

**NON-ADHERENCE TO HIV TREATMENT AMONG PATIENTS IN CAMEROON:
PREVALENCE, PREDICTORS AND EFFECTIVE STRATEGIES IMPROVING
TREATMENT ADHERENCE**

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Abstract

Amos Buh: Non-adherence to HIV treatment among patients in Cameroon: prevalence, predictors and effective strategies improving treatment adherence.

(Under the supervision of Karen Phillips, PhD & Sanni Yaya, PhD)

The Human Immunodeficiency Virus (HIV) epidemic remains a major global public health problem, with sub-Saharan Africa (SSA) at its epicentre. Despite the use of antiretroviral therapy (ART) to reduce new infections and deaths, SSA reports the highest HIV incidence, constituting two-thirds of global new infections. Cameroon is one of SSA countries where HIV care decentralization is enforced as a national policy but follow up of people living with HIV (PLWH) is provider-oriented, with limited patient involvement in clinical monitoring. The purpose of this dissertation was to explore predominant barriers and facilitators influencing ART adherence and identify effective interventions enhancing ART adherence across SSA. Furthermore, we sought to assess the prevalence and predictors of ART non-adherence among PLWH, and factors influencing non-adherence among PLWH who have experienced ART non-adherence in Cameroon.

We conducted a comprehensive systematic review and meta-analysis on studies examining barriers to ART adherence and interventions boosting adherence. Forty-five studies were selected (30 for narrative synthesis and 15 for meta-analysis). Identified barriers and facilitators to ART adherence were categorized into seven principal factors: patient-related, health system-related, medication-related, stigma, poor mental health, socioeconomic and socio-cultural-related factors. Adherence-enhancing interventions encompassed counselling, incentives, mobile phone short message service, peer delivered behavioral intervention, community ART delivery, electronic adherence service monitoring device, lay health worker lead group intervention and food assistance. The

meta-analysis revealed a statistically significant difference in ART adherence between intervention and control groups (pooled OR=1.56, 95%CI:1.35 - 1.80, $p<0.01$).

Using a cross-sectional study of adult PLWH in HIV treatment centres in Cameroon, we explored the prevalence and predictors of ART non-adherence. A total of 451 participants with mean age 43.42 years (SD: 10.42), were enrolled. Overall, ART non-adherence was 37.78%. Reasons for missing ART include forgetfulness, business and traveling without drugs. Significant factors associated with ART non-adherence include age, education, and alcohol consumption.

In a qualitative study of 43 adult PLWH who had experienced ART non-adherence, adherence barriers included those related to patient, medication, health service, stigma, use of alternative treatment, resource limitation, environmental/social, and political instability. Adherence facilitators included social support, aligning treatment with patient's daily routines, use of reminders, health sector/caregiver support, and awareness of HIV status/ART knowledge.

To harness full potential of ART and mitigate HIV burden in SSA countries, stakeholders engaged in HIV management must recognize and integrate barriers, facilitators, and adherence-enhancing interventions when formulating policies or crafting treatment strategies. Continuous information provision and unflinching support both from patients' families and caregivers are needed to improve adherence. Future studies focusing on specific underrepresented demographics - HIV-infected children, adolescents, and pregnant women in SSA are needed to uncover appropriate barriers, facilitators and interventions tailored to each group's unique needs. Other studies focusing on assessing long-term non-adherence trends and determinants using larger samples of PLWH in many regions are necessary. Also, studies using both in-depth and focused group discussions, and quantitative approaches are required to uncover the ART non-adherence-related burden.

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List of abbreviations

AIDS	Acquired Immune Deficiency Syndrome
aOR	Adjusted Odds Ratio
ART	Anti-retroviral Therapy
ARV	Antiretroviral
CD4	Cluster of Differentiation 4
CDC	Centers for Disease Control and Prevention
CI	Confidence Interval
COVID-19	Corona Virus Disease 2019
CNEC	Cameroon National Ethics Committee
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HBM	Health Belief Model
HIV	Human Immunodeficiency Virus
IDI	In-Depth Interview
IQR	Interquartile Range
IRB	Institutional Review Board
JB	Joanna Briggs Institute
JBIMASARI	Joanna Briggs Institute for Meta-Analysis of Statistical Assessment and Review Instrument
KM	Kilometers
LIMICs	Low- and Middle-Income Countries
ml	Milliliters
N	Frequency
NA	Not Applicable
OR	Odds Ratio
PLWH	People Living With HIV
PLWHA	People Living With HIV and AIDS
PRISMA-P	Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols

PROSPERO	International Prospective Register of Systematic Reviews
REB	Research Ethics Board
Ref	Reference variable
SD	Standard Deviation
SSA	Sub-Sahara Africa
TB	Tuberculosis
US	United States
USA	United States of America
WHO	World Health Organization
XAF	African Financial Community Franc

Definition of operational terms

ART Adherence	Adherence to ART is taking all ARV pills in the correctly prescribed doses at the right time
Optimal ART Adherence	Proportion of those who take their ART over 95% of the time
Sub-optimal Adherence	Proportion of those who take their ART for less than 95% of the time
Prevalence of ART non-adherence	The number of PLWH on ART who are not taking their treatment as prescribed in the population at a specific time divided by the number of people on ART in the population at that time.
Viral load	Levels of virus found in the blood per 10 milliliters (ml/copies)

Chapter 1: Introduction, problem statement, research objectives and hypothesis

1.1 Introduction

The human immunodeficiency virus (HIV) is a retrovirus that attacks the cells of the immune system which it destroys or renders ineffective. In the early stages of infection, the individual does not exhibit symptoms. However, the evolution of the infection leads to a weakened immune system and an increased susceptibility to opportunistic infections such as tuberculosis, cancer, pneumonia or diarrhea [1,2]. The final stage of the HIV infection in a person is the Acquired immune deficiency syndrome (AIDS), which is a fatal clinical condition [3].

The HIV/AIDS pandemic is and continues to be a major global public health issue. Since the start of the epidemic to the end of 2021, 84.2 million (64.0 – 113.0 million) people have been infected with HIV and about 40.1 million (33.6 – 48.6 million) people have died of HIV [4]. In 2021, an estimated 38.4 million people were living with HIV worldwide, 1.5 million new infections were registered and 650,000 (510,000 – 860,000) deaths from AIDS-related illnesses were reported [4,5]. Despite efforts to prevent new infections and deaths, sub-Saharan Africa (SSA), bears the heaviest burden of HIV and AIDS with nearly 1 in every 25 adults (3.4%) living with HIV and accounting for more than two-thirds of people living with HIV worldwide [4,6]. Cameroon is one of the countries with a high prevalence of HIV in the West and Central African Sub Region [7]. The prevalence of HIV in this country stands at 3.4%, with 400,000 new cases of the disease but only 224,000 people living with HIV (PLWH) are on antiretroviral therapy in Cameroon [8].

Evidence informs that once people are diagnosed as HIV-positive, it is important to ensure that they can be effectively linked to care [9] and since no cure has been discovered yet, the only

modality of treatment to prolong life and to improve the quality of life of people living with HIV/AIDS at present is anti-retroviral therapy (ART) [10,11]. To be effective, ART has to be taken life-long with 100% adherence [12,13]. Poor or non-adherence – not taking ART every day and exactly as prescribed, can lead to drug resistance and treatment failure [14].

However, non-adherence to ART is still observed in SSA countries where the burden of the disease is high [15]. Some studies have reported that the patient, disease, therapy and relationship of patients with healthcare providers are associated with ART adherence issues [16,17]. Nevertheless, factors affecting non-adherence to HIV treatment are not well known especially in regions with insecurity as well as in a resource poor setting like Cameroon.

1.2 Problem statement

Cameroon is one of the countries in sub-Saharan Africa with a high prevalence of HIV [7]. HIV care decentralization has been enforced as a national policy in this country with few attempts to examine the performance of this policy and its role in preventing HIV [18]. Besides this, the follow-up of PLWH in Cameroon is provider oriented with little patient education and limited patient involvement in clinical monitoring [19]. Little is known about the proportion of PLWH who do not adhere to this kind of treatment in the country.

Furthermore, the healthcare system in Cameroon often experiences low access to drugs, inadequate staffing, coordination and management of commodities for HIV. A few studies have been done all in the capital city of the country (Yaoundé), assessing patients' adherence to ART and examining the socio-economic, clinical and psychological factors associated with self-reported ART interruption [15,20,21]. There is limited or no literature available on the socio-demographic/structural factors associated with non-adherence to HIV treatment in this country.

Finally, it is hard to find literature on the views of patients who have actually experienced non-adherence with HIV treatment as well as literature on age and regional trends in HIV treatment non-adherence in Cameroon. Thus, information for policy development to improve HIV control and management is limited.

To assess the prevalence and predictors of ART non-adherence and the barriers to ART adherence among PLWH that have experienced ART non-adherence in a resource-poor setting like Cameroon, this study explored the following specific objectives:

1.3 Specific research objective 1

To describe the barriers to ART adherence and the effective interventions proven to improve ART adherence in SSA countries.

Rationale: The burden of HIV lies heavily in SSA countries that often have weak healthcare systems and limited resources for HIV treatment. Reviewing common barriers to ART adherence and the effective interventions proven to improve ART adherence in these countries could help countries and organizations involved in the fight against HIV to design management policies that can be implemented in these countries to rapidly curb the pandemic.

Hypothesis: We hypothesize that there exist common barriers to ART adherence and common interventions that can be implemented to improve ART adherence across SSA countries.

1.4 Specific research objective 2

To determine the prevalence and predictors of HIV treatment non-adherence in PLWH in the Northwest, Southwest and Littoral regions of Cameroon.

Rationale: The prescription of HIV treatment or antiretroviral therapy (ART) as soon as someone is diagnosed HIV-positive and the maintenance of a patient on treatment daily as prescribed, is

necessary to avoid the development of drug resistance, treatment failure and patient mortality from HIV-related causes. Determining the socio-demographic/structural characteristics that predict non-adherence to ART will help stakeholders and personnel involved in management of patients derive effective strategies to deter patients' non-adherence to treatment. We will develop a predictive model for ART non-adherence in PLWH in Cameroon.

Hypothesis: We hypothesize that non-adherence to ART is prevalent in PLWH in Cameroon and that readily available socio-demographic/structural characteristics could be used to predict ART non-adherence. We further hypothesized that these characteristics could be used in guiding the development of policies and or management strategies that will keep patients on treatment.

1.5 Specific research objective 3

To assess the factors that influence non-adherence to HIV treatment in PLWH who have experienced HIV treatment non-adherence in Cameroon.

Rationale: ART is the only modality of treatment for HIV at present and taking it life-long with 100% adherence is necessary for it to be effective. Assessing the factors that drives non-adherence among PLWH that have actually experienced non-adherence to ART will help stakeholders and policy makers design policies that will ensure optimal ART adherence among patients taking ART thereby preventing treatment failure and development of drug resistance. We will use in-depth interviews to uncover the barriers to ART adherence in PLWH who have experienced ART non-adherence.

Hypothesis: We hypothesize that PLWH who have experienced ART non-adherence have specific barriers hindering them from adhering to treatment. We further hypothesize that these barriers

could be used in guiding stakeholders in deriving better management strategies that will make patients adhere to treatment.

1.6 Overview

To achieve these objectives, we conducted three distinct studies: a cross-sectional descriptive study of PLWH in HIV treatment centres in Cameroon who were interviewed on their demographic and structural characteristics and their experience with taking HIV treatment; a descriptive qualitative study of PLWH who had experienced non-adherence with HIV treatment in Cameroon; and a systematic review of barriers to ART adherence and effective interventions proven to improve ART adherence in SSA countries.

Chapter 2: Literature review

In this section, we present the burden of HIV, its pathogenesis and risk factors and the preventive and treatment measures. We then summarize the literature on HIV prevalence and predictors, barriers to HIV treatment adherence, interventions improving ART adherence and a theoretical/conceptual framework that explains ART adherence.

2.1 HIV/AIDS

2.1.1 Epidemiology

The acronym HIV refers to the human immunodeficiency virus – a retrovirus that attacks and destroys the cells of the immune system. A person infected with HIV exhibits no symptoms in the early stages of infection but as the infection evolves and progressively weakens the immune system, the infected individual's susceptibility to opportunistic infections such as tuberculosis, cancer, pneumonia or diarrhea is increased [1,2]. Following a weakened immune system in an HIV infected person is the Acquired Immune Deficiency Syndrome (AIDS) – a fatal clinical condition which is the final stage of the HIV infection in a person [3].

Globally, 84.2 million (64.0 – 113.0 million) people have become infected with HIV since the start of the epidemic. In 2021, an estimated 38.4 million people were living with HIV worldwide, 1.5 million new infections were registered and 650,000 (510,000 – 860,000) deaths from AIDS-related illnesses were reported [4,5]. Sub-Saharan Africa is the region with the heaviest burden of the pandemic, with nearly 1 in every 25 adults (3.4%) living with HIV and accounting for more than two-thirds of people living with HIV worldwide [4,6]. Women and girls are the most affected in this region and they accounted for 59% of all new HIV infections in the region in 2019, with 4500 adolescent girls and women 15 -24 years old becoming infected with HIV every week [22].

2.1.2 HIV pathogenesis and risk factors

When a person is infected with HIV, the virus targets the immune system and weakens the individual's defense against other infections. As the virus progressively destroys and impairs the functions of the immune cells, the infected individual becomes immunodeficient and his susceptibility to many infections, cancers and other diseases increases [23].

The HIV virus is transmitted primarily through blood, semen, genital fluids, or breast milk of infected persons and to new born infants from infected mothers [24]. Transmission of the virus occurs most commonly through heterosexual sex, sex between men, mother to child transmission and through exchange of blood products (by sharing needles and syringes for intravenous drug users and transfusion of infected blood) [25]. An individual cannot be infected through ordinary day-to-day contact such as kissing, hugging, shaking of hands or sharing personal objects or food or water. The factors that places an individual at greater risk of contracting HIV include having unprotected anal or vaginal sex; having another sexually transmitted infection such as syphilis, herpes, chlamydia, gonorrhea, and bacterial vaginosis; sharing contaminated needles, syringes and other injecting equipment and drug solutions when injecting drugs; receiving unsafe injections, blood transfusions, tissue transplantation, medical procedures that involve unsterile cutting or piercing; and experiencing accidental needle stick injuries, including among health workers [23]. In Cameroon, the risk factors responsible for the rapid spread of HIV include multiple sex partners, low use of condoms, low status of women (with few economic opportunities and great power differential with men, women do not have the power to demand safer sex), high prevalence of other sexually transmitted infections which facilitates HIV transmission through unprotected sexual relations, harmful socio-cultural practices and migration [26,27].

2.1.3 Management of HIV

Once people are diagnosed as HIV-positive, it is important to ensure that they can be effectively linked to care [28]. At present, no cure has been discovered yet, and the only modality of treatment to prolong life and to improve the quality of life of people living with HIV/AIDS (PLWHA) is anti-retroviral therapy (ART) [14,29]. ART has completely revolutionized the course of the HIV disease, transforming the HIV infection from a life-threatening infection to a manageable chronic condition [30]. ART prevents further replication or multiplication of the virus, reduces the patient's viral load, increases CD4 counts, reduces the patient's likelihood of opportunistic infections and hospitalizations, improves patient's quality of life and reduces mortality [10,11,31]. The increase in the patient's CD4 cell count allows the individual's immune system to recover and produce more CD4 cells which fights off infections and other HIV-related cancers [14]. To be effective, ARTs has to be taken life-long as prescribed, with 100% adherence [12,29]. Adherence to ART reduces the viral load in an individual's body, prevents treatment failure and the likelihood of the emergence of drug-resistant strains of the virus and also prevents further transmission of the virus to non-infected persons [14,32–34].

2.2 Review of previous studies

2.2.1 Studies on the prevalence and predictors of ART adherence in PLWH

Although ART enables immune recovery and improves survival in PLWH [33], most healthcare systems in SSA face numerous challenges emanating from scaling up ART for PLWHA. The most prominent of these challenges include suboptimal adherence to ART, poor retention in care and congestion of primary health care facilities [35]. In fact, a series of studies have been conducted on ART adherence and the prevalence of non-adherence have been reported ranging from 7.5% in Lesotho [36] to over 39% in Australia [30]. High levels of ART adherence have also been reported in other studies ranging from 62% [37] to over 95% [38]. Nevertheless, current information about

ART adherence in Cameroon is limited. The situation is hypothesized to be worse, given the COVID-19 pandemic and political crisis in the country which might further limit access to ART.

With regards to factors associated with non-adherence to ART, various studies have shown varied factors ranging from patient related factors (such as seeing positive results, fear of disclosure, being depressed); to beliefs about medications (e.g. side effects, faith on how well the drugs work); to daily schedules of patients (e.g. using reminder tools, disruption to routines); and to interpersonal relationships (e.g. trusting relations with health care providers, social isolation) [34]. Reported factors significantly associated with ART adherence include trust in medication, trust in healthcare system and interpersonal relationship with physicians and peers [37] and HIV status disclosure, drug dependency, health service satisfaction and perceive need for medical treatment [39]. Non-adherence with ART have been reported to be associated with side effects of the drugs, social isolation and complexity of the antiretroviral (ARV) regimens [40]; physical, economic and emotional stress [41]; poor or lack of ability to follow prescribed treatment, no visits in a month, anxious and or depressed mood, difficulty in taking medication, cannabis consumption and receiving methadone treatment [42]; and having an older age, being a female sex worker and having moderate-to-severe depression [43].

2.2.2 Studies on barriers to ART adherence and interventions improving ART adherence

The barriers to ART adherence have been established in some studies. The identified major obstacles to ART adherence include stigma, negative perception, lack of family and community support [44,45]. However, other factors such as disclosure of status, unemployment, lack of transport to go to the health facility for ART, insufficient feeding, inadequate follow ups, lack of patient confidentiality, lack of disability grants and alternative forms of therapy have also been reported as common barriers to ART adherence [45]. Besides these, physical, economic and

emotional stresses, travel from home, business with other things, depression, alcohol or drug use and ART dosing frequency have also been reported as barriers to adherence [41,46]. However, evidence is limited to the specific barriers to ART adherence that are common in all SSA and or low- and middle-income countries.

With regards to interventions improving ART adherence, it has been reported that patients on ART face multiple barriers to adherence, and no single intervention is sufficient to ensure optimal adherence. As such, health providers need to consider a series of approaches that first identifies patients at risk of poor adherence and then seeks to establish the support that is needed to overcome the barriers to adherence [47]. Some of the interventions include home-based nursing of patients on treatment, peer support for adolescents and the prescription of LPV/r-containing regimens [48]. Also, another study identified that cognitive behavioral interventions, education, treatment supporters, directly observed therapy and active adherence reminder devices (such as mobile phone text messages) are interventions that can increase patients adherence to ART [49]. However, literature on the specific interventions that are effective in improving adherence to ART in SSA countries is limited.

2.3 Theoretical/conceptual framework

A series of theories have attempted to conceptualize the phenomenon of ART adherence. Some of these theories include the Information-Motivation-Behavior, Social Action theory or the theory of planned behavior and Health behavior or Health belief model [50,51]. All these theories do not vividly explain why and how the elements they identify combine to explain adherence or non-adherence to ART, but they provide possible generative mechanisms that explain how and why patients adhere or not to ART [50]. However, most theories have identified motivation, self-efficacy, perceived social support, empowerment, perceived threat, perceived benefits, and

perceived barriers as elements that contribute to patients' adherence to ART [50,51]. The Health behavior model (HBM) usefully describes demographic and psychological factors that influence motivation and also identifies factors that perpetuates actual adherence behavior [50]. It is thus the best model that explains the conceptual framework of this study.

2.3.1 The Heath Behavior or belief Model (HBM)

The HBM was originally developed in the 1950s by social psychologists working with the United States (U.S) Public Health Service to explain why many people did not participate in health programs such as Tuberculosis (TB) and cervical cancer screening [52,53]. The model was subsequently extended by Leventhal, Rosenstock, Becker and others to explain varying reactions to disease symptoms and variations in adherence to treatment [53,54]. It has also been used to guide the design of interventions to improve compliance with preventive procedures used in patients with a wide variety of diseases [55]. The HBM suggests that people's beliefs about health problems, perceived benefits of action and barriers to action, and self-efficacy influence engagement or lack of engagement in health promoting behavior. For the health promoting behavior to be triggered, a stimulus or cue to action must be present [56].

Similar with HIV prevention programs such as condom use, delay of sexual debut and treatment of sexually transmitted infections, the wisdom associated with ART adherence is that given the facts and presented with alternatives, patients will adhere [51]. The HBM follows this approach and has conceptualized the beliefs and attitudes of an individual taking ART to represent perceived threats and net benefits [50]. In fact, for a patient on ART, HIV positive status, CD4 cell counts, and the quality of life constitute the health concern; the prospect of deterioration in health status leading ultimately to death is the perceived threat and factors such as stigma could be considered perceived barriers to treatment [51]. An individual's subjective assessments of the severity of the

consequences of non-adherence to ART, the personal risk of developing problems with regard to ART non-adherence, the value of adhering to ART and an assessment of the obstacles to taking the medication, represent possible mechanisms that could trigger an enforcement of adherence behavior [50,57,58]. Besides these, demographic variables and psychological characteristics of patients as well as the patient's readiness to be concerned about health matters are other important conditions that could trigger an enforcement of adherence behavior [50,59,60]. Specific to the management of HIV/AIDS, the HBM describes interactive states of belief that affects adherence to ART – perceived susceptibility, perceived seriousness, perceived benefits and perceived barriers [61].

Perceived susceptibility: perceived susceptibility of a disease makes an individual conscious of the fact that he could contract the disease [61,62]. Once an individual believes he is at risk of developing a disease, he is motivated to seek preventive medical care. In the case of HIV, an individual who was engaged in an activity placing him at risk of contracting the infection is likely to seek medical intervention [61], such as ART.

Perceived seriousness: this is the tendency of an individual to be proactive in the prevention of any disease perceived to be more serious. Combined with susceptibility, perceived seriousness of a disease forms a real threat to an individual [61,63]. With regards to HIV, perceived seriousness are consequences of the virus such as pain, disability, opportunistic infections, lifelong therapy on ARVs and death [61,64].

Perceived benefits: this is an individual's thoughts of the effectiveness of a given health behavior. A health behavior is perceived as effective if it results in an immediate benefit that is rapid and noticeable [62]. The immediate benefits of ART such as avoidance of opportunistic infections could motivate HIV infected individuals to adhere to the treatment.

Perceived barriers: these are the factors an individual perceives as obstacles to pursuing a given health action. These might include feelings that treatment (such as ART) takes too much time, requires much effort or it is difficult to obtain. An individual will adhere to a health action only when the perceived susceptibility is high and the perceived benefits of the action outweighs the perceived barriers [61,62].

Overall, in the context of adherence to ART, the HBM translates to the desire to achieve a good quality of life and the belief that adherence to ART will improve the patient's health; and this further influences the patient's adherence or not to treatment. An individual with a high perceived threat towards disease (HIV), low barriers to adopting healthy behaviors, and a high perceived benefit to action that will avoid disease has an increased likelihood of adhering to ART [50,53]. The conceptual framework of the HBM is clearly shown in Figure 1 below.

2.3.2 Conceptual framework

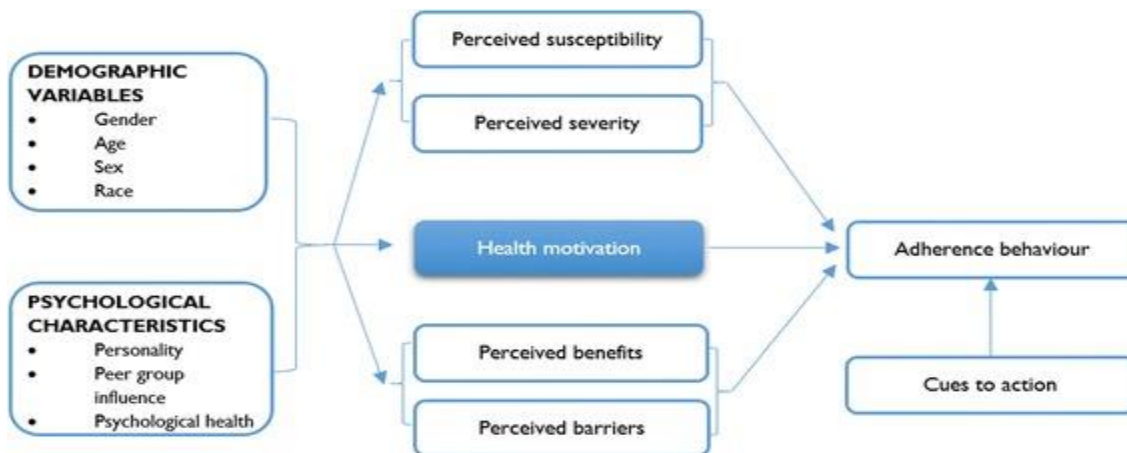


Figure 2. 1: *Health Belief Model*

Source: adapted from Munro and others [50,52,53,65].

Chapter 3: Methodology

3.1 Methods to assess the barriers to ART adherence and effective interventions proven to improve ART adherence in sub-Saharan Africa (SSA)

3.1.a Study design:

This was a systematic review of published studies that have assessed the barriers to ART adherence and interventions improving patients' adherence to ART in resource poor settings (SSA countries). This protocol was developed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) criteria [24].

3.1.b Inclusion criteria

To select appropriate studies for this review, we used the PICO (population, intervention, comparator and outcome) criteria. This allowed us to find and select the right studies that addressed our research questions. Our inclusion criteria therefore comprised:

Population:

This review included studies conducted between 2010 and 2023 on adult HIV-positive patients aged 15 or above in SSA.

Intervention:

All studies that assessed the barriers to ART adherence and or evaluated interventions aimed at improving ART adherence among adults PLWH in SSA were included in this review.

Comparator:

The interventions were in comparison with other strategies to identify the most effective and/or were in comparison to no strategies/interventions (regular basic management).

Outcomes:

The review included studies that assessed the following outcomes:

Primary outcome: Proportion of patients adhering to treatment following implementation of specific strategies.

Secondary outcomes: Proportion of patients retained in care, prevalence of opportunistic infections and or the worsening/severity of the patient's stage of HIV infection following specific treatment interventions. Included studies either measured viral load and or CD4 cell counts as an indication of the treatment adherence and efficacy.

Types of studies:

This review involved experimental and quasi-experimental studies. These included randomized and non-randomized controlled trials as well as comparative before and after studies, and observational studies (cross-sectional studies, case studies, case-control studies, cohort studies, prospective and retrospective studies). Only studies conducted between 2010 and 2023, in SSA, and involving adults 15 years and above were included in this review.

Language:

Only studies written in English and or French were included in this systematic review.

3.1.c Search strategy

A three-step strategy was used to find published studies on barriers to ART adherence and interventions improving adherence to ART among adult PLWH in SSA. An initial search through the Medline Ovid database was first conducted using an analysis of text words found in the title and abstract, and the index terms used in describing the article. Secondly, keywords and index terms were identified to search for studies in selected databases. Finally, additional studies not found in the databases were looked for using the reference list of selected studies from the first and second searches.

For this review, the databases that were searched included Medline Ovid, CINAHL, Embase, and Scopus. We also used databases such as Google scholar and Centres for Disease Control and Prevention (CDC) to search for unpublished studies.

The keywords we used for our initial searches in Medline Ovid included “ART”, “adherence”, “retention in care”, “non-adherence”, “barriers to ART adherence”, “adherence strategies”, “HIV”, “adults PLWH”, “sub-Saharan African countries”.

