the access barriers (both geographic and financial) associated with having to travel to secondary or tertiary-level facilities which may be located in large urban areas that may be far from the homes of HIV patients residing in rural areas. Task-shifting transfers some HIV-related tasks to health cadres with less clinical training and provides more human resources for health in areas with a shortage of physicians and other formally trained clinicians, which is characteristic of most resource-limited settings such as Eswatini. This is related to community-based care, which brings care from the health facilities and closer to the patients' homes, usually involving health cadres with less formal clinical training such as community health workers (CHWs), and helps make care more accessible to patients residing far from health facilities. Finally, integration of care provides a "one-stop" set of services and minimizes the number of visits HIV patients have to make to the health facility as they can receive all the care they need at one place during one visit, reducing transport costs and the time patients have to take away from work and other responsibilities.

While removal of access and financial constraints may enable HIV patients to engage in care in general in Eswatini, stigma mitigation and psychosocial support, together with good clinical services, emerged as essential factors affecting linkage to care at a specific clinic. These findings imply that clinics which provide opportunities for newly diagnosed HIV patients to engage with other HIV patients through peer support groups may enable initial and perhaps continual engagement of HIV patients in care. The training of health providers to meet the specific needs of HIV patients and treat them with respect is also crucial. Clinics that are well-

staffed, have no drug stock-outs, provide timely and efficient lab services are also more likely to attract HIV patients than those without good clinical services. More resources should be invested in minimizing staff shortages, providing ongoing training of health facility staff, and addressing the supply and logistical challenges that many health facilities face in resource-limited settings.

Several of the proposed interventions are encompassed in WHO's guidelines for differentiated service delivery for HIV patients.[5] Eswatini's current differentiated service delivery guidelines recommend five differentiated care models for HIV positive patients who have been on ART for at least one year and have an undetectable viral load,[6] but the same strategies could be used for patients who are yet to achieve viral load suppression. These models are:

1. Mainstream care (for clients requiring close clinical attention because of detectable viral load, co-morbidities or other health concerns)
2. Fast-track model (ART refills separated from clinic visits to reduce client waiting time at clinics)
3. Facility-based treatment clubs (group consultations, ART refills and counseling every quarter and individual clinical attention every six months)
4. Community-based ART groups (community level social support, rotational monthly ART refills for each member on behalf of the group and one individual clinical consultation every six months)
5. ART outreach model (community-based ART refill and clinical consultations by clinical staff)

The implementation of these models in Eswatini began in 2016.

The psychometric methods proposed in this dissertation can lead to the development of a tool that can quantify patient reasons for engagement or non-engagement in care in relation to other factors at every stage of the HIV care continuum and can help providers in determining the best differentiated service delivery model for their patients. As the world battles with the upheavals caused by the COVID-19 pandemic, resource-limited settings with generalized epidemics have been faced with a dual pandemic characterized with disruptions in HIV services.[7] Differentiated service delivery models that are adaptable to meet the specific needs of HIV patients have been crucial in mitigating the additional burdens placed on the health systems by these two pandemics. Indeed, differentiated service is "an approach that simplifies and adapts HIV services to better serve the needs of the people living with and at risk of acquiring HIV and reduce unnecessary burdens on the health system."[5]

Psychometric methods provide an essential framework for the development of a scale to measure patient reasons for engagement or non-engagement in HIV care, predict future engagement, and recommend differentiated service delivery models, which does not currently exist for generalized HIV epidemics. A scale is relevant even in the "treat all" era because it provides a precision approach to identifying patients who need help with engagement in care and aids efficient utilization of time and resources. Scale development is an iterative process that results in a measurement instrument made up of a collection of items combined into composite scores to reveal the theoretical constructs not readily observable. This dissertation fulfilled most of the steps of scale development and can be an important framework for future studies specifically designed to collect data on barriers and enablers of engagement in care using Likert

scale-type questions.[2,8] The methods presented in this dissertation for scale development are also applicable to high-income settings with concentrated epidemics.

The importance of psychometric methods was also evident in Chapter 4 because latent measures were difficult to capture without the use of validated tools. Perceived stigma measured at baseline appeared to have a minimal relationship with viral load suppression. However, the relationship was opposite of the one hypothesized (with low perceived stigma being marginally associated with less viral load suppression), and perceived stigma at baseline was not associated with perceived stigma at the 12 months follow-up time. This finding also suggests that barriers to engagement in care are not static and should be assessed at multiple steps of the care continuum. Additionally, HIV stigma may be perceived differently in a setting like Eswatini with the highest HIV prevalence in the world (at 27% in the adult population),[9,10] and may be less of a barrier to engagement in care as HIV may be more normalized in this setting compared to a setting like Mozambique with a lower (less than half of Eswatini) but still high prevalence (at 13% of the adult population),[11] or other settings with a much lower prevalence in the general population. This could explain why the preliminary exploratory factor analysis (EFA) suggested that mitigation of HIV stigma might enable HIV patients to link and retain in care in Mozambique, yet the enabler did not affect future engagement in care in Eswatini, nor did the corresponding barrier of perceived stigma hinder engagement in care in Eswatini, but instead, patients with less perceived stigma were less likely to be virally suppressed.

Interventions to mitigate barriers to engagement in care should be targeted, and sensitive to the changing nature of complex barriers as HIV patients grow accustomed to their HIV status. Since regular clinic attendance did not have a differential effect on viral load suppression

compared to mere study retention in this study, frequent clinic visits among patients who may otherwise be adherent to ART may not have additional value.[12]

In conclusion, this dissertation showed that there is a scarcity of predictive quantitative studies measuring barriers and enablers of engagement in the HIV care continuum among HIV patients. Psychometric studies are particularly useful in measuring the most prominent underlying factors, and this dissertation showed that these methods can be used to capture latent enablers of engagement and to longitudinally assess the effect of these enablers on future engagement and viral load suppression. The most prominent enablers among HIV patients in care in Eswatini were financial and access advantages. The barriers to engagement may change over time and need to be measured with validated tools. Retention in care did not appear to be a good proxy for ART adherence and did not mediate the relationship between perceived stigma at baseline and viral load suppression at 12 months. Future studies should be designed a priori to collect psychometric data more deliberately, and validated tools should be developed to standardize the measurements of barriers and enablers of engagement across HIV studies and programs and to predict future engagement.

5.4 References

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Appendix A: Search Terms Used for Systematic Review

PUBMED (731 Articles)

(((((("hiv"[MeSH Terms] OR "hiv"[All Fields]) OR "HIV Infections"[Mesh] OR "HIV Infections/drug therapy"[Mesh] OR "HIV Infections/prevention and control"[Mesh] OR "HIV Infections/psychology"[Mesh] OR "HIV Infections/therapy"[Mesh]) AND ("antiretroviral therapy"[All Fields] OR "Anti-Retroviral Agents"[Mesh]) OR "Anti-Retroviral Agents/therapeutic use"[Mesh] OR "HIV disease management"[All Fields]) AND ("Retention in Care"[Mesh] OR "retention"[All Fields] OR "retain*"[All Fields] OR "Continuity of Patient Care"[Mesh] OR "Treatment Adherence and Compliance"[Mesh] OR ("genetic linkage"[MeSH Terms] OR "genetic linkage"[All Fields]) OR "genetic"[All Fields] OR "linkage"[All Fields] OR "link*"[All Fields] OR "continuum of care"[All Fields] OR "care cascade"[All Fields] OR "treatment cascade"[All Fields]) AND ("barrier*"[All Fields] OR "facilitator*"[All Fields] OR "enabler*"[All Fields] OR "reason*"[All Fields]) AND English[Language] AND ("1996/01/01"[PDAT] : "2020/01/31"[PDAT]))))

PSYCHINFO (1,398 articles)

"HIV" AND ("antiretroviral therapy" OR "HIV disease management") AND ("retention" OR "retain*" OR "linkage" OR "link*" OR "continuum of care" OR "care cascade" OR "treatment cascade") AND ("barrier*" OR "facilitator*" OR "enabler*" OR "reason*")

SCOPUS (594 articles)

TITLE-ABS-KEY (*"HIV"*) AND TITLE-ABS-KEY (*"antiretroviral therapy"* OR *"ART"* OR *"HIV disease management"*) AND TITLE-ABS-KEY (*"retention"* OR *"retain*"* OR *"linkage"* OR *"link*"* OR *"continuum of care"* OR *"care continuum"* OR *"care cascade"* OR *"treatment cascade"*) AND TITLE-ABS-KEY (*"barrier*"* OR *"facilitator*"* OR *"enabler*"* OR *"reason*"*) AND (LIMIT-TO (DOCTYPE , *"ar"*)) AND (LIMIT-TO (PUBYEAR , *2020*) OR LIMIT-TO (PUBYEAR , *2019*) OR LIMIT-TO (PUBYEAR , *2018*) OR LIMIT-TO (PUBYEAR , *2017*) OR LIMIT-TO (PUBYEAR , *2016*) OR LIMIT-TO (PUBYEAR , *2015*) OR LIMIT-TO (PUBYEAR , *2014*) OR LIMIT-TO (PUBYEAR , *2013*) OR LIMIT-TO (PUBYEAR , *2012*) OR LIMIT-TO (PUBYEAR , *2011*) OR LIMIT-TO (PUBYEAR , *2010*) OR LIMIT-TO (PUBYEAR , *2009*) OR LIMIT-TO (PUBYEAR , *2008*) OR LIMIT-TO (PUBYEAR , *2007*) OR LIMIT-TO (PUBYEAR , *2006*) OR LIMIT-TO (PUBYEAR , *2005*) OR LIMIT-TO (PUBYEAR , *2004*) OR LIMIT-TO (PUBYEAR , *2003*) OR LIMIT-TO (PUBYEAR , *2002*) OR LIMIT-TO (PUBYEAR , *2001*) OR LIMIT-TO (PUBYEAR , *2000*) OR LIMIT-TO (PUBYEAR , *1999*) OR LIMIT-TO (PUBYEAR , *1998*) OR LIMIT-TO (PUBYEAR , *1997*) OR LIMIT-TO (PUBYEAR , *1996*)) AND (LIMIT-TO (LANGUAGE , *"English"*))

Appendix B: Summary of Studies Included in Systematic Review (n = 228)

Author and Year	Country	Primary Research Question	Barriers and Enablers Assessment	Study Population	Sample Size for Barriers and Enablers Assessment of HIV patients	Primary Measurement Approach for Barriers and Enablers	Secondary Measurement Approach for Barriers and Enablers	Barriers Measured	Enablers Measured	Longitudinal Assessment with Barriers/Enablers?	Overall Study Quality
Adams et. al., 2017	Eswatini	Investigation of how men perceived the Test and Start program, and how their perceptions shaped their acceptance of the program	Investigation of barriers of getting on HIV **treatment**	A purposive sample of adult **men** living in the Kwaluseni and Ludzeludze peri-urban areas	76	Qualitative (focus group discussions, in-depth interviews; informal conversations)	N/A	Lack of hospitality in hospitals; fear of starting treatment early related to ART side effects; poverty; lack of trust in the financial stability of the government; negative social consequences of accessing ART services	N/A	No	Fair

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Adelekan et. al., 2019	Nigeria	Examination of the social barriers in accessing care by clients who returned to care after transient LTFU	Justification for choosing specific health facilities to access HIV **care**	HIV+ participants from 99 Health Care Facilities across 10 of Nigeria's 36 states and Federal Capital Territory previously LTFU but returning to care after tracking **(clinical cohort)**	438	Descriptive (cross-sectional survey)	N/A	N/A	Availability of female providers; availability of drugs; proximity to workplace; trust in provider/quality of service; timeliness/promptness of service; low cost; referral/recommendation	No	Fair
Ahmed et. al., 2017	Eswatini	Assessment of the barriers to ART initiation for children living with HIV from a socio-ecological perspective	Assessment of the barriers to **ART initiation** for children living with HIV from a socio-ecological perspective	**Mothers and caregivers** of HIV+ children aged 2-18 months from registers from purposively selected health facilities	34	Qualitative (focus group discussions)	N/A	Denial; guilt; poor perception of and problems with taking ART; lack of knowledge; TB/HIV co-infection; HIV-related stigma; lack of money; long distance to clinics; failure to disclose HIV status to partner or	N/A	No	Good

Author and Year	Country	Primary Research Question	Barriers and Enablers Assessment	Study Population	Sample Size for Barriers and Enablers Assessment of HIV patients	Primary Measurement Approach for Barriers and Enablers	Secondary Measurement Approach for Barriers and Enablers	Barriers Measured	Enablers Measured	Longitudinal Assessment with Barriers/Enablers?	Overall Study Quality
								family; delays in ART initiation process; unavailability of counselling and education; poor treatment at health facilities; lack of privacy and confidentiality			
Akinde et. al., 2019	United States	Assessment of psychosocial and structural factors influencing engagement in care and ART adherence during pregnancy and the postpartum period; assessment of the acceptability of a peer mentor	Assessment of psychosocial and structural factors influencing **engagement in care** and **ART adherence** during pregnancy and the postpartum period	Black and/or Hispanic HIV+ **women, pregnant** or at most 6 months **postpartum**, attending routine prenatal care or PNC appointments at a comprehensive HIV and obstetrics and gynecology care clinic	15	Qualitative (semi-structured interviews)	N/A	Stigma and isolation; fear of disclosure; depression and/or anxiety; adjustment associated with infant care and responsibilities; structural/psychosocial challenges (related to housing instability and lack of	Social support; concern for infants' well-being (prevention of perinatal HIV)	No	Good

Author and Year	Country	Primary Research Question	Barriers and Enablers Assessment	Study Population	Sample Size for Barriers and Enablers Assessment of HIV patients	Primary Measurement Approach for Barriers and Enablers	Secondary Measurement Approach for Barriers and Enablers	Barriers Measured	Enablers Measured	Longitudinal Assessment with Barriers/Enablers?	Overall Study Quality
		intervention in serving the needs of pregnant and postpartum women in a resource-rich setting		in Philadelphia, Pennsylvania				employment)			
Alfonso et. al., 2009	United States	Exploration of experiences of Multi-drug rescue therapy (MDRT) patients and their providers in order to identify gaps in treatment and factors that may impact adherence to MDRT	Exploration of factors that impact MDRT patients to adhere to **treatment**	MDRT Patients at a tertiary referral HIV specialty clinic in an urban center **(clinical cohort)**	12	Qualitative (semi-structured interviews)	N/A	Side effects; pill burden; toxicities; dealing with comorbid conditions; negative outcome expectancies (belief in treatment); ambivalence; lack of readiness	Having a good patient/provider relationship (support)	No	Good

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Ali et. al., 2018	Pakistan	Determination of the adherence level to ART among HIV+ intravenous drug users in Karachi	Determination of reasons for missing **ART** among HIV+ intravenous drug users in Karachi	HIV+ patients purposively sampled from the ART Unit of the Civil Hospital, Karachi, aged ≥ 18 years, **who had injected drugs** at least once in the previous 12 months	375	Descriptive (cross-sectional survey)	N/A	Forgetting; lack of family support; avoiding adverse effects; pill burden; feeling sick after taking ART	N/A	No	Fair
Anand et. al., 2017	Thailand	Assessment of barriers to ART adherence and clinic visit retention, identification of how eHealth could help reduce those barriers and address HIV care needs, and exploration of preferences for eHealth interventions to	Assessment of barriers to **ART adherence** and clinic visit **retention**	Young **MSM and transgender women** previously diagnosed as HIV+ at The Thai Red Cross AIDS Research Centre and receiving ART for at least 6 months across multiple sites in Bangkok	18	Qualitative (in-depth interviews)	N/A	HIV-related stigma; limited clinic hours; travel requirements; lack of perceived confidentiality at clinics; poor patient-provider communication	Hope of being cured; HIV treatment knowledge; sense of self-worth; responsibility towards family members; improved health outcomes; desire for social support; positive patient-provider relationships	No	Fair

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		optimize HIV treatment and care outcomes									
Anígilájé et. al., 2014	Nigeria	To assess the impact of social leisure and psychosocial support on ART adherence and clinic attendance in a pediatric ART program among children previously LTFU	Assessment of reasons for missed clinic **appointments** and the challenges of clinic **attendance**	**Children and adolescents** in a pediatric ART program at the Pediatric ART Clinic of the Riverside Specialist Clinics of the FMC, Makurdi, previously LTFU **and their caregivers**	33 child-caregiver dyads (quantitative assessment); 8 children/adolescents and 4 child-caregiver dyads (qualitative assessment)	Mixed method (Descriptive quantitative part)	Mixed method (Qualitative focus group discussion part)	Financial constraints; engagement in farming; frequent hospital visits for pharmacy refill; long distance to the clinic; clinic date coinciding with a "market day"; transportation problems; forgetting; getting busy; traveling; feeling sick;	N/A	No	Fair

Author and Year	Country	Primary Research Question	Barriers and Enablers Assessment	Study Population	Sample Size for Barriers and Enablers Assessment of HIV patients	Primary Measurement Approach for Barriers and Enablers	Secondary Measurement Approach for Barriers and Enablers	Barriers Measured	Enablers Measured	Longitudinal Assessment with Barriers/Enablers?	Overall Study Quality
								death of caregiver; not being able to leave visitors at home			
Ankomah et. al., 2016	Ghana	Assessment of access-related barriers faced by HIV+ persons already on ART	Assessment of **access-related** barriers faced by HIV+ persons already on ART	HIV+ persons receiving ART at 4 treatment centers in the Eastern and Greater Accra regions **(clinical cohort)**	540	Mixed method (Descriptive quantitative part)	Mixed method (Qualitative open-ended questions in survey part)	Delays in receiving care from treatment centers; long distance to clinic; high financial costs of accessing and receiving ART; job insecurity arising from regular leave of absence to	Beliefs that ART will suppress the HIV virus; desire to maintain good health and prolong life; desire not to infect unborn children; desire to avoid death; desire to become a good therapeutic citizen	No	Good

Author and Year	Country	Primary Research Question	Barriers and Enablers Assessment	Study Population	Sample Size for Barriers and Enablers Assessment of HIV patients	Primary Measurement Approach for Barriers and Enablers	Secondary Measurement Approach for Barriers and Enablers	Barriers Measured	Enablers Measured	Longitudinal Assessment with Barriers/Enablers?	Overall Study Quality
								receive ART; shortage of drugs and other commoditie s; fear of medication side effects; stigma	(abide by doctors' advice)		
Assefa et. al., 2010	Ethiopia	Description of the challenges encountered in the move toward universal access to HCT and ART services during the 4 years (2005–2008) of free ART services in Ethiopia	Exploration of reasons for poor **linkage to and retention** in care among HIV patients	Patients on ART in each of 32 hospitals and 23 health centers in all regions of the country **(general population)**	275-835	Qualitative (semi-structured interviews)	N/A	Fear of stigma; feeling healthy; lack of trust in the services; long distance to treatment centers; transport cost; lack of support; use of alternative traditional medicines; lack of adequate nutrition;	N/A	No	Poor

Author and Year	Country	Primary Research Question	Barriers and Enablers Assessment	Study Population	Sample Size for Barriers and Enablers Assessment of HIV patients	Primary Measurement Approach for Barriers and Enablers	Secondary Measurement Approach for Barriers and Enablers	Barriers Measured	Enablers Measured	Longitudinal Assessment with Barriers/Enablers?	Overall Study Quality
								poor patient handling			
Assemie et. al., 2019	Ethiopia	Determination of the outcomes (alive or dead) of patients LTFU from ART and identification of factors associated with successful tracing and mortality of these patients	Assessment of rationale for discontinuing treatment among patients LTFU from **ART**	All adult patients aged ≥ 18 years, who started ART at Pawi General Hospital in Benishangule Gumuz Region in Northwest Ethiopia and previously classified as LTFU **(clinical cohort)**	249	Descriptive (cross-sectional survey)	N/A	Spiritual beliefs; side effects; belief in being cured	N/A	No	Fair

Author and Year	Country	Primary Research Question	Barriers and Enablers Assessment	Study Population	Sample Size for Barriers and Enablers Assessment of HIV patients	Primary Measurement Approach for Barriers and Enablers	Secondary Measurement Approach for Barriers and Enablers	Barriers Measured	Enablers Measured	Longitudinal Assessment with Barriers/Enablers?	Overall Study Quality
Atanga et. al., 2017	Cameron	Assessment of linkage and retention in care along the PMTCT cascade in HIV+ pregnant and breastfeeding women initiating Option B+ in Cameroon	Assessment of reasons for **discontinuing treatment** among HIV+ pregnant and breastfeeding women initiating Option B+	HIV+ **women attending ANC, post-natal** and infant welfare services and receiving Option B+ ART at 5 sites within the Kumba Health District, South West Region	36	Descriptive (prospective cohort)	N/A	Denial of HIV status; stigma and discrimination; religious reasons; lack of transport fare to visit clinic	N/A	No	Good
Attonito et. al., 2014	United States	Exploration of the direct effect of several psychosocial variables on viral load and their indirect association with viral load via full mediation of ART adherence	Assessment of barriers to **ART adherence**	HIV+ adults with a history of alcohol abuse or dependence within the last 2 years participating in a RCT recruited from community-based organizations in low-income areas of Miami-Dade and Broward counties,	246	Predetermined scale (barriers to adherenece tool)	N/A	Feeling worse when taking pills; forgetting to take pills; being away from home; having problems taking pills at specified times	N/A	Yes	Fair