3.1.d Study screening and selection

Studies that were identified in searched databases were saved in Zotero and exported to the Covidence software for screening. The inclusion and exclusion criteria of this study was also imported to the Covidence software, and the software was used for title, abstract and full-text screening. After importing references and inclusion/exclusion criteria into the software, two independent reviewers screened titles of included studies following the eligible criteria. All conflicts between the two reviewers were resolved either through discussion or by a third reviewer. This same procedure was applied for abstract screening. After the abstract screening, full texts of potentially eligible studies were retrieved and independently assessed for eligibility by two reviewers. Any conflicts or disagreement between the two reviewers over the eligibility of a given study was resolved in a similar manner as for the title and abstract screening.

3.1.e Assessment of methodological quality

Two independent reviewers were used to assess the methodological validity of the studies that were selected for retrieval using standard critical appraisal tools from the Joanna Briggs Institute for Meta-Analysis of Statistics Assessment and Review Instrument (JBI-MASARI) (Appendix 1). Any disagreement between the two reviewers was settled through discussions or by a third reviewer.

3.1.f Data Extraction

Data was extracted from selected studies using a standardized data extraction tool from the Joanna Briggs Institute Meta-Analysis of Statistics Assessment and Review instrument (Appendix 2). The extracted data included specific details about the barriers to ART adherence, strategies or interventions improving ART adherence, study populations, study methods and outcomes significant to the review question and objective. In the event of any missing data from a study, the corresponding author of the study was contacted to provide the missing data. The data was independently extracted by two reviewers.

3.1.g Data synthesis

We conducted both a meta-analysis and a narrative synthesis of the various interventions improving ART adherence. The meta-analysis was done to identify the interventions with a significant impact in improving patients' adherence to ART. Nevertheless, we also did a narrative synthesis of the barriers to ART adherence in SSA.

For the meta-analysis, we first assessed the statistical heterogeneity with I^2 , which indicates the percentage of the total variation across studies; where 0% - 40% indicates low heterogeneity, 30% - 60% indicates moderate heterogeneity, 50% - 90% indicates substantial heterogeneity, and 75% - 100% indicates considerable heterogeneity. We also examined sources of heterogeneity through subgroup analyses. We used Chi-square test to test the heterogeneity and considered P-values < 0.05 as statistically significant. We selected a fixed-effects model for significant homogeneous studies; otherwise, we applied a random-effects model. All outcomes were summarized using odds ratios (OR) and 95% confidence intervals (CI). An OR<1 indicates a lower rate of outcome among the group of patients who were treated following a given intervention. Publication bias was assessed by visual inspections of funnel plots and Egger's test.

For the narrative synthesis, we described the barriers to ART adherence and the interventions promoting adherence to ART, following Popay's guidance on the conduct of a narrative synthesis [24]. The narrative synthesis was structured by describing the studies following the barriers assessed and the type of strategies used to improve ART adherence. The identified barriers to ART adherence and the interventions improving adherence were first presented in a table followed by detailed description of each ART adherence barrier and intervention promoting treatment adherence.

3.1.h Ethical considerations

This review used data that is published and available in the public domain. There was no primary data collection in the review and as such no ethical considerations were needed for the review. However, the study strictly adhered to the procedures outlined in this protocol in reviewing published and unpublished material in line with the review objectives. The protocol was registered with PROSPERO and also published in the Plos One journal.

3.2 Methods to determine the prevalence and predictors of HIV treatment non-adherence in PLWH in Cameroon.

3.2.a Study design and population

Study design: Cross-sectional descriptive study.

Study setting: The study was conducted in Cameroon – a country in sub-Saharan Africa with a high prevalence of HIV. The country has a population of over 28 million inhabitants [66], it is divided into ten regions and shares boundaries with Nigeria in the west, Chad in the north, Central African Republic in the east and Gabon, Equatorial Guinea, Congo in the south. Participants for the study were enrolled in HIV treatment centres in three selected regions (Littoral, Southwest and Northwest regions – all selected through balloting) in Cameroon. In each of the selected regions,

the study was conducted in only one HIV treatment centre that was purposefully selected based on probability proportionate to the size of patients registered in the centre. The centres were chosen such that on average, about 20% of PLWH and registered for ART in the centres were recruited per week in order to achieve the required sample size in a reasonable short period of time.

Study population: The study targeted PLWH and who were receiving ART in HIV treatment centres in the three selected regions of the country.

Selection criteria: To be eligible for the study, a participant had to be a patient living with HIV, receiving treatment or being followed up in a treatment centre within the country, be at least 21 years old, on treatment for at least six months and had consented to participate in the study.

Sample size consideration: We calculated the sample size using the formula for estimating the sample size of a single population proportion for a prevalence study of an infinite population [67]. We assumed the prevalence of non-adherence to ART in Cameroon was 50%; and with a margin of error of 5% at 95% confidence level, a sample size of 384 was determined using the formula:

$$n = \frac{z^2 p(1 - p)}{d^2}$$

Where n = sample size, Z = Z statistic for a level of confidence (1.96 at 95 % confidence level), P = assumed proportion of non-adherence to ART in Cameroon (50 %) and d = precision (5%).

However, we anticipated having a non-response rate of 10% from participants in the study. To account for this, we increased the 384-sample by 10% to have a sample size of 422. Overall, irrespective of the assumed proportion of non-adherence of 50% used to calculate our sample size, we enrolled a large enough sample of 451 participants that enabled us to estimate the prevalence of non-adherence to ART in our study.

3.2.b Study procedures

After obtaining ethical and administrative approvals to conduct this study, we trained six (6) interviewers (two from each of the three selected regions where the study was conducted) with a background training in health to collect our data. These interviewers ensured that study procedures and participant sampling were implemented correctly.

Sampling and participant recruitment: A multistage sampling technique was used to select participants for this study. Firstly, a list of all the ten regions of the country with HIV treatment centres and their corresponding populations of PLWH was made. Next, balloting was used to select three regions and in each selected region, the HIV treatment centre with the highest population of PLWH registered was further selected. The overall sample size was divided into three to obtain the number of participants to interview in each centre. Study interviewers used the systematic random sampling approach in each centre to recruit participants. After providing the usual care in each centre, clinicians referred selected patients to study interviewers who then explained the study to each eligible patient.

Data collection: Data for this study was collected within the period of November to December 2021. Prior to data collection, study interviewers obtained written informed consent from participants and then collected data on demographic/structural characteristics using a standardized ART adherence self-reported questionnaire adapted from similar studies [30,49,68–70]. Prior to data collection, the questionnaire was pretested in an ART treatment centre (not included in the study) in Cameroon. Data collection was monitored weekly in each centre and collected data was entered into an electronic questionnaire for further analysis.

3.2.c Data analysis

The collected data was entered into MS Access interface on Epi-info and analyzed using the statistical software program STATA version 14. The participants' socio-demographic/structural characteristics were described using frequencies and percentages for categorical variables and means, medians, ranges, and standard deviations for continuous variables.

To determine the proportion of participants who had not adhered to HIV treatment, the percentage of participants who reported having once missed treatment was computed. To investigate the socio-demographic/structural factors associated with non-adherence to HIV treatment, bivariate and multivariate analysis were done. The bivariate analysis comprised of using non-adherence to HIV treatment as a binary outcome variable and participants' socio-demographic/structural characteristics as predictors. Unadjusted odds ratios, 95% confidence intervals and P-values were computed and all variables having P-values ≤ 0.25 in the bivariate analysis were considered as having a possible association with non-adherence to HIV treatment [71]. For the multivariate analysis, non-adherence to HIV treatment was considered as a binary outcome variable and all variables with P-values ≤ 0.25 in the bivariate analysis were considered as predictors and included in the multivariate logistic regression model. Adjusted odds ratios, 95% confidence intervals and p-values were computed. All variables with p-values < 0.05 were considered to have a statistically significant association with non-adherence to HIV treatment. Results have been presented in tables and figures.

3.2.d Ethical considerations

Ethical clearance for the study was obtained from the Health Sciences and Science Research Ethics Board (REB) of the University of Ottawa (Ethics File Number: H-08-21-7274) and the Cameroon Baptist Convention Health Board Institutional Review Board (CBCHBIRB) (IRB study number: IRB2021-53). Administrative authorization was also obtained from the Regional Delegate of Public Health of the Southwest Region (Ref: 1211/MINSANTE/SWR/RDPH/P5/810/725) and the

Regional Hospital Buea (Ref /MPH/SWRDPH/BRH/IRB). Participation in the study was voluntary and written informed consent was obtained from all participants prior to the administration of the questionnaires. Names of participants were not recorded. Information collected from participants was kept confidential and participants were free to withdraw from the study at any moment if they so desired without being asked to give reasons and without incurring any penalties. No harmful procedures were involved in the study and the findings of the study were used strictly for the study's purpose and have been published.

3.2.e Limitations and strengths of study

Although we sampled participants in treatment centres, we acknowledge that the sample may not be representative of all PLWH in Cameroon as our sample was drawn from only three regions of the country. Furthermore, the study included only a cross section of PLWH in Cameroon. Thus, the prevalence of non-adherence we obtained reflects only the detection of cases of non-adherence in our study settings and not necessarily the incidence of non-adherence or the overall prevalence of non-adherence in the population. Participants' differences in access to HIV treatment may also have contributed to an increased prevalence of non-adherence to treatment in patients more likely not to visit treatment centres for their treatment. Again, there is the possibility of response bias as participants may not have revealed the truth of their past adherence to treatment history. There may equally be recall bias as participants may not have fully remembered whether they were non-adherent to HIV treatment or not.

Despite the limitations, the study was however strengthened by the fact that it was conducted in multiple randomly selected settings reflecting the diversity of patients in the country, interviewers were trained to ensure adequate data collection and primary data that ensures that questions pertaining to this study are directly ascertained were collected. Our statistical analysis also allowed

for a more accurate description of the prevalence trends of non-adherence and the factor more likely to be associated with non-adherence to HIV treatment in the context of Cameroon.

3.3 Methods to assess the barriers to ART adherence on PLWH who have experienced ART non-adherence in Cameroon.

3.3.a Study design and population

Study design: Exploratory, descriptive qualitative study.

Study setting: This is identical to the setting for objective 2, described in section 3.2.a above.

Study population: This study targeted only PLWH, who were receiving ART and who had experienced ART non-adherence in Cameroon.

Selection criteria: This is identical to the selection criteria for objective 2, described in section 3.2 above. In addition, only PLWH who had experienced HIV treatment non-adherence in Cameroon were eligible for this study.

PLWH who were severely sick, had poor mental health or other ailments or disabilities obstructing them from providing information requested by the study were excluded from the study.

Sample size: We anticipated up to 30 participants in each centre. However, the number of participants in this study was largely dependent on responses received from participants. As long as there was variation in participant opinions, more participants were recruited. Recruitment of new participants in each centre (after recruiting a minimum of 10 participants per centre) stopped once saturation was attained.

3.3.b Study procedures

Sampling and participant recruitment: These are identical to the selection criteria for objective 2, described in section 3.2.b above. In addition, only the PLWH who had experienced non-adherence with HIV treatment in any of the three centres were purposefully retained to participate in the study. This procedure continued until saturation was reached.

Data collection: Data was collected during the same period as in the cross-sectional study. Semi-structured in-depth interviews (IDIs) were conducted on PLWH who experienced non-adherence with ART. Open ended questions adapted from similar studies [72,73], were used to collect data on participants' perceptions about factors contributing to their non-adherence to ART. The interviews were conducted in French or English by trained interviewers. All interviews were conducted in an arranged office in each treatment centre and participants' responses to questions were recorded.

Prior to analysis, the audio-recorded data were transcribed word verbatim and coded into common themes with the assistance of translators. This was cross-checked by other data collectors and the principal investigator for consistency, just to ensure that strict methodological rigor was followed. The data were further analyzed using the NVIVO version 12 software.

3.3.c Data analysis

The collected data were analyzed using the NVIVO 12 software. Content analysis was done by transcribing and coding the collected data into sub-themes and themes following the Braun & Clarke's [74] guide for conducting a thematic analysis. This guide was used because it enabled a transparent and rigorous analysis that produced pertinent information required for this study. Two researchers independently read the transcripts repeatedly to get immersed into the raw data and made note of initial topics and ideas relevant to the research question. The transcripts were coded in an iterative manner, revisiting the transcripts and altering and modifying the codes as reflected by the data and the emerging patterns. As coding word-by-word or line-by-line reduces the ability

to see patterns among and between pieces of data [75], lines of text from transcripts were broadly coded, ranging from a sentence to several sentences such that intentions from the participants' views were not lost. In the end, the two independent coders discussed their codes and resolved any differences by reaching a consensus agreement. Themes and subthemes were then developed from the codes to respond to study objectives. The sub-themes were grouped under major themes and then, a description of the various themes was made.

3.3.d Trustworthiness

In conducting a qualitative study, trustworthiness is very crucial to ensure that the study is rigorous and that it produces findings capable of impacting policy and practice [76]. To ensure trustworthiness in this study, trained personnel were recruited to collect data, transcribed it, code it and analyze it. The primary investigator closely monitored the data collection process to ensure that data was properly collected. Following data collection, two independent individuals transcribed and coded the data and then discussed their codes together in order to reconcile any differences. The primary investigator and his supervisor then reviewed the coded data in order to validate it and ensured that the codes and themes resulting from the transcripts were credible. Any issues such as contradictions, thematic misinterpretations and factual errors discovered by the primary investigator and his supervisor were discussed and clarifications made. An external auditor skillful in qualitative research together with the primary investigator's supervisor reviewed the coded data to further ensure dependability.

Also, to ensure that findings reflected the reality of the barriers to ART adherence, data were only collected from people who had actually experienced ART non-adherence. The data were collected across three regions of the country and this data triangulation helped enrich and deepened understanding of study findings.

3.3.e Positionality and partnership

A researcher's identities and biases can shape aspects of a research process. To perceive how this can occur, it is important to examine the researcher's positionality [77]. For all the influences a researcher can exert on a research process, the awareness of his/her positionality makes the researcher strive to avoid obvious, conscious or systematic biases in the research process and enables him/her to be as neutral as possible in the collection, interpretation and presentation of data [78].

This study was conducted in three different regions of Cameroon and just the uniqueness of each region poses challenges and opportunities that necessitates the exploration of the role of the researcher in generating data for this study. The identity of the primary investigator (citizen of Cameroon) affected his engagement in this research process in various ways. Firstly, as a citizen, the primary investigator knew the country, and this facilitated his movement to and from the various study sites prior to and during data collection. Secondly, the primary investigator had prior study and work experience in all the three study regions of the country where the study was conducted. Thus, his familiarity with traditional cultural norms, health institutions offering HIV care and administrative procedures in these regions facilitated access to stakeholders involved in HIV care with whom he collaborated in the implementation of study procedures as well as the dissemination of study findings. Thirdly, the primary investigator as a citizen, understood the official and commonly used languages in the study regions – this eased his direct communication with people throughout the research implementation process.

Despite the above advantages, a serious challenge that awaited the researcher was the fact that he is studying abroad. With this awareness, it was likely that most participants will believe that the researcher had much money and should pay them and or provide them with incentives for them to participate in the study. To avoid this, recruitment of participants and data collection in this study was done by trained data collectors. This prevented the researcher meeting participants and

influencing some aspects of the research implementation process. Also using the data collectors fostered the development of a network through which the researcher will continue to work in collaboration with even when the research ends.

3.3.f Ethical considerations

This is identical with the ethical considerations presented in section 3.2.d above.

3.3.g Limitations and strengths of study: The study included only a cross section of PLWH that showed up at the treatment centre and admitted that they had not been adherent to treatment. This might not be representative of the population of patients that do not adhere to treatment in the country. Thus, results of the study may not be generalizable to other communities out of Cameroon. Again, there is the possibility of response bias as participants may not have revealed the truth of their past adherence to treatment history. There may equally be recall bias as participants may not have fully remembered whether they had been non-adherent to HIV treatment or not.

Nonetheless, the strengths of the study are that it was conducted in multiple randomly selected settings reflecting the diversity of patients in the country, interviewers were trained to ensure adequate data collection and primary data that insured that questions pertaining to this study are directly ascertained were collected not just from PLWH but precisely from those that had experienced non-adherence with ART.

Chapter 4: Adherence barriers and interventions to improve ART adherence in Sub-Saharan African countries: a systematic review protocol

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4.1 Abstract

Background: The HIV/AIDS pandemic continues to be a major public health concern, particularly in Sub-Saharan Africa (SSA). Despite efforts to reduce new infections and deaths with the use of antiretroviral therapy (ART), SSA countries continue to bear the heaviest burden of HIV/AIDS globally, accounting for two-thirds of global new infections. The goal of this review is to identify common barriers to ART adherence as well as common effective interventions that can be implemented across SSA countries to improve ART adherence.

Methods: A systematic review of published studies on adult HIV-positive patients aged 15 or above, that have assessed the barriers to ART adherence and interventions improving patients' adherence to ART in SSA countries shall be conducted. We will conduct electronic searches for articles that have been published starting from January 2010 onwards. The databases that shall be searched will include Medline Ovid, CINAHL, Embase, and Scopus. The review will include experimental and quasi-experimental studies such as randomized and non-randomized controlled trials as well as comparative before and after studies, and observational studies - cross-sectional studies, cohort studies, prospective and retrospective studies. Two independent reviewers will screen all identified studies, extract data and appraise the methodological quality of the studies

using standard critical appraisal tools from the Joanna Briggs Institute. The extracted data will be subjected to a meta-analysis and narrative synthesis.

Discussion: This review will synthesize existing evidence on ART adherence barriers and strategies for improving patient adherence to ART in SSA countries. It will identify common barriers to adherence and common interventions proven to improve adherence across SSA. We anticipate that the findings of this review will provide information policy makers and stakeholders involved in the fight against HIV, will find useful in deriving better ways of not only retaining patients on treatment but having them adhere to their treatment.

Review registration: This protocol has been registered with the International Prospective Register of Systematic Reviews (PROSPERO); registration number CRD42021262256.

4.2 Introduction

The HIV/AIDS pandemic remains a significant global public health issue. From the beginning of the epidemic to the end of 2019, 75.7 million people (55.9 million – 100 million) have been infected with HIV [1]. In 2019, an estimated 38.0 million people worldwide were living with HIV, 1.7 million new infections occurred, and 690,000 (500,000 - 970,000) deaths from AIDS-related illnesses were reported [1,2]. Despite efforts to reduce new infections and deaths, Sub-Saharan Africa (SSA) bears the world's heaviest burden of HIV and AIDS, accounting for two-thirds of global new infections and 25.7 million HIV-positive people [3].

Evidence suggests that once people are diagnosed with HIV, it is critical to ensure that they are effectively linked to care [4]. At the moment, no cure has been discovered, and anti-retroviral therapy (ART) is the only treatment modality available to prolong life and improve the quality of life of people living with HIV/AIDS (PLWHA) [5,6]. ART has completely changed the course of HIV disease, transforming it from a potentially fatal infection to a manageable chronic condition

[7]. ART prevents further virus replication or multiplication, lowers the patient's viral load, raises CD4 counts, lowers the patient's risk of opportunistic infections and hospitalizations, improves the patient's quality of life, and lowers mortality [8–10]. The increase in the patient's CD4 cell count allows the individual's immune system to recover and produce more CD4 cells which fights off infections and other HIV-related cancers [1]. To be effective, ARTs has to be taken life-long as prescribed, with 100% adherence [2,3]. Adherence to ART reduces the viral load in an individual's body, prevents treatment failure and the likelihood of the emergence of drug-resistant strains of the virus and also prevents further transmission of the virus to non-infected persons [1,4–6]. Poor or non-adherence – not taking ART every day and exactly as prescribed, can lead to drug resistance and treatment failure [1].

Although ART enables immune recovery and improves survival in PLWH [5], most healthcare systems in SSA face numerous challenges emanating from scaling up ART for PLWHA. The most prominent of these challenges include suboptimal adherence to ART, poor retention in care and congestion of primary health care facilities [7]. These challenges might contribute to the continuous observance of non-adherence to ART in SSA countries where the burden of the disease is high [8]. Some studies have reported that the patient, disease, therapy and relationship of patients with healthcare providers are associated with ART adherence issues [9,10]. Other studies have identified that, the major barriers to ART adherence include stigma, negative perception, lack of family and community support [11,12]. Other factors that have been reported as common barriers to ART adherence include disclosure of status, unemployment, a lack of transportation to the health facility for ART, insufficient feeding, inadequate follow-ups, a lack of patient confidentiality, disability grants, and alternative forms of therapy [12]. Physical, economic, and emotional stress, travel away from home, business with other things, depression, alcohol or drug

use, and ART dosing frequency have all been identified as barriers to adherence [13,14]. Nonetheless, evidence on the specific barriers to ART adherence that are common in all SSA countries is limited.

With regards to ART adherence interventions, it has been reported that patients on ART face multiple barriers to adherence, and no single intervention is sufficient to ensure optimal adherence. As a result, health providers should consider a series of approaches that first identify patients at risk of poor adherence and then seek to establish the support needed to overcome adherence barriers [15]. Home-based nursing of patients on treatment, peer support for adolescents, and the prescription of LPV/r-containing regimens are among the interventions [16]. Another study found that cognitive behavioural interventions, education, treatment supporters, directly observed therapy, and active adherence reminder devices (such as mobile phone text messages) can help patients stick to their ART regimen [17]. However, there is a scarcity of literature on common specific interventions that are effective in improving adherence to ART in SSA countries.

Given that the HIV burden is disproportionately concentrated in SSA countries, which frequently have underdeveloped healthcare systems and limited resources for HIV treatment. Reviewing common barriers to ART adherence and effective interventions proven to improve ART adherence in these countries could assist countries and organizations involved in the fight against HIV in SSA in developing management policies that can be implemented in these countries to quickly curb the pandemic. As a result, the purpose of this review is to answer the question, "What are the common barriers to ART adherence, and what are the common effective interventions that can be implemented to improve ART adherence across SSA countries?"

4.3 Methods

4.3.1 Study design

This will be a systematic review of published studies that examined the barriers to ART adherence and interventions that improved patients' adherence to ART in resource-limited settings (SSA countries). The Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) criteria (Appendix 1) were used to develop this protocol[18]. We will use the PRISMA diagram (Appendix 2) to show how studies for this review shall be selected.

4.3.2 Inclusion criteria

To select appropriate studies for this review, we will use the PICO (population, intervention, comparator, and outcome) criteria. This will allow us to find and select the right studies that can address our research questions. Our inclusion criteria will therefore comprise:

Population:

This review will include studies conducted between 2010 and 2022 on adult HIV-positive patients aged 15 or above in SSA.

Intervention:

All studies that assessed the barriers to ART adherence and or evaluated interventions aimed at improving ART adherence among adults PLWH in SSA shall be included in this review.

Comparator:

The interventions may be in comparison with other strategies to identify the most effective and/or may be in comparison to no strategies/interventions (regular basic management).

Outcomes:

The review will include studies that assessed the following outcomes:

Primary outcome: Proportion of patients adhering to treatment following implementation of specific strategies.

Secondary outcomes: Proportion of patients retained in care, prevalence of opportunistic infections and or the worsening/severity of the patient's stage of HIV infection following specific treatment interventions. Included studies must measure viral load and CD4 cell counts as an indication of the treatment adherence and efficacy.

Types of studies:

This review will include experimental and quasi-experimental studies such as studies with controlled interventions that have assessed barriers to ART adherence and interventions improving ART adherence in SSA countries. These will include randomized and non-randomized controlled trials as well as comparative before and after studies, and observational studies (cross-sectional studies, cohort studies, prospective and retrospective studies). Only studies conducted between 2010 and 2022, in SSA, and involving adults 15 years and above shall be included in this review.

Language:

Only studies written in English and or French will be included in this systematic review.

4.3.3 Search strategy

A three-step strategy shall be used to find published studies on barriers to ART adherence and interventions improving adherence to ART among adult PLWH in SSA. An initial search through the Medline Ovid database shall first be conducted using an analysis of text words found in the title and abstract, and the index terms used in describing the article. Secondly, keywords and index terms shall be identified to search for studies in selected databases. Finally, additional studies not found in the databases shall be looked for using the reference list of selected studies from the first and second searches.

For this review, the databases that shall be searched will include Medline Ovid, CINAHL, Embase, and Scopus. We will also use search engines and directories such as Google scholar and Centres for Disease Control and Prevention (CDC) to search for unpublished studies.

Some of the keywords we have used for our initial searches in Medline Ovid include *“ART”*, *“adherence”*, *“retention in care”*, *“non-adherence”*, *“barriers to ART adherence”*, *“adherence strategies”*, *“HIV”*, *“adults PLWH”*, *“sub-Saharan African countries”* (Appendix 3).

4.3.4 Study screening and selection

Studies that shall be identified in searched databases shall be saved in Zotero and exported to the Covidence software for screening. The inclusion and exclusion criteria of this study shall also be imported to the Covidence software, and the software will be used for title, abstract and full-text screening. After importing references and inclusion/exclusion criteria into the software, two independent reviewers will screen titles of included studies following the eligible criteria. All conflicts between the two reviewers will be resolved either through discussion or by a third reviewer. This same procedure will be applied for abstract screening. After the abstract screening, full texts of potentially eligible studies shall be retrieved and independently assessed for eligibility by two reviewers. Any conflicts or disagreement between the two reviewers over the eligibility of a given study shall be resolved in a similar manner as for the title and abstract screening.

4.3.5 Assessment of methodological quality

Two independent reviewers shall be used to assess the methodological validity of the studies that shall be selected for retrieval using standard critical appraisal tools from the Joanna Briggs Institute for Meta-Analysis of Statistics Assessment and Review Instrument (JBI-MASARI) (Appendix 4). Any disagreement between the two reviewers shall be settled through discussions or by a third reviewer.

4.3.6 Data Extraction

Data shall be extracted from selected studies using a standardized data extraction tool from the Joanna Briggs Institute Meta-Analysis of Statistics Assessment and Review instrument (Appendix 5). The extracted data shall include specific details about the barriers to ART adherence, strategies or interventions improving ART adherence, study populations, study methods and outcomes significant to the review question and objective. In the event of any missing data from a study, the corresponding author of the study shall be contacted to provide the missing data. The data shall be independently extracted by two reviewers.

4.3.7 Data synthesis

If we end up with many studies (10 or more), we will conduct both a meta-analysis and a narrative synthesis of the various interventions improving ART adherence. The meta-analysis will be done to identify the interventions with a significant impact in improving patients' adherence to ART. However, if we end up with few studies, we will just do a narrative synthesis of the barriers to ART adherence and the interventions improving adherence in SSA.

For the meta-analysis, we will first assess the statistical heterogeneity with I^2 , which indicates the percentage of the total variation across studies; where 0% - 40% indicates low heterogeneity, 30% - 60% indicates moderate heterogeneity, 50% - 90% indicates substantial heterogeneity, and 75% - 100% indicates considerable heterogeneity. If there is a substantial amount of heterogeneity (75%), then sources of heterogeneity will be examined through subgroup and sensitivity analyses. We will also use Chi-square test to test the heterogeneity and consider P-values < 0.05 as statistically significant. We will select a fixed-effects model for significant homogeneous studies; otherwise, we will apply a random-effects model. All outcomes will be summarized using odds ratios (OR) and 95% confidence intervals (CI). An OR<1 will indicate a lower rate of outcome

among the group of patients who were treated following a given intervention. Publication bias will be assessed by visual inspections of funnel plots and Egger's test.

For the narrative synthesis, we will describe the barriers to ART adherence and the interventions promoting adherence to ART, following Popay's guidance on the conduct of a narrative synthesis[19]. The narrative synthesis shall be structured by describing the studies following the barriers assessed and the type of strategies used to improve ART adherence. The identified barriers to ART adherence and the interventions improving adherence shall first be presented in a table followed by detailed description of each ART adherence barrier and intervention promoting treatment adherence.

4.3.8 Confidence in Cumulative Evidence

The quality of evidence that shall be used in this review will be assessed by the Grades of Recommendation, Assessment, Development and Evaluation (GRADE)[20].

4.4 Discussion

This review will synthesize existing evidence on ART adherence barriers and strategies for improving patient adherence to ART in SSA countries. We acknowledge that other reviews have been done in this area although with some limitations - some of the reviews are a little old, some have limitations in methods, and some included only articles published in English. For instance, in 2008, a review was published on barriers to access to antiretroviral treatment in developing countries. This review included articles published between 1996 and 2007 and only included articles published in English from the PubMed, FamMed and Cochrane databases [21]. In 2012, another review on adherence to ART in Cameroon described the trend in adherence rates and factors associated with adherence. This review included only studies conducted in one SSA country - Cameroon from January 1999 to May 2012 [22]. In yet another study assessing the

effectiveness of treatment supporter interventions in ART adherence in sub-Saharan Africa, only studies published in English from 2003 to February 2019 were included in the review [23]. Finally, another review on interventions to improve adherence in sub-Saharan Africa only included published articles from the PubMed, Medline and Google Scholar databases [24]. All these reviews likely missed studies not found in the few accessed databases and those published in French.

In view of the limitations of the above published reviews, this review will include articles published in SSA countries from 2010 onward, in both English and French, and searches will be done in more databases than previous studies. It will identify recent evidence on common adherence barriers and common interventions that have been shown to improve adherence across SSA. We anticipate that the findings of this review will provide information that policymakers and stakeholders involved in the HIV fight will find useful in devising better ways to help patients adhere to ART. This protocol is an original systematic review protocol; any changes must be documented and updated in PROSPERO, as well as stated in the final review manuscript. The review findings will be published in a peer-reviewed journal at the conclusion of this study.

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Chapter 5: Barriers and facilitators for interventions to improve ART adherence in Sub-Saharan African countries: a systematic review and meta-analysis.

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5.1 Abstract

Background: The HIV/AIDS pandemic remains a significant public health issue, with sub-Saharan Africa (SSA) at its epicentre. Although antiretroviral therapy (ART) has been introduced to decrease new infections and deaths, SSA reports the highest incidence of HIV/AIDS, constituting two-thirds of the global new infections. This review aimed to elucidate the predominant barriers and facilitators influencing ART adherence and to identify effective strategies to enhance ART adherence across SSA.

Methods: A comprehensive review was conducted on studies examining barriers to ART adherence and interventions to boost adherence among HIV-positive adults aged 15 and above in SSA, published from January 2010 onwards. The research utilized databases like Medline Ovid, CINAHL, Embase, and Scopus. Included were experimental and quasi-experimental studies, randomized and non-randomized controlled trials, comparative before and after studies, and observational studies such as cross-sectional, cohort, prospective and retrospective studies. Two independent reviewers screened the articles, extracted pertinent data, and evaluated the studies' methodological integrity using Joanna Briggs Institute's standardized appraisal tools. The compiled data underwent both meta-analysis and narrative synthesis.

Results: From an initial pool of 12,538 papers, 45 were selected (30 for narrative synthesis and 15 for meta-analysis). The identified barriers and facilitators to ART adherence were categorized into seven principal factors: patient-related, health system-related, medication-related, stigma, poor mental health, socioeconomic and socio-cultural-related factors. Noteworthy interventions enhancing ART adherence encompassed counselling, incentives, mobile phone short message service (SMS), peer delivered behavioural intervention, community ART delivery intervention, electronic adherence service monitoring device, lay health worker lead group intervention and food assistance. The meta-analysis revealed a statistically significant difference in ART adherence between the intervention and control groups (pooled OR=1.56, 95%CI:1.35 - 1.80, $p < 0.01$), with evidence of low none statistically significant heterogeneity between studies ($I^2 = 0 \%$, $p = 0.49$).

Conclusion: ART adherence in SSA is influenced by seven key factors. Multiple interventions, either standalone or combined, have shown effectiveness in enhancing ART adherence. To optimize ART's impact and mitigate HIV's prevalence in SSA, stakeholders must consider these barriers, facilitators, and interventions when formulating policies or treatment modalities. For sustained positive ART outcomes, future research should target specific underrepresented groups like HIV-infected children, adolescents, and pregnant women in SSA to further delve into the barriers, facilitators and interventions promoting ART adherence.

5.2 Introduction

The HIV/AIDS pandemic remains a pervasive global public health challenge. From the epidemic's inception until the close of 2021, approximately 84.2 million individuals (range: 64.0 – 113.0 million) contracted HIV, resulting in an estimated 40.1 million deaths (range: 33.6 – 48.6 million) due to the virus [1]. In 2021 alone, there were 38.4 million people living with HIV, 1.5 million new infections, and between 510,000 and 860,000 AIDS-related deaths [1,2]. Sub-Saharan Africa

(SSA), or the World Health Organization (WHO) African region, continues to bear the heaviest HIV/AIDS burden. Here, nearly 1 in every 25 adults (3.4%) is living with HIV, comprising over two-thirds of the global HIV population [1,3].

After an HIV diagnosis, timely and effective linkage to care is pivotal [4,5]. Currently, there is no cure for HIV. Anti-retroviral therapy (ART) remains the sole treatment that can enhance the lifespan and life quality of people living with HIV/AIDS (PLWHA) [5,6]. ART has revolutionized the management of HIV, transforming a once-fatal disease into a manageable chronic condition [7]. This therapy inhibits the virus' replication, reduces the patient's viral load, increases CD4 counts, and thus decreases the patient's risk of opportunistic infections and hospitalizations. This boosts a patient's quality of life and reduces mortality [8–10]. As the patient's CD4 counts rises, their immune system is rejuvenated, effectively combating infections and HIV-related cancers [6]. For ART to be effective, it must be consistently taken as prescribed [5,7–9]. When properly adhered to, ART minimizes the individual's viral load, prevents drug resistance, reduces the risk of transmission, and lowers treatment failure rates [6,10–12]. Conversely, inconsistent adherence can lead to drug resistance and compromised treatment efficacy [6].

Despite ART's potential benefits - enabling immune recovery and improving survival in PLWH [11], healthcare systems across SSA grapple with multiple challenges in scaling up ART provision. Key issues include suboptimal ART adherence, poor retention of PLWHA in care, and overloaded primary health care facilities [13]. Such challenges might be contributing to observed ART non-adherence, particularly in regions with high disease prevalence [14]. Research has indicated that patient factors, the nature of the disease, treatment modalities, and the patient-healthcare provider relationship can impact adherence [15,16]. Notable barriers encompass stigma, negative perceptions, lack of family and community support, status disclosure issues, unemployment,

transportation challenges, insufficient nutrition, inadequate follow-ups, confidentiality concerns, and dependency on alternative therapies [17,18]. Also, physical, economic, and emotional stress, travel away from home, business with other things, depression, alcohol or drug use, and ART dosing frequency have all been identified as barriers to adherence [19,20]. On the positive side, several facilitators to ART adherence have been documented, including social support [21,22], HIV status disclosure, health improvement due to ART, use of reminder aids and receiving education and counselling [21,23]. Community knowledge and understanding of the HIV infection, increasing collaboration between Western and Traditional providers, peer and family level support, decreasing cost and distance to ART clinic [24] as well as clear instructions for taking ART, service providers' positive attitude towards patients, benefits of adhering to ART and dangers of defaulting [23] have also been documented as factors facilitating ART adherence. Despite this plethora of research, comprehensive insights into the predominant barriers and facilitators common across all SSA countries remain sparse.

Patients on ART frequently face multifaceted barriers to consistent adherence, implying that a single intervention strategy may not suffice. Healthcare providers are thus encouraged to adopt a multifaceted approach - identifying at-risk patients and then tailoring support to address specific adherence obstacles [25]. Documented interventions include home-based care, peer support, and specific treatment regimens [26]. Also, cognitive behavioural interventions, education, treatment supporters, directly observed therapy, and active adherence reminder devices (such as mobile phone text messages) can help patients stick to their ART regimen [27]. However, comprehensive data on interventions universally effective across SSA is scanty.

Considering the acute HIV burden in SSA, coupled with often under-resourced healthcare systems, understanding common barriers to and effective interventions for ART adherence is vital. Such

insights can aid countries and organizations in framing effective strategies to curtail the pandemic in the region. This review, therefore, sought to pinpoint the prevalent barriers and facilitators influencing ART adherence and to unearth universally effective interventions that could enhance ART adherence across SSA.

5.3 Methods

5.3.1 Study design

This was a systematic review and meta-analysis of published studies that examined the barriers and facilitators to ART adherence and interventions that improved patients' adherence to ART in SSA countries. The review is reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) criteria [28]. The review's protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO number CRD42021262256) and published in the Plos One journal [5].

5.3.2 Inclusion criteria

To select appropriate studies for this review, we used the PICO (population, intervention, comparator, and outcome) criteria. This allowed us to find and select the right studies that can address our research questions. Our inclusion criteria therefore comprised:

Population:

This review included studies conducted between 2010 and 2023 on adult HIV-positive patients aged 15 or above in SSA.

Intervention:

All studies that assessed the barriers and facilitators to ART adherence and/ or evaluated interventions aimed at improving ART adherence among adults PLWH in SSA were included in this review.

Comparator:

The interventions were either in comparison with other strategies to identify the most effective and/or were in comparison to no strategies/interventions (regular basic management).

Outcomes:

The review included studies that assessed the following outcomes:

Primary outcome: Proportion of patients adhering to treatment following implementation of specific strategies.

Secondary outcomes: Proportion of patients retained in care, prevalence of opportunistic infections and or the worsening/severity of the patient's stage of HIV infection following specific treatment interventions. Included studies measured viral load and CD4 cell counts as an indication of the treatment adherence and efficacy.

Types of studies:

This review encompassed both experimental and quasi-experimental studies from SSA that evaluated barriers to ART adherence and interventions aimed at enhancing such adherence. Included studies consisted of randomized and non-randomized controlled trials, comparative pre-and-post studies, and various observational studies such as cross-sectional, cohort, prospective and retrospective investigations. The scope of this review was limited to studies conducted between 2010 and 2023 and involved adult participants aged 15 years and older.

Language:

Only studies written in English and or French were included in this systematic review.

5.3.3 Search strategy

A three-step strategy was used to find published studies on barriers to ART adherence and interventions improving adherence to ART among adult PLWH in SSA. An initial search through the Medline Ovid database was first conducted using an analysis of text words found in the title and abstract, and the index terms used in describing the article. Secondly, keywords and index terms were identified to search for studies in selected databases. Finally, additional studies not found in the databases were looked for using the reference list of selected studies from the first and second searches.

For this review, the databases that were searched included Medline Ovid, CINAHL, Embase, and Scopus. We also used search engines and directories such as Google scholar and Centres for Disease Control and Prevention (CDC) to search for unpublished studies.

Some of the keywords we used for our initial searches in Medline Ovid included “*ART*”, “*adherence*”, “*retention in care*”, “*non-adherence*”, “*barriers to ART adherence*”, “*adherence strategies*”, “*HIV*”, “*adults PLWH*”, “*sub-Saharan African countries*”.

5.3.4 Study screening and selection

Studies that were identified in searched databases were saved in Zotero and exported to the Covidence software for screening. The inclusion and exclusion criteria of this study was also imported to the Covidence software, and the software was used for title, abstract and full-text screening. After importing references and inclusion/exclusion criteria into the software, two independent reviewers screened titles of included studies following the eligible criteria. All conflicts between the two reviewers were resolved either through discussion or by a third reviewer. This same procedure was applied for abstract screening. After the abstract screening, full texts of potentially eligible studies were retrieved and independently assessed for eligibility by two

reviewers. Any conflicts or disagreement between the two reviewers over the eligibility of a given study were resolved in a similar manner as for the title and abstract screening.

5.3.5 Assessment of methodological quality

Two independent reviewers were used to assess the methodological validity of the studies that were selected for retrieval using standard critical appraisal tools from the Joanna Briggs Institute for Meta-Analysis of Statistics Assessment and Review Instrument (JBI-MASARI). Any disagreement between the two reviewers was settled through discussions or by a third reviewer.

5.3.6 Data Extraction

Data was extracted from selected studies using a standardized data extraction tool from the Joanna Briggs Institute Meta-Analysis of Statistics Assessment and Review instrument. The extracted data included specific details about the barriers to ART adherence, strategies or interventions improving ART adherence, study populations, study methods and outcomes significant to the review question and objective. In the event of any missing data from a study, the corresponding author of the study was contacted to provide the missing data. The data were independently extracted by two reviewers.

5.3.7 Data synthesis

We conducted both a meta-analysis and a narrative synthesis of the various interventions improving ART adherence. The meta-analysis was done to identify the interventions with a significant impact in improving patients' adherence to ART.

For the meta-analysis, we first assessed the statistical heterogeneity with I^2 , which indicates the percentage of the total variation across studies; where 0% - 40% indicates low heterogeneity, 30% - 60% indicates moderate heterogeneity, 50% - 90% indicates substantial heterogeneity, and 75%

- 100% indicates considerable heterogeneity. If there was a substantial amount of heterogeneity (75%), then sources of heterogeneity were examined through subgroup and sensitivity analyses. We also used Chi-square test to test the heterogeneity and consider P-values < 0.05 as statistically significant. We selected a fixed-effects model for significant homogeneous studies; otherwise, we applied a random-effects model. All outcomes were summarized using odds ratios (OR) and 95% confidence intervals (CI). An OR<1 indicated a lower rate of outcome among the group of patients who were treated following a given intervention. Publication bias was assessed by visual inspections of funnel plots and Egger's test.

For the narrative synthesis, we have described the barriers and facilitators to ART adherence and the interventions promoting adherence to ART, following Popay's guidance on the conduct of a narrative synthesis [29]. The narrative synthesis has been structured by describing the studies following the barriers and facilitators assessed and the type of strategies used to improve ART adherence. The identified barriers and facilitators to ART adherence and the interventions improving adherence have first been presented in a table followed by detailed description of each ART adherence barrier and or facilitator and intervention promoting treatment adherence.

Confidence in Cumulative Evidence

The quality of evidence used in this review was assessed by the Grades of Recommendation, Assessment, Development and Evaluation (GRADE)[30].

5.4 Results

5.4.1 Characteristics of Included Studies

Twelve thousand five hundred and thirty-eight (12538) potential papers were identified for this study. After screening the titles and abstracts, 435 papers were selected for retrieval. When the papers were reviewed, 47 of the 435 papers retrieved for full text screening were found to fully meet our inclusion criteria. The papers were critically appraised using the JBI-MAsARI critical appraisal tool by two independent reviewers and 2 papers were further excluded due to missing outcome measures for different arms of the study. Only 45 papers (30 for narrative synthesis and 15 for meta-analysis) were finally found to be of sufficient quality and were retained (Fig 5.1).

For the meta-analysis, the majority of the studies included were RCTs in design ($n = 14$), while more than half (16) of the studies included in the narrative synthesis were qualitative in design. Each included study was either conducted only in one SSA country or in two or more SSA countries. Participants in the studies were both adult male and female PLWH aged 15 and above. Details about the studies are summarized in Table 5.1.

5.4.2 Quality appraisal

Tables 5.2 and 5.3 present the quality appraisal of studies included in this review. For the included non-randomized control studies, 17 of them had an overall high rate of methodological quality ($>90\%$), 13 had a moderate methodological quality ranging between 80 and 90% and only one had a methodological quality rate of less than 80%. The variation in methodological quality was because some studies did not adequately explain how confounding factors were dealt with, did not sufficiently explain participant follow up and the criteria used to objectively assess outcomes in a reliable way (Table 5.2).

For the included randomized control trials, 6 had a high methodological quality rate (>90%), 6 had a rate between 80-90% and 2 had a methodological quality rate of less than 80%. The variations in methodological quality among trials was because some trials did not conceal the allocation of treatment from allocators, outcomes of participants who withdrew from the trials were not described nor included in the analysis and those assessing outcomes were not blind to treatment allocation (Table 5.3).

5.4.3 Common barriers and facilitators to ART adherence in SSA

Thirty studies [18,31–59] reported barriers to ART adherence and 11 of the studies [31–34,37,39,43,46,53,55,56] also reported facilitators to ART adherence. Both the barriers and facilitators can be grouped under the same seven broad categories – patient, health system, medication, stigma, poor mental health, socio-economic and socio-cultural-related factors (Table 5.4). Specific details of the studies with the barriers and facilitators reported can be found on Table 5.1.

5.4.4 Common ART adherence interventions and their outcome in SSA

Common interventions used in improving ART adherence in SSA countries include counselling [60,61], incentives [62,63], mobile phone short message service (SMS) [60,64–69], peer delivered behavioural intervention [70], community ART delivery intervention [71], electronic adherence monitoring device [69,72], lay health worker lead group intervention [73] and food assistance [74]. The counselling intervention (either used alone or in combination with another intervention such as SMS), peer delivered intervention, food assistance, community ART delivery as well as lay health worker lead group interventions have a significant effect in improving patients' adherence

to ART. However, incentives (either financial or in kind), SMS and electronic adherence monitoring device interventions have varying statistically significant or non-significant effects in different settings (Table 5.5).

5.4.5 Effect of interventions on ART adherence - meta-analysis

Fourteen RCTs and 1 cohort study reported ART adherence as an outcome. All 15 included studies were pooled in the meta-analysis. The total number of participants in the pooled studies was 3877 PLWH who were on ART. Of these 3877 participants, 2110 received an ART adherence intervention and 1520 of them were ART adherent after the intervention. Overall, the results of the pooled analysis from both the RCTs and cohort study included showed a statistically significant difference in ART adherence rates between the intervention and controlled groups (pooled OR=1.56, 95%CI:1.35 - 1.80, $p<0.01$), with evidence of low none statistically significant heterogeneity between studies ($I^2 = 0\%$, $p= 0.49$) (Fig 5.2).

In the subgroup analysis of RCTs and cohort study, the individual and pooled ORs for ART adherence are shown in Fig 5.3. The results of the pooled analysis from the RCTs showed a statistically significant difference in ART adherence between the intervention and control groups (pooled OR=1.65, 95%CI:1.34 – 2.03, $p<0.01$), with evidence of moderate none statistically significant heterogeneity between studies ($I^2 = 41\%$, $p= 0.06$). Similarly, the result of the analysis from the cohort study showed a statistically significant difference in ART adherence between the intervention and control groups (OR=2.87, 95%CI: 1.17 - 7.02; $p=0.02$).

Furthermore, in the subgroup analysis of studies by region (West and Central African region, East African region, and Southern African region), the results of the pooled analysis from studies in the West and Central African as well as those from the East African region showed a statistically

significant difference in ART adherence between intervention and control groups but with no statistically significant heterogeneity between studies. A moderate none statistically significant heterogeneity ($I^2 = 44\%$, $p = 0.13$) was only observed in the Southern African region studies which also showed a none statistically significant difference in ART adherence between intervention and control groups ((pooled OR=1.51, 95%CI:0.86 - 2.63, $p=0.15$), (Fig 5.4).

5.4.6 Confidence in the evidence

The assessment of the quality of the evidence used in this review shows that there is high certainty of evidence in intervention effect on the domain of patients' adherence to ART. The certainty of evidence on the outcome domains of retention in care and CD4 cell counts is low. Lastly, certainty of evidence on the viral load outcome domain is very low (Table 5.6).

5.5 Discussion

ART regimens are life-long requirement of strict compliance by patients and needs to be taken as prescribed to achieve treatment success and prevent drug resistance [7,8,75]. As clinical and immunological improvement as well as viral suppression are only expected when individuals adhere to ART [5,7–9], the efficacy and durability of ART drug regimens require near perfect adherence rates as high as 95% or more [76–78].

This systematic review and meta-analysis synthesized existing evidence on ART adherence barriers, facilitators and strategies or interventions for improving patients' adherence to ART in SSA countries. We document that 30 studies included in this review reported barriers to ART adherence, 11 of them also reported facilitators to ART adherence and 15 studies reported interventions improving ART adherence in SSA. The common barriers reported are grouped under seven major factors: patient-related (age, use of alcohol or other drugs, forgetfulness, business with

other things, non-status disclosure, limited HIV knowledge, leaving house without drugs, perceived wellness or feeling healthy), health system-related (poor clinic infrastructure, health workers knowledge and attitudes, long waiting times, poor service delivery, rupture of drugs), medication-related (side effects, pill burden/dosing, treatment fatigue), stigma (gossips, fear of status disclosure), poor mental health (depression, anger and hopelessness, sleep disorders, feeling overwhelmed with life demands), socioeconomic (unemployment, poverty, food insecurity, no disability grants, lack of partner/family support) and socio-cultural-related (use of alternative medicines, intimate partner violence, religious beliefs/practices, belief in witch doctors, lack of community support) factors. Similarly, the common facilitators to ART adherence are also group under the same seven major factors as barriers and they include: patient-related (use of reminders, having routines, disclosing status and HIV/ART education), health system-related (caregiver support, decentralization of ART care units, improved relationship with care providers), medication-related (awareness of regimen, benefits of ART), stigma (accept status, view ART as life-saving, improve knowledge and understanding of HIV/ART), poor mental health (motivation to be healthy for self and others, counselling, belief in eminent HIV cure discovery, desire to raise offspring), socioeconomic (disability grants, financial support) and socio-cultural-related (partner/family support, social support, community support, encouragement from community health workers). The interventions improving ART adherence include counselling, incentives, mobile phone short message service (SMS), peer delivered behavioural intervention, community ART delivery intervention, electronic adherence service monitoring device, lay health worker lead group intervention and food assistance. These interventions are either effective individually or when combined and the results of our meta-analysis revealed an improvement in ART adherence in favour of ART interventions.

There have been several reviews in the realm of ART adherence, each with its distinct scope and limitations. Some are somewhat dated, others might have methodological constraints, and a significant portion focuses exclusively on English-language publications. Specifically: a 2008 review centred on barriers to accessing antiretroviral treatment in developing nations, emphasizing studies from 1996 to 2007 and exclusively sourcing from PubMed, FamMed and Cochrane databases [79]. A 2012 examination reviewed ART adherence trends in Cameroon, covering studies between January 1999 and May 2012 [80]. Another review from 2003 to February 2019 addressed the efficacy of treatment supporter interventions for ART adherence in SSA, but it considered only English-language studies [81]. A further review regarding strategies to bolster adherence in sub-Saharan Africa exclusively considered articles from PubMed, Medline and Google Scholar databases [82].

Our study fills a unique niche in this spectrum: it provides an all-encompassing view of barriers, facilitators, and interventions to enhance ART adherence in SSA, embracing both English and French publications. This makes our review distinct as no similar comprehensive study has been identified.

Delving into our findings, we observed that the reported barriers align with those from other reviews, specifically those relating to patient factors, medication, stigma and health services [25]. Nonetheless, our review offers a broader scope, encompassing barriers that have been somewhat overlooked by others, like transport [83] and food insecurity issues [84]. Other reviews focused exclusively on population and health system level barriers [79] and depression and alcohol use related barriers [85]. Furthermore, our findings regarding facilitators mirror those from other reviews, noting common themes like social support, reminders, status disclosure and the importance of establishing robust patient-provider relationships [86].

Regarding interventions, our review highlights a variety of strategies, some potent as standalone measures, and others more effective in tandem with complementary interventions. This is consistent with another review asserting the necessity of multiple interventions due to the diverse barriers faced by ART patients [25]. While our review doesn't single out the most impactful intervention, our meta-analysis underscores an overarching improvement in adherence when ART interventions are implemented. This is in line with other analyses which have demonstrated increased adherence with the introduction of interventions [87]. It is also noteworthy that some specific groups, like pregnant and lactating women, show heightened adherence when given targeted interventions [88]. Community-based ART delivery, as observed in other reviews, also emerges as a potent strategy, enhancing patient retention, accessibility to HIV services, and overall treatment engagement [89–91].

Strengths and limitations:

This review has the following strengths – eligible studies were identified through a comprehensive search on several databases and sources, it included recent articles published in SSA countries from 2010 onward, studies published in either English and or French were included, and two persons independently evaluated each study for inclusion and data extraction. Furthermore, this review alone has synthesized recent evidence on common adherence barriers and facilitators, and common interventions that have been shown to improve ART adherence across SSA in one single review than any previous review has done.

However, our review is limited by the fact that we included some cohort studies which may bias the overall estimate effect due to unmeasured confounding not adjusted for in multivariable analysis. Also, included studies for our meta-analysis did not measure the outcome (adherence) in

the same way nor using the same tool; this might impact the results of our pooled analysis. Lastly, we did not include unpublished studies and might have missed some eligible articles.

Conclusion:

The barriers and facilitators to ART adherence in SSA countries can be categorized under seven primary factors: patient-related, health system-related, medication-related, stigma, poor mental health, socioeconomic and socio-cultural-related factors. Common interventions that enhance ART adherence encompass counselling, incentives, mobile phone short message services (SMS), peer delivered behavioural intervention, community ART delivery intervention, electronic adherence service monitoring device, lay health worker lead group intervention and food assistance. These strategies prove effective either as standalone approaches or in conjunction with other methods. To harness the full potential of ART and mitigate the HIV burden in SSA countries, stakeholders engaged in HIV prevention and treatment must recognize and integrate these barriers, facilitators, and adherence enhancing interventions when formulating policies or crafting treatment strategies. Ensuring sustained optimal outcomes from ART may necessitate further research, particularly focusing on specific underrepresented demographics such as HIV-infected children, adolescents, and pregnant women in SSA. This research will aim to uncover the most appropriate barriers, facilitators and interventions tailored to each group's unique needs.