Author and Year	Country	Primary Research Question	Barriers and Enablers Assessment	Study Population	Sample Size for Barriers and Enablers Assessment of HIV patients	Primary Measurement Approach for Barriers and Enablers	Secondary Measurement Approach for Barriers and Enablers	Barriers Measured	Enablers Measured	Longitudinal Assessment with Barriers/Enablers?	Overall Study Quality
				Florida **(other key population)**							
Avong et. al., 2015	Nigeria	Assessment of the level of adherence to ART and adherence determinants among participants on ART	Description of factors that constrain and motivate **adherence to ART**	HIV+ adults aged ≥ 18 years on ART for ≥ 12 months and attending the ART clinic of the Abuja University Teaching Hospital (AUTH), the largest tertiary hospital in the region **(clinical cohort)**	502	Descriptive (cross-sectional survey)	N/A	Forgetting to take medication; travelling away from home; running out of medication; being busy at work; lacking food; having medication stolen	Improvement of health condition; having a desire to live; having family support; having a support group	No	Good

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Ayieko et. al., 2018	Uganda and Kenya	Assessment of barriers to engagement in HIV care, particularly testing, ART initiation and viral suppression steps of the cascade	Assessment of barriers to engagement in HIV care, particularly **ART initiation** and **viral suppression** steps of the cascade	HIV+ members of a community cohort, randomly selected from household rosters established by the Sustainable East African Research for Community Health (SEARCH) socio-economic survey, a community-level cluster randomized HIV test-and-treat trial implemented in 32 rural communities in Uganda and Kenya **(general population)**	63	Qualitative (semi-structured interviews)	N/A	HIV-related stigma; denial; fear of disclosure; poverty (lack of food and transport); competing demands (care-seeking interfering with work); feeling healthy; lack of social support; prior negative experiences with health services; drug side effects; negative beliefs and attitudes about ART; treatment fatigue	N/A	No	Good

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Bajunirwe et. al., 2018	Uganda	Exploration of factors that influence access, availability, and utilization of HIV services in rural Uganda in the setting of a large donor funded program	Exploration of barriers that affect access to **HIV services**	Clients presenting for HIV care and treatment services at health facilities randomly selected in 19 districts of 5 rural regions in northern Uganda **(general population)**	Not stated	Qualitative (focus group discussions)	N/A	Drug shortages; long distance to health facility; staffing shortages; HIV services offered at inconvenient hours; lack of adequate atttention/time from health care workers; lack of privacy at health facility; stigma persistence; lack of social and economic support initiatives to aid retention in treatment	N/A	No	Poor

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Balcha et. al., 2011	Ethiopia	Exploration of the major barriers to sustained treatment and to follow-up of ART patients at hospital and health center levels in Oromia Region	Exploration of the major barriers to sustained **treatment** and to follow-up of ART patients at hospital and health center levels in Oromia Region	HIV+ clients aged ≥ 18 years purposively samples from hospitals and health centers in the Oromia Region **(general population)**	11	Qualitative (focus group discussions)	N/A	Perception of ART as a long-term life support for an incurable illness; perception of free ART as expensive (because of additional laboratory and nutritional expenses); financial constraints; stigma; lack of community support	N/A	No	Fair
Bam et. al., 2015	Nepal	Measurement of overall adherence levels, identification barriers and facilitators to adherence and identification of gaps in ART adherence monitoring and support of ART	Identification barriers and facilitators to **adherence** of **ART** patients	Clients on ART for ≥ 6 months, aged ≥ 15 years from the 25 ART sites of the Nepal, covering all the 5 development regions of the country **(general population)**	21	Descriptive (cross-sectional survey)	N/A	Side effects; being away from home; lack of ART knowledge; forgetfulness; not wearing a wristwatch; road closures (strikes); death of the spouse; transportation problems; lack of	Wearing a wristwatch; support from family and friends; having access to a radio; timely availability of medicine; collecting medicine before scheduling ART visit	No	Good

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		patients in different clinics in all 5 regions of the country						access to medications			

Author and Year	Country	Primary Research Question	Barriers and Enablers Assessment	Study Population	Sample Size for Barriers and Enablers Assessment of HIV patients	Primary Measurement Approach for Barriers and Enablers	Secondary Measurement Approach for Barriers and Enablers	Barriers Measured	Enablers Measured	Longitudinal Assessment with Barriers/Enablers?	Overall Study Quality
Barfod et. al., 2006	Denmark	Comparison of the self-reported reasons for missed doses between patients with higher and lower HAART adherence in a population-based cohort of patients	Examination of patients' self-reported reasons for missing doses of **HAART**	All HIV-infected patients aged ≥ 16 receiving HIV care in western Denmark (Danish HIV Cohort Study) and patients at the HIV clinic at Rigshospitalet in Copenhagen **(general population)**	840	Descriptive (prospective cohort)	N/A	Forgetting; being away from home; having a change in daily routine; being busy with other things; falling asleep through the dose time; having problems taking pills at specified times; feeling sick or ill; having drunk alcohol; not wanting others to notice them taking medication; feeling depressed/overwhelmed; feeling good; wanting to avoid side effects; wanting a break from	N/A	No	Fair

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								thinking about HIV; having difficulty taking the pills because of taste or size; having too many pills to take; thinking the medicine would work just as well anyway; running out of pills; feeling like the drug was toxic/harmful; lacking support form partner, family or friends; using drugs; misunderstanding the information about medications or dosing; having a poor relationship			

Author and Year	Country	Primary Research Question	Barriers and Enablers Assessment	Study Population	Sample Size for Barriers and Enablers Assessment of HIV patients	Primary Measurement Approach for Barriers and Enablers	Secondary Measurement Approach for Barriers and Enablers	Barriers Measured	Enablers Measured	Longitudinal Assessment with Barriers/Enablers?	Overall Study Quality
								with physician			

Author and Year	Country	Primary Research Question	Barriers and Enablers Assessment	Study Population	Sample Size for Barriers and Enablers Assessment of HIV patients	Primary Measurement Approach for Barriers and Enablers	Secondary Measurement Approach for Barriers and Enablers	Barriers Measured	Enablers Measured	Longitudinal Assessment with Barriers/Enablers?	Overall Study Quality
Bassett et. al., 2017	South Africa	Evaluation of the impact of self-perceived barriers to health care on 1-year mortality among newly diagnosed HIV patients in Durban	Assessment of perceived barriers to **care** during the previous 6 months	Newly diagnosed HIV+ patients aged ≥ 18 enrolled at 4 sites in the greater Durban area **(clinical cohort)**	1,887	Assessing association or causation (prospective cohort)	N/A	Poor service delivery; financial constraints; personal health perception; logistical problems; structural issues	N/A	Yes	Good
Beer et. al, 2012	United States	Assessment of mechanisms through which concerns about medications act as barriers to HIV care	Assessment of barriers to HIV **care**	Never in Care (NIC) Project HIV+ individuals not enrolled in care sampled from the Enhanced HIV/AIDS Reporting System (eHARS) from Indiana, New Jersey, New York City, Philadelphia, and Washington State during 2008–2010	134 (quantitative assessment) and 48 (qualitative assessment)	Mixed method (Descriptive quantitative part)	Mixed method (Qualitative structured interviews)	Perception that medications may be harmful or unnecessary; preference for alternative medical care; concerns about prescription practices; preservation of future treatment options; mistrust of medications and medical care providers;	N/A	No	Fair

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				(general population)				concerns that medications may cause more harm than good			
Betancur et. al., 2017	Brazil	Description of the clinical, demographic and psychological characteristics, and quality of life of HIV patients with poor ART adherence	Assessment of self-reported reasons for **non-adherence to ART**	HIV+ patients aged 18-65 on ART for at least 1 year with viral load > 500 copies/mL and receiving care at the AIDS outpatient clinics of the Prof. Edgard Santos University Hospital	47	Descriptive (cross-sectional survey)	N/A	Feeling well; running out of pills; having problems taking pills at specified times; feeling depressed; feeling sick or indisposed; sleeping when time to take dose; feeling the drug is toxic/harmf	N/A	No	Fair

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				(HUPES), Salvador, Bahia **(clinical cohort)**				ul; having a change in daily routine; Not wanting to be noticed taking the meds; avoiding undesirable side effects; having too many pills to take; forgetting; being busy with other things; being away from home			
Bezabhe et. al., 2014	Ethiopia	Examination of the barriers and enablers of ART adherence and retention in follow-up care among HIV+ adult patients and healthcare providers	Examination of the barriers and enablers of **ART adherence and retention** in follow-up care among HIV+ adult patients	HIV+ patients aged ≥ 18 receiving ART for at least a month from Felege-Hiwot Hospital and Gondar University Hospital, Amhara Region **(clinical cohort)**	24	Qualitative (semi-structured interviews)	N/A	Economic constraints; perceived stigma and discrimination; fasting; being baptized with holy water; medication side effects; dissatisfaction with healthcare services	Disclosure of HIV status; social support; use of reminder aids; responsibility for raising children; improved health due to ART; receiving education and counseling	No	Good

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Black et. al., 2014	South Africa	Examination of the acceptability of rapid initiation of lifelong ART by pregnant women	Examination of the barriers to and facilitators of **ART commencement**	HIV+ **pregnant women** enrolled in a rapid ART initiation in pregnancy program attendinig ANC at a midwife-driven ANC clinic in Cape Town	27	Qualitative (semi-structured interviews)	N/A	Non-acceptance of being pregnant; Non-acceptance of HIV status; ART ineligibility; fear of treatment side effects; pill burden; non-disclosure of HIV status	Desire to protect unborn child from virus; protection of own health and longevity; counseling; social support; disclosure of HIV status; constructive family; community role models	No	Fair
Boehme et. al., 2014	United States	Description of barriers and facilitators of HIV care adherence among HIV-infected postpartum women	Description of barriers and facilitators of HIV **care adherence** among HIV-infected postpartum women	HIV+ **postpartum women** having given birth to a child within the last 5 years and receiving care from 4 HIV care clinics in Alabama	18	Mixed method (Descriptive quantitative part)	Mixed method (Focus group discussions, individual interviews and nominal group technique rankings qualitative part)	Transportation problems; problems with work schedule; children's schedule problems; long duration of appointments; length of time between appointments; fear of bad news; fear of symptoms	Desire to stay healthy; good health of child; desire to live a long life; support from health-care providers/ peer advocates; appointment reminders; flexible scheduling; family support; transportation	No	Good

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								worsening; disease stabilization; fear of child's HIV serostatus; clinic/copay expenses; stigma; difficulty swallowing pills; disclosure concerns; lack of health education regarding the importance of ART medication or meaning of HIV status	arrangements; social service support; childcare encouragement		
Bofill et. al., 2014	Argentina	Exploration and identification of factors associated with patient engagement and retention in care in Buenos Aires	Exploration and identification of factors associated with patient **engagement and retention** in care in Buenos Aires	HIV+ patients aged ≥ 18 receiving care from 2 clinics located in urban Buenos Aires **(clinical cohort)**	6	Qualitative (focus group discussions and key informant interviews)	N/A	Low self-efficacy; fear and concerns about HIV; lack of provider involvement in treatment; stigma; fear of medication side effects; frequent	Long-term relationship with provider; acceptance of HIV status; integration of medication ingestion into daily routines;	No	Fair

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								changes of primary care provider at clinic; difficulties obtaining physician appointments or other health care services	social support		
Bogart et. al., 2013	South Africa	Identification of barriers to linkage to care among PLHIV not yet on ART	Identification of barriers to **linkage to care** among PLHIV not yet on ART	HIV+ patients receiving care at McCord Hospital in Durban, KwaZulu-Natal and not yet on ART **(clinical cohort)**	51	Qualitative (focus group discussions and semi-structured interviews)	N/A	Stigma; financial and transport issues; inconvenient clinic hours; long queues; difficulty in appointment scheduling; disrespect from staff	N/A	No	Good

Author and Year	Country	Primary Research Question	Barriers and Enablers Assessment	Study Population	Sample Size for Barriers and Enablers Assessment of HIV patients	Primary Measurement Approach for Barriers and Enablers	Secondary Measurement Approach for Barriers and Enablers	Barriers Measured	Enablers Measured	Longitudinal Assessment with Barriers/Enablers?	Overall Study Quality
Braitstein et. al., 2011	Kenya	Identification of the vital status and reasons for children becoming LTFU from an HIV program in Kenya	Identification of reasons for children becoming **LTFU** from an HIV program in Kenya	HIV+ or HIV exposed **children** attending AMPATH centre clinic at the urban Moi Teaching and Referral Hospital (MTRH) in Eldoret, or the rural sub-District Hospital in Burnt Forest, and who were LTFU and their **caregivers**	97	Descriptive (prospective cohort)	N/A	Transport costs; family commitments; work commitments of the child or the caregiver; child or caregiver too ill to come to clinic; school commitments; disclosure issues; insecurity (afraid to travel); having travelled; having been displaced (from post-election violence); forgetting about appointments; refusal of care by child or caregiver (due to family discrimination,	N/A	No	Fair

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								community discrimination, belief in alternatiive/ faith/traditional/herbal healing)			
Brown et. al., 2019	Uganda and Kenya	Assessment of factors that lead to high retention in care among men in a universal treatment setting	Assessment of facilitators and barriers to **retention** in care among men in a universal treatment setting	HIV+ **men** who were residents of rural communities undergoing the SEARCH cluster-randomized trial	109	Mixed method (Descriptive and multivariable prospective cohort part)	Mixed method (Qualitative in-depth interview part)	N/A	Maintaining physical health; a patient-centered treatment environment; supportive partnerships; few negative consequences to disclosure; ability to seek care in facilities outside community of residence	No	Good

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Buchanan et. al., 2012	United States	Examination of the agreement between child and caregiver perceptions of barriers to ART adherence and associated factors	Examination of the agreement between child and caregiver perceptions of barriers to **ART adherence** and associated factors	HIV exposed and infected **children** participating in the PACTG P1042S longitudinal sub-study of PACTG P219C, **and their caregivers**	151	Assessing association or causation (prospective cohort)	N/A	Inability of child to get meds; failure to refill meds; scheduling interference; having multiple caregivers; child being away from home; being busy with other things; having a change in daily routine; falling asleep through dose time; not being able to keep the pill or liquid down; having too many pills to take; avoiding side effects; feeling like medication is toxic or harmful; having problem	N/A	No	Good

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								taking pills as directed; child refusing to take pills; child feeling sick or ill; child feeling good; concerns about being noticed taking medications; feeling depressed or overwhelmed			
Busza et. al., 2014	Zimbabwe	Exploration of the barriers and facilitators experienced by caregivers of HIV+ children in sustaining HIV treatment and care to inform the	Exploration of the barriers and facilitators experienced by caregivers of HIV+ children in sustaining HIV **treatment and care**	Primary **caregivers** of HIV+ children aged 6-15 enrolled at the Harare Central Hospital HIV clinic	15	Qualitative semi-structured interviews)	N/A	Distance to hospital; transportation costs; fear of disclosing HIV status to the child or others; unstable family structure; drug stock-outs;	Openness within the family; availability of practical assistance; psychosocial support from community	No	Fair

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		design of a community-based intervention to support caregivers to increase children's retention in care						healthcare worker absenteeism; unsympathetic school environments			
Byakika-Tusiime et. al., 2005	Uganda	Determination of level of adherence and reasons for non-adherence to ART among HIV+ patients purchasing ART in resource-limited setting	Determination of reasons for **non-adherence to ART** among HIV+ patients purchasing ART in resource-limited setting	HIV+ patients purchasing ART from 3 treatment centers in Kampala **(clinical cohort)**	304	Mixed method (Descriptive and multivariable cross-sectional part)	Mixed method (Qualitative unstructured interview part)	Shortage of drugs due to lack of money; forgetfulness; drug in-accessibility; adverse effects of the drug; travelling away from home; unclear instructions by the health provider; being too busy; regimen being too complex; fear of wasting	N/A	No	Poor

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								drug; presence of other disease conditions			
Byakika-Tusiime et. al., 2009	Uganda	Assessment of the effect of family-based treatment on ART adherence amongst HIV+ parents and their HIV+ children attending an MTCT Plus program	Assessment of reasons for incomplete **ART adherence** amongst HIV+ parents and their HIV+ children attending an MTCT Plus program	HIV+ **mothers** attending an MTCT Plus program at Mulago Hospital in Kampala, Uganda	15	Qualitative (focus group discussions)	N/A	Lack of transportation money; perceived stigma; fear of disclosure to partner; drug packaging; cost of therapy	Desire to stay alive in order to care and support children and other family members; good clinical response to ART in children	No	Fair

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Camlin et. al., 2016	Kenya, Uganda and Tanzania	Assessment of reasons for not returning to clinic among HIV+ patients LTFU and the influence of those reasons on subsequent care reengagement	Assessment of reasons for **not returning to clinic** among HIV+ patients LTFU and the influence of those reasons on subsequent care reengagement	HIV+ patients LTFU from clinics participating in the East Africa International Epidemiologic Databases to Evaluate AIDS **(clinical cohort)**	430	Psychometric (factor analysis)	N/A	Poverty; transport costs; interference with work responsibilities; poor treatment by providers; fear of disclosure of HIV status; feeling healthy; treatment fatigue/seeking spiritual alternatives to medicine	N/A	Yes	Fair
Castel et. al., 2018	United States	Assessment of the feasibility and acceptability of video gaming to improve ART adherence among HIV+ adolescents and young adults	Description of the barriers and facilitators of **ART adherence** among HIV+ adolescents and young adults	HIV+ **adolescents and young adults** aged 13-24 who had disclosed their HIV status and received care at Washington University and Children's National Medical Center Special	12	Qualitative (focus group discussions)	N/A	Disclosure of HIV status; irregular daily schedules (time management challenges); difficulty swallowing pills; not wanting to be different from peers; forgetfulness	Use of alarms and pillboxes as reminders; motivation from family	No	Fair

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				Immunology Services in the DC metropolitan region							
Castro et. al., 2015	Pueto Rico	Identification of barriers and facilitators of HAART adherence among HIV+ people in Southern Puerto Rico using a Social Ecological framework	Identification of barriers and facilitators of **HAART adherence** among HIV+ people in Southern Puerto Rico	HIV+ persons on HAART from clinics, communities, and government based organizations that provide health services to HIV+ patients in southern Puerto Rico **(general population)**	12	Mixed method (Descriptive quantitative part)	Mixed method (Qualitative in-depth interview part)	Treatment regimen issues; poor mental health; poor interpersonal relations; poor health literacy; environmental/organizational issues; health system challenges; transportation issues; stigma/discrimination	Patient desire to live/spiritual practices/health concerns; social support; desire to take care of children; referrals and support from health care professionals	No	Good

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Cataldo et. al., 2017	Malawi	Exploration of the experiences of patients and healthcare workers regarding the implementation of Option B+ for PMTCT	Exploration of the barriers to **retention** in care among women enrolled in Option B+	HIV+ **pregnant or breastfeeding women** newly enrolled in an Option B+ ART program in 6 health facilities participating in the PURE trial	24	Qualitative semi-structured interviews)	N/A	Lack of male involvement; privacy and confidentiality concerns; stigma; long distance to health facility	N/A	No	Fair
Chakrapani et. al., 2011	India	Exploration of barriers to ART access among HIV+ MSM and transgender women in Chennai	Exploration of barriers to **ART access** among HIV+ MSM and transgender women in Chennai	HIV+ **MSM and transgender women** in Chennai affiliated with 4 CBOs that work with MSM and transgender persons	34	Qualitative (focus group discussions)	N/A	Stigma; lack of family support; unmet basic needs (such as food and shelter); negative experiences with healthcare providers; logistical procedures at clinic; inadequate counseling services; lack of confidentiality; insufficient ART training	N/A	No	Fair

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								among outreach workers; delays in HIV testing; fatalism; alcohol use; insufficient knowledge about ART and belief in alternative cures			

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Chakrapani et. al., 2014	India	Exploration of barriers to free ART access at government ART centers among HIV+ IDUs in Chennai	Exploration of barriers to free **ART access** at government ART centers among HIV+ IDUs in Chennai	HIV+ **IDUs** affiliated with 2 community agencies that work with IDUs and PLHIV	19	Qualitative (focus group discussions)	N/A	Lack of family support; fear of societal discrimination; unmet basic needs (such as food and shelter); unfriendly hospital environment; logistical procedures at clinic; lack of provider confidence in patient adherence; inadequate counseling services; lack of confidentiality; lack of effective linkages between ART centers, needle/syringe programs, and drug dependence treatment centers;	N/A	No	Fair

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								active drug use; lack of self-efficacy in ART adherence; low motivation to initiate ART; inadequate knowledge about ART			
Chakravarty et. al., 2016	India	Identification of defaulters from HIV care and exploration of reasons for defaulting among HIV+ patients in a pre-ART program	Exploration of reasons for **defaulting from care** among HIV+ patients in a pre-ART program	PLHIV in pre-ART care at the ART center of the Centre of Excellence in HIV Care, Banaras Hindu University (BHU), who had defaulted from care	83	Descriptive (cross-sectional interview)	N/A	Inconvenient clinic timing; need for multiple modes of transport; perceived improved health; long distance to clinic; lack of social support; financial difficulty	N/A	No	Poor