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Table 5. 1: Characteristics of included studies

Study (first author, year)	Setting	Study design	Participants/ sample size	Intervention	Comparison	Outcomes	ART barriers	ART facilitators
Ajuna et al, 2021	Two primary health care facilities in southwestern Uganda	Qualitative descriptive study	23 Young adults living with HIV (YALWH). Age: 18-24 years	NA	NA	Barriers and facilitators of ART adherence	Structural barriers to ART adherence (e.g., stigma) were the most cited, followed by medication- (e.g., pill burden), and patient-related barriers (e.g., non-disclosure of HIV status)	Bonding (family, friends, and neighbors), bridging (informal groups), and linking (health professionals) social networks.
Axelsson et al, 2015	Senkatana HIV Clinic in Maseru, Lesotho	Qualitative, semi-structured interview study	28 HIV-positive adults (17 women and 11 men) Age: 18 years and older	NA	NA	Role of timing of ART intake, information patients received from health workers, local adherence patterns, barriers	Interruption of daily routines or leaving the house without sufficient medicine	Use of mobile phone alarms, phone clocks and support from family and friends

						and facilitators of ART adherence		
Azia et al, 2016	Vredenburg regional hospital, Western Cape, South Africa	Descriptive qualitative study	18 non-adhering patients on ART Age: 18-63	NA	NA	Challenges faced by patients on ART	Stigma, disclosure, unemployment, lack of transport, insufficient feeding, disability grants and alternative forms of therapy	NA
Balcha et al, 2011	ART clinics in the Oromia region in Ethiopia	Qualitative study	14 HIV positive patients on ART Age: 26-37 years	NA	NA	Major reasons of patient attrition from treatment at hospital and health center levels.	stigma, financial challenges, and lack of community support, strong belief in holy water and witch doctors among a large segment of the society	disclosure, community support, and decentralization of ART to primary health care units
Becker et al, 2021	Four rural communities in Eswatini	Mixed methods (An exploratory	166 rural women living with HIV and receiving ART	NA	NA	Magnitude to which identified barriers	household food insecurity, maltreatment by clinic staff, forgetfulness,	NA

		sequential design)	Age: 20-49 years			impacted ART adherence	stress, gossip, mode of transport, age, and lack of community support	
Biomndo et al, 2021	Twelve HIV clinics in government health facilities in Kenya	Cross-sectional survey	408 HIV-positive women receiving free ART Age: 18-69 years	NA	NA	Intimate partner violence (IPV) exposure by a current partner, ART adherence rate, and other factors that affect ART adherence	Experiencing physical IPV, sexual IPV, or controlling behavior	Higher education level and having an HIV-positive partner
Bukenya et al, 2019	Kalungu and Wakiso districts in Uganda	Qualitative cross-sectional study	30 individuals on ART Mean age: 41.7 years	NA	NA	How the environmental, social, economic and behavioral experiences of people living with HIV with poor viral suppression could explain their non-adherence to long term ART.	Travel for work or social activities, stigma, receiving little or no continuous ART adherence education, alcohol consumption and use of alternative 'HIV cure' medicines, ART side effects, treatment fatigue, belief that long-term ART or God can 'cure HIV', and food security	

Buregyeya et al, 2017	Three rural districts (Masaka, Mityana and Luwero) in Uganda	Cross-sectional qualitative study	57 pregnant and breastfeeding women receiving care in six health facilities, who had been on lifelong ART for at least 6 months. Age: 16-42 years	NA	NA	Experiences of HIV infected pregnant and breastfeeding women regarding barriers and facilitators to uptake and adherence to lifelong ART.	Fear to disclose HIV status to partners, drug related factors (side effects and the big size of the tablet), and HIV stigma	Support from male partners and peer family support groups.
Duff et al, 2010	Antenatal clinic in a regional hospital in western Uganda	Exploratory , descriptive qualitative study	51 HIV positive Women who had attended antenatal care and received pre-test HIV counselling. Age: 18 years and older	NA	NA	Barriers to accessing and accepting highly active antiretroviral therapy (HAART) by HIV-positive mothers in the Ugandan Kabarole District's Programme for the Prevention of Mother to Child Transmission-Plus (PMTCT-Plus)	Economic factors (e.g., lack of transportation); social/environmental factors (e.g., stigma towards HIV/AIDS); health care factors (e.g., long waiting times); HIV/HAART knowledge; and HIV disease progression (e.g., physical constraints to attending clinics regularly as an outpatient)	NA

Dzansi et al, 2020	A teaching hospital in Accra, Ghana	A phenomenological qualitative study	26 adult patients receiving ART Age: 18–65 years	NA	NA	Explored adherence behaviour among patients diagnosed with HIV in a teaching hospital in Accra, Ghana	forgetfulness, secrecy, waiting time, religious beliefs, and sleep.	perception of ART as part of daily routines, benefits of the ART, awareness of regimen, access to food, and transparency.
Essomba et al, 2015	L'hôpital de référence Laquintinie de Douala, Cameroon	Cross-sectional analytic study	521 PLWHIV Age: 15 years and above	NA	NA	Explored factors associated with nonadherence to ART among PLWHIV	Forgetfulness, rupture of medication in hospital, business with other things	NA
<i>Idindili et al, 2012</i>	Tumbi Hospital and Chalinze Health Centre in Pwani Region in eastern Tanzania	Case-control study	316 adult HIV infected people (79 cases and 237 controls matched by age and sex were studied) Age: 18-75 years	NA	NA	Explored factors associated with non-adherence among HIV-infected individuals in Pwani Region	Lack of bus fare, disclosure to confidants only and failure to disclose HIV-test positive status, alcohol use, not satisfied with providers	NA
Kagee et al, 2012	Public hospital in South Africa	Qualitative study	10 patients receiving ART (seven men and three women).	NA	NA	Identified structural barriers that influenced adherence among patients who	Structural barriers: time away from work, transport expenses, long	NA

			Age: 22-37 years			were enrolled in the national ART programme in South Africa	waiting times and negative experiences with clinic staff. Pill-taking barriers: food insecurity, stigma and discrimination	
Kim et al, 2016	one rural and three urban Malawi Ministry of Health (MOH) facilities in Lilongwe District, Malawi	Qualitative study	65 HIV-infected women who were pregnant or postpartum Age: 16–44	NA	NA	Barriers and facilitators to uptake and adherence to ART	Initiation barriers: concerns about partner support, feeling healthy, needing time to think, ART barriers: ART-related side effects and lack of partner support	Encouragement from community health workers, side effects subsiding, decline in health, change in partner, and fear of future sickness, desire to prevent transmission and improve health
Koole et al, 2016	18 purposively selected health facilities in Tanzania,	Cross-sectional study	4425 ART patients	NA	NA	Reasons patients miss taking their ART, the proportion who miss their ART because	Forgetting, ART-related hunger or not having enough food and symptoms	NA

	Uganda, and Zambia		Age: 18 years or older			of symptoms; and the association between symptoms and incomplete adherence.	(feeling sick or uncomfortable because of the ART), lack of transport, being away from home and asked to stop ART by traditional healer.	
Mabunda et al, 2019	Letaba HIV clinic, South Africa	Cross-sectional survey	281 HIV-infected young adults Age: 18-35 years	NA	NA	Factors associated with ART nonadherence	Forgetting, feeling good, fear and running out of treatment	NA
Masa et al, 2017	Two rural communities in eastern Zambia	Cross-sectional study	101 people living with HIV (PLHIV) Age: 18-50 years	NA	NA	Barriers and facilitators of antiretroviral therapy adherence	Having monetary debt, non-farming-related occupation, owning more transportation-related assets, living in community with fewer economic opportunities, place of residence	owning more livestock, place of residence, self-perceived health status (rated as better)
Miller et al, 2010	An NGO clinic in Limpopo Province and a public hospital in	Qualitative study	28 adult patients receiving ART Mean age: 31 years	NA	NA	Assessed reasons for ART default	transport costs, time needed for treatment, and logistical challenges,	

	Gauteng Province, South Africa						stigma, ART side effects	
Mitiku et al, 2013	Hiwot Fana and Jugal hospitals in Ethiopia	Cross-sectional study	239 PLWHIV Age: >18 years	NA	NA	Explored factors for non-adherence to ART	forgetting, traveling, and being busy doing other things	
Moomba and Wyk, 2019	Livingstone General Hospital, Zambia	Explorative , qualitative study	42 patients on ART Age: 18 years and above	NA	NA	Assessed social and economic barriers to ART adherence	Economic factors: poverty, unemployment, and the lack of food Social factors: traditional medicine, religion, lack of family and partner support, and disclosure	NA
Mtetwa et al, 2013	Public HIV clinic in Harare, Zimbabwe	Qualitative study	38 HIV-positive sex workers Age: 18-41 years	NA	NA	explored the reasons for non-attendance and the high rate of attrition	Being demeaned and humiliated by health workers, social stigma, being identified and belittled within the health care environment, competing time commitments and costs of transport	

							and some treatment	
Ndirangu et al, 2022	Public health clinics and substance use treatment programmes in Cape Town, South Africa	Qualitative study	69 Women living with HIV Age: 18 and 45 years	NA	NA	Barriers to HIV treatment adherence among women	Intrapersonal-level factors (substance use, financial constraints, food insecurity; community-level factors (anticipated and enacted stigma, community violence) and institutional-level factors (patient-provider relationships, health facility barriers, environmental stigma).	NA
Ngarina et al, 2013	Mitra Plus clinic located within the Muhimbili National Hospital compound, Dar es Salaam, Tanzania	Qualitative study	23 HIV-infected women enrolled in the Mitra Plus PMTCT study with a CD4 cell count of < 200/ μ L Age: 25- 45 years	NA	NA	Reasons for poor adherence to antiretroviral therapy postnatally	Lack of motivation after successfully protecting their child from becoming infected, not feeling ill, feeling hopeless, living in poverty, overwhelming	NA

							demands of everyday life, having to hide their ART due to the stigma of being HIV-infected	
Nsoh et al, 2021	Four hospitals in Yaoundé, Cameroon	Cross-sectional study	271 PLHIV Age: 20 years and above	NA	NA	Assessed predictors of treatment interruption amongst PLHIV and motivating factors to treatment adherence	Transport cost and stigmatization	Belief in the discovery of an eminent HIV cure and the desire to raise offspring
<i>Okoronkwo et al, 2013</i>	Adult retroviral clinic of the Nnamdi Azikiwe University Teaching Hospital, Nnewi, southeast Nigeria.	Cross-sectional descriptive survey	221 adult HIV-infected patients Age: 20-49 years	NA	NA	Explored nonadherence factors in relation to their socioeconomic characteristics	Forgetfulness, busy schedule, side effects of drugs, and stigma	NA
Rasmussen et al, 2013	Simão Mendes HIV Treatment Center	Grounded theory design	20 adult, HIV infected individuals receiving ART at	NA	NA	Assessed barriers and facilitators to patient ART adherence	Limited HIV knowledge, treatment-related costs and competing	Experienced treatment benefits and complementi

	in Bissau, Guinea-Bissau		a HIV treatment centre Age: 15 - 65 years				livelihood needs; poor clinic infrastructure; perceived stigma; and traditional practices	ng social networks.
Schatz et al, 2019	Three Level III health centers and the Medical Research Council/Ugan da Virus Research Institute (MRC/UVRI) Health Clinic, Uganda	Qualitative study	40 persons living with HIV Age: 50 - 96 years	NA	NA	Assessed barriers and facilitators to antiretroviral therapy (ART) access and adherence among older Africans	Transportation costs, food insecurity, and healthcare workers' knowledge, attitudes, and behaviors	High levels of health literacy, the use of a variety of reminder strategies and viewing ART as life- saving
Tsega et al, 2015	ART clinic of the University of Gondar referral hospital, Ethiopia	Cross- sectional study	351 ART patients Age: > 18 years	NA	NA	ART adherence, associated factors and reasons for nonadherence	forgetfulness (29 [43.3%]), missing appointments (14 [20.9%]), running out of medicine (9 [13.4%]), depression, anger, or hopelessness (4 [6.0%]), side effects of the medicine used (2 [3.0%]), and	

							nonbelief in the ART	
Wakibi et al, 2011	HIV/AIDS treatment centre in the Kenyatta National Hospital, Kenya Medical Research Institute (KEMRI) and Riruta Health centre in Nairobi, Kenya	Cross-sectional study	416 HIV+ outpatients Age: 18 years or more	NA	NA	Adherence to ART and identified factors responsible for non-adherence	being busy, forgetting, distance of clinic from home and difficulty with dosing schedule	NA
Weiser et al, 2010	AIDS treatment programs in Mbarara and Kampala, Uganda	Grounded theory design	47 HIV-infected adults Age: 18 years or older	NA	NA	How food insecurity interferes with ARV therapy regimens	Food insecurity: intolerable hunger in the absence of food, Side effects of ARVs were exacerbated in the absence of food, Participants believed they should skip doses if they could not afford the added nutritional burden,	NA

							competing demands between costs of food and medical expenses, forgot medication doses while working.	
Maduka & Tobin-West, 2013	A tertiary health care institution in Nigeria	RCT	104 HIV positive clients who had been HAART experienced for at least three months prior to commencement of the study Age: 20-69 years	Adherence counseling and short message reminders (52 participants received monthly adherence counseling and twice weekly short message reminders for four months + standard care).	Standard care (52 participants received only standard care)	Self-reported adherence and CD4+ cell counts measured pre- and post-intervention (At post-intervention, 76.9% of the intervention group and 55.8% of the control group achieved adherence Also, median CD4+ cell count of the intervention group increased from 193 cells/ml to 575.0 cells/ml against 131.0 cells/ml to 361.5 cells/ml in the	NA	NA

						control group (P = 0.007).		
Graham et al, 2020	A research clinic run by KEMRI in Mtwapa, Kenya	RCT	60 gay, bisexual, and other men who have sex with men (GBMSM) living with HIV Age: 18 years or older	The <i>Shikamana</i> intervention (combined modified Next Step Counseling by providers with support from trained peers) to improve adherence (27 (45%) of participants were assigned to the intervention (16 ART-experienced and 11 ART-naïve)	Standard care (33 (55%) of participants were assigned to standard care (17 ART-experienced and 16 ART-naïve)	Feasibility, acceptability, safety, and initial intervention effects - differences in self-reported adherence and virologic suppression. (Feedback on feasibility and acceptability was positive based on exit interviews. After adjustment for baseline viral suppression and confounding, the intervention group had 6-fold increased odds of viral suppression during follow-up).	NA	NA
Fahey et al, 2020	Four health facilities in Shinyanga region, Tanzania	RCT	530 Adults with HIV who had started ART	Cash incentive for monthly clinic attendance	Usual care (184 patients received the usual care)	Retention in care with viral suppression (At 6 months, approximately 134	NA	NA

			Age: 18 years or older	(172 in the smaller incentive group, and 174 in the larger incentive group, received monthly incentives for 6 months via mobile health technology		(73%) participants in the control group remained in care and had viral suppression, compared with 143 (83%) in the smaller incentive group (risk difference [RD] 9·8, 95% CI 1·2 to 18·5) and 150 (86%) in the larger incentive group (RD 13·0, 4·5 to 21·5); we identified a positive trend between incentive size and viral suppression (p trend=0·0032), although the incentive groups did not significantly differ (RD 3·2, -4·6 to 11·0))		
Mbuagbaw et al, 2012	Yaoundé Central Hospital (YCH) Accredited Treatment	Randomized two-arm parallel design trial	200 HIV-positive adults on ART Age: 21 years and above	Motivational mobile phone text messages (SMS)	Usual care (99 participants received the usual care	At 6 months, overall retention was 81.5%. We found no significant effect on adherence by		

	Centre (ATC), Yaounde, Cameroon			(101 participants received a weekly standardized motivational text message e.g “You are important to your family. Please remember to take your medication. You can call us at this number: +237 xxxx xxxx.”)		VAS>95% (risk ratio [RR] 1.06, 95% confidence interval [CI] 0.89, 1.29; p=0.542; reported missed doses (RR 1.01, 95% CI 0.87, 1.16; p>0.999) or number of pharmacy refills (mean difference [MD] 0.1, 95% CI: 0.23, 0.43; p=0.617 (SMS did not significantly improve adherence to ART).		
Magidson et al, 2021	Khayelitsha community, Western Cape, South Africa	RCT	61 HIV positive people on ART Age: 18-65 years	Khanya, a task-shared, peer-delivered behavioral intervention to improve ART adherence (30 participants received a six-session peer-delivered behavioral intervention, each 60 minutes	Enhanced treatment as usual (ETAU) (31 participants received ETAU – initial screening and referral to t	Ninety-one percent of participants (n = 56) were retained at six months. The intervention was highly feasible, acceptable, appropriate and delivered with fidelity (>90% of components delivered as		

				long, that integrates several evidence-based intervention components – behavioral activation, problem solving, motivational interviewing and mindfulness-based relapse prevention)		intended by the peer). There was a significant treatment-by-time interaction for ART adherence (estimate = -0.287 [95% CI = -0.507 , -0.066]), revealing a 6.4 percentage point increase in ART adherence in <i>Khanya</i> , and a 22.3 percentage point decline in ETAU.		
Linnemayr et al, 2017	Mildmay clinic, Kampala, Uganda	RCT	155 HIV-infected men and women Age: 19–78	Behavioural incentives (in-kind incentives from a choice of one of three items – a coffee mug, an umbrella or a water bottle)	Standard care	individuals receiving incentives were 23.7 percentage points more likely to achieve 90% antiretroviral adherence compared with the control group [95% confidence interval (CI), 6.7–40.7%]. Specifically, 63.3% (95% CI, 52.9–72.8%) of participants in the		

						pooled intervention groups maintained at least 90% mean adherence during the first 9 months of the intervention, compared with 39.6% (95% CI, 25.8–54.7%) in the control group.		
Lester et al, 2010	ART clinics in Kajiado and Nairobi, Kenya	RCT	538 HIV-infected adults initiating antiretroviral therapy (ART) in three clinics in Kenya Age: 18 years and above	Mobile phone short message service (SMS) (273 participants received weekly SMS messages from a clinic nurse and were required to respond within 48 h)	Standard care (265 participants received standard care)	Adherence to ART was reported in 168 of 273 patients receiving the SMS intervention compared with 132 of 265 in the control group (relative risk [RR] for non-adherence 0.81, 95% CI 0.69–0.94; p=0.006). Suppressed viral loads were reported in 156 of 273 patients in the SMS group and 128 of 265 in the control group, (RR for virologic failure 0.84, 95%		

						CI 0·71–0·99; p=0·04). Patients who received SMS support had significantly improved ART adherence and rates of viral suppression compared with the control individuals		
Barnabas et al, 2020	Rural and peri-urban settings in South Africa and Uganda	Randomised trial	1315 People living with HIV Age: 18 years or older	community-based delivery of ART	clinic-based ART delivery	Retention in care and viral suppression (Retention at the month 12 visit was 95% (n=1253). At 12 months, community-based ART increased viral suppression compared with the clinic group (306 [74%] vs 269 [63%], RR 1·18, 95% CI 1·07–1·29; p ^{superiority} =0·0005)	NA	NA
Abiodun et al, 2021	HIV clinics in two states in southwest Nigeria	RCT	209 medication-non-adherent	Interactive and tailored short message reminders to	104 participants received the standard of care and two	ART adherence assessed using the visual analog scale, viral	NA	NA

			adolescents living with HIV Age: 15-19 years	enhance antiretro-viral therapy adherence. 105 participants received daily SMS reminder + Received the standard of care and two clinic visit reminders every four weeks	clinic visit reminders every four weeks. one SMS reminder each for follow-up appointments, 48 hours and 24 hours before the follow-up visit date	suppression, pill count, and ACTG scores; the feasibility of the intervention by the SMS delivery and response (overall and individual) rates; and acceptability using self-report, willingness to continue receiving the intervention, and desire for its scale-up. (Viral load parameters showed statistically significant differences between control and intervention groups - mean difference for viral load between the two groups was 30,998.42 (95% CI 903.35e61,093.48) copies/		
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						ml with a p-value of .044).		
Orrell et al, 2015	Hannan Crusaid Treatment Centre (HCTC) in Gugulethu, Cape Town, South Africa	RCT	230 ART-naive adults and adolescents Age: ≥ 15 years	Real-time electronic adherence monitoring device that records dosing time (115 participants received SoC and automated text reminders if dosing >30 minutes late)	standard of care (SoC) (115 participants received 3 pretreatment education sessions)	Median adherence was 82.1% (interquartile range, 56.6%–94.6%) in the intervention arm, compared with 80.4% (interquartile range, 52.8%–93.8%) for SoC [adjusted odds ratio for adherence 1.08; 95% confidence interval (CI): 0.77 to 1.52]. Text message reminders linked to late doses detected by real-time adherence monitoring did not significantly improve adherence or viral suppression.	NA	NA
Peltzer et al, 2012	Ladysmith Hospital in the Uthukela District of	RCT	152 HIV-infected adults on ART	Lay health worker leads	Standard care (76 participants individually)	There was a significant improvement of ART adherence	NA	NA

	KwaZulu-Natal, South Africa		Age: 18 years and above	structured group intervention (76 participants received three monthly 1 h sessions of medication information combined with problem-solving skills in an experiential/interactive group format)	attend monthly one visit to review their health status with their medical practitioner – 20 minutes, standard of care)	and CD4 count and a significant reduction of depression scores over time in both intervention and control conditions; however, no significant intervention effect between intervention and control conditions was found.		
Pop-Eleches et al, 2011	Chulaimbo Rural Health Center (CRHC) in Nyanza Province, Kenya	RCT	720 Adult patients who had initiated ART Age: > 18 years	Short message service (SMS) reminders (70 participants received short daily reminder messages, 72 received long daily reminders, 73 received short weekly reminders, and 74 received long weekly reminders)	No SMS (139 participants received no SMS)	53% of participants receiving weekly SMS reminders achieved adherence of at least 90% during the 48 weeks of the study, compared with 40% of participants in the control group ($P = 0.03$)	NA	NA

Reid et al, 2017	Independence Surgery, an urban private clinic in Gaborone, Botswana	RCT	108 treatment-experienced adult patients Age: 21 years and above	Cellular phone short message service (SMS) reminders (54 participants received SMS reminders three days prior, one day prior, and the morning of the scheduled monthly pharmacy pickup)	No intervention (54 participants received no SMS)	There were no significant differences in the changes of CD4 count between the intervention and control groups. While mean log HIV VL was lower in the intervention group at the end of six months (5.31 vs. 3.88, $p = 0.05$), the difference in VL from baseline across the groups was not statistically significant (-0.24 vs. 0.09 , $p = 0.14$).		
Sumari-de Boer et al, 2021	Kilimanjaro Christian Medical Centre and Majengo Health Centre, Tanzania	RCT	249 PLWH Age : 18-65 years	Digital adherence tools (DATs) - Real-time medication monitoring device + SMS reminder (80 participants received reminder short message service (SMS) texts,	Standard care only (81 participants received standard care only)	The average (over 48 weeks) adherence in the SMS, RTMM, and control arms was 89.6%, 90.6%, and 87.9% for pharmacy refill; 95.9%, 95.0%, and 95.2% for self-report in the past week; and 97.5%, 96.6%, and 96.9%	NA	NA

				followed by a question SMS. 82 participants received a real-time medication monitoring (RTMM) device (Wisepill) with SMS reminders)		for self-report in the past month, respectively (<i>P</i> values not statistically significant).		
Tirivayi et al, 2012	four Lusaka public-sector ART clinics that distributed food rations (Mtendere, Chawama, Kanyama, and George) and four control clinics that did not distribute rations (Bauleni, Chipata, Matero Reference, and Chilenje), Zambia	Cohort study	400 ART patients receiving food assistance Age: 18 years and above	Food assistance (144 participants received food assistance	No food assistance (147 participants received no food assistance	After 6 months, food assistance recipients (n=145) had higher ART adherence compared to non-recipients (n=147, 98.3% versus 88.8%, respectively; <i>p</i> <0.01), but no significant effects were observed for weight or CD4+ lymphocyte count change.	NA	NA

Table 5. 2: JBI critical appraisal results for non-randomize control trial studies.

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Total (%)
Ajuna, 2021	1	1	0	1	1	N/A	1	1	1	87.5*
Axelsson, 2015	1	1	0	1	1	N/A	1	1	1	87.5*
Azia, 2016	1	1	0	1	1	N/A	1	1	1	87.5*
Balcha, 2011	1	1	0.5	1	1	N/A	1	1	1	93.8*
Becker, 2021	1	1	1	1	1	N/A	1	1	1	100.0*
Biomndo, 2021	1	1	1	1	1	N/A	1	1	1	100.0*
Bukenya, 2019	1	1	0	0.5	1	N/A	1	0.5	1	75.0*
Buregyeya, 2017	1	1	0	1	1	N/A	1	1	1	87.5*
Duff, 2010	1	1	0	1	1	N/A	1	1	1	87.5*
Dzansi, 2020	1	1	0.5	1	1	1	1	1	1	94.4
Essomba, 2015	1	1	1	1	1	N/A	1	1	1	100.0*

Idindili, 2012	1	1	1	1	1	1	1	1	1	100.0
Kagee, 2012	1	1	0	1	1	N/A	1	1	1	87.5*
Kim, 2016	1	1	0	1	1	N/A	1	1	1	87.5*
Koole, 2016	1	1	1	1	1	N/A	1	1	1	100.0*
Mabunda, 2019	1	1	1	1	1	N/A	1	1	1	100.0*
Masa, 2017	1	1	1	1	1	N/A	1	1	1	100.0*
Miller, 2010	1	1	0.5	1	1	1	1	1	1	94.4
Mitiku, 2013	1	1	1	1	1	N/A	1	1	1	100.0*
Moomba, 2019	1	1	0	1	1	N/A	1	1	1	87.5*
Mtetwa, 2013	1	1	0	1	1	N/A	1	1	1	87.5*
Ndirangu, 2022	1	1	1	1	1	1	1	1	1	100.0
Ngarina, 2013	1	1	0	1	1	N/A	1	1	1	87.5*

Nsoh, 2021	1	1	1	1	1	1	1	1	1	100.0
Okoronkwo, 2013	1	1	1	1	1	N/A	1	1	1	100.0*
Rasmussen, 2013	1	1	0	1	1	N/A	1	1	1	87.5*
Schatz, 2019	1	1	0	1	1	N/A	1	1	1	87.5*
Tsega, 2015	1	1	1	1	1	N/A	1	1	1	100.0*
Wakibi, 2011	1	1	1	1	1	0.5	1	1	1	94.4
Weiser, 2010	1	1	0	1	1	N/A	1	1	1	87.5*
Tirivayi, 2012	1	1	1	1	1	1	1	1	1	100.0

1 = Yes, 0= No, 0.5 = Unclear, N/A = not applicable

* Score is out of 8 due to an inapplicable item

Table 5. 3: JBI critical appraisal results for randomized controlled trial studies

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Total (%)
Maduka, 2013	1	1	1	1	1	1	1	1	1	1	100.0

Graham, 2020	1	1	1	0.5	1	1	1	1	1	1	95.0
Fahey, 2020	1	1	0.5	N/A	0.5	1	1	1	1	1	88.9*
Mbuagbaw, 2012	1	1	1	1	1	1	1	1	1	1	100.0
Magidson, 2021	1	1	1	1	0.5	1	1	1	1	1	95.0
Linnemayr, 2017	1	1	0.5	0.5	0.5	1	1	1	1	1	85.0
Lester, 2010	1	1	1	0	1	1	1	1	1	1	90.0
Barnabas, 2020	1	1	0	0	0	1	1	1	1	1	70.0
Abiodun, 2021	1	1	1	0	1	1	1	1	1	1	90.0
Orrell, 2015	1	1	1	0	0.5	1	1	1	1	1	85.0
Peltzer, 2012	1	1	0.5	0	0.5	1	1	1	1	1	80.0

Pop- Eleches, 2011	1	1	0.5	0	0.5	1	1	1	1	1	80.0
Reid, 2017	1	1	1	N/A	0	1	1	1	1	1	88.9*
Sumari-de Boer, 2021	1	1	0	0	0	1	1	1	1	1	70.0

1 = Yes, 0= No, 0.5 = Unclear, N/A = not applicable

* Score is out of 9 due to an inapplicable item

Table 5. 4: Common barriers and facilitators to ART adherence in SSA

Category	Barriers	Facilitators
Patient-related factors	• Travel for work or social activities • Business with other things • Forgetfulness • Perceived wellness or feeling healthy • HIV disease progression • Non status disclosure • Limited HIV/ART knowledge • use of alcohol or other drugs • Age • Stress • Leaving house without sufficient drugs	• Use of reminders • Having routines • Disclosing status • HIV/ART education
Health system-related factors	• Poor relationship with care providers • Poor clinic infrastructure • Health workers knowledge, attitudes and behaviour • Long waiting times • Poor service delivery • No continuous ART adherence education • Rupture of drugs	• Caregiver support • Decentralization of ART to primary care units • Improved relationship with care providers
Medication-related factors	• Side effects • Pill burden/ dosing	• Awareness of regimen • Benefit of ART

	• Big size of tablet • Treatment fatigue • ART-related hunger	
Stigma-related factors	• Gossips • Fear of status disclosure	• Accept HIV status • View ART as lifesaving • Improve knowledge and understanding of HIV/ART
Poor mental health-related factors	• Depression • Anger or hopelessness • Feeling overwhelmed with demands of daily life • Sleep disorders	• Motivation to be healthy for self and others • Counseling • Belief in eminent HIV cure discovery • Desire to raise offsprings
Socio-economic-related factors	• Unemployment • Poverty • Lack of partner/family support • No disability grants • Food insecurity	• Disability grants • Financial support
Socio-cultural-related factors	• Use of alternative medicines • Intimate partner violence • Community violence • Religious beliefs/practices • Belief in witch doctors • Lack of community support	• Partner/family support • Social support • Community support • Encouragement from community health workers

Table 5. 5: ART adherence interventions and their outcomes in SSA

Study	Intervention	Control	Outcome of intervention
Maduka, 2013	Adherence counseling and short message reminders	Standard care	Significant effect on ART adherence and CD4 cell count
Graham, 2020	The <i>Shikamana</i> intervention (combined modified Next Step Counseling by providers with support from trained peers) to improve adherence	Standard care	Significant effect on viral suppression
Fahey, 2020	Cash incentive for monthly clinic attendance	Usual care	Significant effect on viral suppression
Mbuagbaw, 2012	Motivational mobile phone text messages (SMS)	Usual care	No significant effect on adherence
Magidson, 2021	Khanya - a task-shared, peer-delivered behavioral intervention to improve ART adherence	Enhanced treatment as usual (ETAU)	Significant treatment-by-time interaction for ART adherence
Linnemayr, 2017	Behavioural incentives (in-kind incentives from a choice of one of three items – a coffee mug, an umbrella or a water bottle)	Standard care	no significant effect on Adherence.
Lester, 2010	Mobile phone short message service (SMS)	Standard care	Significant effect on ART adherence and viral suppression

Barnabas, 2020	Community-based delivery of ART	clinic-based ART delivery	Significant effect on viral suppression
Abiodun, 2021	Interactive and tailored short message reminders to enhance antiretroviral therapy adherence.	Standard care & two clinic visit reminders every four weeks.	Significant effect on viral load suppression
Orrell, 2015	Real-time electronic adherence monitoring device that records dosing time	standard of care (SoC)	No significant improvement in adherence or viral suppression.
Peltzer, 2012	Lay health worker lead structured group intervention	Standard care	Significant improvement of ART adherence and CD4 count
Pop-Eleches, 2011	Short message service (SMS) reminders	No SMS	Significant effect on ART adherence
Reid, 2017	Cellular phone short message service (SMS) reminders	No intervention	No significant differences in the changes of CD4 and viral load
Sumari-de Boer, 2021	Digital adherence tools (DATs) - Real-time medication monitoring device + SMS reminder	Standard care only	No statistically significant difference in ART adherence
Tirivayi, 2012	Food assistance	No food assistance	Significant effect on ART adherence, but no significant effects were observed for weight or CD4+ lymphocyte count

Table 5. 6: GRADE certainty of evidence ratings

Outcome domain/ studies	Sub-outcomes	Methodology	Inconsistency	Indirectness	Imprecision	Publication bias	Level of certainty of evidence
Adherence to ART [Abiodun, Maduka, Mbuagbaw, Reid, Lester, Linnemayr, Magidson, Pop-Eleches, Tirivayi, Peltzer, Sumari-de Boer]	a. self-reported adherence b. pharmacy pickups c. pharmacy refill d. pill count or tablet return	No serious concerns	No serious concerns	No serious concerns	No serious concerns	Minor concerns (some studies did not disaggregate sub-outcomes)	HIGH CERTAINTY - ⊕⊕⊕⊕ (minor concerns about publication bias)
Retention in care [Barnabas, Pop-Eleches, Fahey, Magidson, Mbuagbaw, Graham]	a. proportion of patients retained after intervention	No serious concerns	Serious concerns (some heterogeneity in outcomes of interest)	No serious concerns	Minor concerns (lack of confidence intervals in some results)	No serious concerns	LOW CERTAINTY - ⊕⊕OO (serious concerns with inconsistency and minor concerns with imprecision)
CD4 cell counts [Graham, Maduka, Peltzer, Reid, Tirivayi]	a. increase in CD4 cell count	No serious concerns	Minor concerns (only five studies)	No serious concerns	Minor concerns (some studies did not report actual CD4 cell counts)	No serious concerns	LOW CERTAINTY - ⊕⊕OO (minor concerns with inconsistency and imprecision)

Viral load [Abiodun, Lester, Reid, Orrell, Fahey, Graham, Barnabas]	a. undetected viral load (< 40 copies /ml)	No serious concerns	Very serious (some heterogeneity in outcomes of interest)	Minor concerns (some studies did not report direct outcomes)	Minor concerns (mixed findings in terms of viral load copies/ml)	Minor concerns (some studies did not disaggregate sub-outcomes)	VERY LOW - ⊕○○○ (serious concerns with inconsistency, indirectness, imprecision, and publication bias)
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⊕⊕⊕⊕ - high certainty, ⊕⊕⊕○ - moderate certainty, ⊕⊕○○ - low certainty, ⊕○○○ - very low certainty.