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				(clinical cohort)							
Chandy et. al., 2019	India	Examination of factors associated with sustained engagement in care among women living with HIV in South India	Examination of barriers to **sustained engagement in care** among women living with HIV in South India	HIV+ women enrolled in the Chenata cluster-randomized trial and receiving care in public and government -aided private ART centers in South India **(clinical cohort)**	264	Assessing association (cross-sectional interview)	N/A	Transportation problems; childcare issues; taking time off from household chores/ work; long wait-times at the clinic	N/A	No	Fair

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Chang et. al., 2019	United States	Evaluation of factors associated with HIV care re-engagement among persons disengaged from HIV care	Assessment of barriers to **care engagement** among HIV+ patients disengaged from care	HIV+ patients in Kings County, Washington, enrolled in the Surveillance Public Health—Seattle and King County (PHSKC) Data to Care (D2C) Care and Antiretroviral Promotion Program (CAPP) **(general population)**	408	Assessing association or causation (prospective cohort)	N/A	Uncertainty about HIV diagnosis; belief in having control over HIV; belief that a doctor would not help; preference for alternative treatments over conventional HIV care and ART	N/A	No	Fair

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Chenneville et. al., 2017	United States	Assessment of medication knowledge, adherence, and factors affecting adherence among HIV+ youth	Assessment of factors affecting medication **adherence** among HIV+ youth	HIV+ **youth** aged 13-24 recruited from a pediatric/adolescent infectious disease program in the Southeastern part of the country	72	Qualitative (structured interviews)	N/A	Treatment side effects; younger age; nutrition/dietary needs; poor knowledge/ understanding; poor memory; medication fatigue; poor motivation; constant reminder of illness; fear of disclosure/ social concerns; emotional concerns; failure to plan; interference with routine activities; number of pills; size of pills; taste of pills; problems with refills; transportation problems	Absence of side effects; adequate nutrition/diet; knowledge/ understanding; memory aids; adequate privacy; meeting goals; having a daily routine; changing lifestyle; number of pills; size of pills; regimen/timing; type of medication; adequate transportation	No	Fair

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Chesney et. al., 2000	United States	Assessment of ART adherence levels among participants in HIV clinical trials	Assessment of reasons for **non-adherence to ART** among participants in HIV clinical trials	HIV+ patients enrolled in clinic trials at 10 Adult AIDS Clinical Trials Units (ACTUs) **(clinical cohort)**	75	Descriptive (cross-sectional survey)	N/A	Simply forgetting; being away from home; being busy with other things; having a change in daily routine; falling asleep through dose; problems with taking meds at specific times; falling ill or sick; avoiding side effects; feeling depressed/overwhelmed; pill burden; fear or being noticed taking meds; feeling drug is toxic/harmful	N/A	No	Fair

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Chime et. al., 2019	Nigeria	Determination of the predictors of adherence to medication and retention among PLHIV in Enugu State	Determination of the reasons for **non-adherence** to medication among PLHIV in Enugu State	HIV+ patients aged ≥18 who accessed care in 8 comprehensive health facilities in Enugu state, who had been on HAART for at least a year prior to the study **(clinical cohort)**	294	Descriptive (cross-sectional survey)	N/A	Being away from home; forgetting; physical discomfort; running out of medication; not being able to hide to take the drugs; fasting	N/A	No	Poor
Chirambo et. al., 2019	Malawi	Exploration of factors associated with non-adherence to ART among adult patients accessing ART services at 2 private urban health facilities in Southern Malawi	Exploration of factors associated with **non-adherence to ART** among adult patients accessing ART services at 2 private urban health facilities in Southern Malawi	HIV+ adults receiving care at 2 private urban health facilities in Southern Malawi **(clinical cohort)**	24	Qualitative (in-depth interviews)	N/A	Forgetfulness; poor risk perception; denial of HIV infection status; fear of disclosure; ARV side effects; ARV fatigue; shortage of trained ART providers; poor financial and geographical	Follow up visits from providers after missed appointments; adequate health education and counseling; supportive relationships	No	Good

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								accessibility; poor relationship with healthcare workers			
Christopoulos et. al., 2015	United States	Assessment of reasons for lack of ART usage among patients retained in care and the motivations for retention in absence of ART usage	Assessment of reasons for lack of **ART usage** among patients retained in care and the motivations for **retention** in absence of ART usage	HIV+ patients not currently on ART but receiving care at 2 academic medical centers in San Francisco and New York **(clinical cohort)**	20	Qualitative (in-depth semi-structured interviews)	N/A	Fears of side effects and drug toxicities; denial and non-disclosure of HIV diagnosis; stigma concerns	Sufficient education on newer ARVs; acceptance of HIV status; social support; increased confidence in adherence ability; strong provider recommendation to start ART; lab monitoring opportunities; good provider relationships; access to social services;	No	Good

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									access to opiate pain medications ; acute symptoms		
Clouse et. al., 2014	South Africa	Identification of challenges to postpartum retention in care among HIV+ women initiating ART under Option B+	Identification of challenges to postpartum **retention** in care among HIV+ women initiating ART under Option B+	HIV+ **pregnant and post-partum women** aged ≥18 years attending ANC and PNC at Witkoppen Health and Welfare Centre (WHWC) in Johannesburg	50	Mixed method (Descriptive quantitative part)	Mixed method (Qualitative semi-structured interview and focus group discussions part)	Lacking money; having work conflicts; poor staff treatment at clinic; mother's belief that she should care more about the baby's health than her own; mother's ignorance or perceived irresponsibility;	N/A	No	Fair

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								mother's denial of her HIV status; mother's non-disclosure of HIV status; long queues or limited hours at clinic; mother's relocation; mother's belief of being cured			
Cocohoba et. al., 2013	United States	Determination of the barriers and facilitator of adherence support among HIV patients who receive ART adherence support and counseling from HIV-focused community pharmacies in the San Francisco Bay	Determination of the barriers and facilitator of **adherence** support among HIV patients who receive ART adherence support and counseling from HIV-focused community pharmacies in the San Francisco Bay	HIV+ patients who obtained ART from a community pharmacy in the San Francisco Bay Area **(clinical cohort)**	19	Qualitative semi-structured interviews)	N/A	Complicated insurance systems; anxiety about not being able to receive medications quickly; feeling ill; concerns about pharmacy location; presence of drug-seeking or intoxicated pharmacy patrons; lack of privacy in	Feeling known by the pharmacy	No	Good

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								the pharmacy counseling area			
Culbert et. al., 2014	United States	Description of men's perceptions of and experiences with HIV care and ART during incarceration	Description of barriers to incarcerated men's willingness and ability to access and adhere to **treatment**	HIV+ **men** recently incarcerated and receiving care at 6 community HIV clinics in Chicago	42	Qualitative (in-depth interviews)	N/A	Physical isolation; interpersonal violence; lack of safety; perceived threats to privacy; correctional officer (CO) apathy or unwillingness; fees for health services	N/A	No	Good

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daSilva et. al., 2015	Mozambique	Exploration of pre-ART LTFU among HIV+ patients in Zambe´zia province	Exploration of factors contributing to **attrition** among pre-ART HIV+ patients in the district of Maganja da Costa in Zambe´zia province	HIV+ patients aged ≥18 receiving care at HIV centers in Vanderbilt University / Friends in Global Health (VU/FGH)-supported clinics in the district of Maganja da Costa in Zambe´zia province **(clinical cohort)**	20	Mixed method (Descriptive quantitative part)	Mixed method (Qualitative semi-structured interview part)	Geographic distance to facility; lack of transport; competing priorities; fear of repercussions from spouses; perceived poor quality of care at facility; discouragement by traditional healers; denial of HIV status/illness; shame	Good clinical services, including counseling and support; assistance with caring for dependents at home; transportation assistance; spouses' awareness of status; wishing to remain in good health; starting ART	No	Fair
Dahab et. al., 2011	South Africa	Investigation of reasons for LTFU and treatment discontinuation among participants enrolled in ART in a public-sector clinic based in a tertiary hospital vs a workplace clinic-based	Investigation of reasons for **LTFU and treatment discontinuation** among participants enrolled in ART in a public-sector clinic based in a tertiary hospital vs a workplace clinic-based	HIV+ patients aged ≥18 receiving ART in a public-sector clinic based in a tertiary hospital or a workplace clinic-based in a tertiary hospital for employees of a mining company	27	Qualitative semi-structured interviews)	N/A	Uncertainty about own HIV status; disbelief in HIV and ART; poor patient–provider relationships; workplace discrimination; moving away; having no money for clinic	N/A	No	Fair

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		in a tertiary hospital for employees of a mining company	in a tertiary hospital for employees of a mining company	**(clinical cohort)**				transport; use of traditional medicines			
Davis et. al., 2018	Kazakhstan	Examination of perceived barriers and facilitators to ART adherence among PWID	Examination of perceived barriers and facilitators to **ART adherence** among PWID	**PWID** in 4 Kazakhstan cities recruited through AIDS Centers, needle-exchange programs, outreach workers, and NGOs that work with PWID and PLHIV	57	Qualitative (focus group discussions)	N/A	Misperceptions about ART; forgetfulness due to effects of illicit drug use; medication side effects; misperceptions about medication assisted therapy (MAT); poverty; legal challenges; disruptions in the ART supply;	Social support; good relationships with healthcare providers	No	Good

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								stigma and discrimination; treatment for co-morbidities			
De et. al., 2013	India	Identification of factors responsible for late ART enrollment among HIV patients with low CD4+ cell count	Identification of factors responsible for late **ART enrollment** among HIV patients with low CD4+ cell count	HIV+ patients receiving care at the ART Center of School of Tropical Medicine (STM), in Kolkata **(clinical cohort)**	100	Descriptive (cross-sectional survey)	N/A	Failure of physician to suspect and refer patient for HIV testing early; health seeking behavior; fear of stigma; depression; lack of family support	N/A	No	Poor
Denison et. al., 2015	Zambia	Exploration of adolescents' and adult caregivers' experiences with ART adherence	Exploration of barriers and facilitators of **ART adherence** among adolescents and their	HIV+ **adolescents (aged 15-18) and their caregivers** receiving care at 2 ART clinics	32 adolescents and 23 caregivers	Qualitative (in-depth interviews)	N/A	Fear of unintended disclosure; anticipated stigma; spiritual beliefs and healings; lack of knowledge	Family support; clinic-sponsored youth groups; wanting to maintain one's health;	No	Good

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			adult caregivers	in Ndola, Zambia				of one's HIV status; side effects; reluctance to take medication daily	using phone and clock alarms		
Deribe et. al., 2008	Ethiopia	Determination of factors associated with defaulting from ART in Jimma	Determination of reasons for defaulting from **ART** in Jimma	HIV+ patients on ART and receiving care at Jimma University Specialized Hospital (JUSH) in Jimma zone **(clinical cohort)**	1,270	Descriptive (case control study)	N/A	Loss of hope in medication; side effects; lack of food; mental illness; holy water; lack of transport money; mental illness; other illnesses; transfer to other ART center; imprisonment; stigma; forgetting	N/A	No	Fair
Diabaté et. al., 2007	Côte d'Ivoire	Assessment of HAART adherence and determination of factors associated with poor adherence among HIV+	Determination of factors associated with poor **adherence** among HIV+ patients in Abidjan	HIV+ patients attending the Unité de Soins Ambulatoires et de Conseils HIV hospital	591	Descriptive (prospective cohort)	N/A	Drug supply interruptions	N/A	No	Fair

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		patients in Abidjan		**(clinical cohort)**							
Dombrowski et. al., 2015	United States	Assessment of barriers to HIV care and ART initiation among persons poorly engaged in care in King County, Washington	Assessment of barriers to HIV **care and ART** initiation among persons poorly engaged in care in King County, Washington	HIV+ persons who are part of the Care and Antiretroviral Promotion Program (CAPP) in King County, Washington **(general population)**	247	Descriptive (cross-sectional survey)	N/A	Insurance problems; practical problems; financial problems; perceived lack of need for medical care; perceived lack of need for medication; forgetting appointments; trouble getting to appointments; lack of transportation; not knowing how to find a doctor; poor relationship with doctor; homelessness; using drugs;	N/A	No	Good

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								preference for alternative therapies including faith-based; depression or other mental health issues; side effect concerns; adherence concerns; resistance concerns; not haviing drugs prescribed by doctor; fear of disclosure; not having accepted HIV+ status; competing priorities; other health problems; wanting a break			

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Duff et. al., 2010	Uganda	Description of barriers to accessing and accepting HAART by HIV+ mothers in a PMTCT program in Kabarole District	Description of barriers to accessing and accepting **HAART** by HIV+ mothers in a PMTCT program in Kabarole District	HIV+ **women receiving ANC** at Kabarole District referral clinic as part of the PMTCT-Plus program	45	Qualitative (in-depth interviews and focus group discussions)	N/A	Economic concerns; transport costs; HIV-related stigma and non-disclosure of HIV status to partners; long waiting times at the clinic; suboptimal provider-patient interactions	N/A	No	Good
Dyrehave et. al., 2016	Guinea-Bissau	Validation of previously found barriers and facilitators to ART adherence and description of the association with HIV-related knowledge in Bissau	Assessment of barriers and facilitators to **ART adherence**	HIV+ patients receiving care at the Hospital Nacional Sima˜o Mendes, in Bissau **(clinical cohort)**	494	Descriptive (cross-sectional survey)	N/A	Side effects; running out of pills; food insecurity; traveling; simply forgetting; being too ill to attend the clinic	N/A	No	Good

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Eholié et. al., 2007	Côte d'Ivoire	Estimation of HAART adherence and determinants of adherence in HIV-infected adults followed in field conditions in Abidjan	Assessment of reasons for **non-adherence to HAART** among HIV-infected adults in Abidjan	HIV+ adults on HAART receiving care at 3 public outpatient clinics in Abidjan **(clinical cohort)**	308	Descriptive (cross-sectional survey)	N/A	Drugs being out of stock in pharmacy; fear of drug side effects; cost of drugs; influence of traditional practitioners; complexity of drug regiments; forgetting; long distance to clinic; unavailability of the referent doctor	N/A	No	Fair
Ekama et. al., 2012	Nigeria	Determination of ART adherence levels and identification of factors that influence adherence during pregnancy	Determination of factors that influence **ART adherence** during pregnancy	HIV+ **pregnant women** receiving ART at the HIV treatment Centre of the Nigerian Institute of Medical Research (NIMR), Lagos	170	Descriptive (cross-sectional survey)	N/A	Forgetfulness; sleeping; work schedule; religious activity; lack of food; fear of disclosure	Protection of unborn child; desire to stay healthy and alive; instruction from counselors; previous PMTCT experience	No	Fair

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Enane et. al., 2018	Botswana	Assessment of critical missed opportunities for HIV care and barriers to care among adolescents hospitalized with HIV at Botswana's tertiary referral hospital	Assessment of barriers to HIV **care** among adolescents hospitalized with HIV at the country's tertiary referral hospital	**Adolescents** living with HIV (ALWHIV) [aged 10–19] hospitalized at Princess Marina Hospital (PMH) in Gaborone **and caregivers**	15 adolescents and caregivers	Qualitative (semi-structured interviews)	N/A	Nondisclosure to adolescents; isolation; mental health concerns; lack of awareness of perinatal HIV infection; illness or death of the mother; fear of HIV diagnosis; logistical problems at clinic; lack of disclosure to family members; lack of family support; stigma and fear of discrimination; mobility; lack of adherence support; poverty; lack of adolescent-	Adolescent disclosure; family disclosure and support; family supervision; mental health support	No	Good

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								centered services			
Enane et. al., 2020	Kenya	Investigation of barriers and facilitators to retention in care experienced by perinatally infected HIV+ adolescents in western Kenya	Investigation of barriers and facilitators to **retention** in care experienced by perinatally infected HIV+ adolescents in western Kenya	**Adolescents** living with HIV (ALWHIV) [aged 10–19] receiving care at Moi Teaching and Referral Hospital (MTRH) and MTRH AMPATH Centre and Rafiki Centre for Excellence in Adolescent Health, in	116 (102 adolescents and 28 caregivers)	Qualitative (key informant interviews and focus group discussions)	N/A	Stigma; poverty; trauma, conflict, or abuse; mental health challenges; fear of disclosures at school; financial difficulties	Good relationships with clinic staff; peer support interventions;	No	Good

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				Eldoret, **and caregivers**							
Farhoudi et. al., 2019	Iran	Exploration of the barriers to ART adherence among the HIV+ prisoners of Ghezelhesar Prison	Exploration of the barriers to **ART adherence** among the HIV+ prisoners of Ghezelhesar Prison	Male HIV+ prisoners not retained on ART at Ghezelhesar Prison **(other key population)**	6	Qualitative (focus group discussions)	N/A	Lack of trust in the effectiveness of ART; drug complications; inadequate nutrition; lack of amenities; social stigma; lack of economic and psychological support; lack of family support; ill treatment from prison	N/A	No	Fair

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								staff; inadequate methadone prescription for those with opium addiction; forgetfulness			
Ferguson et. al., 2002	United States	Examination of racial differences in patient-perceived barriers to ARV adherence and reported adherence	Examination of perceived barriers to ARV **adherence**	HIV+ patients receiving care at a university-based HIV outpatient clinic **(clinical cohort)**	149	Assessing association (cross-sectional interview)	N/A	Poor knowledge and attitudes about medicines; lack of social support; negative perception of qualities of medicine; scheduling problems; forgetting	N/A	No	Good

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Ferguson et. al., 2014	Kenya	Assessment of uptake of long-term HIV care and treatment services among women testing HIV+ in pregnancy-related services and exploration of barriers and facilitators to navigating these services	Exploration of barriers and facilitators of long-term HIV **care and treatment** services among women testing HIV+ in pregnancy-related services	**Pregnant women** newly diagnosed with HIV and receiving ANC care at Naivasha District Hospital, Rift Valley Province	19	Qualitative (semi-structured interviews)	N/A	Partner's negative attitude to HIV status; negative interactions with health workers; poor clinical services; financial obstacles	Social support; positive interactions with health workers	No	Fair
Franse et. al., 2017	Rwanda	Assessment of timely linkage-to-HIV-care in health facilities before and after the introduction of PITC in the OPDs	Assessment of reasons for **non-enrollment in** HIV **care** after the introduction of PITC in the OPDs of health facilities	Participants of a a cluster non-RCTof a PITC intervention in OPDs of 6 Rwandan health facilities who had not been enrolled into pre-ART care within 90 days	34	Descriptive (cross-sectional survey)	N/A	Non-acceptance of HIV status; stigma concerns; problems with healthcare services; not having time to go back to the clinic; feeling healthy; not seeing the utility of	N/A	No	Poor

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				(clinical cohort)				medicines; belief in faith-based healing			
Fuente-Soro et. al., 2019	Mozambique	Estimation of the linkage and long-term retention in care of PLHIV newly diagnosed during two cross-sectional community-based serosurveys and identifcation of factors interfering with engagement along the HIV-care continuum in southern	Identifcation of factors interfering with **engagement** along the HIV-care continuum in southern Mozambique	PLHIV newly diagnosed during either one of the two previous cross-sectional community-based serosurveys (2010 and 2012) in the Manhiça District, southern Mozambique **(general population)**	73	Qualitative (semi-structured interviews)	N/A	Competitive needs; alternative/traditional healers/ medicine; health system compliance; health system approaches to increase linkage and retention to care; HIV-care workflow; side effects of ARTs; ART stock outs	Value of health status; health literacy; social support; familiar/partner support; empowerment of PLHIV; health system compliance; health system approaches to increase linkage and retention to care; HIV-care workflow; self-perception	No	Good

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		Mozambique							of disease control through CD4 counts; wiliness to take ART; ART therapeutic options		
Genberg et. al., 2015	United States	Assessment of how barriers to ART adherence are related and their differential impact on adherence over time	Assessment of barriers to **ART adherence**	Participants of an RCT intervention recruited from academic, community, general medicine practice, and private infectious disease practice medical centers in the New England area	151	Psychometric (factor analysis)	N/A	Medication and health concerns; stigma; family responsibilities; problems with schedule and routine	N/A	Yes	Good

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				(clinical cohort)							
Geng et. al., 2016	Kenya, Uganda and Tanzania	Assessment of retention and patient reported barriers to care after newly initiating ART	Assessment of patient reported barriers to **care** after newly initiating ART	HIV+ patients no longer in care from 14 clinic sites in Kenya, Uganda and Tanzania that contribute data to the East Africa International Epidemiologic Databases to Evaluate AIDS (EA-IeDEA) consortium	78	Descriptive (cross-sectional survey)	N/A	Lack of transportation; work or child care responsibilities; feeling healthy; lack of food; alcohol consumption; inconvenient clinic logistics; being too sick; negative advise from family/others; medication side effects;	N/A	No	Good

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				(clinical cohort)				perceived ineffectiveness of medication; financial problems; poor relationship with providers; burden of taking drugs; alternative/traditional healing; family conflicts; fear of disclosure			
Ghalehkhani et. al., 2019	Iran	Assessment of the HIV treatment cascade of PLWH in Iran and the reasons for gaps in HIV services	Assessment of reasons for the gaps in HIV **services** and HIV **treatment** cascade of PLHIV	PLHIV reported to the national HIV surveillance till September 2014 **(general population)**	273	Mixed method (Cross-sectional survey part)	Mixed method (Qualitative focus group discussion part)	Poor self-care; shortage of supplies; competing priorities; poor access to health system; stigma; lack of competent counselors; transport problems; adverse drug reactions; negative	N/A	No	Fair

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								perception about the effects of ARTs; pill burden; mental health problems; conflicts with family members; fear of disclosure			
Go et. al., 2019	Indonesia, Ukraine and Vietnam	Description of environmental and population barriers to and facilitators of ART uptake and adherence among PWID	Description of environmental and population barriers to and facilitators of **ART** uptake and adherence among PWID	**PWID** who were participants of the HPTN 074 RCT at baseline and were randomized to the intervention arm (use of systems navigators and psychosocial counseling to access HIV care, treatment, and retention	37	Qualitative (semi-structured interviews)	N/A	Lack of clinic access; financial problems; fear of HIV infection and drug side effects; drug use and withdrawal symptoms; lack of social support; stigma	Internal motivation due to feeling sick; social support	No	Good

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Gokarn et. al., 2012	India	Assessment of the rate of ART adherence and factors that influence adherence	Assessment of factors that influence **ART adherence**	HIV+ patients who received care in the ART center of the out-patient department of a tertiary care hospital in Aurangabad **(clinical cohort)**	300	Descriptive (cross-sectional survey)	N/A	Traveling; being too busy; medication side effects;forgetting to take pills; feeling well; fear of disclosure; advised by a doctor to stop medications; lack of health improvement from medications; pill burden	N/A	No	Fair
Gold et. al., 2000	Australia	Identification of reasons for not taking ART among HIV infected people in Sydney and Melbourne	Identification of reasons for not taking **ART** among HIV infected people in Sydney and Melbourne	HIV+ mostly **gay or bisexual men** in Sydney or Melbourne not on ART	270	Psychometric (factor analysis)	N/A	Hostility to conventional medicines/preference for alternative medicines; resignation towards death; psychological stress of being on medication; following negative examples from other	N/A	No	Fair

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								people to not take medication; cost of medication; poor risk perception; waiting for development of better drugs; bad experiences with ARVs in the past; having lived with HIV for a long time			
Gold et. al., 2001	Australia	Identification of reasons for not taking ART among HIV infected people in Sydney and Melbourne	Identification of reasons for not taking **ART** among HIV infected people in Sydney and Melbourne	HIV+ **gay or bisexual men** in Sydney or Melbourne not on ART	20	Qualitative	N/A	Fear of side effects; fear of toxicity; the inconvenience of taking medication; fear of disrupting positive mental attitude; absence of symptoms	N/A	No	Fair

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Goudge et. al, 2011	South Africa	Exploration of the effect of food insecurity and lack of social cohesion on ART adherence	Exploration of the effect of food insecurity and lack of social cohesion on **ART adherence**	PLWHIV receiving care from local public sector clinics in Gauteng Province **(clinical cohort)**	22	Qualitative interviews	N/A	Food insecurity; poverty; gendered inequalities	N/A	No	Poor
Graney et. al., 2003	United States	Assessment of relationship between HIV medication regiment and adherence and factors that affect adherence	Assessment of factors that affect HIV medication **adherence**	HIV+ adults aged ≥18 from an inner city clinic **(clinical cohort)**	57	Descriptive (cross-sectional survey)	N/A	Lack of privacy; interference of social life; work/school interference; forgetting; fear; feeling well; perceiving clinic as reminder of disease	Social support; desire to live and avoid illness; deteriorating health; improving health; altruism; good relationship with provider	No	Poor

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Gugsa et. al., 2017	Malawi	Examination of pregnant women's experiences with ART adherence and retention in care during periods of pregnancy and lactation	Examination of factors affecting ART **adherence and retention** in care during periods of pregnancy and lactation	**Pregnant and lactating women** on ART receiving care at Bwaila District Hospital in Lilongwe	39	Qualitative (in-depth semi-structured interviews)	N/A	Lack of emotional and financial support from male partners; lack of sufficient counseling from providers at ART initiation; lack of strong support system; mobility; transport problems; alternative/faith-based healing; denial of illness; fear of taking drugs; negative advice from provider; drug side effects; forgetting to take drugs	Strong support systems; positive health outlook; positive effects of drugs; desire to be healthy; knowing or seeing other people on ART	No	Good

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Guise et. al., 2016	Kenya	Assessment of barriers and facilitators of accessing HIV care among PWID living with HIV	Assessment of barriers and facilitators of accessing HIV **care** among PWID living with HIV	**PWID** living with HIV in Nairobi, Malindi and Ukunda	44	Qualitative (in-depth interviews)	N/A	The hardship of addiction and the costs of care; silencing of HIV in the community; discrimination in the clinic	Supportive providers	No	Fair
Harper et. al., 2019	United States	Examination of barriers transgender and other gender-diverse youth (TGDY) face at each stage of the HIV continuum of care, as well as across socioecological systems	Examination of barriers transgender and other gender-diverse youth (TGDY) face at **each stage of the HIV continuum** of care	**Transgender** and other gender-diverse youth (TGDY) who were participants of the Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN)	66	Qualitative (in-depth interviews)	N/A	Societal oppression and discrimination; housing problems; laws and policies; poor access; distrust of medical system; financial problems; confidentiality and privacy issues; distant location of service; poor service delivery; lack of availability and awareness	N/A	No	Good

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								of services; difficulty navigating the system; negative provider interactions; lack of social support and social undermining; lack of instrumental support; fear of disclosure of HIV status			

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Harris et. al., 2011	Dominica n Republic	Determinati on of risk factors for non-adherence to ART among HIV infected individuals	Determinati on of barriers to **ART adherence** among HIV infected individuals	HIV+ adults aged ≥18 receiving care from 2 clinics in the (in Puerto Plata and Santo Domingo) **(clinical cohort)**	300	Descriptive (cross-sectional survey)	N/A	Forgetting; feeling too ill; being away from home; being too busy; fear of side effects; difficulty carrying out instructions; running out of medications ; feeling well; feeling depressed; falling asleep; perceiving medications as harmful; having a change in routine; pill burden; frequency of clinic visits; transportatio n problems; financial problems; conflicts with work; long waiting times at clinic; difficulty finding	N/A	No	Good

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								someone to care for children			
Hendrickson et. al., 2018	South Africa	Assessment of treatment outcomes and facilitators of long-term ART adherence and retention in care	Assessment of barriers and facilitators of long-term **ART adherence and retention**	HIV+ adults aged ≥18 receiving care at a large public-sector HIV clinic in Johannesburg, Gauteng Province **(clinical cohort)**	24	Qualitative	N/A	Stigma; medication side effects; travel; hospitalization; abuse; fear of disclosure; negative provider attitudes; long waiting times;	Supportive counseling; informal support groups; desire to need to support family;	No	Good

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Hendrickson et. al., 2019	South Africa	Exploration of barriers and facilitators around decision-making along the HIV care cascade	Exploration of barriers and facilitators around decision-making **along the HIV care cascade**	HIV+ adults aged ≥18 on ART for ≥ 10 years and receiving care at a large public-sector HIV clinic in Johannesburg **(clinical cohort)**	24	Qualitative (in-depth interviews)	N/A	Changing clinic conditions; fear of side-effects; stigma	Physical wellbeing and a desire to survive; responsibility for raising children; supportive clinic staff; having support networks; experiencing improvements in health on ART	No	Fair
Hendrickson et. al., 2019	Côte d'Ivoire	Examination of men's perceptions of ART and how ART mitigates HIV's threats to men's values	Examination of men's perception of benefits and challenges of **ART adherence**	HIV+ **men** aged between 25 and 49 from 3 urban sites across Côte d'Ivoire—Abidjan at Yopougon-Ouest-Songon, Bouaké, and San Pédro	28	Qualitative (in-depth interviews and focus group discussions)	N/A	Restriction of schedules; fear of medication side effects	Reduction of risk of HIV transmission; minimization of job and productivity loss; maintenance of men's roles as decision makers and providers; mitigation of HIV-related stigma	No	Good

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Hightow-Weidman et. al., 2017	United States	Assessment of barriers and facilitators to engagement in care, missed visits, ARV uptake, adherence and viral suppression among young black men who have sex with men (YBMSM)	Assessment of barriers and facilitators to engagement in **care**, missed visits, antiretroviral uptake, **adherence and viral suppression** among young black men who have sex with men (YBMSM)	HIV+ young black **men who have sex with men** (YBMSM) participating in the HMP trial	193	Descriptive (cross-sectional survey)	N/A	Inconvenient location or transportation; financial problems; ART adherence concerns; fear of side effects; not having found a doctor	N/A	No	Good
Hoffmann et. al., 2016	Brazil	Exploration of barriers affecting HIV-infected men at each stage of the care cascade in Salvador	Exploration of barriers affecting HIV-infected men at **each stage of the care cascade** in Salvador	HIV+ **men** receiving care at the State Reference Center in Salvador	25	Qualitative (semi-structured interviews)	N/A	Poor quality of care; long wait times; lack of reliable drug supply; fear of disclosure; difficulty accepting HIV infection; transportation difficulties; absenteeism at work or school; low perceived	N/A	No	Fair

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								risk of HIV; toxicity and complexity of ARV regimens			
Holtzman et. al., 2015	United States	Identification and comparison of barriers and facilitators to retention and adherence and evaluatuation of how these barriers and facilitators map to Andersen's Behavioral Model (ABM)	Identification and comparison of barriers and facilitators to **retention and adherence**	HIV+ adults aged ≥18 from 3 urban, Ryan White Program funded clinics in Philadelphia **(clinical cohort)**	51	Qualitative (semi-structured interviews)	N/A	Stigma; mental illness; substance abuse; housing problems; insurance problems; illness; competing life activities; poor provider relations; transportation problems; negative clinic experiences; appointment scheduling problems; pill burden; medication side effects; poor	Social support; reminder strategies; colocation of services; good provider relations; positive clinic experiences; flexible appointment scheduling; good pharmacy services; good health literacy	No	Good

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								pharmacy services; poor health literacy			
Inguane et. al., 2016	Mozambique	Assessment of enrolment and retention in HIV care among HIV+ adults in Central Mozambique and identification of barriers and facilitators	Identification of barriers and facilitators of **enrolment and retention** in HIV care among HIV+ adults in Central Mozambique	HIV+ adults and adolescents aged ≥18 in the catchment area of 8 health facilities in Sofala and Manica Provinces **(general population)**	42	Qualitative (in-depth interviews and focus group discussions)	N/A	Lack of symptoms; lack of respect by health workers; poor quality of care; financial and transport problems	Presence of symptoms; proximity to health facility;	No	Poor

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Intasan et. al., 2014	Thailand and Cambodia	Comparison of 3 different adherence monitoring tools in predicting virologic failure as part of the PREDICT RCT	Assessment of barriers to **taking medicines** among children in the PREDICT trial	HIV+ **children** aged 1–12 years (**and their caregivers**) participating in the in the PREDICT trial and on ART for ≥ 6 months	207	Assessing association or causation (prospective cohort)	N/A	Running out of drug supply because of delayed visits to clinic; child forgetting to take medicine; child refusing to take medicine	N/A	Yes	Fair
Iroezi et. al., 2013	Malawi	Assessment of barriers and facilitators to HIV care for pregnant and postpartum women	Assessment of barriers and facilitators to HIV **care** for pregnant and postpartum women	HIV+ **pregnant and postpartum women** receiving ANC or PNC at Nkhoma Hospital and 2 referring health clinics in Nkhoma, central Malawi	22	Qualitative (in-depth structured interviews)	N/A	Lack of transportation to clinic; stigma; food insecurity; negative provider attitudes	HIV prevention information; desire for infant to be healthy; nutrition resources	No	Poor

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Iroha et. al., 2010	Nigeria	Determination of ART adherence levels among pediatric patients at an outpatient clinic, the reasons for non-adherence, and the factors associated with adherence	Determination reasons for **non-adherence to AR**T among pediatric patients at an outpatient clinic	**Caregivers of children** who had been on HAART for at least 30 days and receiving care at the Pediatric Special Clinic at Lagos University Teaching Hospital (LUTH) in Lagos	212	Descriptive (cross-sectional survey)	N/A	Drug exhaustion at home; child sleeping through; caregiver being away; caregiver forgetting; child being away; child vomiting	N/A	No	Good
Janssen et. al., 2015	Gabon	Evaluation of treatment outcomes of HIV patients and identification of factors associated with LTFU and mortality	Identification of factors associated with **LTFU** among HIV patients	HIV+ patients receiving care at the at the HIV clinic in Lambaréné, Gabon (Centre de Traitement Ambulatoire, Lambaréné) **[clinic cohort]**	15	Qualitative (focus group discussions)	N/A	Adverse effects; long distance to the clinic; time constraints; financial problems; stigma; poor clinic logistics; negative attitudes of clinic staff	N/A	No	Poor

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Jeffrey Edwards et. al., 2019	Trinidad and Tobago	Evaluation of the implementation and outcomes of a patient tracing program	Evaluation of reasons for **LTFU** among HIV patients after implementation of a patient tracing program	HIV+ patients who were part of the Medical Research Foundation of Trinidad and Tobago (MRFTT) and were LTFU **(clinical cohort)**	589	Descriptive (cross-sectional survey)	N/A	Forgetting appointments; being too busy/working; fear of disclosure	N/A	No	Fair
Johnson et. al., 2009	United States	Assessment of group differences in self-reported reasons for not taking ART among diverse HIV patients	Assessment of reasons for not taking **ART** among diverse HIV patients	HIV+ patients in 4 US cities (San Francisco, Los Angeles, Milwaukee, and New York City) who were participants of a randomized behavioral prevention trial **(general population)**	399	Assessing association (cross-sectional interview)	N/A	Wanting to hide HIV status; having changed provider/clinic; waiting for CD4/viral load counts to worsen; not having been offered ART by provider; not receiving medical care; wanting to avoid side effects	N/A	No	Fair

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Joseph et. al., 2018	Nigeria	Determination of ART adherence levels among HIV infected pregnant women on a PMTCT program	Determination of factors that contribute to poor **ART adherence** among HIV infected pregnant women on a PMTCT program	HIV+ **pregnant women** receiving care at the PMTCT clinic of Federal Teaching Hospital, Abakaliki, Ebonyi State	268	Descriptive (cross-sectional survey)	N/A	Fear of disclosure; pregnancy related illness; forgetting; running out of pills; losing pills; pill burden; perception of harmful effects of medication on baby	N/A	No	Fair
Kagee et. al., 2012	South Africa	Identification of structural barriers that influenced ART adherence among HIV patients enrolled in the national ART program	Identification of structural barriers that influenced **ART adherenc**e among HIV patients enrolled in the national ART program	HIV+ patients enrolled in the national ART program and receiving care from a hospital in the Western Cape region **(clinical cohort)**	10	Qualitative (semi-structured interviews)	N/A	Having to take time away from work; food insecurity; transport expenses and long distance to clinic; long waiting times; negative experiences with providers; poor access to substance abuse treatment programs; stigma and discrimination	N/A	No	Fair

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Kalichman et. al., 2017	United States	Examination of the use of ART adherence strategies and barriers to adherence among non-adherent HIV patients	Examination of barriers to **ART adherence** among non-adherent HIV patients	Men and women living with HIV in Atlanta, Georgia **(general population)**	1,101	Descriptive (cross-sectional survey)	N/A	Forgetting; not having the right pills; being too busy; being confused; dealing with something unexpected; medication side effects; sleeping through dose time; feeling depressed and overwhelmed; fear of disclosure; running out of pills; inability to get to the pharmacy; inability to afford medications; being too drunk or high; drinking; using drugs	N/A	No	Fair

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Kamal et. al., 2018	Switzerland	Identification of factors associated with high or low ART adherence among HIV patients in an interprofessional medication adherence programme (IMAP)	Identification of factors associated with high or low **ART adherence** among HIV patients in an interprofessional medication adherence programme (IMAP)	HIV patients in an interprofessional medication adherence programme (IMAP) receiving care at the Community Pharmacy of the Department of ambulatory care & community medicine, University of Lausanne in collaboration with the infectious diseases service of the University Hospital **(clinical cohort)**	522	Qualitative (semi-structured interviews and computational text analysis)	N/A	Poor communication with providers; pill burden and medication side effects; irregular dose timing; disruptive schedule; psycho-social and economic problems; stigma; forgetting; co-morbidities; irregular use of Medication Electronic Monitoring System (EM); smoking	Positive reinforcements; regular dose timing; social support; experiencing a higher quality of life; better treatment management	No	Fair

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Karki et. al., 2016	India	Assessment of the problems faced by ART users in HIV care	Assessment of the reasons for **non-ART adherence** among patients in HIV care	HIV+ patients on ART receiving care at Sukraraj Tropical and Infectious Disease Control Hospital, Teku, and Bir Hospital **(clinical cohort)**	82	Descriptive (cross-sectional survey)	N/A	Forgetting to take medication; forgetting to collect medication; medication side effects; poor perception of the effectiveness of ART	N/A	No	Poor
Katirayi et. al., 2016	Malawi	Exploration of barriers and facilitators that affect a woman's decision to initiate and to adhere to Option B +	Exploration of barriers and facilitators that affect a woman's decision to initiate and to **adhere** to Option B +	**Pregnant and postpartum** HIV+ **women** enrolled in Option B + from Likuni Mission Hospital, Kabadula Community Hospital and Dedza and Mchinji District Hospitals	39	Qualitative (in-depth interviews and focus group discussions)	N/A	Being skeptical about life-long treatment	Perceiving drugs as health-enhancing; experiencing positive effects of drugs	No	Good

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Katz et. al., 2011	South Africa	Determination of rates of ART refusal in newly diagnosed HIV patients and the impact of ART refusal on initiation of care in Soweto	Determination of reasons for **ART** refusal in newly diagnosed HIV patients in Soweto	HIV+ adults aged ≥18 receiving care at the Zazi outpatient center of the Perinatal HIV Research Unit (PHRU) for HIV testing in Soweto **(clinical cohort)**	148	Descriptive (cross-sectional survey)	N/A	Feeling healthy; being unable to disclose HIV status; medication side effects; inability to adhere; cultural beliefs; stigma	N/A	No	Fair
Kayabu et. al., 2018	Tanzania	Determination of factors influencing effective linkage of newly diagnosed PLHIV into care	Determination of factors influencing effective **linkage** of newly diagnosed PLHIV into care	HIV patients aged ≥18 enrolled in care and treatment centers in 3 districts in Tanga Region **(clinical cohort)**	45	Qualitative (in-depth interviews and focus group discussions)	N/A	Stigma; falling sick; denial of HIV status; poor counseling	Being escorted to clinic	No	Fair
Kebaabetswe et. al., 2019	Botswana	Exploration of barriers to and facilitators of linkage to care and ART initiation	Exploration of barriers to and facilitators of **linkage** to care and **ART initiation**	HIV+ patients aged 18-64 participating in the Ya Tsie community randomized trial and randomized to	49	Qualitative (in-depth interviews and focus group discussions)	N/A	Stigma and discrimination; overcrowded clinics; negative staff attitudes; denial of HIV status; non-	Support from healthcare providers; social support; perceived benefits of ART	No	Good

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				intervention **(general population)**				disclosure of HIV status; gender dynamics; lack of social/family support; religious beliefs			
Kelly et. al., 2011	Papua New Guinea	Assessment of the relationship between HIV and ART, the extent of nutritional counselling for HIV patients, and food security in Papua New Guinea	Assessment of the reasons for **non-ART adherence** among HIV patients in Papua New Guinea	HIV patients aged ≥16 from 6 provinces in Papua New Guinea **(general population)**	374	Mixed method (Cross-sectional survey part)	Mixed method (Qualitative in-depth interview part)	Forgetting; being too busy; not having enough food; perceiving medication as a reminder of HIV status; medication side effects; fear of disclosure; financial problems; perceived lack of effectiveness of ART/pursuit of alternative healing; being too sick; having difficulty	N/A	No	Poor

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								swallowing medication; pill burden; being drunk			
Kelly et. al., 2019	Sierra Leone	Assessment of the reasons for being LTFU during pre-ART care among HIV patients in Freetown	Assessment of the reasons for being **LTFU** during pre-ART care among HIV patients in Freetown	HIV patients LTFU during their first 12-months of pre-ART care at the Connaught Hospital in Freetown **(clinical cohort)**	41	Qualitative (semi-structured interviews)	N/A	Financial constraints; being busy; negative provider attitudes; confidentiality concerns; poor treatment by providers; long clinic wait times; fear of disclosure; stigma	N/A	No	Fair

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Kemnitz et. al., 2017	United States	Identification of modifiable risk factors for poor engagement in HIV care and non-adherence to ART during the transition from prisons to communities	Identification of modifiable risk factors for poor engagement in HIV **care** and non-adherence to **ART** during the transition from prisons to communities	HIV+ adults aged ≥18 participating in the Wisconsin Transitions Study who received HIV care while residing in a Wisconsin state prison and intended to receive HIV care in the community upon release **(other key population)**	32	Qualitative (semi-structured interviews)	N/A	Stigma	Supportive relationships with care providers; professional case managers; supportive peers	No	Good
Kerr et. al., 2004	Canada	Identification of psychosocial determinants of HAART adherence among HIV-infected IDUs, and self-reported reasons for non-adherence to HAART	Identification of self-reported reasons for non-**adherence** to HAART among HIV-infected IDUs	HIV+ participants of the Vancouver Injection Drug Users' Study (VIDUS) who had **injected illicit drugs** at least once in the previous month and resided in the Greater	108	Descriptive (cross-sectional survey)	N/A	Forgetting; sleeping through doses; pill burden; being too busy; being away from home; privacy concerns; being too sick; dose-schedule conflicts; changes in routine; being too	N/A	No	Good