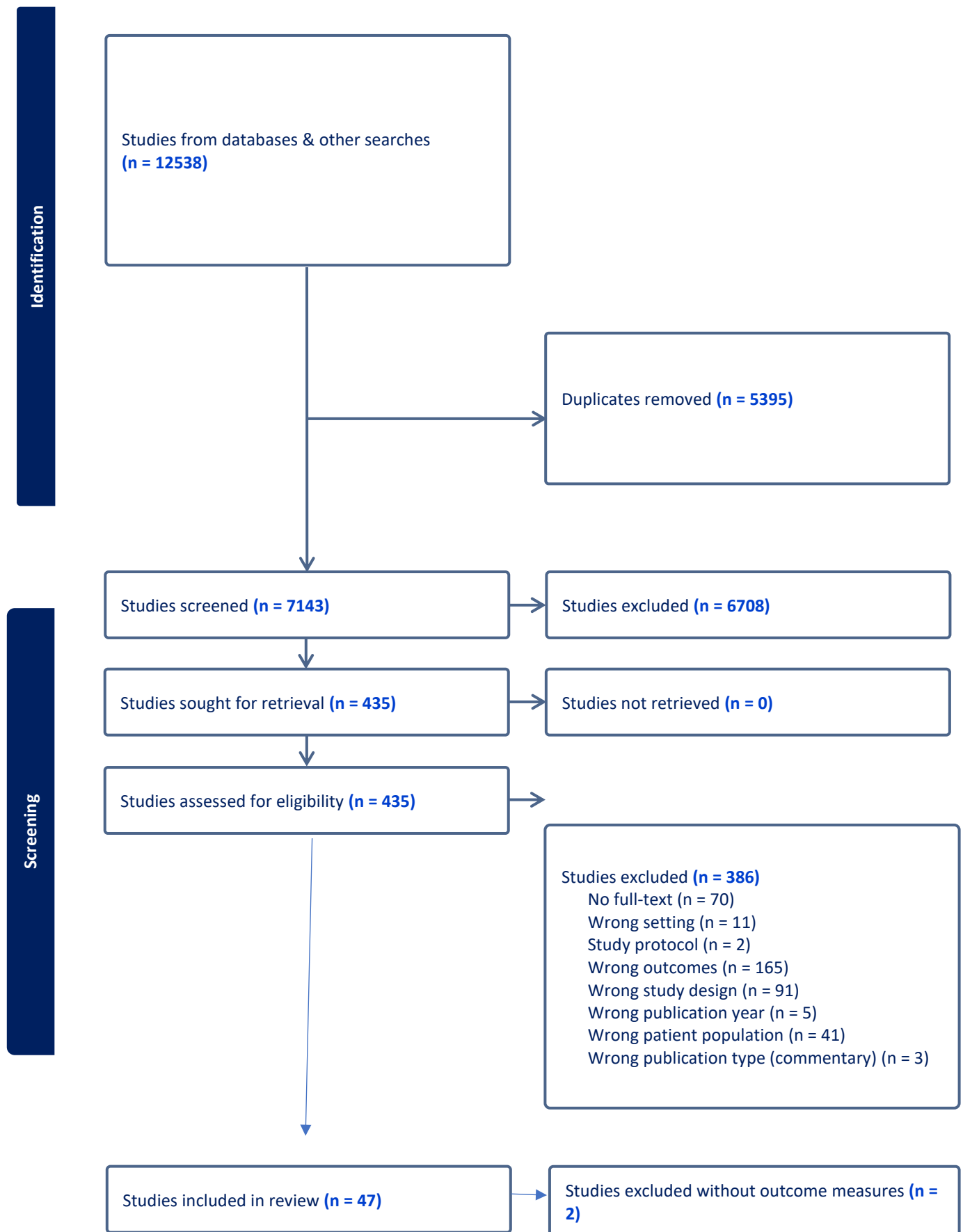
Figure legends

Fig 5.1. PRISMA flowchart of selection process

Fig 5.2. Forest plot of ART adherence comparing adherence interventions versus control

Fig 5.3. Forest plot of ART adherence comparing adherence interventions versus control in subgroup RCTs and cohort study analysis

Fig 5.4. Forest plot of ART adherence comparing adherence interventions versus control in subgroup analysis by region



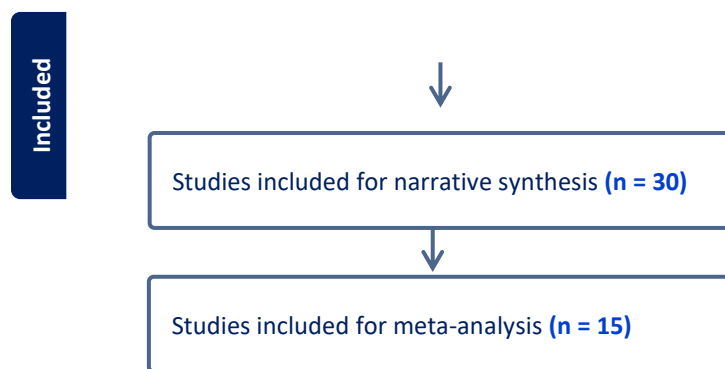


Figure 5. 1: *PRISMA flowchart of selection process*

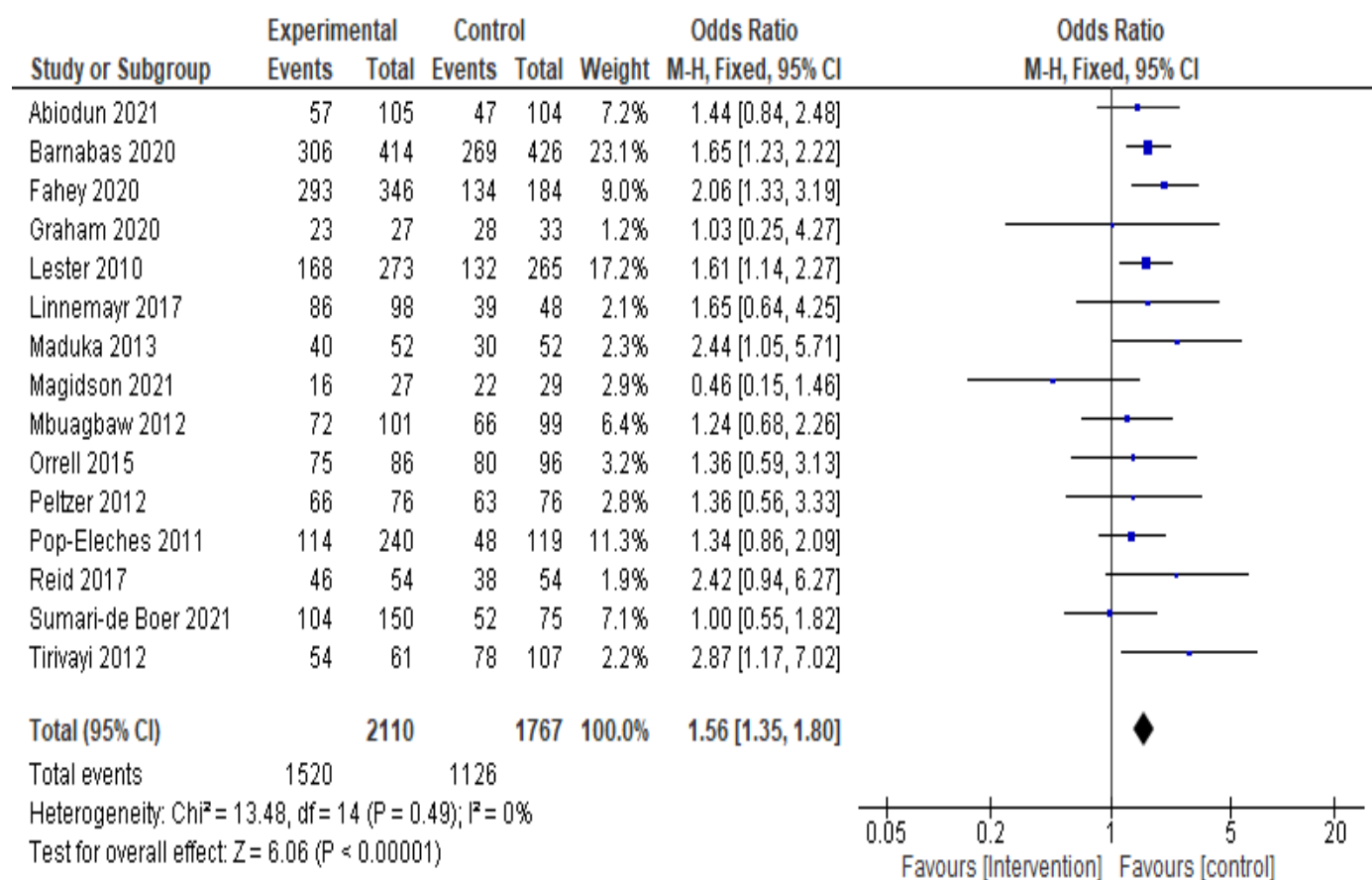


Figure 5. 2: *Forest plot of ART adherence comparing adherence interventions versus control*

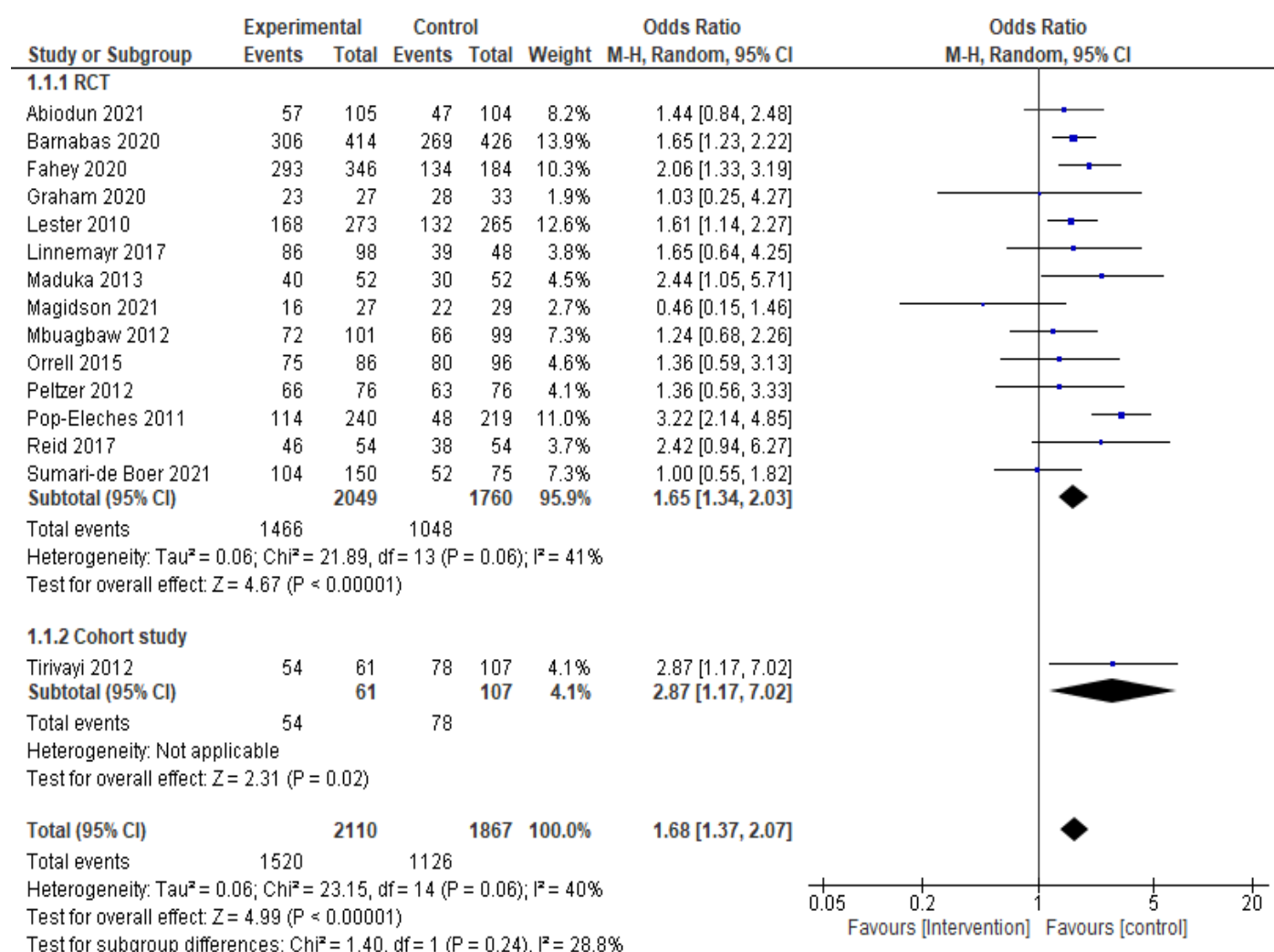


Figure 5. 3: Forest plot of ART adherence comparing adherence interventions versus control in subgroup RCTs and cohort study analysis

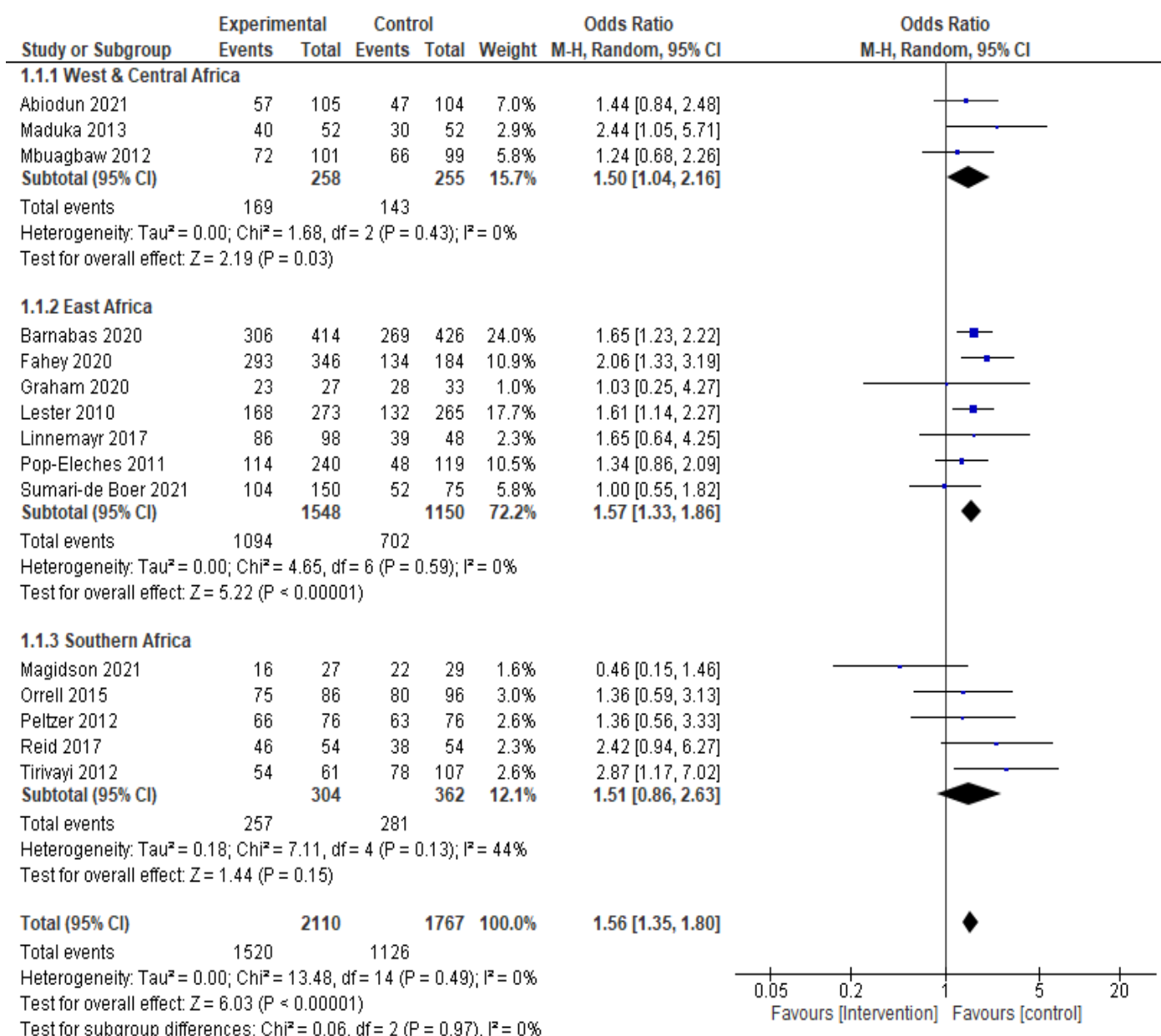


Figure 5. 4: Forest plot of ART adherence comparing adherence interventions versus control in subgroup analysis by region

Chapter 6: Prevalence and factors associated with HIV treatment non-adherence among people living with HIV in three regions of Cameroon: a cross-sectional study

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6.1 Abstract

Background: In Cameroon, HIV care decentralization is enforced as a national policy, but follow-up of people living with HIV (PLWH) is provider-driven, with little patient education and limited patient participation in clinical surveillance. These types of services can result in low antiretroviral therapy (ART) adherence. The objective of this study was to assess the prevalence and predictors of ART non-adherence among PLWH in Cameroon.

Methods: A cross-sectional descriptive study of PLWH in HIV treatment centres in Cameroon was conducted. Only PLWH, receiving treatment in a treatment centre within the country, who had been on treatment for at least six months and who were at least 21 years old were included in the study. Individuals were interviewed about their demographics and ART experiences. Data were collected using a structured interviewer-administered questionnaire and analyzed using STATA version 14.

Results: A total of 451 participants participated in this study, 33.48% were from the country's Southwest region. Their mean age was 43.42 years (SD: 10.42), majority (68.89%) were females. The overall proportion of ART non-adherence among participants was 37.78%, 35.88% missed taking ART twice in the last month. Reasons for missing ART include forgetfulness, business and traveling without drugs. Over half of participants (54.67%) know ART is life-long, 53.88% have

missed ART service appointments, 7.32% disbelieve in ART benefits, 28.60% think taking ART gives unwanted HIV Status reminder and 2.00% experienced discrimination seeking ART services. In the multivariate analysis, odds of ART non-adherence in participants aged 41 and above was 0.35 times (95%CI: 0.14, 0.85) that in participants aged 21-30 years, odds of ART non-adherence comparing participants who attained only primary education to those who attained higher than secondary education was 0.57 times (95%CI: 0.33, 0.97) and the odds of ART non-adherence in participants who are nonalcohol consumers was 0.62 times (95%CI: 0.39, 0.98) that in alcohol consumers.

Conclusion: High proportion of participants are ART non-adherent, and the factors significantly associated with ART non-adherence include age, education and alcohol consumption. However, some reasons for missing ART are masked in participants' limited knowledge in taking ART, disbelief in ART benefits, feelings that ART gives unwanted HIV status reminder and experiencing discrimination when seeking ART services. These underscores need to improve staff (health personnel) attitudes, staff-patient-communication, and proper ART prior initiation counselling of patients. Future studies need to focus on assessing long-term ART non-adherence trends and predictors using larger samples in many treatment centres and regions.

6.2 Introduction

The HIV/AIDS pandemic remains a major global public health problem. From the start of the epidemic to the end of 2021, 84.2 million (64.0 – 113.0 million) people have been infected with HIV and about 40.1 million (33.6 – 48.6 million) people have died of HIV [1]. In 2021, an estimated 38.4 million people were living with HIV worldwide, 1.5 million new infections were registered and 650,000 (510,000 – 860,000) deaths from AIDS-related illnesses were reported [1,2]. Despite efforts to prevent new infections and deaths, sub-Saharan Africa (SSA) or the World

Health Organization (WHO) African region, bears the heaviest burden of HIV with nearly 1 in every 25 adults (3.4%) living with HIV and accounting for more than two-thirds of people living with HIV worldwide [1,3]. Cameroon is one of the countries with a high prevalence of HIV in the West and Central African Sub Region [4]. The prevalence of HIV in this country stands at 2.9% [5,6]. In 2021, 15000 new cases of the disease were recorded but only 78% of people living with HIV (PLWH) are on antiretroviral therapy in Cameroon [6–8].

Evidence informs that once people are diagnosed as HIV-positive, it is important to ensure that they can be effectively linked to care [9,10] and since no cure has been discovered yet, the only modality of treatment to prolong life and to improve the quality of life of people living with HIV/AIDS at present is anti-retroviral therapy (ART) [10–12]. It has also been documented that ART regimens are life-long requirement of strict compliance by patients and needs to be taken as prescribed to achieve treatment success and prevent drug resistance [13–15]. Therefore, to be effective, ART has to be taken life-long with 100% adherence, as clinical and immunological improvement as well as viral suppression are only expected when individuals adhere to ART [10,13,14,16]. Poor or non-adherence – not taking ART every day and exactly as prescribed, can lead to drug resistance and treatment failure [10,17].

However, non-adherence to ART is still observed in SSA countries where the burden of the disease is high [18]. Some studies have reported that the patient, disease, therapy and relationship of patients with healthcare providers are associated with ART adherence issues [19,20]. Nevertheless, factors affecting non-adherence to HIV treatment are not well known especially in regions with insecurity as well as in a resource poor setting like Cameroon.

In Cameroon, decentralization of HIV care has been enforced as a national policy, with few attempts to examine the performance of this policy and its role in HIV prevention [21]. Apart from that, the follow-up of PLWH in Cameroon is provider oriented with little patient education and limited patient involvement in clinical surveillance [22]. Little is known about the proportion of PLWH who do not adhere to this kind of treatment in the country.

Furthermore, the healthcare system in Cameroon often experiences low access to drugs, inadequate staffing, coordination and management of commodities for HIV. A few studies have been conducted, all in the country's capital city (Yaoundé), to assess patient adherence to ART and examine the socio-economic, clinical and psychological factors associated with self-reported ART interruption [18,23,24]. There is limited or no literature on the socio-demographic/structural factors associated with non-adherence to HIV treatment in this country. The aim of this study therefore was to determine the prevalence and predictors of HIV treatment non-adherence among PLWH in the Northwest, Southwest and Littoral regions of Cameroon.

6.3 Methods

6.3.1 Study design and setting

A cross-sectional descriptive study was conducted on adult PLWH who were receiving ART treatment in selected HIV treatment centres in three regions of Cameroon.

Briefly, the study was conducted in Cameroon – a country in sub-Saharan Africa with a high prevalence of HIV. The country has a population of over 28 million inhabitants [25], it is divided into ten regions and shares boundaries with Nigeria in the west, Chad in the north, Central African Republic in the east and Gabon, Equatorial Guinea, Congo in the south. Participants for the study were enrolled in HIV treatment centres in three selected regions (Littoral, Southwest and

Northwest regions – all selected through balloting) of the country. In each of the selected regions, the study was conducted in only one HIV treatment centre (Mboppi Baptist Hospital Douala in the Littoral region, the Regional Hospital Buea in the Southwest region, and the Nkwen Baptist Hospital Bamenda in the Northwest region) that was purposefully selected based on probability proportionate to the size of patients registered in the centre. The centres were chosen such that on average, about 20% of PLWH and registered for ART in the centres were recruited per week in order to achieve the required sample size in a reasonable short period of time. In all the selected treatment centres, patients are managed and followed-up by doctors, nurses, and other health personnel. Patients are received in the centres from Monday to Friday, between 8:00 a.m. to 3:00 p.m. Each centre has a reception room where patients are registered in order of their arrival, a waiting room where patients wait before being consulted and consultation rooms where patients are consulted and counseled.

6.3.2 Study population, participants, and sampling

The study targeted PLWH who were receiving ART in HIV treatment centres in the Northwest, Southwest and Littoral regions of the country. To be eligible for the study, a participant had to be a patient living with HIV, receiving treatment, or being followed up in a treatment centre within the country, be at least 21 years old, had been on treatment for at least six months and must have consented to participate in the study.