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				Vancouver Region				high; feeling depressed; avoiding medication side effects			
Kerr et. al., 2005	Canada	Identification of psychosocial determinants of HAART discontinuation among HIV-infected IDUs, and self-reported reasons for discontinuation of HAART	Identification of self-reported reasons for **discontinuation of HAART** among HIV-infected IDUs	HIV+ participants of the Vancouver Injection Drug Users' Study (VIDUS) who had **injected illicit drugs** at least once in the previous month and resided in the Greater Vancouver Region	160	Descriptive (cross-sectional survey)	N/A	Being fed-up with HAART; interactions with methadone; traveling; medication side effects; being in jail	N/A	No	Good

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Kesselring et. al., 2019	Canada	Examination of factors associated with delayed ART initiation in British Columbia (BC)	Examination of factors associated with delayed **ART initiation** in British Columbia (BC)	HIV+ BC residents aged ≥19 who were ART treatment-naïve and part of the Engage Study **(general population)**	87	Assessing association or causation (prospective cohort)	N/A	Fear of side effects; perceived financial cost; reluctance to rely on ART for life; perceiving ART as unnecessary to survive; alternative treatments; perception that ART would do more harm than good	N/A	Yes	Fair
Khawcharoenporn et. al., 2017	Thailand	Assessment of the feasibility of active targeted HTC and linkage to care among MSM	Assessment of barriers to **linkage** to care among MSM	**MSM** attending a gay saunas Pathumthani province who had tested HIV+ but not linked to care and successfully traced during follow-up	2	Descriptive (prospective cohort)	N/A	Financial problems; time constraints; inability to be absent from work; disclosure concerns	N/A	No	Poor

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Kiwanuka et. al., 2018	Uganda	Assessment of retention in care among women on Option B+ in Uganda	Assessment of barriers and facilitators of **retention** in care among women on Option B+ in Uganda	**Pregnant and breastfeeding women** who started Option B+ in Gomba district	12	Qualitative (in-depth interviews)	N/A	Medication side effects; not being ready for treatment; inadequate counseling; stigma; unsupportive partner	Adequate partner counseling and support; disclosure; desire to stay alive and raise uninfected children	No	Fair
Knight et. al., 2015	South Africa	Exploration of barriers and facilitators of linkage to and retention in care among HIIV patients who received HBCT in rural KwaZulu-Natal	Exploration of barriers and facilitators of **linkage to and retention** in care among HIV patients who received HBCT in rural KwaZulu-Natal	HIV+ patients who participated in a HBCT project which included interventions to facilitate linkages to HIV care in rural KwaZulu-Natal **(general population)**	25	Qualitative (semi-structured interviews)	N/A	Negative facility-based logistics; stigma	Supportive counseling; follow-up care; support of family and friends; same day POC CD4 testing and counseling	No	Fair

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Koole et. al., 2016	Tanzania, Uganda and Zambia	Identification of reasons HIV patients miss taking ART, the proportion who miss their ART because of symptoms, and the association between symptoms and poor ART adherence	Identification of reasons HIV patients miss taking **ART**	HIV+ adults aged ≥18 participating in a cross-sectional study from 18 clinic sites from different levels in the health system who had initiated ART at least 6 months prior to study **(clinical cohort)**	1,278	Descriptive (cross-sectional survey)	N/A	Forgetting; not having enough food; medication side effects; financial problems; transport problems; starting TB treatment; feeling well; being away from home; advised by doctor to stop ART; advised by traditional healer to stop ART; lack of availability of ART at pharmacy; perceiving ART as not helpful	N/A	No	Fair
Kuchinad et. al., 2016	United States	Exploration of barriers and facilitators of engagement and retention in care among PLHIV with	Exploration of barriers and facilitators of **engagement and retention** in care among PLHIV with	PLHIV engaged in HIV care in an urban HIV clinic who were recent **substance users**	34	Qualitative (semi-structured in-depth interviews)	N/A	Denial of HIV diagnosis; perceived inevitability of death from HIV; forgetting medications /appointmen	Illness/disease progression; development of a ritual associated with medication; positive relationship	No	Good

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		substance use	substance use					ts due to drug use; prioritizing drug use over HIV treatment; medication side effects	with provider		
Kumarasamy et. al., 2005	India	Examination of barriers and facilitators of ART adherence among HIV patients in Chennai	Examination of barriers and facilitators of **ART adherence** among HIV patients in Chennai	HIV+ patients receiving care at Y.R. Gaitonde Center for AIDS Research and Care (YRG CARE) in Chennai **(clinical cohort)**	60	Qualitative (in-depth interviews)	N/A	Cost of ART; stigma; lack of social support; non-disclosure of HIV status; lack of trust in the efficacy of ART; fear of side effects	Good social support systems; perceived benefits of ART; perceived negative consequences of nonadherence	No	Good
Kutnick et. al., 2017	United States	Assessment of patterns of linkage to HIV care and clinical outcomes among high-risk heterosexuals and assessment of barriers and facilitators	Assessment of barriers and facilitators of HIV **care engagement** among high-risk heterosexuals	Newly diagnosed HIV+ patients considered high-risk heterosexuals **(other key population)**	15	Qualitative (semi-structured in-depth interviews)	N/A	Denial of HIV diagnosis; stigma; fear of disclosure; transport problems; financial problems	Negative consequences of nonadherence; not wanting to infect others	No	Good

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		of HIV care engagement									
Lacombe-Duncan et. al., 2019	Canada	Assessment of the engagement of transgender women living with HIV (WLWH) in HIV care and the barriers and facilitators to HIV care cascade engagement	Assessment of the barriers and facilitators to HIV **care cascade engagement** among transgender women living with HIV (WLWH) in HIV care and the	**Transgender women** living with HIV (WLWH) participating in the Canadian HIV Women's Sexual and Reproductive Health Cohort Study (CHI-WOS)	50 (11 for qualitative)	Mixed method (Cross-sectional survey part)	Mixed method (Qualitative semi-structured interview part)	Rejection/disbelief; grief; self-blame/shame; negative perception of effects of medication; concerns about drug–drug interactions; changes to medication routine; medication fatigue; competing life circumstances; stigma; poor clinic logistics; financial problems; depression; geographical distance;	Increasing self-worth; psychosocial support; declining physical health; treatment advancements; perceived benefits of ART; good relationships with providers; good health education	No	Fair

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								medical and psychological logistics			
Layer et. al., 2014	Tanzania	Exploration of multi-level barriers and facilitators affecting entry into and engagement in the HIV care continuum in Iringa	Exploration of multi-level barriers and facilitators affecting **entry into and engagement** in the HIV care continuum in Iringa	HIV infected clients in facilities and communities in Iringa **(general population)**	165	Qualitative (in-depth interviews and focus group discussions)	N/A	Feeling healthy; separately located services; challenging clinic logistics; ineffective systems for CD4 testing; drug stock-outs; poor treatment by providers; spiritual healing; stigma	Perceiving HIV as a normal disease; support groups; use of home-based care providers	Yes	Good

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Lifson et. al., 2013	Ethiopia	Exploration of experiences with and barriers to attending clinic appointments among HIV patients	Exploration barriers to **attending clinic appointments** among HIV patients	HIV+ patients aged ≥18 receiving care at the Arba Minch Hospital HIV Clinic **(clinical cohort)**	21	Qualitative (focus group discussions)	N/A	Misunderstandings about ART; alternative healing methods; drug/alcohol use; long distance to clinic; negative experiences with providers; financial problems; medication side effects; stigma; competing domestic/work priorities; lack of food; lack of psychosocial support	N/A	No	Fair
Liu et. al., 2016	China	Ascertainment of the knowledge, beliefs, attitudes, and practices among HIV infected Chinese MSM	Ascertainment of the barriers and facilitators to **linkage and engagement** in care among HIV infected	**MSM** living with HIV affiliated with the Chaoyang Chinese AIDS Volunteer Group (CCAVG) in Beijing	40	Qualitative (focus group discussions)	N/A	Perceived discrimination from providers; fear of disclosure; lack of guidance or follow-up care; inconvenien	Referral and accompaniment by peers; support from HIV-positive MSM counselors; provision of free care;	No	Fair

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			Chinese MSM					t clinic time or location; treatment concerns; psychological burden of HIV care commitment	standardization of good HIV care; good health information regarding linking MSM to care		
Lubega et. al., 2010	Uganda	Exploration of reasons for drop-out from pre-ARV care among HIV patients in a resource-poor setting	Exploration of reasons for **drop-out** from pre-ARV care among HIV patients in a resource-poor setting	HIV+ patients who received care from government facilities in Iganga district **(clinical cohort)**	10	Qualitative (in-depth interviews)	N/A	Inadequate counseling; use of traditional/spiritual healers; gender inequalities; long waiting time at clinic; transportation costs	N/A	No	Fair
Lubega et. al., 2013	Uganda	Exploration of barriers or motivators to regular PMTCT attendance from a client perspective in eastern Uganda	Exploration of barriers or motivators to regular PMTCT **attendance** from a client perspective in eastern Uganda	PMTCT clients (**pregnant or post-partum HIV+ women**) receiving care in health centers in Iganga district in eastern Uganda	10	Qualitative (in-depth interviews)	N/A	Sex inequality; inadequate counseling; high transport costs; non-disclosure; fear of disclosure	N/A	No	Fair

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Mabunda et. al., 2019	South Africa	Identification of factors associated with ART adherence among HIV+ young adults	Identification of factors associated with **ART adherence** among HIV+ young adults	HIV+ young adults aged 18 to 35 and receiving ART from Letaba hospital HIV clinic **(other key population)**	281	Descriptive (cross-sectional survey)	N/A	Forgetting; feeling good; fear; running out of drugs	N/A	No	Fair
MacPherson et. al., 2012	Malawi	Assessment of barriers and facilitators to progression through the HIV care continuum	Assessment of barriers and facilitators to **progression through the HIV care continuum**	HIV+ patients aged ≥16 receiving care at Ndirande and Chilomoni Health Centres **(clinical cohort)**	30	Qualitative (semi-structured interviews)	N/A	Gender norms; lack of psychosocial support; infantilizing of patients; providers not prescribing treatment	Gender norms; psychosocial support	No	Good
Maixenchs et. al., 2015	Mozambique	Exploration of the effect of clinical symptoms on ART adherence factors, perceptions, and attitudes associated with ART adherence among HIV patients	Exploration of factors, perceptions, and attitudes associated with **ART adherence** among HIV patients	HIV+ patients aged ≥18 on ART for > 8 months, who were participants of the RITA study and receiving care at the Manhiça District Hospital (MDH)	51	Qualitative (in-depth interviews)	N/A	Post-ART symptoms; poor treatment from clinic staff	Psychosocial support; financial support; desire be able to look after children	No	Fair

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				(clinical cohort)							

Marcus et. al., 2015	Belgium, France, Republic of Ireland, the Netherlands, the United Kingdom, Denmark, Finland, Norway, Sweden, Austria, Switzerland, Germany, Luxemburg, Greece, Spain, Italy, Portugal, he Czech Republic, Hungary, Poland, Slovenia, Slovakia, Bulgaria, Cyprus, Malta, Romania, Bosnia and Herzegovina, Croatia, Macedonia, Serbia, Turkey, Estonia, Lithuania, Latvia, Belarus,	Assessment of ART coverage and reasons for never starting or stopping ART among HIV-infected MSM in 38 European countries	Assessment of reasons for never starting or stopping **ART** among HIV-infected MSM in 38 European countries	**MSM** participating in the European MSM Internet Survey (EMIS)	3,627	Psychometric (factor analysis)	N/A	Fear of consequences; perceived lack of need; ART inaccessibility	N/A	No	Fair

	Moldova, Russia, and Ukraine										

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Marhefka et. al., 2008	United States	Examination of the association between pediatric HIV medication adherence and regimen responsibility, adherence barriers, and strategies for remembering medications	Examination of pediatric HIV medication **adherence** and strategies for remembering medications	HIV-infected **children** aged 2-15 **and their caregivers** who were participants of the Perinatally Exposed Children (PACTS-HOPE) study	127 pairs	Assessing association (cross-sectional interview)	N/A	Forgetting; change in daily routine; not being able to obtain drugs; being busy; child refusing to take medication; fear of side effects; running out of medicine; lack of privacy	Pairing medication-taking with another activity; consistent schedule or routine; using cues such as pill boxes, calendars, beepers for reminders; child and caregiver taking medication at the same time; reminder from child or another person	No	Fair
Marson et. al., 2013	Kenya	Analysis of characteristics, reasons for transferring, and reasons for discontinuing care among patients LTFU from ATR care	Analysis of reasons for discontinuing care among patients **LTFU** from **ART care**	HIV+ patients aged ≥18 receiving care from the Coptic Hope Center for Infectious Diseases in Nairobi and LTFU **(clinical cohort)**	15	Descriptive (cross-sectional survey)	N/A	Having moved; not feeling the need to start ART; alternative/faith-based healing	N/A	No	Fair

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Maskew et. al., 2007	South Africa	Identification of causes of LTFU among HIV patients	Identification of causes of **LTFU** among HIV patients	HIV patients LTFU from Themba Lethu Clinic at Helen Joseph Hospital in Johannesburg **(clinical cohort)**	70	Descriptive (cross-sectional survey)	N/A	Financial difficulty; medication stopped by doctor; having moved; receiving private treatment; social problems; taking alternative/traditional medication; medication side effects	N/A	No	Poor
Maughan-Brown et. al., 2018	South Africa	Assessment of factors causing delays to ART initiation among HIV patients referred to HIV care clinics from a mobile health clinic in Cape Town	Assessment of factors causing delays to **ART initiation** among HIV patients referred to HIV care clinics from a mobile health clinic in Cape Town	HIV+ patients aged ≥18 referred for ART by a mobile health clinic in Cape Town and participating in the iLink Study **(general population)**	41	Qualitative (in-depth interviews)	N/A	Health service logistical challenges; difficulty navigating the clinic system; negative interactions with providers	N/A	No	Fair

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Maughan-Brown et. al., 2019	South Africa	Assessment of linkage to care and uptake of ART after ARTreferral by a mobile clinic in Cape Town	Assessment of barriers and facilitators of **linkage** to care and uptake of **ART** after ART-referral by a mobile clinic in Cape Town	HIV+ patients aged ≥18 referred for ART by a mobile health clinic in Cape Town and participating in the iLink Study **(general population)**	86 (41 for qualitative)	Mixed method (Cross-sectional survey part)	Mixed method (Qualitative in-depth interview part)	Not ever wanting to start ART; being unable to get time off work; not knowing where to go; not having money for transportation; confidentiality concerns; perceived poor treatment from clinic staff; fear of disclosure at clinic; being too ill to go to clinic; long wait lines at clinic; fear of ART side-effects; denial of HIV status; food insecurity	Good perception of positive ART effects; follow-up telephone counselling; having familial responsibilities; desire to maintain health to avoid disclosure	No	Fair

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Mayston et. al., 2016	India	Description of the pathways to care, examination of the influence of common mental disorder, hazardous alcohol use and cognitive impairment on the pathways, and exploration of the effect of other psychosocial factors on HIV patients' experience with HIV testing and care	Exploration of the effect of psychosocial factors on HIV patients' experience with HIV **care**	HIV+ patients receiving care at the Integrated Counselling and Testing Centre (ICTC) of the Goa Medical College (GMC) in Goa state **(clinical cohort)**	15	Qualitative interviews	N/A	Stigma; hopelessness	Psychosocial support; nutritional support; health insurance assistance; health education; desire to support and provide for family members; belief in efficacy of medication	No	Fair

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McAllister et. al., 2013	Australia	Assessment of the association between financial stress and ART adherence in a resource-rich setting	Assessment of the association between financial stress and **ART adherence** in a resource-rich setting	HIV+ patients attending the HIV, Immunology and Infectious Diseases Unit, St Vincent's Hospital in Sydney **(clinical cohort)**	335	Assessing association (cross-sectional interview)	N/A	Medication costs; transport costs;	N/A	No	Poor
McGrath et. al., 2012	Uganda	Examination of women's experiences in accessing HIV care in order to identify avenues to improve access to care	Examination of barriers and facilitators of accessing HIV **care** among HIV infected women	HIV+ women aged ≥18 receiving care at the Joint Clinical Research Centre (JCRC) in Kampala **(other key population)**	52	Descriptive (cross-sectional survey)	N/A	N/A	Occurrence of symptoms; advice from health care provider, parent or partner	No	Poor

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McLean et. al., 2017	Malawi, Tanzania and Uganda	Exploration of the factors that influence acceptance and adherence to Option B+, and the role of pregnancy	Exploration of the factors that influence acceptance and **adherence** to Option B+	HIV+ **pregnant women** enrolled in the Bottlenecks Study undertaken health and demographic surveillance sites (HDSS)	22	Qualitative (in-depth interviews)	N/A	Negative interactions with clinic staff; lack of support from partner	Feeling ready; previous knowledge of HIV-positive status; positive interactions with clinic staff; supportive relationship with partners; desire to protect unborn infant; desire to stay alive to support child; desire to protect HIV-negative partner	No	Good

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McMahon et. al., 2015	Australia	Determination of retention and loss to follow up in HIV care and subsequent reasons among HIV patients in the state of Victoria	Determination of reasons for interruptions in HIV **care** among HIV patients in the state of Victoria	HIV+ patients receiving care from the 6 main HIV clinical care sites in the state of Victoria **(clinical cohort)**	29	Descriptive (cross-sectional survey)	N/A	Feeling well; being too busy; having difficulty attending clinic (because of transport or clinic logistical issues); financial problems; psychosocial stress; having difficulty accepting HIV diagnosis; having apathy and lowered mood; wanting a break from care; traveling overseas; being incarcerated; negative experiences at clinic; running out of drugs; not believing in	N/A	No	Fair

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								conventional treatments; having needle phobia			

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Mesic et. al., 2019	Zambia	Assessment of barriers and facilitators of engagement in the HIV continuum of care among adolescents living with HIV/ AIDS (ALHA)	Assessment of barriers and facilitators of **engagement in the HIV continuum of care** among adolescents living with HIV/ AIDS (ALHA)	**Adolescents** living with HIV/ AIDS (ALHA) [aged 16-19] receiving care from 6 HIV clinics across 3 districts in Zambia	373 (43 for qualitative and 330 for quantitative part)	Mixed method (Cross-sectional multivariable part)	Mixed method (Qualitative focus group discussions and in-depth interviews part)	Adolescent responsibilities (school, social activities, chores and work); poverty; poor nutrition; stigma; fear of disclosure; disrespectful treatment by providers; poor clinical services or lack of providers; lack of adolescent specific services at clinic, schools or communities; lack of clinic resources; lack of collaboration among organizations; poor clinic logistics; medication	Having good knowledge about ART; being motivated; having accepted HIV status; believing in the efficacy of ART; positive interactions with health providers; home visits; text message/phone reminders; improved quality of care at clinic	No	Fair

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								side effects; not believing in the efficacy of ART; lack of psychosocial support from family, friends and teachers; social norms; feeling well; lack of transportation; forgetting; family commitments			
Miller et. al., 2010	South Africa	Assessment of reasons why HIV patients default ART care	Assessment of reasons why HIV patients default **ART care**	HIV+ patients receiving care at 2 treatment centers in Limpopo and Gauteng provinces who had defaulted or transferred from care	28	Qualitative interviews	N/A	Transport costs; being unable to take time off work to go to clinic; inconvenient clinic logistics; stigma; medication side effects; use of alternative/t	N/A	No	Fair

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				(clinical cohort)				raditional medications			
Mimiaga et. al., 2010	Ukraine	Exploration of barriers and facilitators to HAART adherence among Ukrainian injection drug users (IDUs)	Exploration of barriers and facilitators to **HAART adherence** among Ukrainian injection drug users (IDUs)	HIV+ injection drug users **(IDUs)** aged ≥18, residing in Kiev, attending treatment at the Kiev City AIDS Center and opioid-dependent	16	Qualitative (semi-structured focus group discussions)	N/A	Harassment and discrimination by police; opioid dependence; complexity of drug regimen; medication side effects; forgetting; having co-occurring mental health problems; HIV stigma	Having cues for taking pills; support and reminders from family, significant other, and friends; opioid substitution therapy; wanting improved health	No	Good