The sample size for the study was calculated using the formula for estimating the sample size of a single population proportion for a prevalence study of an infinite population [26]. Since the proportion of patients who do not adhere to ART in Cameroon was not known, we assumed the prevalence of non-adherence to ART in Cameroon was 50%; and with a margin of error of 5% at 95% confidence level, a sample size of 384 was determined. However, we anticipated having a

non-response rate of 10% from participants in the study. To account for this, we increased the 384-sample by 10% to have a sample size of 422. Nonetheless, in order to have a large enough sample that will enable us to estimate the prevalence of non-adherence to ART in our study we enrolled 451 participants in this study.

Participants were sampled and enrolled into the study between the period of November and December 2021 by six (6) trained interviewers (two from each of the three selected regions where the study was conducted) with a background training in health. A multistage sampling technique was used to select participants for this study. Firstly, a list of all the ten regions of the country with HIV treatment centres and their corresponding populations of PLWH was made. Next, balloting was used to select three regions and in each selected region, the HIV treatment centre with a high population of PLWH registered was further selected. The overall sample size was divided into three to obtain the number of participants to interview in each centre. Study interviewers used the systematic sampling approach in each centre to recruit participants. After providing the usual care in each centre, clinicians referred selected patients to study interviewers who then explained the study to each eligible patient.

6.3.3 Data collection

Data on demographic/structural characteristics of participants and participants' experiences taking ART was collected using a standardized ART adherence self-reported questionnaire adapted from similar studies [27–31]. Prior to data collection, the questionnaire was pretested in an ART treatment centre (not included in the study) in Cameroon. In this study, we considered participants non-adherent to ART to be those participants who reported having once missed treatment (missed taking their ART in the past 4 weeks prior to participating in the study at least one time). Our data

collection was monitored weekly in each centre and the collected data was entered in an electronic questionnaire for further analysis.

6.3.4 Data management and analysis

The collected data was entered into an MS Access interface on Epi-info and analyzed using the statistical software program STATA version 14. The participants' socio-demographic/structural characteristics have been described using frequencies and percentages for categorical variables and means, medians, inter-quartile ranges and standard deviations for continuous variables.

To determine the proportion of participants who have not adhered to HIV treatment, the percentage of participants who reported having once missed treatment was computed.

To investigate the socio-demographic/structural factors associated with non-adherence to HIV treatment, bivariate and multivariate analysis were done. The bivariate analysis comprised of using non-adherence to HIV treatment as a binary outcome variable and participants' socio-demographic/structural characteristics as predictors. The odds of not adhering to ART between participants using unadjusted odds ratios, 95% confidence intervals and P-values were computed. A P-value ≤ 0.25 was set as the determining point in the bivariate analysis for a variable to be considered as appearing to have an association with non-adherence to HIV treatment and be included in the multivariate logistic model [32]. For the multivariate analysis, non-adherence to HIV treatment was considered as a binary outcome variable and all variables with P-values ≤ 0.25 in the bivariate analysis were considered as predictors and included in the multivariate logistic regression model. Adjusted odds ratios, 95% confidence intervals and p-values were computed. All variables with p-values < 0.05 were considered to have a statistically significant association with non-adherence to HIV treatment (ART).

6.3.5 Ethics approval and consent to participate: Ethical clearance for the study was obtained from the Health Sciences and Science Research Ethics Board (REB) of the University of Ottawa (Ethics File Number: H-08-21-7274) and the Cameroon Baptist Convention Health Board Institutional Review Board (CBCHBIRB) (IRB study number: IRB2021-53). Administrative authorization was also obtained from the Regional Delegate of Public Health of the Southwest Region (Ref: 1211/MINSANTE/SWR/RDPH/P5/810/725) and the Regional Hospital Buea (Ref /MPH/SWRDPH/BRH/IRB). Written informed consent was obtained from all participants prior to their participation in the study.

6.4 Results

6.4.1 Participants' characteristics

The characteristics of the 451 participants included in this analysis are presented in Table 6.1. More than one third of the participants in the study 151 (33.48%) were from the Southwest region of the country. The mean age of participants was 43.42 years (SD: 10.42) and majority of the participants (68.89%) were females. Two hundred and one (44.57%) of the participants were married and 156 (34.59%) had attained only the primary school level of education. One hundred and eighty-three (40.58%) of participants were Roman Catholic Christians. Two hundred and six (45.78%) of the participants were self-employed and the median monthly income of participants was 50,000 XAF (IQR: 30,000-80,000XAF). Both the median number of months of participants since they were first diagnosed HIV positive, and the median number of months participants have been taking ART was 84 months (IQR: 48-132). A vast majority of the participants 402 (89.33%) had a once daily ART dosing frequency. Most participants' 344 (76.44%) means of transportation from their homes to the HIV treatment centre was by car/taxi, with the median distance from participants homes to the HIV treatment centre being 8 Km (IQR:5-17) and the median time spent

by participants from their homes to the treatment centre being 30 minutes (IQR: 15-45). Participants had a mean number of 5 people (SD: 2.62%) living in their homes with 42.54% of those people being their children and majority of the participants 363 (80.85%) had disclosed their HIV status to their family/friends.

6.4.2 Non-adherence to ART among participants

Table 6.2, Figs 6.1 and 6.2 shows participants' ART non-adherence characteristics. Overall, the proportion of participants that did not adhere to their ART (defined as ever missed taking ART at least once in the last month prior to their participation in this study) was 37.78% (Table 6.2). The number of times participants missed taking their ART in the last four weeks varied from once to more than five times – with more than one third of these participants 61 (35.88%) missing their ART twice (Fig 6.1).

With regards to the reasons for missing their ART in the last four weeks, 60 (35.29%) of the participants stated that they forgot, 27.65% of the participants stated that they were busy while 12.35%, 7.65% and 5.29% of the participants respectively stated traveled to the village/other location, run out of medicines and stigma as their reasons for missing their ART (Fig 6.2).

6.4.3 HIV related hospitalizations among participants

The proportion of participants that had been hospitalized for HIV-related concerns prior to their participation in this study was 27.33%. Prominent among the specific reasons for hospitalization was prolonged fever - reported by 42.74% of participants. However, TB/pneumocystis, chronic diarrhea, and other health issues (malaria, anemia, cancer, diabetes, toxoplasmosis, candidiasis) were respectively reported in 12.10%, 11.29% and 16.13% of patients (Table 6.2).

6.4.4 Health risk behaviors among participants

The health risk behaviors practiced by participants are presented in Table 6.2. A proportion of participants were engaged in health risky behaviors such as consumption of alcohol and no physical activity - reported in 36.36% and 58.00% of the participants respectively. Also, use of unprescribed drugs was reported in 25.17% of participants as well as having multiple sex partners which was reported in 8.67% of participants.

6.4.5 Participants' knowledge, experiences, and views about ART

The views and experiences of participants are presented in Table 6.3. Over half (54.67%) of the participants know and strongly agree that ART is lifelong, with 257 (57.11%) of the participants reporting that their health status has been stable since ART initiation. Nevertheless, 243 (53.88%) of participants reported having ever missed an ART service appointment. Although 279 (61.86%) of participants disagreed that they experienced physical adverse events related to ART, 84 (18.67%) of participants reported having ever experienced ARV side effects, 33 (7.32%) of participants do not believe in the benefits of ART and 129 (28.60%) of participants strongly agree that taking ART tablets gives them an unwanted reminder of their HIV status. One hundred and seventy-six (39.02%) of the participants did not express any worries that ART might stop working in future, but a small proportion of the participants (2.00%) reported that they had experienced health service discrimination while seeking HIV treatment services.

6.4.6 Correlates of participants' non-adherence to ART

The sociodemographic/structural correlates of patients' non-adherence to ART offered in treatment centres in Cameroon are presented in Tables 6.4 and 6.5. In the bivariable analysis, the factors that appeared to be associated with patients' non-adherence to ART included sex (being

female when compared to being male), being of age 31-40 and 41 and above when compared to age 21-30, being married/cohabiting and being divorced/separated/widow when compared to being single/never married, attaining primary and secondary level of education when compared to those that attained higher than secondary level of education, being 5-9 years and 10 or more years since HIV positive diagnosis when compared to being less than one year since diagnosis, taking ART for 5-9 years and 10 or more years when compared to taking ART for less than one year, having no job when compared to having a self-employed/ government/ private sector job, being a Muslim/Animist/Pentecostal Christian when compared to being a protestant Christian, having more than two people living in their homes when compared to having two or less people living in their homes, living with their children when compared to living with their parents, being a nonsmoker when compared to being a smoker and being a nonalcoholic when compared to being an alcoholic. In fact, the odds of non-adherence to ART in female participants was 0.77 times (95%CI: 0.51, 1.16) that in male participants. The odds of non-adherence to ART comparing participants aged 41 and above to participants 21-30 years of age was 0.34 times (95%CI: 0.18,0.64). Also, the odds of non-adherence to ART in divorced/separated/widowed participants was 0.60 times (95%CI: 0.33, 1.11) that in single/never married participants. The odds of not adhering to ART in participants with secondary or less level of education was 0.66 times (95%CI: 0.42, 1.06) that in participants that had attained greater level of education beyond secondary school. With regards to the number of years since HIV positive diagnosis, the odds of not adhering to ART in participants who were 10 or more years since their HIV positive diagnosis was 0.35 times (95%CI: 0.14, 0.91) that in participants who had not been up to a year since their HIV positive diagnosis. Again, the odds of not adhering to ART in participants 10 or more years since their initiation of ART was 0.37 times (95%CI: 0.14, 0.98) that in participants who had been on

ART for less than a year. The odds of not adhering to ART comparing participants who had no job to participants who were either self-employed or working with the government or private sector was 0.76 times (95%CI: 0.50, 1.16). when considering participants' religion, the odds of not adhering to ART in participants who were either Muslim, Animist or Pentecostal in faith was 0.67 times (95%CI: 0.40,1.13) that in participants who were protestant Christians. The odds of not adhering to ART comparing participants living with more than 2 persons in their homes to those living with 2 or lesser persons was 0.75 times (95%CI: 0.47, 1.19) while the odds of not adhering to ART in participants living with their children was 0.43 times (95%CI: 0.20, 0.95) that in participants living with their parents. When comparing nonsmokers to smokers, the odds of not adhering to ART was 0.47 times (95%CI: 0.18, 1.22). Finally, the odds of not adhering to ART in participants who said they do not drink alcohol was 0.59 times (95%CI: 0.40, 0.87) that in participants who said they drink alcohol (Table 6.4).

After adjusting for potential confounding by each of the socio-demographic/ structural characteristics that appeared to have an association with non-adherence to ART in the bivariate analysis, only being of a younger age (21-30), attaining only the primary level of education and being an alcohol consumer remained significant predictors of non-adherence to ART. The odds of not adhering to ART in participants aged 41 and above was 0.35 times (95%CI: 0.14, 0.85) that in participants aged 21-30 years. Similarly, the odds of not adhering to ART in participants aged 31-40 was 0.42 times (95%CI: 0.17, 1.02) that in participants who were aged 21-30 years. Also, the odds of not adhering to ART comparing participants who attained only a primary level of education to those who attained a level of education higher than the secondary school was 0.57 times (95%CI: 0.33, 0.97). Finally, the odds of not adhering to ART in participants who said they do not consume

alcohol was 0.62 times (95%CI: 0.39, 0.98) that in participants who said they were alcohol consumers (Table 6.5).

6.5 Discussion

The only treatment modality to prolong life and improve quality of life in people living with HIV/AIDS (PLWHA) is anti-retroviral therapy (ART) [17,33]. ART has completely revolutionized the course of the HIV disease, transforming the HIV infection from a life-threatening infection to a manageable chronic disease [27]. It prevents further replication or multiplication of the virus, reduces the patient's viral load, increases CD4 counts, reduces the likelihood of opportunistic infections and patient hospitalizations, improves patient's quality of life and reduces mortality [11,12,34]. Adherence to ART reduces the viral load in an individual's body, prevents treatment failure and the likelihood of emergence of drug-resistant viral strains, and also prevents further transmission of the virus to uninfected individuals [17,35–37].

In this study assessing the extent of ART non-adherence among PLWH treated in HIV treatment centres in the Northwest, Southwest and Littoral regions of Cameroon, we evaluated the proportion of PLWH who are ART non-adherent, the number of times ART was missed in the last month and reasons for non-adherence to treatment. We document that the proportion of ART non-adherence in patients in these centres is high. Approximately, 38% of patients are non-adherent to their ART, a high proportion of concern since ART must be taken as prescribed for life, with 100% adherence for it to be effective [13,16,33]. Also, the frequency with which participants missed their ART (between one and more than five times in the past month) and reasons for missing ART (such as forgetfulness, preoccupied with other things, traveling somewhere else without drugs) are also documented. In this study, the available socio-demographic/structural characteristics of the participants, both individually and as a group, did not accurately discriminate between participants

who adhere to ART and those who do not. Nonetheless, younger age (21-30), achieving only elementary education and consuming alcohol had statistically significant associations with participants' non-adherence to ART.

The clinical implication of missing one or more doses of ART are development of drug resistance and treatment failure [10,17]. Although it has been documented that the best response to ART is seen when adherence is 100% [16], however, with the advent of new drugs such as the integrase strand transfer inhibitors and newer protease inhibitors, adherence with these drugs do not necessarily need to be 100% as the drugs could provide undetectable viral loads even with lower levels of adherence [38–40]. Nevertheless, the efficacy and durability of ART drug regimens still requires near perfect adherence rates as high as 95% or more [41–43].

While the level of ART non-adherence among participants in this study appears high (37.78%), it is within the range reported among participants in similar studies conducted elsewhere. We found no studies on ART non-adherence conducted in different regions of Cameroon prior this study, but the prevalence of ART non-adherence ranges from 7.5% in Lesotho [44] to over 39% in Australia [27]. In contrast, high ART adherence was also reported in other studies ranging from 62% in USA [45] to over 95% in Malawi [46].

A series of studies have documented the reasons for ART non-adherence including stigma, negative perception, lack of family and community support [47,48]. Other factors such as disclosure of status, unemployment, lack of transport to go to the health facility for ART, insufficient feeding, inadequate follow ups, lack of patient confidentiality, lack of disability grants and alternative forms of therapy have also been reported as common obstacles to ART adherence [48]. Besides these, physical, economic and emotional stresses, travel from home, business with

other things, depression, alcohol or drug use and ART dosing frequency have also been reported to hinder ART adherence [49,50]. In this study however, some of the reasons for missing ART included forgetfulness, being busy with other things and travelling to a different location without drugs reported in 35.29%, 27.65% and 12.35% of participants respectively. However, only 54.67% of participants know ART should be taken life-long, 7.32% do not believe in the benefits of ART, 28.60% think taking ART gives an unwanted reminder of HIV status and 2.00% of participants said they have experienced health service discrimination while seeking ART services – these could be masked reasons for participants’ non-adherence to ART and reiterates a need to improve health workers attitudes towards patients, improve staff-patient-communication and proper counselling of patients on the importance of adhering to ART prior to their ART initiation.

Some studies have found that factors significantly associated with ART adherence include trust in medication, trust in healthcare system and interpersonal relationship with physicians and peers [45] and disclosure of HIV status, drug addiction, satisfaction with health service and perception of the need for medical treatment [51]. While our sample size was sufficient to estimate the proportion of ART non-adherence among participants, only a limited number of covariates appeared to have an association with non-adherence and could be considered as potential predictors - age, education, and alcohol consumption. Our findings are similar to those of other studies that found age [52,53], education [19,54,55] and alcohol consumption [56] as factors associated with ART non-adherence. Nonetheless, our findings differ from studies that found ART non-adherence to be associated with side effects of the drugs, social isolation and complexity of the antiretroviral (ARV) regimens [57]; physical, economic and emotional stress [49]; poor or inability to follow prescribed treatment, no visits in a month, anxious and or depressed mood,

difficulty in taking medication, cannabis consumption and receiving methadone treatment [58]; and being a female sex worker and suffering from moderate-to-severe depression [52].

Limitations and strengths of this study

The level of ART non-adherence in this study could be influenced by population characteristics, the COVID-19 pandemic and the current political crisis in the country which might further be limiting access to ART. Although we sampled participants in three regions of the country, the sample may not have been representative of all PLWH and seeking ART services in these regions as the study did not include all treatment centres in each selected region. Furthermore, the study included only a cross section of PLWH in Cameroon. Thus, the prevalence of non-adherence obtained reflects only the detection of cases of non-adherence in our study settings and not necessarily the incidence of non-adherence or the overall prevalence of non-adherence in the population. Participants' differences in access to HIV treatment may also contribute to an underestimation of the prevalence of non-adherence to treatment in patients more likely not to visit treatment centres for their treatment. Again, there is the possibility of response bias as participants may not have revealed the truth of their past adherence to treatment history. There may equally be recall bias as participants may not have fully remembered whether they have been non-adherent to HIV treatment or not.

Despite these limitations, the study was strengthened by the fact that it was conducted in multiple randomly selected settings reflecting the diversity of patients in the country, interviewers were trained to ensure appropriate data collection, and primary data that ensures that questions pertaining to this study are directly ascertained was collected. Our statistical analysis also allowed

for a more accurate description of the prevalence of non-adherence and the factors more likely associated with non-adherence to HIV treatment in the context of Cameroon.

Conclusion

A high proportion of participants are not adhering to their ART. However, some of the reasons for missing ART are forgetfulness, being busy with other things and travelling to another place without drugs. Some of the reasons for missing ART are masked in participants limited knowledge in taking their ART as prescribed, disbelief in the benefits of ART, feelings that taking ART gives an unwanted reminder of HIV status and experience of discrimination when using ART services. This underscores the need to improve the attitude of staff working in HIV treatment centres, improve staff-patient-communication and provide patients with appropriate counselling on the importance of adhering to their ART prior to their ART initiation. There was a significant relationship between non-adherence to ART and only three participants' socio-demographic/structural characteristics (younger age (21-30), attainment of only the primary education and alcohol consumption), other factors that could possibly contribute to participants' non-adherence to ART needs to be explored. To guide policy making, future studies need to focus on assessing long-term ART non-adherence trends and determinants or predictors of ART non-adherence using larger samples of people living with HIV in many treatment centres and regions.

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Table 6. 1: Characteristics of the overall study population (N (%) or Mean (SD) or Median (IQR)).

Characteristic	N or Mean or Median	% or SD or IQR
Region of residence		
Northwest	150	33.26
Southwest	151	33.48
Littoral	150	33.26
Age (years)	43.42	10.42
Sex		
Male	140	31.11
Female	310	68.89
Marital status		
Single	170	37.69
Married	201	44.57

Divorced	17	3.77
Separated	18	3.99
Never married	19	4.21
Widowed/widower	26	5.76
Education*		
Primary	156	34.59
Secondary	153	33.92
High school	73	16.19
University	69	15.30
Religion		
Muslim	17	3.77
Catholic	183	40.58
Protestant	169	37.47
Pentecostal	79	17.52
Animist	3	0.67
Working status		
No job	138	30.67
Self-employed	206	45.78
Government staff	49	10.89
Private staff	57	12.67
Monthly income (XAF)	50000	30000-80000
Distance to centre (KM)	8	5-17
Time to centre (minutes)	30	15-45
Transportation means to centre		

By foot	43	9.56
Bike	63	14.00
Car/taxi	344	76.44
Number of people in home	5	2.62
Persons living with		
Spouse/partner	20	4.45
Children	191	42.54
Parents	29	6.46
Relatives	178	39.64
Nobody	31	6.90
Disclosed HIV status to family/friend		
No	86	19.15
Yes	363	80.85
HIV months	84	48-132
ART months	84	48-132
ART daily dosing		
Once daily	402	89.33
Twice daily	48	10.67

*Primary education involves at most seven years, secondary at most twelve, high school at most fourteen and university above fourteen years of education. N=frequency, %=frequency in percentage, SD=standard deviation and IQR=inter quartile range, KM= Kilometers, XAF= African Financial Community Franc.

Table 6. 2: ART adherence, health risk behaviors and HIV related hospitalizations among participants

Variable	N	%
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Ever missed taking ART last month		
No	280	62.22
Yes	170	37.78
HIV related hospitalization		
No	327	72.67
Yes	123	27.33
Reasons for hospitalization		
Chronic diarrhea	14	11.29
Chronic herpes simplex	7	5.65
TB/pneumocystis	15	12.10
Meningitis	4	3.23
Prolong fever	53	42.74
Weight loss	9	7.26
Jaundice	2	1.61
Other (malaria, anemia, cancer, diabetes, toxoplasmosis, candidiasis)	20	16.13
Health risk behaviors		
Smoking	18	3.99
Alcohol	164	36.36
Unprescribed drug use	113	25.17
Multiple sex partners	39	8.67
No physical exercises	261	58.00
N=frequency, %=frequency in percentage		

Table 6. 3: Participants' knowledge, experiences and views about ART

Variable	N	%
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Health status since ART initiation		
Worse	4	0.89
Stable	257	57.11
Better	189	42.00
Ever had ARV side effects		
No	366	81.33
Yes	84	18.67
Ever missed ART service appointment		
No	208	46.12
Yes	243	53.88
Know ART is life long		
Strongly agree	246	54.67
Agree	157	34.89
Uncertain	24	5.33
Disagree	12	2.67
Strongly disagree	11	2.44
Do not believe in benefits of ART		
Strongly agree	26	5.76
Agree	33	7.32
Uncertain	48	10.64
Disagree	209	46.34
Strongly disagree	135	29.93
Taking tablets gives unwanted HIV status reminder		
Strongly agree	129	28.60
Agree	106	23.50
Uncertain	38	8.43

Disagree	131	29.05
Strongly disagree	47	10.42
Worried ART will stop working in future		
Strongly agree	37	8.20
Agree	54	11.97
Uncertain	123	27.27
Disagree	176	39.02
Strongly disagree	61	13.53
Experienced physical adverse events in last 12 months		
Strongly agree	18	3.99
Agree	37	8.20
Uncertain	10	2.22
Disagree	279	61.86
Strongly disagree	107	23.73
Experienced health service discrimination in last 2 years		
Strongly agree	9	2.00
Agree	4	0.89
Uncertain	9	2.00
Disagree	167	37.03
Strongly disagree	262	58.09
N=frequency, %=frequency in percentage		

Table 6. 4: Correlates of participants non-adherence with ART- bivariable analysis.

Characteristic	N	%	<u>Participants non-adherence with ART</u>		P-values
			OR*	95% CI	
Region of residence					

Southwest	59	39.07	Ref		
Northwest	55	36.91	0.91	0.57-1.45	0.70
Littoral	56	37.33	0.93	0.58-1.48	0.76
Age					
21-30	29	59.18	Ref		
31-40	50	39.68	0.45	0.23-0.89	0.02
41+	91	33.09	0.34	0.18-0.64	<0.01
Sex					
Male	59	42.14	Ref		
Female	111	35.92	0.77	0.51-1.16	0.21
Marital status					
Single/never married	81	42.86	Ref		
Married /cohabiting	70	35.00	0.72	0.48-1.08	0.11
Divorced/separated/widow	19	31.15	0.60	0.33-1.11	0.11
Education**					
Primary	48	30.97	0.52	0.32-0.83	0.01
Secondary	56	36.60	0.66	0.42-1.06	0.09
Greater than secondary	66	46.48	Ref		
HIV years***					
<1	11	55.00	Ref		
1-4	53	50.00	0.82	0.31-2.14	0.68
5-9	55	35.48	0.45	0.18-1.15	0.10
10+	51	30.18	0.35	0.14-0.91	0.03
ART years					
<1	10	52.63	Ref		
1-4	53	49.53	0.88	0.33-2.35	0.80
5-9	60	36.59	0.52	0.20-1.35	0.18
10+	47	29.38	0.37	0.14-0.98	0.05

Working status					
Self-employed/ government/ private staff	123	39.55	Ref		
No job	46	33.33	0.76	0.50-1.16	0.21
Distance					
≤25	146	37.63	0.96	0.55-1.66	0.87
>25	24	38.71	Ref		
Religion					
Protestant	68	40.48	Ref		
Catholic	71	38.80	0.93	0.61-1.43	0.75
Muslim/ Animist/ Pentecostal	31	31.31	0.67	0.40-1.13	0.14
Monthly income (XAF)					
≤50000	74	39.57	0.85	0.46-1.55	0.59
51000 – 100000	29	36.25	0.73	0.36-1.48	0.39
>100000	24	43.64	Ref		
Transportation means to centre					
Bike	27	42.86	Ref		
Car/taxi	127	37.03	0.78	0.45-1.35	0.38
By foot	16	37.21	0.79	0.36-1.75	0.56
Number of people in home					
≤2	42	43.30	Ref		
>2	121	36.45	0.75	0.47-1.19	0.22
Persons living with					
Parents	15	51.72	Ref		
Children	60	31.58	0.43	0.20-0.95	0.04
nobody	13	41.94	0.67	0.24-1.87	0.45
Relatives	72	40.45	0.63	0.29-1.39	0.26

Spouse/partner	10	50.00	0.93	0.30-2.92	0.91
Smoke					
Yes	10	55.56	Ref		
No	160	37.04	0.47	0.18-1.22	0.12
Alcohol					
Yes	75	45.73	Ref		
No	95	33.22	0.59	0.40-0.87	0.01
Unprescribed drugs					
Yes	45	39.82	Ref		
No	125	37.31	0.90	0.58-1.39	0.64

*OR=unadjusted odds ratio, **Primary education at most seven years, secondary education is at most five years after primary education and above five years of education after primary education for greater than secondary, ***HIV years=number of years since HIV-positive diagnosis, OR=odds ratio, Ref= reference variable category, CI=confidence interval, P-values<0.25 suggests possible association to satisfaction, XAF= African Financial Community Franc.

Table 6. 5: Correlates of participants non-adherence with ART- multivariable analysis

Characteristic	N	%	<u>Participants non-adherence with ART</u>		P-values
			aOR*	95% CI	
Age					
21-30	29	59.18	Ref		
31-40	50	39.68	0.42	0.17-1.02	0.05
41+	91	33.09	0.35	0.14-0.85	0.02
Sex					
Male	59	42.14	Ref		
Female	111	35.92	1.04	0.64-1.70	0.87
Marital status					
Single/never married	81	42.86	Ref		
Married /cohabiting	70	35.00	0.95	0.55-1.61	0.84

Divorced/separated/widow	19	31.15	0.84	0.40-1.74	0.63
Education**					
Primary	48	30.97	0.57	0.33-0.97	0.04
Secondary	56	36.60	0.66	0.40-1.10	0.11
Greater than secondary	66	46.48	Ref		
HIV years***					
<1	11	55.00	Ref		
1-4	53	50.00	1.22	0.09-16.38	0.88
5-9	55	35.48	0.12	0.01-2.57	0.18
10+	51	30.18	0.23	0.01-5.64	0.37
ART years					
<1	10	52.63	Ref		
1-4	53	49.53	0.78	0.05-11.14	0.85
5-9	60	36.59	5.26	0.22-124.78	0.30
10+	47	29.38	2.00	0.07-55.17	0.68
Working status					
Self-employed/ government/ private staff	123	39.55	Ref		
No job	46	33.33	0.66	0.39-1.10	0.11
Religion					
Protestant	68	40.48	Ref		
Catholic	71	38.80	0.83	0.51-1.34	0.45
Muslim/ Animist/ Pentecostal	31	31.31	0.78	0.43-1.40	0.40
Number of people in home					
≤2	42	43.30	Ref		
>2	121	36.45	1.04	0.57-1.89	0.89

Persons living with					
Parents	15	51.72	Ref		
Children	60	31.58	1.01	0.38-2.70	0.98
nobody	13	41.94	1.55	0.33-7.16	0.58
Relatives	72	40.45	1.34	0.52-3.46	0.54
Spouse/partner	10	50.00	1.82	0.49-6.80	0.37
Smoke					
Yes	10	55.56	Ref		
No	160	37.04	0.45	0.13-1.54	0.20
Alcohol					
Yes	75	45.73	Ref		
No	95	33.22	0.62	0.39-0.98	0.04

*aOR=adjusted odds ratio, **Primary education at most seven years, secondary education is at most five years after primary education and above five years of education after primary education for greater than secondary, ***HIV years=number of years since HIV-positive diagnosis, OR=odds ratio, Ref= reference variable category, CI=confidence interval, P-values<0.05 are statistically significant.

Figure legends

Fig 1. Proportion of patients who missed ART in past 4 weeks versus number of times ART was missed.

Fig 2. Proportion of patients that missed ART versus reasons ART was missed.

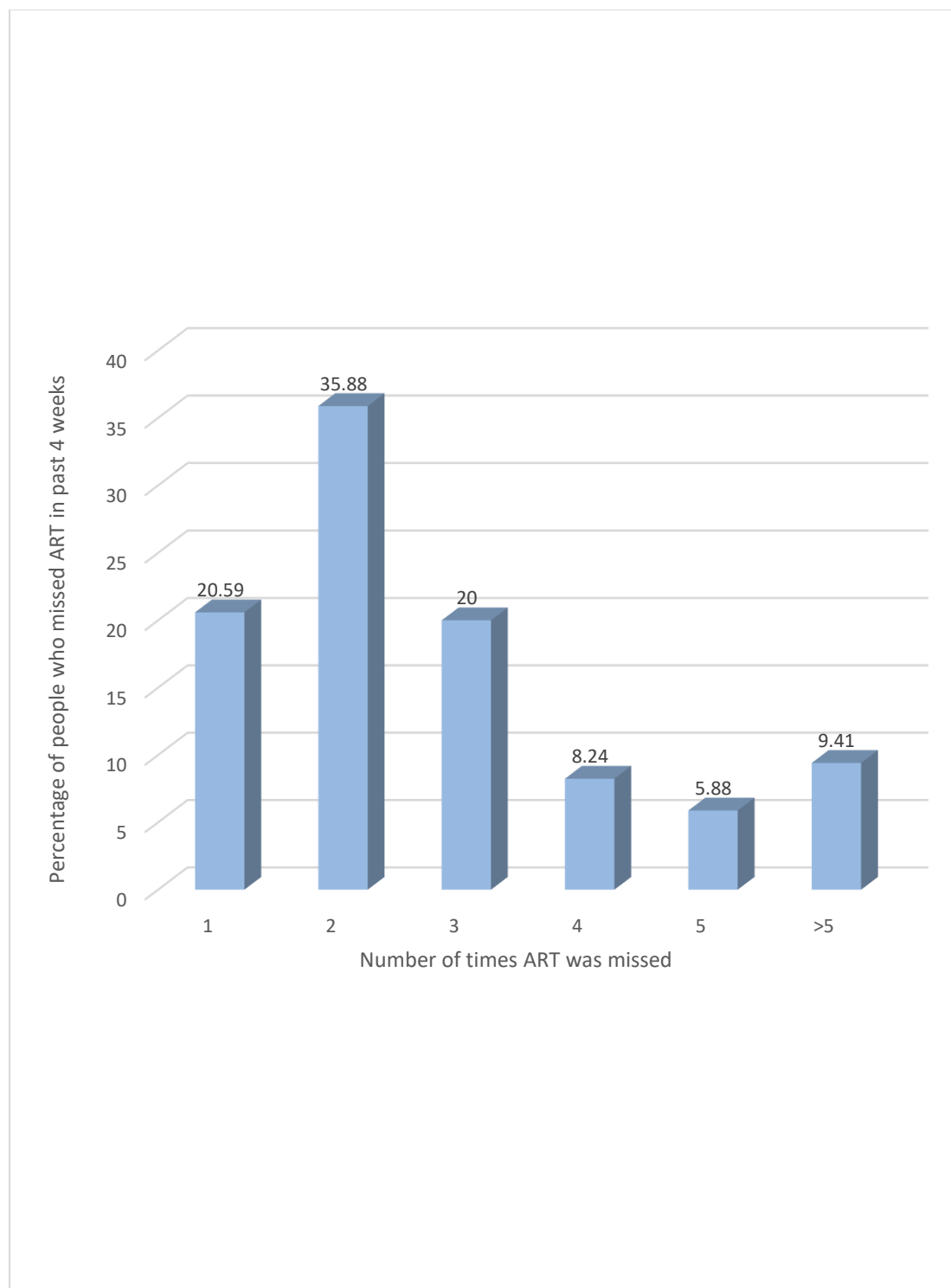


Figure 6. 1: Proportion of patients who missed ART in past 4 weeks versus number of times ART was missed.

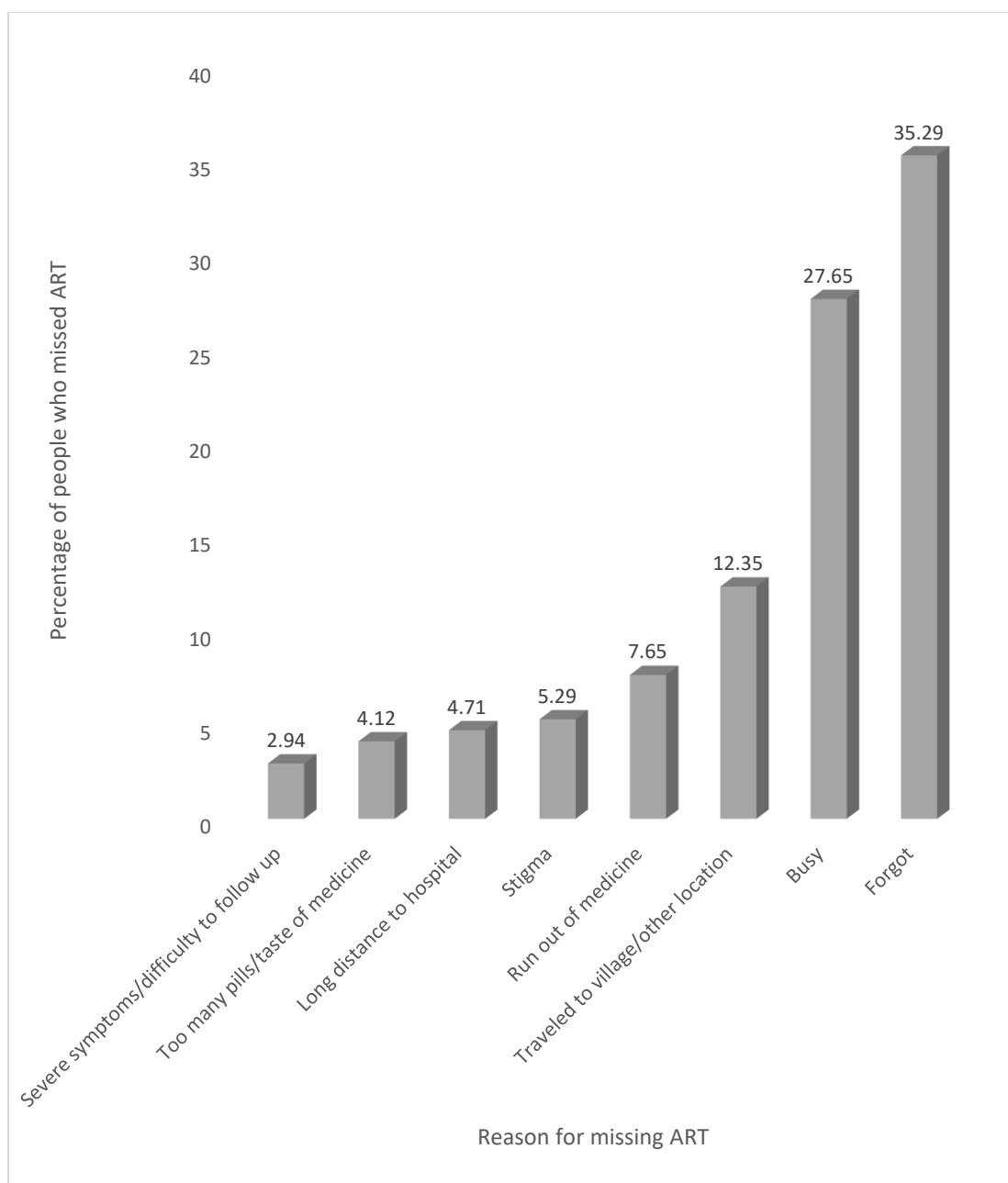


Figure 6. 2: Proportion of patients that missed ART versus reasons ART was missed.

Chapter 7: Barriers and facilitators to ART adherence among ART non-adherence people living with HIV in Cameroon: a qualitative phenomenological study

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7.1 Abstract

Background: Antiretroviral therapy (ART) needs to be taken for life with near perfect levels of adherence for it to be effective. Nonetheless, ART non-adherence is still observed in sub-Saharan African (SSA) countries such as Cameroon. The objective of this study was to assess the factors influencing non-adherence and or adherence among people living with HIV (PLWH) who have experienced non-adherence to ART in Cameroon.

Methods: A descriptive qualitative study of PLWH who have experienced non-adherence with ART in Cameroon was conducted. Data were collected using in-depth interviews. Collected data were analyzed using the NVIVO 12 software.

Results: In total, 43 participants participated in this study. The Southwest and Littoral regions each contributed 15 (34.88%) of participants, participants' mean age was 37.1 years (SD: 9.81) and majority 34 (82.93%) were females. ART adherence barriers include those related to patient (forgetfulness, business with other things, unwillingness to swallow drugs daily), medication (side effects), health service (arrogance of caregivers, occasional drug shortages at treatment centre, poor counseling of patient), stigma (fear of status disclosure), use of alternative treatment (traditional medicine, prayers and deliverance), resource limitation (limited food, limited finances), environmental/social (limited or no home support), and political instability (disruption

of free circulation by ghost towns, roadblocks and gunshots in some regions). ART adherence facilitators include social support (family and peer support), aligning treatment with patient's daily routines (align ART with schedule of family members), use of reminders (phone alarm, sound of church bell), health sector/caregiver support (messages to patient, financial support, proper counseling), and patient's awareness of HIV status/ART knowledge (awareness of HIV positive status, Knowledge of ART benefits).

Conclusion: ART adherence barriers in Cameroon include those related to patient, medication, health service, stigma, use of alternative treatment, resource limitation, environmental/social, and political instability. ART adherence facilitators include social support, aligning treatment with patient's daily routines, use of reminders, health sector/caregiver support, and patient's awareness of HIV status/ART knowledge. Given these barriers and facilitators, continuous information provision and consistent support both from patients' families and caregivers are needed to improve adherence among patients. Further studies including many regions and larger samples using both in-depth and focused group discussions as well as quantitative approaches are required to uncover the burden related to ART non-adherence.

7.2 Introduction

Antiretroviral therapy (ART) is typically a combination of three or more drugs that interrupts the Human Immunodeficiency Virus (HIV) replication, enables immune recovery and improves survival among people living with HIV (PLWH) [1]. However, poor retention in care and non-adherence to ART continues to undermine the success of HIV treatment and care programs across the world, especially in sub-Saharan Africa (SSA) where the burden of HIV is heaviest [2–4].

When a person is infected with HIV, the virus targets the immune system and weakens the individual's defense against other infections. As the virus progressively destroys and impairs the

functions of the immune cells, infected individuals become immunodeficient and their susceptibility to many infections, cancers and other diseases increases [5]. To avoid a progressive destruction of the immune cells, it is important that people should be effectively linked to care once they are diagnosed as HIV-positive [6].

At the moment, there is no cure discovered for HIV; the only treatment modality to prolong life and to improve quality of life of PLWH is ART [7,8]. ART has revolutionized the course of the HIV disease, transforming the HIV infection from a life-threatening infection to a manageable chronic condition [4]. It prevents further replication or multiplication of the virus, reduces the patient's viral load, increases CD4 counts, reduces the patient's likelihood of opportunistic infections and hospitalizations, improves patient's quality of life and reduces HIV related morbidity and mortality [9–11]. The increase in the patient's CD4 cell count allows the individual's immune system to recover and produce more CD4 cells which fights off infections and other HIV-related cancers [7]. To be effective however, ART has to be taken life-long as prescribed, with near perfect levels of adherence [8,12]. Adherence to ART reduces the viral load in an individual's body, prevents treatment failure and the likelihood of the emergence of drug-resistant strains of the virus and also prevents further transmission of the virus to non-infected persons [1,7,13,14]. In fact, with timely access to ART, PLWH can expect a near normal life expectancy [1,13,14]. Despite this, most health care systems in SSA face numerous challenges emanating from scaling-up ART for PLWH – prominent among these challenges are poor retention in care, congestion of the primary health care facilities and sub-optimal adherence to ART [3].

The barriers to ART adherence have been established in some studies. The identified major obstacles to ART adherence include stigma, negative perception, and lack of family and community support [15,16]. Other factors such as disclosure of status, unemployment, lack of

transport to go to the health facility for ART, insufficient feeding, inadequate follow ups, lack of patient confidentiality, lack of disability grants and alternative forms of therapy have also been reported as common barriers to ART adherence [16]. Besides these, physical, economic and emotional stresses, travel from home, business outside the home, depression, alcohol or drug use and ART dosing frequency have also been reported as barriers to adherence [17,18].

Some studies have also reported facilitators to ART adherence including social support [19,20], responsibility for raising children, disclosure of HIV status, improved health on ART, use of reminder aids and receiving education and counseling [19,21]. Community knowledge and understanding of the HIV infection, increasing collaboration between Western and Traditional providers, peer and family level support, decreasing cost and distance to ART clinic [22] as well as clear instructions for taking ART, service providers' positive attitude towards patients, benefits of adhering to ART and dangers of defaulting [21] have also been documented as factors facilitating ART adherence. Nevertheless, evidence is limited about the specific barriers and facilitators to ART adherence that are common in some SSA and or low- and middle-income countries such as Cameroon. More specifically, it is hard to find literature on the views of patients who have actually experienced non-adherence with HIV treatment concerning their barriers and facilitators to treatment adherence. As such, information for policy development targeting specific ART adherence barriers in order to improve HIV control and management is limited.

Also, Cameroon has been undergoing a political crisis since 2016. It has been documented that political conflicts leads to disruption of health care and displacement of patients [23]. Besides political conflicts, the COVID-19 pandemic has also been reported to have disrupted HIV care [24]. Thus, the political instability in Cameroon and the COVID-19 pandemic might have further limited access to ART for PLWH in this country. The objective of this study therefore was to

assess the factors that influence non-adherence and or adherence to HIV treatment in PLWH who have experienced HIV treatment non-adherence in Cameroon.

7.3 Methods

7.3.1 Study design

A qualitative phenomenological study design was used in this study. This design was conducted on adult PLWH who have experienced ART non-adherence in Cameroon.

7.3.2 Research setting

Briefly, the study was conducted in Cameroon – a country in sub-Saharan Africa with a high prevalence of HIV. The country has a population of over 28 million inhabitants [25] and it is divided into ten regions. Participants for the study were enrolled in HIV treatment centres in three selected regions (Littoral, Southwest and Northwest regions – all selected through balloting; this process involved making a list of the ten regions of the country, writing them on pieces of paper in a basket and then randomly picking three regions for the study) of the country. In each of the selected regions, the study was conducted in only one HIV treatment centre that was purposefully selected based on probability proportionate to the size of patients registered in the centre.

7.3.3 Study population, participants and sampling

This study only included PLWH who were on ART and had experienced ART non-adherence in Cameroon. To be eligible for the study, a participant had to be a PLWH receiving treatment in a treatment centre in the country, be at least 21 years old, have been on treatment for at least six months and have given their consent to participate. Furthermore, this study only included PLWH who had experienced HIV treatment non-adherence in Cameroon. PLWH who were severely sick,

having poor mental health, or had other ailments or disabilities that prevented them from providing the study with the requested information were excluded from the study.

We anticipated recruiting up to 30 participants in each centre. However, the number of participants in this study was largely dependent on responses received from participants. As long as there was variation in participant opinions, more participants were recruited. Recruitment of new participants in each centre (after recruiting a minimum of 10 participants per centre) stopped once saturation was attained. Overall, a total of 43 participants were enrolled in the study between the period of November and December 2021.

The sampling and enrollment of participants in this study was done by six trained interviewers (two from each of the selected regions where the study was conducted) with background training in health. The purposive sampling technique was employed by study interviewers to recruit participants in each study centre. Only PLWH who had experienced non-adherence (missed refill, ART appointment, taking ART as prescribed and had detectable viral loads) with ART in any of the three selected study centres were purposefully retained to participate in the study. This procedure continued until saturation was reached in each centre.

7.3.4 Data collection

To collect data for this study, in-depth interviews (IDIs) were conducted on PLWH who had experienced non-adherence with ART. Open ended questions adapted from similar studies [26,27], were used to collect data on participants' perceptions about factors contributing to their non-adherence to ART. The interviews were conducted in French or English by trained interviewers. To ensure privacy, all interviews were conducted in an arranged office in each treatment centre and participants' responses to questions were recorded.

Prior to analysis, the audio-recorded data were transcribed word verbatim and coded into common themes with the assistance of translators. This was cross-checked by other data collectors and one of the investigators for consistency, to ensure that strict methodological rigor was followed.

7.3.5 Data analysis

The NVIVO 12 software was used to analyze data. The collected data were transcribed and coded into themes and sub-themes for thematic analysis, as per Braun & Clarke's [28] guide for conducting a thematic analysis. This guide was used because it allowed for a transparent and rigorous analysis that produced relevant information for this study. Two people independently read the transcripts multiple times to immerse themselves in the raw data and made notes on initial topics and ideas relevant to the research question. The transcripts were coded iteratively, returning to the transcripts and altering and modifying the codes in response to the data and emerging patterns. Because coding word-by-word or line-by-line limits the ability to see patterns among and between pieces of data [29], lines of text from transcripts were broadly coded, ranging from a sentence to several sentences, so that participants' intentions were not lost. Finally, the two independent coders discussed their codes and reached a consensus agreement to resolve any differences. The codes were then used to create themes and subthemes that would respond to study objectives. The sub-themes were organized into major themes, and then each theme was described.

7.3.6 Trustworthiness

In conducting a qualitative study, trustworthiness is crucial to ensure that the study is rigorous and that it produces findings capable of impacting policy and practice [30]. To ensure trustworthiness in this study, trained personnel were recruited to collect data, transcribe, code and analyze the data. One of the investigators (AB) closely monitored the data collection process to ensure that data were properly collected. Following data collection, two independent individuals (AB and IKK)

transcribed and coded the data and then, they discussed their codes together in order to reconcile any differences. Two investigators (AB and SY) then reviewed the coded data in order to validate it and ensure that the codes and themes resulting from the transcripts were credible. Any issues such as contradictions, thematic misinterpretations and factual errors discovered by the investigators were discussed and clarifications made. An external auditor (CBM) skillful in qualitative research together with one of the investigators (SY) reviewed the coded data to further ensure dependability.

Also, to ensure that findings reflected the reality of the barriers to ART adherence, data were only collected from people who had actually experienced ART non-adherence. The data were collected across three regions of the country and this range of data helped enrich and deepened understanding of study findings.

7.3.7 Ethical considerations: Ethical clearance for the study was obtained from the Health Sciences and Science Research Ethics Board (REB) of the University of Ottawa (Ethics File Number: H-08-21-7274) and the Cameroon Baptist Convention Health Board Institutional Review Board (CBCHBIRB) (IRB study number: IRB2021-53). Administrative authorization was also obtained from the Regional Delegate of Public Health of the Southwest Region (Ref: 1211/MINSANTE/SWR/RDPH/P5/810/725) and the Regional Hospital Buea (Ref /MPH/SWRDPH/BRH/IRB). Written informed consent was obtained from all participants prior to their participation in the study.

7.4 Results

7.4.1 Participants' characteristics

The characteristics of the 43 participants that took part in this study are presented in Table 7.1. The Southwest and Littoral regions of the country each contributed 15 participants in the study and the

mean age of participants was 37.1 years (SD: 9.81). Most participants (34) in the study were females. Single and married participants each represented more than a third (16) of participants in the study. More than half (24) of the participants attained only the secondary level of education and less than one third (14) of them were Roman catholic Christians. Few (11) of the participants were engaged in business activities and the ART dosing frequency for all participants in the study was once daily. The median number of years participants had been on ART was 7 years (IQR: 3-10); in fact, more than one third (41.86%) of participants had been on ART for 6-10 years (Figure 7.1).

7.4.2 Barriers to ART adherence among ART non-adherent participants in Cameroon

Table 7.2 shows the details of the barriers to ART adherence among ART non-adherent participants. The barriers are separated into main themes and are described with some participants' views in quotations.

Patient-related barriers: These are patients' behavioral factors or activities that prevent them from taking their medication. Patient-related barriers are linked to the fact that patients displace themselves from home without their drugs, either overnight or return too late for them to take their drugs. Added to this, some patients feel tired of taking drugs daily and others simply forget to take them.

“Nothing hinders me except that I forget because if I forget I know that I have passed that day without taking it so it is only for the next day that I will take it.” [56 years old, female].

“I don't like swallowing medicines every day, each time I take it, I ask God, when is this going to end.” [36 years old, female].

“I went for a burial and slept there and came back to the house when 6A.M had already passed so I could not take it again.” [36 years old, female].

Medication barriers: These are drug reactions on the patients when they swallow the drugs. These are mostly due to side effects of the Antiretroviral drugs (ARVs) such as nausea, dizziness and nightmares experienced by some patients when taking the drugs.

“I think the most difficult part is that when I go to work the medicine makes me weak.” [40 years old, male].

“Well, when I started taking the medicine it used to turn my neck, it used to make me feel like I will vomit as if I was pregnant, but it was just when I started the medicine” [66 years old, female].

“I used to have so many dreams at night especially about death when I started taking the medicines, but after a while this stopped.” [38 years old, female].

Health service barriers: These are barriers encountered by patients in the healthcare facilities which prevent or discourage patients from taking their ART. These stem from drug shortages to caregiver attitudes which cause patients to wait for extended periods of time when they go to collect their drugs in treatment centres. This makes some patients feel frustrated and they will abandon their ARVs. Besides this, poor counseling of patients on importance of adhering to their treatment makes patients non-adherent to ARVs.

“Some of the nurses are harsh, like when somebody just comes in, they’ll be like “come, na ya book this? (Come, is this your book?).” [26 years old, female].

“The hardest part is when I come to the hospital like this to come and take it, and when they are delaying to give my medicine like that, it really bothers me.” [33 years old, female].

Stigma related barriers: Fear of disclosure of status makes some patients feel ashamed of moving around with their drugs or even taking them in the midst of others. As such, they leave drugs at home when they travel and even when they are in possession of the drugs, they would not take them if they were in the company of others.

“I feel uneasy to take it because when I travel like that, maybe I may go with people I feel uneasy taking the drugs in the midst of people.” [35 years old, female].

“Number 1 problem is forgetfulness and number 2 is that whenever I’m elsewhere and it is time for drugs, I cannot remove it to drink when people are around.” [45 years old, male].

Alternative treatment: The belief that traditional medicine cures a patient of HIV or that prayers to God could make a patient receive deliverance from HIV renders some patients non-adherent to their ARVs when they go in search for this alternative treatment.

“I stopped taking it for some time because I believed that God has the final say, God is the healer, and he can do anything to be possible so that made me to stop taking it for some time.” [47 years old, male].

“I don’t have anything that is really difficult for me, it’s just that I’m not really happy that every day I have to take them because it is showing that what we are taking are chemicals which aren’t good for humans ... at times I feel like I should even go for these herbs, I have a specialist I went to him to try to treat it and he showed me some amount of people that have come to him concerning HIV, it’s just that it is expensive.” [38 years old, female].

Resource limitation: Patients are often advised to eat well before swallowing their ARVs; when there is neither food nor money to buy food, some patients simply abandon their drugs. Besides this, some patients need money to pay transport to the treatment centre to collect/refill their drugs;

in case of lack of money, they simply stay home and cannot continue taking their drugs when the drugs get finish.

“The most difficulty I face when taking my medicine is when I don’t have the transport to go and take it every day. That is the only difficulty.” [34 years old, male].

“As I am taking this medicine, they said I should be eating fruits, vegetables, and many other things but with this crisis someone is just short of money, you see food, but you are not able to buy it.” [47 years old, female].

Environmental/social barriers: Some patients are faced with multiple problems – intermittent lack of support for childcare as well as limited transportation to go to health centre for treatment. For instance, some of the patients’ spouses or family members who provide support to help them take their drugs occasionally travel – leaving the patients with no support and at such moments, patients are non-adherent to their drugs.

“At times I forget my rendezvous like when my husband travels, I have difficulty in coming because it is far plus with the children so at times my rendezvous comes, and he is not there, and he’s the one who always carries me to come here, so, when he travels like that, to come here it is difficult with the kids; that is why at times it disturbs me.” [21 years old, female].

Poor mental health: Some patients are suffering from poor mental related health issues such as depression. Such patients find no meaning/reason in living or being alive. This makes them lose hope on their treatment to the point where they give up on taking ART in preference to death.

“See it’s because I lost my children and I also lost my workshop, that’s where I just gave up, it’s not like I was ignorant. I just wanted to give up that it is just better for me to die.” [33 years old, male].

Intrapersonal and cognitive barriers: Some patients have a challenging time seeing themselves as the only one taking ART in the house or family. Even when they have social support or people to help remind them adhere to their treatment, these patients perceive the help as unwanted because those providing the help are not taking the treatment.

“The most difficult part is that everyone in the house is not taking it and you’re the only one taking it; so, like when, might be someone will remind you, like you just get angry that this person is not taking it and the person is telling me to go and take my medicine, it doesn’t concern the person like don’t remind me to take them.” [21 years old, male].

Political instability: Two of the regions (Northwest and Southwest regions) where the study was conducted are experiencing an ongoing political crisis – there are sometimes roadblocks, gunshots, and organization of ghost towns (days in which all activities including movement of people in a city are closed down) on some days which obstructs circulation and scares patients from going to collect/refill their drugs when they are finished. When patients run out of drugs during these periods, they have no option but to stop taking treatment.

“The challenge I have is only that the last time I went to the village, I overstayed there which wasn’t my plan because they blocked the roads, so I wasn’t able to come back, that is the only challenge I have.” [31 years old, male].

“... because of these gunshots we can run to a different quarter to go and sleep, so the thing disturbed me and just that one day that I didn’t take my medicine it disturbed me a lot.” [47 years old, female].

“...with all these ghost towns at times we make 2 weeks at home without going anywhere and my medicine got finished.” [37 years old, female].

“... I went to make 2 weeks in the village, and they locked the roads, so I made one month and did not take medicine for 2 weeks.” [42 years old, female].

7.4.3 Facilitators to ART adherence among ART non-adherent participants in Cameroon

Table 7.3 shows factors helping patients’ adherence to ART. Major factors facilitating ART adherence among patients include:

Social support: Most patients would adhere to treatment if they were supported emotionally, materially, and financially by their family members and or peers.

“At times when I forget my rendezvous, it is my husband who reminds me himself, he even brings me here to collect my medicines when I have my rendezvous. He is really helping me take my medicines.” [32 years old, female].

Patients’ daily routines: Aligning the time patients are supposed to take their drugs to coincide with the time certain routine schedules occur helps patients remember to take their drugs. For instance, taking drugs before spouse/family member leaves for work every morning or after brushing teeth in the morning or just when children are preparing to go to school.

“When I wake up and brush, I just take my medicine and I eat well, if there is fruit to eat I will eat on top of it.” [34 years old, female].

Reminders: Setting up an alarm on a phone at a particular time when drugs should be taken or programming to take drugs when the church bell rings, for patients staying besides the church or when children are about going to school helps some patients remember to take their drugs.

“I’m just beside the church so when they ring the bell I just wake up and take it.” [38 years old, female].

“... Once I hear the alarm on my phone ring every morning it just indicates that I have to take it.” [30 years old, female].