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Moriarty et. al., 2017	Ghana	Examination of the role of medication stock-outs in contributing to treatment interruption and the effect on medication adherence	Examination of the role of medication stock-outs and other factors in contributing to **treatment** interruption	HIV+ adults receiving care from the adult HIV clinic and antenatal clinics at the Komfo Anokye Teaching Hospital (KATH) in Kumasi **(clinical cohort)**	57	Qualitative (semi-structured interviews)	N/A	Stock-outs; work or financial difficulties; medication side effects	N/A	No	Good
Mshana et. al., 2006	Tanzania	Identification and mitigation of barriers to seeking ART between HIV testing enrolling in the new government ART program	Exploration of perceptions and experiences of barriers to accessing **ART** in the new government ART program	HIV+ residents of Kisesa ward **(general population)**	12	Qualitative (focus group discussions and in-depth interviews)	N/A	Financial constraints; poor treatment at health facility; difficulties in sustaining long-term treatment; stigma concerns	N/A	No	Fair
Mtetwa et. al., 2013	ZImbabwe	Exploration of reasons for non-retention in care among HIV-infected sex workers	Exploration of reasons for **non-retention** in care among HIV-infected sex workers	HIV+ **sex workers** who were part of the Sisters with a Voice (SWV) program	38	Qualitative (focus group discussions)	N/A	Poor treatment by health workers; stigma; competing time commitments; transport and	N/A	No	Fair

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								treatment costs			
Mueller et. al., 2018	Germany	Adaptation and validation of the Adherence Barriers Questionnaire (ABQ) to the specific needs of HIV patients	Adaptation and validation of the **Adherence** Barriers Questionnaire (ABQ) to the specific needs of HIV patients	HIV+ patients aged ≥18 on ART for at least a year in Southwest Germany **(general population)**	370	Psychometric (factor analysis)	N/A	Unintentional adherence barriers (financial problems, lack of privacy, forgetting, difficulty taking medication, traveling, fear of side effects); disease/treatment knowledge (good medication literacy, good relationship with provider, regular medication schedule); intentional adherence barriers (perceiving medication as	N/A	No	Fair

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								poisonous, feeling healthy, avoidance of side effects)			
Mukumbang et. al., 2017	Zambia	Conceptualization of the factors affecting retention in care of HIV patients on ART using the ecological framework	Conceptualization of the factors affecting **retention** in care of HIV patients on **ART**	HIV+ patients on ART from 3 clinics in Kabwe district **(clinical cohort)**	45	Qualitative (in-depth semi-structured interviews)	N/A	Medication side effects; gaining weight (as a sign of good health); belief in alternative/faith healing; use of herbal remedies; alcohol use; stigma; fear of disclosure; long waiting times; long travel distances; high transportatio	N/A	No	Good

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								n costs; medication stock outs; staff shortages; food shortages; traveling			
Murphy et. al., 2003	United States	Investigation of barriers to HAART adherence among HIV–infected adolescents and corresponding association with non-adherence	Investigation of barriers to **HAART adherence** among HIV–infected adolescents	HIV-infected **adolescents** aged 12-19 who were part of the Reaching for Excellence in Adolescent Care and Health (REACH) study	114	Psychometric (factor analysis)	N/A	Medication-related adverse effects (both physical and psychological); complications in day-to-day routines	N/A	No	Fair

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Musa et. al., 2019	Nigeria	Exploration of factors that facilitate retention in care of children with HIV from the caregivers' perspective	Exploration of factors that facilitate **retention** in care of children with HIV from the caregivers' perspective	**Caregivers** of HIV-infected **children** receiving care at the paediatric HIV clinic of ABUTH in Zaria	38	Qualitative (in-depth interviews)	N/A	N/A	Good financial resources; high education level; residing close to the clinic; reliable psychosocial support from family; HIV status disclosure; having a parent/ grandparent as caregiver; community support; positive clinic staff attitude; good quality of healthcare; having a peer support group	No	Good

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Musumari et. al., 2013	Democratic Republic of Congo	Exploration of barriers and facilitators of ART adherence among HIV patients	Exploration of barriers and facilitators of **ART adherence** among HIV patients	HIV+ participants receiving care at the Centre Hospitalier Monkole (CHM) and the NGO Actions Communautaires Sida/Avenir Meilleur pour les Orphelins (ACS/Amo-Congo) in Kinshasa **(clinical cohort)**	38	Qualitative (in-depth semi-structured interviews)	N/A	Food insecurity; financial constraints; forgetfulness; fear of disclosure/stigma; religious beliefs; medication side effects; alcohol consumption; travel/migration; feeling hopeless; traditional medicines	Religious beliefs	No	Good
Mutwa et. al., 2013	Rwanda	Assessment of barriers and successes in ART adherence among adolescents	Assessment of barriers and successes in **ART adherence** among adolescents	HIV infected **adolescents** aged 12–21 receiving care at the HIV outpatient clinic of the Center for Treatment and Research on AIDS, Tuberculosis and Malaria (TRACplus)	42 adolescents and 10 caregivers	Qualitative (focus group discussions and in-depth interviews)	N/A	Stigma; non-disclosure of HIV status; lack of psychosocial support; lack of privacy; desire to be normal; medication side effects; non-acceptance of HIV status;	Belief in the efficacy of ART; disclosure of HIV status; psychosocial support	No	Fair

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				and their **caregivers**				difficulty obtaining medication refills; pill burden; insufficient nutritional support			
Mwamba et. al., 2018	Zambia	Assessment of how Zambian health system tangible components and work practices and behavior influence the decisions of HIV patients lost to care to disengage from care	Assessment of how Zambian health system factors influence the decisions of HIV patients lost to care to **disengage from care**	HIV patients receiving care from 12 clinics, selected from 4 provinces **(clinical cohort)**	55	Qualitative (in-depth interviews)	N/A	Long distance to clinic; poor clinic logistics; privacy concerns; chronic understaffing; drug rationing and inflexibility in visit schedules; alternative treatment; negative attitude of clinic staff	N/A	No	Good

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Nabaggala et. al., 2018	Uganda	Assessment of the effect of tracking PLHIV after missed clinic visits and of factors associated with them returning to care	Assessment of the factors associated with PLHIV **returning to care** after missed clinic visits	PLHIV receiving HIV care at Moroto Regional Referral Hospital (RRH) who had missed a scheduled visit **(clinical cohort)**	381	Assessing association or causation (retrospective cohort)	N/A	Forgetting; having adequate drug supplies; long distance to clinic; traveling; having a tight work schedules; stigma; medication side effects; lack of food	N/A	Yes	Fair
Nabukeera-Barungi et. al., 2015	Uganda	Description of ART-adherence levels and factors associated with retention among HIV-infected adolescents in Uganda	Exploration of barriers and facilitators of ART-**adherence and retention** in care among HIV-infected adolescents in Uganda	HIV-infecte **adolescents** from all 10 districts in Uganda and their **caregivers**	227 adolescents and 46 caregivers	Qualitative (focus group discussions and in-depth interviews)	N/A	Stigma; laxity; poverty; medication side effects; disclosure challenges; poor self-image and identity; pill burden; depression; fatigue; myths and misconceptions about ARVs	Peer support groups; counseling; supportive health care workers; conducive scheduling (during school holidays); food support; short waiting time; transportation assistance; phone/sms follow-up	No	Fair

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Nakanwagi et. al., 2016	Uganda	Exploration of the barriers and facilitators of linkage to HIV care among FSWs	Exploration of the barriers and facilitators of **linkage** to HIV care among FSWs	**FSWs** receiving HIV care from Reach Out Mbuya HIV/AIDS Initiative (ROM), a community-based organization in peri-urban Uganda	28	Qualitative (in-depth interviews)	N/A	Negative attitude of health workers; rigid treatment policies; perceived stigma; lack of HIV education; denial; fear of disclosure; fear and myths about ART; lack of time to attend clinic; financial constraints; work-related factors	Perceived good quality of health services; community peer support systems; need to remain healthy; having alternative sources of income; observing experiences of other HIV-infected people	No	Good
Napúa et. al., 2016	Mozambique	Formative research to inform the design of a pilot facility-level intervention to improve retention and ART adherence in the context B+ among	Assessment of barriers and facilitators of **retention and ART adherence** in the context B+ among HIV+ pregnant women	HIV+ **pregnant women** receiving care at 6 high-volume health centers providing PMTCT and ART services in the	51	Qualitative (focus group discussions)	N/A	Long wait times; short consultations; poor counseling; stigma; being unready to accept HIV status and begin treatment	N/A	No	Poor

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		HIV+ pregnant women		Mozambican National Health System							
Ngarina et. al., 2013	Tanzania	Exploration of perceived barriers to ART adherence post-delivery and after the cessation of breastfeeding among post-partum women	Exploration of perceived barriers to **ART adherence** post-delivery and after the cessation of breastfeeding among post-partum women	HIV+ **postpartum women** with detectable viral load and receiving care at the Mitra Plus clinic of the Muhimbili National Hospital compound in Dar es Salaam	23	Qualitative (semi-structured interviews)	N/A	Lack of motivation after protecting child from perinatal infection; feeling well; feeling of hopelessness; being busy; forgetting; overwhelming demands of everyday life; poverty; lack of empowerment; fear of disclosure	N/A	No	Good

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Njie-Carr et. al., 2016	United States	Exploration of barriers and facilitators of engagement in HIV care among PLHIV	Exploration of barriers and facilitators of **engagement in HIV care** among PLHIV	HIV+ patients aged ≥18 receiving care at a large urban metropolitan clinic in Baltimore **(clinical cohort)**	14	Qualitative (focus group discussions and in-depth interviews)	N/A	Mental and physical illness; interruption in routine activities; drug and alcohol problems	A desire to live and stay well; positive influence from support systems; supportive clinic and staff; system reminders to stay in care; a desire and need to help others	No	Good
Nkosi et. al., 2016	South Africa	Exploration of linkages between notions of masculinity, alcohol consumption, and ART adherence among HIV+ men	Exploration of linkages between notions of masculinity, alcohol consumption, and **ART adherence** among HIV+ men	HIV+ **men** aged ≥18 on ART for at ≥3 months, who had consumed alcohol in the past 3 months and receiving care at at 5 PEPFAR ART clinics in Tshwane (Pretoria)	27	Qualitative (focus group discussions)	N/A	Normative notions of masculinity in the men's social circles; fears of alcohol-ART interactions; negative healthcare provider-patient power dynamics	Normative notions of masculinity in the men's social circles	No	Good

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Ntela et. al., 2018	Democratic Republic of Congo	Assessment of the influence of local media, religion and cultural beliefs on ART adherence among PLHIV	Assessment of the influence of local media, religion and cultural beliefs on **ART adherence** among PLHIV	HIV+ patients aged ≥18 receiving ART from 2 rural hospitals in the central Kongo Province **(clinical cohort)**	50	Qualitative (semi-directional individual interviews)	N/A	Disagreement between media messages and those provided by healthcare providers; negative advice from religious leaders; belief in traditional/alternative healing	Positive advice from religious leaders	No	Fair
Nyaku et. al., 2019	United States	Examination of the prevalence, non-persistence to ART medication among patients in HIV care, the association between non-persistence and sustained HIV-viral suppression, and the reasons for non-persistence	Examination of the reasons for non-persistence to **ART** medication among patients in HIV care	HIV+ patients aged ≥18 non-persistent to ART and recorded in the Medical Monitoring Project (MMP), a nationally representative HIV surveillance system **(general population)**	1,446	Descriptive (cross-sectional survey)	N/A	Medication side effects; treatment fatigue; other drug or alcohol use; traveling; feeling good; being depressed and having other mental health problems; lack of access to medication	N/A	No	Good

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Nyato et. al., 2019	Tanzania	Exploration of the factors affecting linkage to HIV care among FSWs	Exploration of the factors affecting **linkage** to HIV care among FSWs	**FSWs** receiving HIV testing through the Sauti Project in 4 regions of Tanzania	21	Qualitative (participatory group discussions)	N/A	Unfriendly service delivery environment; confidentiality concerns; negative attitudes of health providers; myths and misconceptions about ART; stigma; fear of losing clients or partners; low perceived risk	Transportation assistance to clinic; friendly health care providers; peer-support networks	No	Good
O'Brien et. al., 2003	United States	Description of factors associated with HAART discontinuation in an urban, outpatient cohort of HIV patients	Description of factors associated with **HAART discontinuation** in an urban, outpatient cohort of HIV patients	HIV+ patients receiving HAART at the HIV Outpatient Clinic (HOP) of the Medical Center of Louisiana, in New Orleans who had discontinued their initial	211	Assessing association or causation (retrospective cohort)	N/A	Treatment failure; adverse event; medication side effects; incarceration; hospitalization; substance abuse	N/A	Yes	Good

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				HAART regimen **(clinical cohort)**							
O'Connor et. al., 2011	South Africa	Assessment of the rate and reasons for LTFU among stable HIV patients on ART in a down-referral model of care	Assessment of reasons for **LTFU** among stable HIV patients on ART in a down-referral model of care	HIV+ patients down-referred to designated primary health care (PHC) facilities in a decentralized care model in Johannesburg **(clinical cohort)**	15	Descriptive (retrospective cohort)	N/A	Fear of disclosure to employer; not wanting to take time off work; having relocated; having personal problems; logistical challenges accessing care in the primary health care facilities	N/A	No	Poor

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O'Laughlin et. al., 2018	Uganda	Investigation of experiences of refugees accessing and taking ART while living in a post-conflict settlement and assessment of the barriers and facilitators to ART adherence	Assesment of the barriers and facilitators to **ART adherence** among refugees while living in a post-conflict settlement and assessment of the	HIV+ adult refugees residing at the Nakivale Refugee Settlement, in rural southwest Uganda and receiving care at the HIV clinic at Nakivale Health Center **(other key population)**	61	Qualitative (semi-structured interviews)	N/A	Difficulty accessing clinic when ill; food insecurity; drug stockouts; violence and unrest in the settlement	Seeking care before being too ill; using medication reminders; carrying ART at all times; register an alternative person to pick up ART	No	Fair
Odili et. al., 2017	Nigeria	Investigation of the level of ART adherence and factors affecting adherence among HIV patients	Investigation of factors affecting **ART adherence** among HIV patients	HIV+ adult patients receiving care at the Antiretroviral Clinic of Central Hospital, Agbor, Delta State **(clinical cohort)**	300	Descriptive (cross-sectional survey)	N/A	Forgetting; being busy; fear of disclosure; medication side effects; pill burden; comorbidities; medication stock outs at clinic	N/A	No	Poor

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Oku et. al., 2014	Nigeria	Determination of the prevalence of HAART adherence and factors associated with adherence among PLHIV in a rural setting	Determination of the factors associated with **HAART adherence** among PLHIV in a rural setting	HIV+ patients aged ≥18 on HAART for at least 3 months and receiving care at the General Hospital (GH), Ugep, Yakuur Local Government area (LGA), Cross River State **(clinical cohort)**	393	Descriptive (cross-sectional survey)	N/A	Being busy; forgetting; religious constraints such as fasting; traveling; being depressed; lack of food; feeling unwell; fear of side effects; disclosure concerns; inconvenient timing	N/A	No	Fair
Oluoch et. al., 2019	Kenya	Exploration of community members' and PLHIV's experiences and perceptions regarding uptake of HIV care in the ART clinics in a large informal settlement in Nairobi	Exploration of PLHIV's experiences and perceptions regarding uptake of HIV **care** in the ART clinics in a large informal settlement in Nairobi	PLWHIV aged ≥18 residing in Kibera informal settlement in Nairobi **(general population)**	46	Qualitative (focus group discussions)	N/A	Negative attitude of health workers	Availability of many health facilities	No	Poor

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Parantha man et. al., 2009	India	Assessment of ART adherence behavior and the factors that affect adherence in children	Assessment of the factors that affect **ART adherence** in children	**Caregivers** of children under 12 living with HIV who were responsible for administering ART to the child (or children) and receiving care at a non-profit medical care and research institution in Chennai	14	Qualitative (semi-structured interviews)	N/A	Medication related factors such as side effects; child's unwillingness to take medication; non-disclosure to child; unsupportive family members; stigma and confidentiality concerns; mistrust in the quality of health care; financial problems	Child's willingness to take medication; supportive family members; access to free medication; child-friendly formulations; adherence counselling	No	Fair
Parsons et. al., 2015	Zambia	Exploration of experiences of persons living with disabilities (PWD) and HIV	Exploration of barriers to **care** of persons living with disabilities (PWD) and HIV	persons living with disabilities (PWD) and HIV who were part of the Sepo Study in Lusaka **(other key population)**	21	Qualitative (semi-structured interviews)	N/A	Stigma	N/A	No	Good

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Patel et. al., 2016	Kenya	Identification of barriers and facilitators of ART initiation and adherence among HIV infected individuals in discordant relationships	Identification of barriers and facilitators of **ART** initiation and adherence among HIV infected individuals in discordant relationships	HIV infected individuals in discordant relationships who were part of the Partners Demonstration Project **(other key population)**	33	Qualitative (in-depth interviews)	N/A	Denial of diagnosis; stigma; disclosure concerns; perceived medication side-effects; challenges in obtaining refills; lack of information and counseling	Desire to love a longer and healthier life; desire to prevent HIV transmission to others; desire to appear normal/healthy and avoid disclosure	No	Fair
Pecoraro et. al., 2014	Russia	Identification of barriers and facilitators of retention in care among HIV patients	Identification of barriers and facilitators of **retention** in care among HIV patients	HIV patients receiving care at the Leningrad Regional AIDS Center and Botkin Hospital for Infectious Diseases **(clinical cohort)**	45	Qualitative (focus group discussions)	N/A	Stigma/discrimination; negative experiences with providers; difficulty accessing treatment; time constraints (being too busy/ employed/ caring for dependents); inaccurate beliefs about the efficacy of ART; medication side-effects;	Desire to live; social support; spirituality; having a healthy/drug-free lifestyle; having effective organizational strategies such as reminders to take ART; positive thinking and experiences with ART; positive experiences with	No	Poor

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								substance use; depression	healthcare providers		
Pell et. al., 2018	Eswatini	Examination of reasons why some newly diagnosed HIV+ clients delay ART initiation	Examination of reasons why some newly diagnosed HIV+ clients delay **ART initiation**	PLHIV who were part of the MaxART study and received care at one of the 8 participating health facilities in Hhohho Region and who delayed ART initiation for ≥90 days **(clinical cohort)**	13	Qualitative (semi-structured interviews)	N/A	Needing time to accept HIV status; feeling healthy; concerns about medication side effects; disclosure concerns	N/A	No	Fair

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Philip et. al., 2019	India	Description of the factors impeding PWID's ability to access ART care	Description of the factors impeding PWID's ability to access **ART care**	**PWID** aged ≥18 who were part of a longitudinal study and recruited from 5 drop-in centers in Delhi	31	Qualitative (in-depth semi-structured interviews)	N/A	Denial of HIV status; fatalistic attitude; depression; hopelessness; being under the influence of drugs; competing demands such as working to earn money for livelihood or drugs; transportation difficulties; logistical challenges at health facilities	Using social networks; using drug peddlers as peer educators; provision of care through mobile health units	No	Fair
Pierre et. al., 2017	Haiti	Assessment of enablers of survival with AIDS among PLHIV	Assessment of enablers of **ART adherence** among PLHIV	PLHIV who survived ≥10 years on ART through and receiving care at Haitian Study Group on Kaposi's Sarcoma and Opportunisti	25	Qualitative (semi-structured interviews)	N/A	N/A	Having a strong spiritual foundation; supportive family; positive interactions with providers; developing a routine for taking medications	No	Good

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				c Infections (GHESKIO) clinics **(clinical cohort)**							
Rachlis et. al., 2013	Malawi	Identification of factors that influence patient LTFU among PLHIV and factors that impede successful tracing efforts	Identification of factors that influence patient **LTFU** among PLHIV	HIV patients who had become LTFU from Zomba Central Hospital or any of the 3 decentralized rural clinics in Zomba district while on ART **(clinical cohort)**	41	Qualitative (concept mapping)	N/A	Stigma and fears; beliefs; acceptance and knowledge of ART; access to ART; poor documentation; social and financial support issues; health worker attitudes	N/A	No	Good

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Rangarajan et. al., 2014	Vietnam	Assessment of barriers to care among PLHIV and their association with late HIV testing and delays in entry into HIV care	Assessment of barriers to **care** among PLHIV	HIV+ patients aged ≥18 receiving care at an urban outpatient clinic (OPC) in Ho Chi Minh City (HCMC) and 2 rural OPCs located in Can Tho and An Giang provinces who were not currently taking ART and were late presenters to care **(clinical cohort)**	196	Assessing association (cross-sectional interview)	N/A	Feeling healthy; stigma concerns; time conflicts with work or school; confidentiality concerns; fear of medication side effects; financial concerns; not wanting to take medications; not knowing where to get care; long distance to clinic; clinic logistical problems; detention or imprisonment; fear of detention or imprisonment; poor perception of service quality at clinic	N/A	No	Fair

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Reback et. al., 2003	United States	Assessment of HIV medication adherence among gay and bisexual methamphetamine-abusing men	Assessment of barriers to HIV medication **adherence** among gay and bisexual methamphetamine-abusing men	Gay and bisexual methamphetamine-abusing men enrolled in a treatment research program for methamphetamine use in Hollywood, California **(other key population)**	23	Qualitative (semi-structured interviews)	N/A	The combination of methamphetamine use and sexual activities; methamphetamine-related disruptions in food and sleep schedules; avoiding potentially harmful effects of combining methamphetamine and HIV medications	N/A	No	Poor
Roura et. al., 2009	Tanzania	Assessment of factors affecting sustained attendance at ART clinics among HIV patients	Assessment of factors affecting sustained **attendance at ART clinics** among HIV patients	PLHIV in Kisesa participating in a community-based cohort study monitoring Tanzania's ART roll-out **(general population)**	42	Qualitative (semi-structured interviews)	N/A	Alternative/ faith healing; lack of trust in efficacy of ART; negative advice from social networks; lack of psychosocial support; financial problems; long	Personal willingness; perceived capacity; positive advice from social networks; psychosocial support; financial support; home-based care; access to health information	No	Fair

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								distance to clinic			
Rudy et. al., 2009	United States	Determination of the prevalence of barriers to ART adherence and how the barriers relate to each other in adolescents	Determination of the barriers to **ART adherence** in adolescents	HIV+ **adolescents and youth** aged 12 to 24 participating in the Adolescent Trials Network for HIV/AIDS Interventions (ATN) or the Pediatric AIDS Clinical Trials Group (PACTG)	396	Descriptive (cross-sectional survey)	N/A	Not having a place to sleep; medical insurance problems; lack of transportation to get medications; lack of transportation to clinic; problems getting medications filled; job or school-related problems; family or child care problems	N/A	No	Good

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Sabin et. al., 2008	China	Assessment of barriers to ART adherence among HIV-infected patients, particularly among IDUs	Assessment of barriers to **ART adherence** among HIV-infected patients who were mostly IDUs	HIV patients at Dali Second People's Hospital (DSPH) in Old Dali, Yunnan province, who were mostly former **IDUs**	36	Qualitative (focus group discussions and in-depth interviews)	N/A	Stigma; mental health issues; financial concerns; forgetting; pill burden and medication scheduling issues; medication side effects; drug or alcohol abuse	N/A	No	Fair
Safren et. al., 2005	India	Examination of the pattern and frequency of ART adherence among HIV patients using clinic chart data and reasons for non-adherence	Examination of reasons for **non-adherence to ART** among HIV patients using clinic chart data	HIV patients with available chart data receiving HIV treatment at Y.R. Gaitonde Center for AIDS Research and Care (YRG CARE) in Chennai **(clinical cohort)**	75	Descriptive (retrospective cohort)	N/A	Cost; inability to return to clinic for a refill; medication side effects; working; having improved health; having personal problems at home; traveling; being depressed; alcohol problems	N/A	No	Poor

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Saleem et. al., 2014	Uganda	Assessment of barriers and facilitators to linkage to long-term HIV care among HIV+ pregnant women diagnosed during ANC	Assessment of barriers and facilitators to **linkage** to long-term HIV care among HIV+ pregnant women diagnosed during ANC	HIV+ **pregnant women** diagnosed during ANC at 11 health facilities in the Eastern region of Uganda	48	Descriptive (retrospective cohort)	N/A	Denial of HIV status; fear of social, physical and medical consequences; feeling healthy; not knowing anyone at the HIV clinic	Support from expert clients; escorted referrals; same-day HIV care registration; coordination between ANC and HIV services	No	Poor
Sangaramoorthy et. al., 2017	United States	Exploration of HIV stigma, retention in care, and ART adherence among HIV-infected older Black women	Assessment of barriers and facilitators of **ART adherence and retention** in care among HIV-infected older Black women	HIV+ Black women aged ≥40 residing in Prince George's County (PGC) **[other key population]**	35	Qualitative (semi-structured interviews)	N/A	Lack of access to health facility; lack of coordination of care; financial hardships	Use of appointment reminders	No	Good

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Sarna et. al., 2014	India	Examination of enrollment into ART services and exploration of barriers to enrollment among PLHIV	Exploration of barriers to **enrollment into ART** services among PLHIV	HIV+ patients enrolled in a cohort study from integrated counseling testing centers (ICTCs) across 6 Indian states and lost to care from ART centers **(clinical cohort)**	189	Descriptive (prospective cohort)	N/A	Feeling healthy; work or family responsibilities; financial concerns; fear of disclosure; long distance to clinic; alternative/traditional healing; disruption of care due to striking health workers; family objection; being too sick; lack of proper documentation; discouragement by health provider; denial of HIV diagnosis	N/A	No	Fair

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Sauceda et. al., 2018	United States	Identification of the most important barriers to ART adherence among HIV patients recruited through an online survey	Identification of the most important barriers to **ART adherence** among HIV patients recruited through an online survey	HIV+ mostly **gay men** aged ≥18 recruited through an online survey and living in the US	1217	Assessing association (cross-sectional survey)	N/A	Falling asleep through dose; being depressed; distracted by day-to-day life; wanting to avoid medication side effects; being under the influence of alcohols or illicit drugs; forgetting; running out of pills; feeling sick; having problems with pharmacy and insurance	N/A	No	Good
Shabalala et. al., 2018	Eswatini	Exploration of HIV+ patients' reasons for discontinuing ART	Exploration of HIV+ patients' reasons for **discontinuing ART**	HIV+ patients aged ≥18 who were part of the MaxART study enrolled in 14 participating public health	9	Qualitative (semi-structured interviews)	N/A	Mobility; negative interactions with clinic staff; medication side-effects; lack of food; stigma concerns; lack of social	N/A	No	Fair

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				facilities in Hhohho Region **(clinical cohort)**				support; precarious employment; negative emotions (such as anxiety and fear); disclosure concerns			
Sharma et. al., 2013	Nepal	Assessment of factors associated with non-adherence among PLHIV	Assessment of factors associated with **non-adherence** among PLHIV	PLHIV receiving ART care at Tribhuvan University Teaching Hospital (TUTH), Maharajgunj Kathmandu **(clinical cohort)**	100	Descriptive (cross-sectional survey)	N/A	Forgetting; lack of finances; attendance to religious ceremony; alcohol use; loss of drugs; strikes/accidents; perceiving ART as unnecessary; depression; lack of family support; lack of privacy	N/A	No	Poor

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Shet et. al., 2016	India	Assessment of the patterns, and predictors of ART adherence over time in relation to virological failure among HIV patients	Assessment of the predictors of **ART adherence** over time in relation to virological failure among HIV patients	HIV patients receiving care from 5 clinics in Karnataka and Tamil Nadu states participating in the HIV-India Trial (HIVIND) **(clinical cohort)**	599	Assessing association or causation (prospective cohort)	N/A	Unavailability of pills; forgetting; dosing confusion; drug toxicity; stigma; depression	N/A	Yes	Good
Sibanda-Kunda et. al., 2015	Zambia	Determination of the effect of gender on access to ART and its relationshiip with neurocognitive impairment	Determination of the effect of gender on access to **ART**	HIV+ adults receiving care at 6 clinics run by the Lusaka Urban District Health Management Team **(clinical cohort)**	34	Qualitative (semi-structured interviews)	N/A	Men's power dominance; stigma; unequal distribution of HIV programs across gender groups	N/A	No	Poor

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Sileo et. al., 2019	Uganda	Exploration of the motivation of alcohol consumption, and its effect on ART adherence among male fisherfolk	Exploration of the effects of alcohol consumption on **ART adherence** among male fisherfolk	HIV infected **male** fisherfolk on ART in Wakiso District who were part of a larger cross-sectional study and receiving care at Mildmay-supported ART clinics	30	Qualitative (in-depth semi-structured interviews)	N/A	Alcohol consumption	N/A	No	Good
Smillie et. al., 2014	Kenya	Exploration of the experiences of PLHIV who have attempted to engage in HIV care and their perceptions on the use of mHealth to enhance their care	Exploration of barriers and facilitators to **care** engagement among PLHIV	HIV+ patients aged ≥18 and receiving care at the Kibera Community Health Centre (KCHC), an African Medical and Research Foundation (AMREF) clinic in Nairobi **(clinical cohort)**	15	Qualitative (semi-structured interviews)	N/A	Poverty; depression; fear of stigma; being too sick to travel; not wanting to leave children	Positive interactions with clinic staff; free treatment; use of appointment reminder strategies	No	Fair

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Smith et. al., 2012	United States	Assessment of barriers and facilitators of retention in HIV care by applying the Information, Motivation, Behavioral Skills (IMB) model of health behavior	Assessment of barriers and facilitators of **retention** in HIV care	HIV-infected adults residing in the Bronx, NY and receiving care through community clinics or outreach teams **(general population)**	18	Qualitative (in-depth semi-structured interviews)	N/A	Poor health information; negative personal attitudes and beliefs; poor risk perception; competing priorities; poor patient–provider relationships; negative social norms and support; negative global constructs of self-care; denial of diagnosis; HIV cognitive and physical impairments; poor mental health	Good health information; positive personal attitudes and beliefs; perceived vulnerability; ability to balance competing priorities; positive relationships with providers; positive social norms and support; acceptance of diagnosis; stigma; positive global constructs of self-care	No	Good

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Soto Blanco et. al., 2005	Spain	Assessment of the frequency of ART non-adherence and of the predictors of non-adherence among HIV-infected prison inmates	Assessment of the predictors of **ART non-adherence** among HIV-infected prison inmates	HIV-infected prison inmates in 2 prisons in Andalusia region who were on ART **(other key population)**	177	Descriptive (cross-sectional survey)	N/A	Medication side effects; missing pills	N/A	No	Good
Sprague et. al., 2014	United States	Assessment of the engagement and retention in HIV care experiences of low-income PLHIV on the AIDS Drug Assistance Program HIV care	Assessment of the barriers and facilitators of **engagement and retention** in HIV care among low-income PLHIV on the AIDS Drug Assistance Program	Low-income PLHIV on the AIDS Drug Assistance Program in 2 sites in Alabama with a health clinic with an AIDS Service Organization (ASO) nearby **(general population)**	25	Qualitative (semi-structured interviews)	N/A	Psychological distress; fear; lack of information; substance use; incarceration; lack of food, transport and housing	Good social infrastructure (good social services); social enablers (use of social workers); enabling spaces (access to information)	No	Good

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StClair-Sullivan et. al., 2019	Zambia	Exploration of barriers to HIV care among young people living with HIV (YPLWHIV) and assessment of the acceptability and feasibility of using mHealth to improve retention in care and ART adherence	Exploration of barriers to HIV **care** among young people living with HIV (YPLWHIV)	**Young people** living with HIV (YPLWHIV) aged 16-24 and receiving care at CIDRZ (Centre for Infectious Disease research in Zambia) supported, government-run health facilities in the Lusaka district	24	Qualitative (focus group discussions)	N/A	Stigma; inconvenient clinic opening hours; long waiting times at clinic; negative experiences with healthcare professionals; unintended disclosure; lack of HIV-related health education; lack of psychosocial support	N/A	No	Fair
Stinson et. al., 2012	South Africa	Investigation of the barriers to initiating lifelong ART during pregnancy and the challenges to postpartum retention in HIV care	Investigation of the barriers to **initiating lifelong ART** during pregnancy and the challenges to postpartum retention in HIV care	HIV+ **pregnant or postpartum women** who were ART-eligible or had initiated ART receiving care at 4 Cape Town public-sector primary	28	Qualitative (structured interviews)	N/A	Late first presentation to care; denial of an HIV diagnosis; fear of disclosure; fear of initiating lifelong ART; fear of treatment side-effects	Prevention of vertical transmission of HIV	No	Fair

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				healthcare facilities							
Stranix-Chibanda et. al., 2019	Argentina, Botswana, Brazil, Haiti, India, Malawi, South Africa, Tanzania, Thailand, Uganda, United States, Zambia, Zimbabwe	Assessment of the uptake of universal ART and reasons for accepting or declining ART among HIV-infected pregnant and postpartum women	Assessment of the reasons for accepting or declining **ART** among HIV-infected pregnant and postpartum women	HIV+ **pregnant or postpartum women** who were part of the PROMISE trial and had not been randomized to ART but were offered universal ART at the initial counselling session	1,492	Descriptive (prospective cohort)	N/A	Wanting more time to consider taking ART; feeling well; having concerns about potential side effects of ART; disclosure concerns; having concerns about committing to life-long treatment; being too busy; knowledge of ineligibility as per local guidelines	Having concerns about health; having concerns about the CD4 count; understanding universal treatment recommendation	No	Fair

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Tabatabai et. al., 2014	Malawi	Evaluation of characteristics of patients resuming ART after treatment interruption and identification of reasons for interrupting ART	Identification of reasons for interrupting **ART** among HIV patients	HIV+ patients aged ≥15 receiving care at Lighthouse Clinic in Lilongwe who resumed ART after treatment interruption **(clinical cohort)**	147	Mixed method (Cross-sectional survey part)	Mixed method (Qualitative in-depth interview part)	Travel; transport costs; negative interactions with healthcare providers; fatigue or forgetfulness; feeling sick; adverse drug effects; conditions related to pregnancy or delivery; religious factors; stigma; use of traditional medicine; clinician advice to stop ART	N/A	No	Good

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Taylor et. al., 2014	United States and Dominican Republic	Determination of the impact of geographic mobility on HIV care engagement and ART adherence among highly mobile, linked populations	Determination of the impact of geographic mobility on HIV **care engagement and ART adherence** among highly mobile, linked populations	HIV+ Dominican patients aged ≥21 who had recently travelled between New York City and Santo Domingo **(other key population)**	35	Qualitative (in-depth interviews)	N/A	Disruption of daily schedule because of travel; perceiving vacation travel as a vacation from medicine; fear of medication side effects during travel; stigma concerns; disclosure concerns; mistrust of physicians in destination country; running out of medications; inability to access medication in destination country; fear of confiscation of medicines by customs	N/A	No	Good

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								officials; transport costs in towns/rural areas in destination country; having medication stolen during travel			
Tiruneh et. al., 2016	Ethiopia	Assessment of retention of HIV patients in care and factors that influence retention	Assessment factors that influence **retention** of HIV patients in care	HIV+ patients receiving ART care at a tertiary teaching hospital in Addis Ababa **(clinical cohort)**	~ 60	Qualitative (focus group discussions)	N/A	Stigma; dissatisfaction with care; financial problems; alternative/faith healing (use of holy water)	Improved health; social support	No	Fair

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Tofighi et. al., 2019	United States	Assessment of factors influencing patient engagement with opioid use disorder (OUD), the HIV care cascade and engagement with integrated primary care treatment of HIV and OUD	Assessment of factors influencing patient **engagement** HIV care cascade among HIV patients with OUD	HIV patients with OUD admitted in Bellevue Hospital's inpatient detoxification unit in New York City **(PWID)**	23	Qualitative (in-depth interviews)	N/A	Lack of insurance coverage; incarceration; transferred care; homelessness; financial insecurity; exposure to peers actively using opioid; stigma; illicit purchases by pharmacies of participant's supplies of ART; disruption in supplies of ART following admissions to OUD treatment program	Insurance coverage; support from peers, family, and clinic coordinators; integrated addiction treatment and HIV care; transportation vouchers	No	Fair

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Tomori et. al., 2014	Tanzania	Examination of socioeconomic and sociocultural barriers and potential facilitators of retention in ART among HIV patients	Examination of socioeconomic and sociocultural barriers and potential facilitators of **retention in ART** among HIV patients	PLHIV residing in Iringa Region **(general population)**	14	Qualitative (semi-structured in-depth interviews)	N/A	Lack of knowledge and misperceptions of treatment; access problems (long distance to clinics and poverty); stigma; lack of psychosocial support; alternative healing	Positive perceptions ART efficacy; improved ART availability; nutritional and financial support; social support	No	Poor
Tran et. al., 2012	Vietnam	Examination of the distribution of CD4 count, evaluation of the linkage between HIV testing and HIV care, and exploration of reasons for late ART initiation among PLHIV	Exploration of reasons for late **ART initiation** among PLHIV	HIV patients receiving care from clinics from 5 provices **(clinical cohort)**	30	Qualitative (semi-structured in-depth interviews)	N/A	Poor linkage between HIV testing and HIV care and treatment services; lack of confidential ART services; limited human resources capacity at ART clinics	N/A	No	Poor

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Treffry-Goatley et. al., 2016	South Africa	Identification of individual and structural factors that can challenge or support ART adherence among PLHIV in resource-limited settings	Identification of individual and structural factors that can challenge or support **ART adherence** among PLHIV in resource-limited settings	PLHIV in in KwaZulu-Natal recruited from primary health clinics **(clinical cohort)**	20	Qualitative (digital storytelling)	N/A	Stigma	Confidence in the effectiveness of ART; perceiving HIV as any other chronic disease that requires lifetime treatment; risk perception; psychosocial support	No	Fair
Tuller et. al., 2010	Uganda	Assessment of structural barriers to ART adherence and clinic care and how transportation costs are perceived, experienced and addressed by PLHIV	Assessment of structural barriers to **ART adherence and clinic care** and how transportation costs are perceived, experienced and addressed by PLHIV	PLHIV attending the Immune Suppression (ISS) Clinic at the Mbarara University of Science and Technology in Mbarara **(clinical cohort)**	41	Qualitative (semi-structured interviews)	N/A	Lack of money for transportation	N/A	No	Fair

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Tweya et. al., 2013	Malawi	Description of misclassification of HIV patients LTFU and explanation of the reasons for ART discontinuation	Explanation of the reasons for **ART discontinuation** among HIV patients	HIV patients receiving care at Lighthouse Trust's two public ART clinics in urban Malawi who were traced after being LTFU **(clinical cohort)**	940	Descriptive (retrospective cohort)	N/A	Forgeting; feeling too weak/sick to go and collect ARVs; travelling; transportation costs; suspected medication side effects; religious beliefs; spouse's disapproval of taking medication; perception of clinic not being helpful; feeling healthy; not being ready for ARVs; lack information about ARVs; work responsibilities	N/A	No	Fair

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Usman et. al., 2019	Nigeria	Determination of the predictors of ART non-adherence among HIV patients	Determination of the predictors of **ART non-adherence** among HIV patients	HIV patients receiving care at the Infectious Diseases Hospital (IDH) and Murtala Muhammad Specialist Hospital (MMSH) in Kano State **(clinical cohort)**	204	Descriptive (case control study)	N/A	Forgetting; feeling better; stigma; running out of medications; being too ill; medication side effects	N/A	No	Poor
Vallabhaneni et. al., 2012	India	Description of the prevalence, duration, reasons, and predictors of treatment interruption among HIV patients	Description of the reasons for **treatment interruption** among HIV patients	HIV+ patients aged ≥18 receiving care at 2 hospitals in Bangalore, Karnataka **(clinical cohort)**	552	Descriptive (prospective cohort)	N/A	Financial constraints; pharmacy stock outs and clinic logistics; medication side effects; instruction by doctor; feeling sick; feeling depressed; being healthy; being away from home; being busy; not understanding regimen; alcohol consumptio	N/A	No	Good

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								n; alternative/traditional medicine			
vanAndel et. al., 2016	The Netherlands	Identification of predictors and reasons for non-attendance at outpatient clinic appointments among HIV patients	Identification of reasons for **non-attendance** at outpatient clinic appointments among HIV patients	HIV+ patients receiving care from outpatient clinics and part of the ATHENA cohort **(clinical cohort)**	447	Descriptive (case control study)	N/A	Forgetting; day-to-day responsibilities; psychosocial problems; feeling well; feeling ill	N/A	No	Good
VanTam et. al., 2011	Vietnam	Description of factors affecting ART adherence among PLHIV and assessment of the acceptability of home-based ART delivery	Description of factors affecting **ART adherence** among PLHIV	HIV patients receiving ART care at the HIV/AIDS outpatient clinic (OPC) in Uong Bi hospital, Quang Ninh province	39	Qualitative (focus group discussions)	N/A	Stigma	N/A	No	Fair

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				(clinical cohort)							
Veinot et. al., 2006	Canada	Assesssment of HIV-positive youths' experiences with, and perceptions of, HIV treatment	Assesssment of HIV-positive youths' experiences with, and perceptions of, HIV **treatment**	HIV+ **youth** aged 12 to 24 recruited through AIDS-serving organizations, youth-serving organizations, hospitals, and health clinics	34	Qualitative (in-depth semi-structured interviews)	N/A	Lack of adequate treatment knowledge; being unprepared for treatment decision-making; difficulties taking medications (due to disruption of social life, administration or side effects);	N/A	No	Fair

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Venables et. al., 2019	Democratic Republic of Congo	Assessment of reasons behind HIV patients' delay in seeking health-care services for advanced HIV	Assessment of reasons behind HIV patients' **delay in seeking health-care** services for advanced HIV	HIV+ patients receiving care at the Médecins Sans Frontières (MSF)-run Centre Hospitalier de Kabinda (CHK) in Kinshasa **(clinical cohort)**	7	Qualitative (in-depth interviews)	N/A	Stigma; religious beliefs; financial constraints	N/A	No	Poor
Wachira et. al., 2018	Kenya	Exploration of the perceptions, experiences and expectations of HIV patients regarding their engagement in care	Exploration of the perceptions, experiences and expectations of HIV patients regarding their **engagement in care**	HIV+ patients aged ≥18 receiving ART care receiving HIV care at one of the 3 participating AMPATHplus clinics **(clinical cohort)**	86	Qualitative (focus group discussions and in-depth interviews)	N/A	Negative patient-provider relationships	Positive patient-provider relationships	No	Fair
Wadunde et. al., 2018	Uganda	Determination of ART adherence levels and the factors affecting adherence among HIV infected children	Determination of factors affecting **ART adherence** among HIV infected children	**Caregivers** of HIV-infected **children** aged 0–14 years receiving ART in 2 hospitals in Kabale district	153	Descriptive (cross-sectional survey)	N/A	Caregiver forgetfulness; transportation problems; school examinations; child having been out playing; child	N/A	No	Fair

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								vomiting drug; running out of medication			
Wanyama et. al., 2007	Uganda	Assessment of the effect of belief in spiritual healing on ART non-adherence among HIV patients	Assessment of the effect of belief in spiritual healing on **ART non-adherence** among HIV patients	HIV patients who were part of a prospective observational cohort at the Makerere University Infectious Diseases Institute (IDI) HIV treatment program **(clinical cohort)**	6	Descriptive (prospective cohort)	N/A	Spiritual healing	N/A	No	Poor
Ware et. al., 2005	United States	Assessment of the effect of illicit drug use on ART adherence	Assessment of the effect of illicit drug use on **ART adherence**	HIV+ patients who use drugs residing in Boston, Massachusetts **(PWID)**	52	Qualitative interviews	N/A	Use of illegal drugs; not carrying medications; competing priorities; redefining regimens to simplify pill-taking, change schedule or	N/A	No	Good

Author and Year	Country	Primary Research Question	Barriers and Enablers Assessment	Study Population	Sample Size for Barriers and Enablers Assessment of HIV patients	Primary Measurement Approach for Barriers and Enablers	Secondary Measurement Approach for Barriers and Enablers	Barriers Measured	Enablers Measured	Longitudinal Assessment with Barriers/Enablers?	Overall Study Quality
								mitigate side effects			
Ware et. al., 2013	Nigeria, Uganda and Tanzania	Assessment of missed clinic visits among HIV patients and subsequent disengagement from HIV/AIDS treatment and care	Assessment of missed clinic visits among HIV patients and subsequent disengagement from HIV/AIDS **treatment and care**	HIV+ patients aged ≥18 receiving care from participating study clinics who had missed scheduled visits for at least 3 months and were successfully traced **(clinical cohort)**	91	Qualitative (in-depth interviews)	N/A	Cultural and family obligations; meeting economic requirements; travel delays and traffic accidents; encounters with violence; transport problems; lack of family and community support; scheduling errors; forgetting; objections to clinic policies; negative interactions with clinic staff	N/A	No	Poor

Author and Year	Country	Primary Research Question	Barriers and Enablers Assessment	Study Population	Sample Size for Barriers and Enablers Assessment of HIV patients	Primary Measurement Approach for Barriers and Enablers	Secondary Measurement Approach for Barriers and Enablers	Barriers Measured	Enablers Measured	Longitudinal Assessment with Barriers/Enablers?	Overall Study Quality
Watson-Jones et. al., 2012	Tanzania	Assessment of the care and referral of HIV-infected women identified through PMTCT and exploration of barriers to clinic attendance	Exploration of barriers to **clinic attendance** among HIV-infected women identified through PMTCT	HIV+ **pregnant women** admitted for delivery at 2 government hospitals in Mwanza city and had not attended an HIV clinic prior to admission	38	Descriptive (prospective cohort)	N/A	Lack of appropriate health education; being too ill; disclosure concerns; wanting to wait until after delivery; long distance to HIV clinic; absence of services when they attended the HIV clinic; time constraints; denial of HIV diagnosis; feeling healthy	N/A	No	Fair
Watt et. al., 2009	Tanzania	Assessment of the dynamics of good ART adherence among HIV patients	Assessment of the dynamics of good **ART adherence** among HIV patients	HIV+ patients aged ≥18 receiving care at an HIV clinic in Arusha **(clinical cohort)**	36	Qualitative (in-depth semi-structured interviews)	N/A	N/A	Improvement of health condition; desire to meet family responsibilities; using specific strategies to remember to take pills; material and	No	Good

Author and Year	Country	Primary Research Question	Barriers and Enablers Assessment	Study Population	Sample Size for Barriers and Enablers Assessment of HIV patients	Primary Measurement Approach for Barriers and Enablers	Secondary Measurement Approach for Barriers and Enablers	Barriers Measured	Enablers Measured	Longitudinal Assessment with Barriers/Enablers?	Overall Study Quality
									emotional support; trusting advise of healthcare providers		
Weidle et. al., 1999	United States	Evaluation of the extent of ART adherence among HIV-infected patients of an inner-city hospital and evaluation of reasons for non-adherence	Evaluation of reasons for **non-adherence to ART** among HIV-infected patients of an inner-city hospital	HIV+ patients receiving care at the Bronx-Lebanon Hospital Center (BLHC) in the South Bronx, New York **(clinical cohort)**	173	Descriptive	N/A	Forgetting; not having access to medicines; medication toxicity; being instructed to not take medication by healthcare provider; perceived or actual inefficacy of medications	N/A	No	Poor

Author and Year	Country	Primary Research Question	Barriers and Enablers Assessment	Study Population	Sample Size for Barriers and Enablers Assessment of HIV patients	Primary Measurement Approach for Barriers and Enablers	Secondary Measurement Approach for Barriers and Enablers	Barriers Measured	Enablers Measured	Longitudinal Assessment with Barriers/Enablers?	Overall Study Quality
Weiser et. al., 2003	Botswana	Assessment of the determinants of ART adherence among HIV patients	Assessment of the determinants of **ART adherence** among HIV patients	HIV+ patients receiving care at 3 private clinics in Gaborone and Francistown **(clinical cohort)**	109	Mixed method (Cross-sectional multivariable part)	Mixed method (Qualitative structured interview part)	Pill burden; long treatment duration; medication side effects; financial constraints; required visit frequency burden; travel and migration; hunger; stigma; forgetting; running out of medication; being too busy; being instructed to not take medication by healthcare provider; long distance to clinic; being unable to follow instructions; being too sick; closure of pharmacy; alcohol use;	N/A	No	Poor

Author and Year	Country	Primary Research Question	Barriers and Enablers Assessment	Study Population	Sample Size for Barriers and Enablers Assessment of HIV patients	Primary Measurement Approach for Barriers and Enablers	Secondary Measurement Approach for Barriers and Enablers	Barriers Measured	Enablers Measured	Longitudinal Assessment with Barriers/Enablers?	Overall Study Quality
								feeling healthy; being stressed at work or home			
Weiser et. al., 2010	Uganda	Assessment of the role of food insecurity in the lives of HIV-infected patients and how food insecurity leads to ART non-adherence and treatment interruptions	Assessment of how food insecurity leads to **ART non-adherence** and treatment interruptions among HIV-infected patients	HIV-infected patients participating in AIDS treatment programs in Mbarara (Immune Suppression Clinic) and Kampala (Adherence Monitoring Ugandan Cohort Study sites) **(clinical cohort)**	47	Qualitative (semi-structured in-depth interviews)	N/A	Food insecurity	N/A	No	Good

Author and Year	Country	Primary Research Question	Barriers and Enablers Assessment	Study Population	Sample Size for Barriers and Enablers Assessment of HIV patients	Primary Measurement Approach for Barriers and Enablers	Secondary Measurement Approach for Barriers and Enablers	Barriers Measured	Enablers Measured	Longitudinal Assessment with Barriers/Enablers?	Overall Study Quality
Wood et. al., 2004	United States	Examination of the patterns, barriers and facilitators to medication adherence in HIV-infected women caring for children	Examination of the barriers and facilitators to **medication adherence** in HIV-infected women caring for children	HIV+ **women caring for children** who were prescribed HAART by their medical providers	36	Qualitative interviews	N/A	Medication side effects; feeling healthy; medication being a reminder of illness; forgetting; fear; guilt; negative relationships with partners and family members; emotional distress	Positive relationships with partners and family members; concern for children	No	Poor
Wringe et. al., 2009	Tanzania	Exploration of factors affecting attendance at HIV clinic appointments among recently diagnosed HIV+ patients	Exploration of factors affecting **attendance** at HIV clinic appointments among recently diagnosed HIV+ patients	Recently diagnosed HIV+ Kisesa residents who were referred to the HIV clinic, and were members of the local home-based care (HBC) organization **(general population)**	42	Qualitative (focus group discussions and in-depth interviews)	N/A	Health systems logistics (queues, travel to clinic); stigma concerns; Low perceived susceptibility to HIV-related illnesses; denial of HIV status; feeling healthy; medication side effects; perceived	Being ill; having improved health; free health education and counseling; self-efficacy	No	Fair

Author and Year	Country	Primary Research Question	Barriers and Enablers Assessment	Study Population	Sample Size for Barriers and Enablers Assessment of HIV patients	Primary Measurement Approach for Barriers and Enablers	Secondary Measurement Approach for Barriers and Enablers	Barriers Measured	Enablers Measured	Longitudinal Assessment with Barriers/Enablers?	Overall Study Quality
								lack of efficacy of medication; lack of psychosocial support from family members; alternative healing; lack of self-efficacy			
Wubshet et. al., 2013	Ethiopia	Determination of reasons and outcomes of patients LTFU from HIV care	Determination of reasons for patients being **LTFU** from HIV care	HIV patients LTFU from the University of Gondar Hospital, northwest Ethiopia and traced through a community tracking survey **(clinical cohort)**	135	Descriptive (cross-sectional survey)	N/A	Preferring traditional medicine and/or holy water; having improved health; having deteriorating health; financial constraints; stigma and social problems	N/A	No	Fair

Author and Year	Country	Primary Research Question	Barriers and Enablers Assessment	Study Population	Sample Size for Barriers and Enablers Assessment of HIV patients	Primary Measurement Approach for Barriers and Enablers	Secondary Measurement Approach for Barriers and Enablers	Barriers Measured	Enablers Measured	Longitudinal Assessment with Barriers/Enablers?	Overall Study Quality
Wutoh et. al., 2005	United States	Application of the health belief model (HBM) to assess the perceptions of older HIV patients regarding their disease, the effect on adherence to medication, use of alternative therapies, and risk behaviors	Assessment of perceived barriers to **ARV medications**	HIV+ patients, aged ≥50 receiving care at 2 HIV clinics in Washington, District of Columbia **(clinical cohort)**	100	Assessing association (cross-sectional survey)	N/A	Medication costs; pill burden; medication side effects; complexity of the medication regimens; inconvenient scheduling; concerns about tolerance to medications	N/A	No	Poor
YildizSevgi et. al., 2017	Turkey	Investigation of the level of ART adherence and determinants of non-adherence among HIV patients	Investigation of determinants of **ART non-adherence** among HIV patients	HIV+ patients aged ≥18 receiving care at 4 tertiary hospitals affiliated with the ACTion against HIV in Istanbul (ACTHIV-IST) Study Group in Istanbul **(clinical cohort)**	263	Descriptive (cross-sectional survey)	N/A	Being away from home; being busy; forgetting; pill burden; wanting to avoid medication side effects; fear of disclosure; having a change in daily routine; perceived drug toxicity/harmfulness;	N/A	No	Fair

Author and Year	Country	Primary Research Question	Barriers and Enablers Assessment	Study Population	Sample Size for Barriers and Enablers Assessment of HIV patients	Primary Measurement Approach for Barriers and Enablers	Secondary Measurement Approach for Barriers and Enablers	Barriers Measured	Enablers Measured	Longitudinal Assessment with Barriers/Enablers?	Overall Study Quality
								falling asleep; feeling sick; feeling depressed/overwhelmed; problems timing pill intake with meals; running out of pills; feeling healthy			
Yu et. al., 2007	Malawi	Assessment of the outcome status of HIV patients LTFU from ART care	Assessment reasons for **LTFU from ART** care among HIV patients	HIV+ patients LTFU from 4 public ART facilities in the northern region of Malawi **(clinical cohort)**	37	Descriptive (cross-sectional interview)	N/A	Transportation costs; religious beliefs; persuasion by relatives to stop ART	N/A	No	Poor
Zahedi-Spung et. al., 2018	United States	Identification of barriers to ART adherence during pregnancy among HIV patients and assessment of patient understanding of	Identification of barriers to **ART adherence** during pregnancy among HIV patients	HIV+ **postpartum women** receiving care at a hospital in Atlanta, Georgia	45	Descriptive (cross-sectional interview)	N/A	Forgetting; financial constraints; medication side effects; not having a desire to take medications	N/A	No	Poor

Author and Year	Country	Primary Research Question	Barriers and Enablers Assessment	Study Population	Sample Size for Barriers and Enablers Assessment of HIV patients	Primary Measurement Approach for Barriers and Enablers	Secondary Measurement Approach for Barriers and Enablers	Barriers Measured	Enablers Measured	Longitudinal Assessment with Barriers/Enablers?	Overall Study Quality
		perinatal transmission									

ART = Antiretroviral Therapy
LTFU = Lost To Follow Up
HIV+ = HIV Positive
TB = Tuberculosis
ANC = Antenatal care
PNC = Postnatal care
MDRT = Multi-Drug Rescue Therapy
MSM = Men who have Sex with Men
HCT = HIV Care and Treatment
PMTCT = Prevention of Mother to Child Transmission (of HIV)
RCT = Randomized Controlled Trial
HAART = Highly Active Antiretroviral Therapy
PLHIV = People Living with HIV
IDUs = Injecting Drug Users
ARVs = Antiretrovirals
PITC = Provider Initiated Testing and Counseling
OPD = Out Patient Department
PWID = People Who Inject Drugs
HTC = HIV Testing and Counseling
HBCT = Home Based HIV Counseling and Testing
OUD = Opioid Use Disorder

Appendix C: Measurements and Definitions for Reasons for Linkage and Retention in Care in Link4Health Study

Measurement	**Definition (Question Asked)**
Linkage to Care in General at 1 Month	Why did you go to the ART clinic after testing positive?
Linkage to Care at a Specific Clinic at 1 Month	Why did you go to that specific ART clinic?
Linkage to Care in General at 12 Months	Why did you go to an HIV care clinic during the last 12 months?
Linkage to Care at a Specific Clinic at 12 Months	Why did you go to that specific ART clinic?
Retention in Care at 12 Months	Why do you continue to get HIV care at that clinic?

Appendix D: Summary of Latent Factors Depicted by Reported Reasons for Linkage and Retention in Care in Engage4Health Study and Corresponding Factor Loadings

Reason for Linkage/Retention	**Latent Factor**	**Correlation [Loading] (and Standard Error) of Reason with Latent Factor**
Health care worker told me	Instructed	0.631 (0.267)*
Study staff told me to		0.98 (0.310)*
Clinic was convenient/close	Access/Financial Reasons	0.155 (0.068)*
Care and treatment are free		0.416 (0.106)*
Transportation is easy/cheap		0.408 (0.066)*
Short clinic waiting time		0.507 (0.112)*
Staff are respectful; nice	Good Clinical Services	0.987 (0.364)*
Care is good		0.729 (0.137)*
There is a doctor there		0.729 (0.137)*
Medications are available		0.636 (0.178)*
Lab tests are available		0.725 (0.213)*
Offers services I need (eg. food)		1.015 (0.171)*
I have a friend/family member who goes	Stigma Mitigation/Psychosocial Support	0.326 (0.153)*
Clinic is far away; HIV status is kept confidential there		0.523 (0.187)*

* Significant association at P< 0.05.

Appendix E.i: Relative Risk Regression for Effect of Retention in Care on Viral Load Suppression with Complete Cases: Link4Health Data, Eswatini, 2013-2014

Retention Measure	Effect on Viral Load Suppression			
	Crude Analysis		Adjusted Analysis[#]	
	RR	95% CI	RR	95% CI
Retained in Care at 12m (not LTFU) [No vs Yes]	1.06	(0.83-1.37)	1.08	(0.83-1.42)
Consistently Engaged in Care (No vs Yes)	1.08	(0.90-1.31)	1.08	(0.89-1.34)
Not Retained and Not Consistent and vs All Other Consistency and Retention Combinations	1.03	(0.74-1.43)	1.05	(0.74-1.50)

[#]Adjusted for intervention arm

Appendix E.ii: Relative Risk Regression for Effect of Retention in Care on Viral Load Suppression with Single Worst-Case Imputations: Link4Health Data, Eswatini, 2013-2014

Retention Measure	Effect on Viral Load Suppression			
	Crude Analysis		Adjusted Analysis[#]	
	RR	95% CI	RR	95% CI
Retained in Care at 12m (not LTFU) [No vs Yes]	1.05	(0.92-1.20)	1.07	(0.92-1.26)
Consistently Engaged in Care (No vs Yes)	1.00	(0.90-1.10)	1.00	(0.98-1.57)
Not Retained and Not Consistent and vs All Other Consistency and Retention Combinations	1.02	(0.87-1.18)	1.04	(0.89-1.23)

[#]Adjusted for intervention arm

Appendix F.i: Relative Risk Regression for Effect of Potential Barriers of Care Engagement on Linkage, Retention and Viral Load Suppression with Complete Cases: Link4Health Data, Eswatini, 2013-2014

Potential Barrier	Effect on Linkage				Effect on Retention				Effect on Viral Load Suppression			
	Crude Analysis		#Adjusted Analysis		Crude Analysis		#Adjusted Analysis		Crude Analysis		#Adjusted Analysis	
	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
Perceived Stigma [Baseline] (Continuous)	1.00	(0.99-1.01)	1.00	(0.99-1.02)	1.00	(0.99-1.02)	1.00	(0.99-1.03)	0.96*	(0.92-0.99)*	0.96	(0.92-1.00)
Perceived Psychosocial Support [Baseline] (Continuous)	1.00	(0.99-1.01)	1.00	(0.98-1.02)	1.00	(0.99-1.02)	1.00	(0.98-1.03)	1.00	(0.93-1.07)	1.00	(0.93-1.09)
Perceived Clinical Staff Competence (No vs Yes)	1.00	(0.91-1.11)	1.00	(0.82-1.23)	1.07	(0.94-1.21)	1.04	(0.84-1.29)	0.92	(0.50-1.67)	0.85	(0.41-1.78)
Employment Status (Employed vs Unemployed) ##	1.00	(0.95-1.05)	1.00	(0.91-1.10)	0.96	(0.90-1.03)	0.97	(0.87-1.09)	1.04	(0.85-1.28)	1.07	(0.82-1.39)
Travel Time to the Health Facility (30 Minutes or More vs Less Than 30 Minutes)	1.00	(0.93-1.09)	1.00	(0.86-1.18)	1.03	(0.92-1.16)	1.06	(0.89-1.28)	1.33	(0.93-1.90)	1.35	(0.85-2.12)

[#]Adjusted for intervention arm, age, gender, education, employment, and marital status (except for the Employment Status potential barrier)
[##]Adjusted for intervention arm, age, gender, education, and marital status
*Significant association

Appendix F.ii: Relative Risk Regression for Effect of Potential Barriers of Care Engagement on Linkage, Retention and Viral Load Suppression with Worst Case Single Imputations: Link4Health Data, Eswatini, 2013-2014

Potential Barrier	Effect on Linkage				Effect on Retention				Effect on Viral Load Suppression			
	Crude Analysis		#Adjusted Analysis		Crude Analysis		#Adjusted Analysis		Crude Analysis		#Adjusted Analysis	
	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
Perceived Stigma [Baseline] (Continuous)	1.00	(0.99-1.01)	1.00	(0.99-1.02)	1.00	(0.99-1.02)	1.00	(0.99-1.03)	0.98	(0.97-1.00)	0.99	(0.96-1.01)
Perceived Psychosocial Support [Baseline] (Continuous)	1.00	(0.99-1.01)	1.00	(0.98-1.02)	1.00	(0.99-1.02)	1.00	(0.98-1.03)	1.00	(0.97-1.04)	1.00	(0.96-1.04)
Perceived Clinical Staff Competence (No vs Yes)	1.00	(0.91-1.11)	1.00	(0.82-1.23)	1.07	(0.94-1.21)	1.04	(0.84-1.29)	1.02	(0.74-1.41)	0.99	(0.65-1.50)
Employment Status (Employed vs Unemployed) ##	1.00	(0.95-1.05)	1.00	(0.91-1.10)	0.96	(0.90-1.03)	0.97	(0.87-1.09)	1.01	(0.89-1.15)	1.01	(0.85-1.21)
Travel Time to the Health Facility (30 Minutes or More vs Less Than 30 Minutes)	1.00	(0.93-1.09)	1.00	(0.86-1.18)	1.03	(0.92-1.16)	1.06	(0.89-1.28)	1.10	(0.87-1.38)	1.13	(0.84-1.51)

#Adjusted for intervention arm, age, gender, education, employment, and marital status (except for the Employment Status potential barrier)

[##]Adjusted for intervention arm, age, gender, education, and marital status
*Significant association

Appendix G.i: Relative Risk Regression for Effect of Staff Competence on Viral Load Suppression Using Best Case (all "Yes" Single Imputation Assumption): Link4Health Data, Swaziland, 2013-2014

	Effect on Viral Load Suppression			
	Crude Analysis		#Adjusted Analysis	
	RR	95% CI	RR	95% CI
Clinical Staff Competence (No vs Yes)	1.28	(0.98-1.66)	1.23	(0.88-1.71)

#Adjusted for intervention arm, age, gender, education, employment, and marital status

Appendix G.ii: Relative Risk Regression for Effect of Staff Competence on Viral Load Suppression Using Worst Case (all "No" Single Imputation Assumption): Link4Health Data, Swaziland, 2013-2014

	Effect on Viral Load Suppression			
	Crude Analysis		#Adjusted Analysis	
	RR	95% CI	RR	95% CI
Clinical Staff Competence (No vs Yes)	0.87	(0.47-1.61)	0.82	(0.39-1.72)

#Adjusted for intervention arm, age, gender, education, employment, and marital status