Health sector/caregiver support: Some patients expressed that, messages, or calls from caregivers reminding them to go for their drugs helps them adhere to treatment. Others state that availability of drugs at the treatment centre at all times, development of alternative ART drug formulations (such as injectables) and provision of financial incentives to assist in patient transportation to go collect drugs at the treatment centre, would help in treatment adherence.

“The only way you people can help me is that if you have a chance, you can call me at that time to remind me so that if I was elsewhere, I could say eh my nurse just bipped me that I should take my medicine because there are times one sleeps and forget.” [47 years old, male].

“It’s just the finances you people could help me with because for the moment I’m not doing anything so coming to take drugs is not easy for me.” [32 years old, female].

“Well, what could help ease the task for me is if the drugs could be given to me through injection.” [40 years old, female].

Patient’s awareness of health status/ART knowledge: Some participants reported that being aware of their HIV status and knowing that ART improves their health, motivates them to continue taking the drugs as prescribed.

“I know that the medicine is a tablet that’s like it’s not that it cures the virus that is in us, but it makes the virus to be weak in a way that it cannot multiply because as long as I am not taking my medicine, the virus multiplies every day plenty. So, when I am taking the medicine, it makes the virus to lose that energy or force to multiply, so it makes it weak, and it just stays in one place. I know that I have the virus, but it is that the virus cannot multiply as long as I drink my medicine.”
[27 years old, female].

7.5 Discussion

Non-adherence or sub-optimal adherence to ART may result in unsuppressed viral load, leading to development of drug resistance, opportunistic infections and ultimately mortality of patient [27,31]. To ensure prolonged benefits of treatment therefore, adherence to ARVs is key [12,27,32].

We assessed the barriers to ART adherence among people who have experienced ART non-adherence, as well as the factors that facilitate ART adherence among these people, in three regions of Cameroon (Northwest, Southwest and Littoral regions). We have documented that the barriers to ART adherence in Cameroon are classified into ten major themes: patient barriers (forgetfulness, other commitments, unwillingness to swallow drugs on a daily basis), medication barriers (drug side effects), health service barriers (arrogance of caregivers, occasional drug shortages at treatment centre, poor patient counseling), stigma-related barriers (fear of status disclosure), use of alternative treatment (traditional medicine, prayers and deliverance), resource limitation (limited food, limited finances), environmental/social barriers (limited or no home support), poor mental health barriers (depression), intrapersonal and cognitive barriers (seeing self as the only one taking ART) and political instability (disruption of free circulation by ghost towns, roadblocks and gunshots in some regions). We identified five major groups of ART adherence facilitators: social support (family and peer support), aligning treatment with patient’s daily

routines (align ART with family members' schedules), use of reminders (phone alarm, sound of church bell), health sector/caregiver support (messages to patient, financial support, proper counseling), and patient's awareness of HIV status/ART knowledge (awareness of HIV positive status, knowledge of ART benefits).

While the barriers to ART adherence in this study represent the reality of study participants living in Cameroon, they reflect ART adherence barriers reported among participants in similar studies conducted elsewhere. Prior to this study, we did not find studies conducted on barriers to ART adherence among ART non-adherent participants in Cameroon, but studies elsewhere have reported similar barriers such as food insecurity [33,34], stigma related disclosures [26,35,36], low social support and poor relationship between patient and caregivers [37–39], mental illness (especially depression) [40,41], intrapersonal and cognitive issues (perceived psychological and behavioral issues) [42,43], preference for traditional medicine and forgetfulness [26,27], and side effects of ARVs [44]. In contrast, other studies have reported additional barriers to ART adherence such as substance abuse, denial of HIV status, treatment longevity, patients' socioeconomic status, social isolation and complexity of regimens [38,45,46], which were not documented in this study. This study has however reported political instability and insecurity (ghost towns, roadblocks and gunshots) as a major barrier to ART adherence experienced by patients especially in the Northwest and Southwest regions of Cameroon which have not been reported previously. During political instability, there is disruption of health care and displacement of patients – limiting patients' access to ART. Unplanned prolonged ART interruption caused by ghost towns for instance have negative effects on HIV treatment outcomes including increased morbidity and mortality, as well as development of drug resistant strains of the virus [23]. Besides political instability, the COVID-19 pandemic also had a major impact on ART adherence. The pandemic disrupted HIV care

[24,47] through lockdowns, physical distancing and isolation restrictions measures that were enforced. COVID-19 restrictions also caused fear and anxiety symptoms in patients resulting in low ART adherence [47–49].

Concerning facilitators to ART adherence reported in this study, other studies have documented similar factors facilitating ART adherence such as use of support groups and social networks [20,22,50], support from health care providers, use of reminder aids [51,52], linking pill-taking with daily activities or events [44,53], and social support [19]. Nevertheless, other studies have also documented additional ART adherence facilitators such as perceived need to meet family responsibilities, perceived positive outcomes, self-motivation, disclosing HIV status to others, responsibility for raising children and experienced treatment benefits [19,50,51,53].

Limitations and strengths of study

The study included only a cross section of PLWH at the treatment centres who acknowledged that they had not been adherent to treatment. This might not be representative of the population of patients that do not adhere to treatment in the country. Thus, results of the study may not be generalizable to other communities in Cameroon. Again, there is the possibility of response bias as participants may not have revealed the real picture of their past adherence to treatment history. There may equally be recall bias as participants may not have fully remembered their reasons for non-adherence to ART or whether they had been non-adherent to HIV treatment or not. Also, we were looking for reasons for non-adherence which change over time; it is possible that respondents did not offer the full range of their reasons or reported only recent reasons for non-adherence.

Nonetheless, the strengths of the study are that it was conducted in multiple randomly selected settings reflecting the diversity of patients in the country, interviewers were trained to ensure

adequate data collection and primary data that ensures that questions pertaining to this study are directly ascertained were collected not just from PLWH but precisely from those who acknowledged they had experienced non-adherence with ART.

Conclusion

The barriers to ART adherence in Cameroon include patient barriers (forgetfulness, business with other things, unwillingness to swallow drugs daily), medication barriers (side effects of drugs), health service barriers (arrogance of caregivers, occasional drug shortages at treatment centre, poor counseling of patient), stigma related barriers (fear of status disclosure), use of alternative treatment (traditional medicine, prayers and deliverance), resource limitation (limited food, limited finances), environmental/social barriers (limited or no home support), and political instability (disruption of free circulation by ghost towns, roadblocks and gunshots in some regions). ART adherence facilitators include factors such as social support (family and peer support), aligning treatment with patient's daily routines (align ART with schedule of family members), use of reminders (phone alarm, sound of church bell), health sector/caregiver support (messages to patient, financial support, proper counseling), and patient's awareness of HIV status/ART knowledge (awareness of HIV positive status, Knowledge of ART benefits). Given these barriers and facilitators, continuous information provision and unflinching support both from patients' families and caregivers are needed to improve ART adherence among patients. Further studies including many regions and larger samples using both in-depth and focused group discussions as well as quantitative approaches (to determine the scale of interruptions especially in conflict areas using objective measures such as medication refill adherence, viral load, and resistance test results) are required to uncover the burden related to ART nonadherence.

7.6 References

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Table 7. 1: Characteristics of the overall study population (N (%) or Mean (SD) or Median (IQR)).

Characteristic	N or Mean or Median	% or SD or IQR
Region of residence		
Northwest	13	30.23
Southwest	15	34.88
Littoral	15	34.88
Age	37.1	9.81
Sex		
Male	7	17.07
Female	34	82.93
Marital status		
Single	16	38.10
Married	16	38.10
Divorced	1	2.38
Separated	3	7.14
Widowed/widower	6	14.29
Education*		
Primary	13	30.95
Secondary	24	57.14
High school	1	2.38
University	4	9.52
Religion		
Muslim	2	4.76
Catholic	14	33.33
Baptist	4	9.52
Presbyterian	7	16.67
Pentecostal	13	30.95
Animist	2	4.76
Occupation		
Business	11	27.50
Cleaner	1	2.50
Designing	1	2.50
Driving	2	5.00
Entrepreneur	1	2.50
Farming	9	22.50
Hairdressing	1	2.50
Housewife	4	10.00
Mechanic	1	2.50

Nursing	1	2.50
Retired	1	2.50
Security officer	1	2.50
Student	2	5.00
Tailoring	2	5.00
Teaching	2	5.00
ART years	7	3-10
ART daily dosing		
Once daily	43	100.00

*Primary education involves at most seven years, secondary at most twelve, high school at most fourteen and university above fourteen years of education. N=frequency, %=frequency in percentage, SD=standard deviation and IQR=inter quartile range.

Table 7. 2: Barriers to ART adherence among people who have experienced ART non-adherence in Cameroon

Themes	Sub-themes	Example
Patient	- Forgetfulness - Business with other things - Hate swallowing drugs	- Went to the farm or work or occasion and unexpectedly slept there or returned late - Feeling tired or not comfortable swallowing drugs daily
Medication	- Side effects	- Nausea - Dizziness - Nightmares
Health service	- Arrogant caregivers - Drug shortages - Poor counseling	- Delay in dispensing drugs to patient when they are in hospital - Unwelcoming attitudes of some caregivers
Stigma related	- Fear of status disclosure	- Carrying drugs around or taking them in public can make people discover patient's status and stigmatize them
Alternative treatment	- Traditional medicine - Prayers and deliverance	- Belief that traditional medicines flushes out

		- virus from one's system - Belief that God can deliver one from illness if they focus on prayers and fasting
Resource limitation	- Limited food - Limited or no finances	- Did not have food to eat before taking drug - Lacked money for transportation to hospital
Environmental/social	- Limited or no home support	- Live alone/spouse travels
Poor mental health	- Depression	- See no meaning in being alive
Intrapersonal and cognitive	- Lone person on ART	- See self as the only one taking ART in family
Political instability	- Disruption of movement by ghost towns	- Roadblocks, gunshots on ghost town days scares people to go for drugs

Table 7. 3: Factors that facilitate ART adherence among people who have experienced ART non-adherence in Cameroon

Themes	Sub-themes	Example
Social support	- Family support - Peer support	- Provide emotional and material/financial support - Help reminding patient to take drugs
Patients' daily routines	- Align ART with recurring routines - Align ART with schedule of family members	- Patient takes drugs when children are preparing to go to school or before spouse/family member goes to work
Reminders	- Phone alarms - Church bell - Living with pupils/students	- Patient is reminded of time to take drugs when phone alarms or when church bell

		rings or when children wakeup to go to study
Health sector/caregiver support	- Messages/calls to patient - Financial support - Proper counseling - Availability of drugs - Alternative drug formulation (injectables)	- Text messages or calls reminding patients to go for their drugs - Continuous education of patients on importance of adhering to treatment
Patient's awareness of health status/ ART knowledge	- Aware of HIV status - Know ART helps	- experience of an improvement in health with ART

Figure Legends

Figure 1. Proportion of participants versus length of time on ART

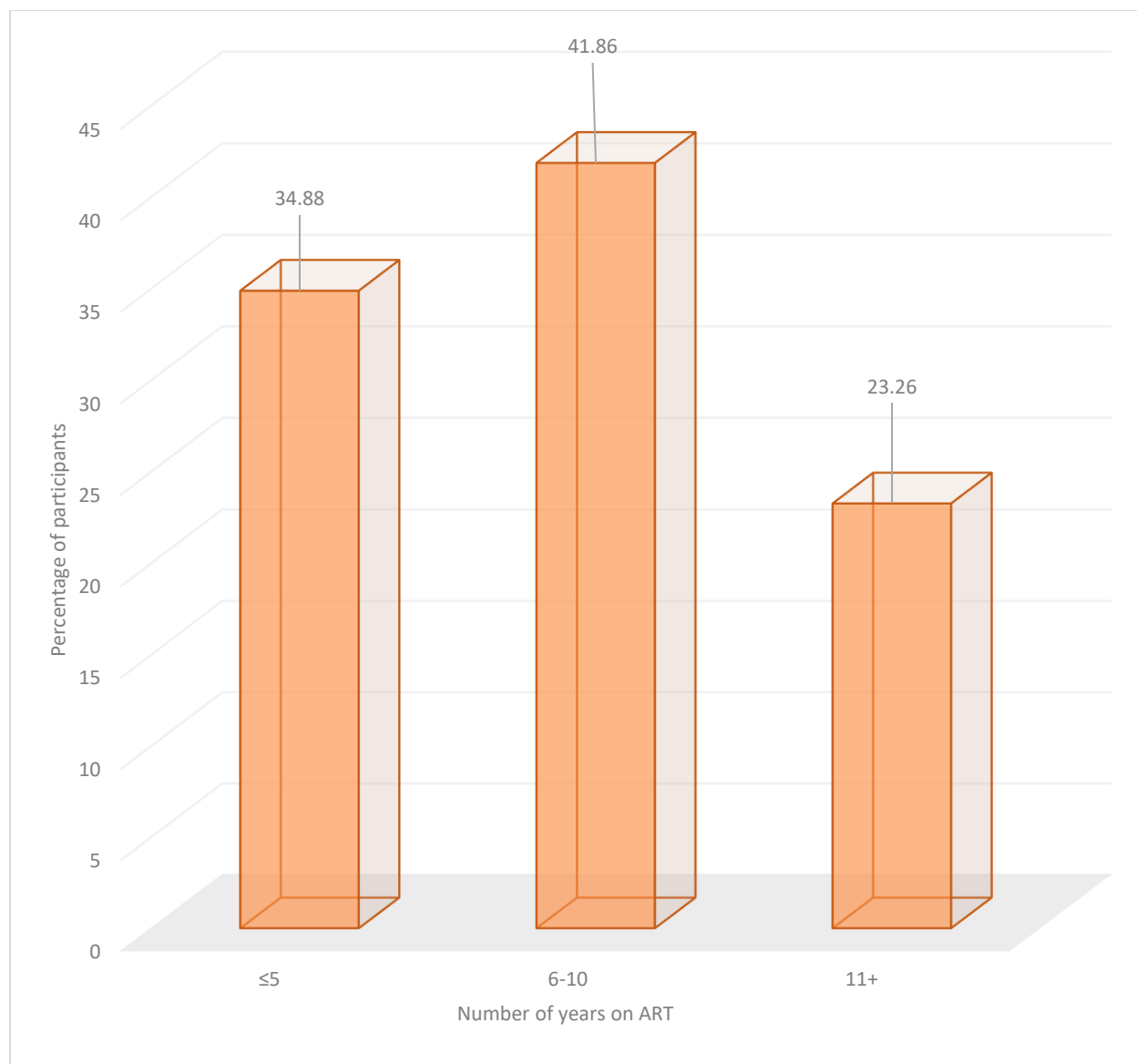


Figure 7. 1: Proportion of participants versus length of time on ART

Chapter 8: Thesis discussion

Thesis contributions to the Body of Knowledge

This dissertation was premised on the hypotheses that there exist common barriers to ART adherence and common interventions that can be implemented to improve ART adherence across SSA countries, that non-adherence to ART is prevalent in PLWH in Cameroon, that readily available socio-demographic/structural characteristics could be used to predict non-adherence, and that people who have experienced ART non-adherence have specific barriers hindering them from adhering to treatment. We therefore sought to provide data that could guide stakeholders involved in HIV management as well as policy makers in deriving better policies or management strategies that will make patients adhere to treatment. This thesis contributes to the body of knowledge on barriers and facilitators to ART adherence, as well as interventions promoting adherence across SSA countries, identified using mixed research methods. Overall, the thesis reveals that if we are to harness the full potential of ART and mitigate the HIV burden, the barriers, facilitators, and adherence enhancing interventions need to be recognized and integrated by stakeholders and policy makers when formulating policies or crafting treatment strategies – failure to do so, only promotes ART non-adherence by patients.

We conducted a comprehensive systematic review and meta-analysis on studies examining barriers to ART adherence and interventions to boost adherence among HIV-positive adults aged 15 years and above in SSA, published from January 2010 onwards. The results reveal that the barriers and facilitators to ART adherence in SSA countries can be categorized under seven primary factors: patient-related, health system-related, medication-related, stigma, poor mental health, socioeconomic and socio-cultural-related factors. Common interventions that enhance ART

adherence encompass counselling, incentives, mobile phone short message services (SMS), peer delivered behavioral intervention, community ART delivery intervention, electronic adherence service monitoring device, lay health worker lead group intervention and food assistance. These strategies prove effective either as standalone approaches or in conjunction with other methods. Even though our review does not identify the most impactful intervention, we nonetheless confirm our hypothesis that there exist common barriers to ART adherence and common interventions that can be implemented to improve ART adherence across SSA countries.

Building on the findings of the systematic review which only identified barriers, facilitators and adherence promoting interventions across SSA without indicating the prevalence and determinants of ART non-adherence, we also conducted a cross-sectional descriptive study on adult PLWH who were receiving ART treatment in selected HIV treatment centres in three regions of Cameroon. Results reveal a high proportion of participants are not adhering to their ART. Some of the reasons for missing ART are forgetfulness, being busy with other things and travelling to another place without drugs. However, some of the reasons for missing ART are masked in participants' limited knowledge in taking their ART as prescribed, disbelief in the benefits of ART, feelings that taking ART gives an unwanted reminder of HIV status and experience of discrimination when using ART services. This underscores the need to improve the attitude of staff working in HIV treatment centres, improve staff-patient-communication and provide patients with appropriate counselling on the importance of adhering to their ART prior to their ART initiation. There was a significant relationship between non-adherence to ART and only three participants' socio-demographic/structural characteristics (younger age (21-30), attainment of only the primary education and alcohol consumption). Although only few variables showed a significant relationship to non-adherence, these results still confirm our hypothesis that non-adherence to ART is prevalent in

PLWH in Cameroon, and that readily available socio-demographic/structural characteristics could be used to predict non-adherence.

These survey findings, together with the systematic review helped inform our qualitative phenomenological study on adult PLWH who had experienced ART non-adherence in Cameroon. The results show that the barriers to ART adherence among these group of patients in Cameroon include patient barriers (forgetfulness, business with other things, unwillingness to swallow drugs daily), medication barriers (side effects of drugs), health service barriers (arrogance of caregivers, occasional drug shortages at treatment centre, poor counseling of patient), stigma related barriers (fear of status disclosure), use of alternative treatment (traditional medicine, prayers and deliverance), resource limitation (limited food, limited finances), environmental/social barriers (limited or no home support), and political instability (disruption of free circulation by ghost towns, roadblocks and gunshots in some regions). ART adherence facilitators include factors such as social support (family and peer support), aligning treatment with patient's daily routines (align ART with schedule of family members), use of reminders (phone alarm, sound of church bell), health sector/caregiver support (messages to patient, financial support, proper counseling), and patient's awareness of HIV status/ART knowledge (awareness of HIV positive status, Knowledge of ART benefits). Considering these results, we again confirm our hypothesis that people who have experienced ART non-adherence have specific barriers hindering them from adhering to treatment.

Unique to this thesis, Cameroon's sociopolitical instability stands out as a major barrier hindering patients from adhering to ART. This is worst in the Northwest and Southwest regions of the country where frequent roadblocks and ghost towns (days in which all activities including movement of people in a city are closed down) prevent patients from seeking ART services. The

impact of this political instability does not only prevent patients from seeking ART services but could also disrupt ART supply chains to affected regions, limit availability of human healthcare resources and other alternatives to care for patients. Thus, delay in the resolution of the ongoing political crisis in Cameroon will not only further fuel non-adherence to ART but might render ART non-efficient due to the development of resistant strains of the virus during periods of treatment interruption.

Limitations

Although most of our participants were female, a gender lens was not embedded in the design of the study. The objectives of our study were limited to assessing the prevalence of ART non-adherence and associated factors as well as the barriers and facilitators to ART adherence. It is possible that gender plays a role in patients' adherence or non-adherence to ART. Nevertheless, the predominance of female participants in our study is not surprising - women are more likely to be captured by health services. In Cameroon, when women go to seek antenatal-related health services, they are screened for HIV and if positive, they are directly linked to ART services. The cultural norms in this country are in favour of men not accompanying their wives to hospital. Since men do not commonly attend childbirth related services, they are typically not captured by health services. Also, women are more likely to contract HIV and other sexually transmitted infections than men – anatomically, women have a greater mucus area that is exposed to HIV during sexual intercourse. All these might contribute to the disproportionate high number of women infected with HIV.

Besides the gender intersectionality limitation of our study, the study was a cross-sectional design and did not include all treatment centres in the selected regions. As such, our sample might not be representative of all PLWH in the regions.

Finally, our study was conceptualized using the HBM which really does not explain how cultural norms and environmental factors contribute to ART non-adherence. We considered other models such as the Social Action theory and the Information-Motivation-Behaviour theory, but discarded these theories as they did not vividly explain why and how the elements combine to explain adherence or non-adherence to ART. The HBM was adopted notwithstanding its limitation because it usefully describes demographic and psychological factors that influence motivation and also identifies factors that perpetuate actual adherence behaviour.

Public health implications

The public health implications of our findings are important. First, to harness the full potential of ART and mitigate the HIV burden in SSA countries, stakeholders engaged in HIV prevention and treatment must recognize and integrate barriers, facilitators, and adherence enhancing interventions when formulating policies or crafting treatment strategies. Failure to recognize these and address them accordingly only fuels non-adherence to ART by patients and the potential for ART to lose its efficacy due to the development of viral strains resistant to ART.

Secondly, given these barriers and facilitators, continuous information provision and unflinching support both from patients' families and caregivers are needed to improve ART adherence among patients. Patients need continuous counseling about HIV and the benefits of ART and support (both material and financial) in order to adhere to ART for their entire lives.

Future directions

Future studies or reviews and meta-analysis, particularly focusing on specific underrepresented demographics such as HIV-infected children, adolescents, and pregnant women in SSA are needed to uncover the most appropriate barriers, facilitators and interventions tailored to each group's unique needs. Other studies focusing on assessing long-term ART non-adherence trends and determinants or predictors of ART non-adherence using larger samples of people living with HIV in many treatment centres and regions will also be necessary. Also, studies including many regions and larger samples using both in-depth and focused group discussions as well as quantitative approaches (to determine the scale of ART interruptions especially in conflict areas using objective measures such as medication refill adherence, viral load, and resistance test results) are required to uncover the burden related to ART non-adherence.

Conclusion

The prevalence of ART non-adherence in SSA is high. ART adherence barriers and facilitators across SSA countries can be categorized under seven primary factors: patient-related, health system-related, medication-related, stigma, poor mental health, socioeconomic and socio-cultural-related factors. Common interventions that enhance ART adherence encompass counselling, incentives, mobile phone short message services (SMS), peer delivered behavioural intervention, community ART delivery intervention, electronic adherence service monitoring device, lay health worker lead group intervention and food assistance. These strategies prove effective either as standalone approaches or in conjunction with other methods. To harness the full potential of ART and mitigate the HIV burden in SSA countries, stakeholders engaged in HIV prevention and treatment must recognize and integrate these barriers, facilitators, and adherence enhancing

interventions when formulating policies or crafting treatment strategies. Ensuring sustained optimal outcomes from ART may necessitate further research, particularly focusing on specific underrepresented demographics such as HIV-infected children, adolescents, and pregnant women in SSA. This research will aim to uncover the most appropriate barriers, facilitators and interventions tailored to each group's unique needs.

Appendices

Appendix 1: PRISMA-P 2015 Checklist

Section/topic	#	Checklist item	Information reported		Line number(s)			
			Yes	No				
ADMINISTRATIVE INFORMATION								
Title: Effective educational interventions for the promotion of sexual and reproductive health and rights for school-age children in low and middle-income countries: A systematic review protocol								
Identification	1a	Identify the report as a protocol of a systematic review	☒	☐				
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	☐	☒				
Registration	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number in the Abstract	☒	☐				
Authors								
Contact	3a	Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author	☒	☐				
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	☒	☐				
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	☐	☒				
Support								
Sources	5a	Indicate sources of financial or other support for the review	☒	☐				
Sponsor	5b	Provide name for the review funder and/or sponsor	☐	☒				
Role of sponsor/funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	☐	☒				
INTRODUCTION								
Rationale	6	Describe the rationale for the review in the context of what is already known	☒	☐				
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	☒	☐				
METHODS								
Eligibility criteria	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language,	☒	☐				

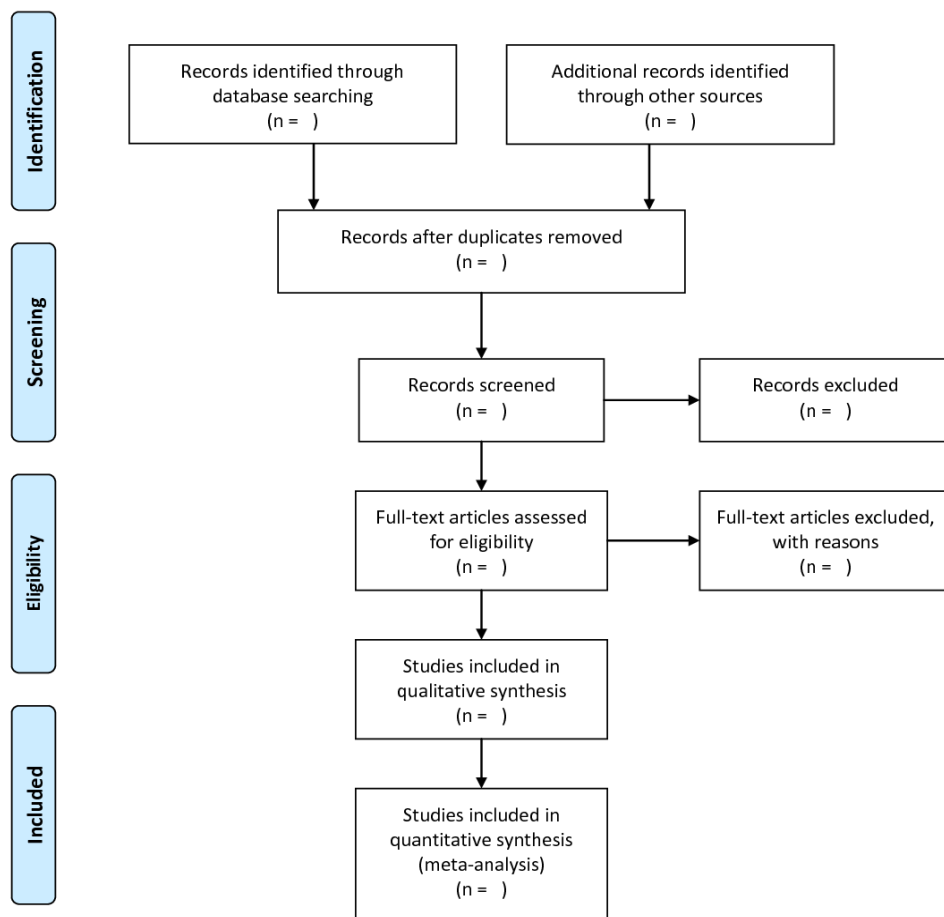
Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
		publication status) to be used as criteria for eligibility for the review			
Information sources	9	Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage	☒	☐	
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	☒	☐	
STUDY RECORDS					
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	☒	☐	
Selection process	11b	State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)	☒	☐	
Data collection process	11c	Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	☒	☐	
Data items	12	List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications	☐	☒	
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	☒	☐	
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	☒	☐	
DATA					
Synthesis	15a	Describe criteria under which study data will be quantitatively synthesized	☒	☐	
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., I^2 , Kendall's tau)	☒	☐	
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)	☐	☒	
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	☒	☐	

Section/topic	#	Checklist item	Information reported		Line number(s)
			Yes	No	
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies)	☐	☒	
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (e.g., GRADE)	☒	☐	

Appendix 2: PRISMA 2009 Flow Diagram



PRISMA 2009 Flow Diagram



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit www.prisma-statement.org.

Appendix 3: Medline (Ovid) Search Strategies and Results

1 test.ti. 173184
2 exp HIV/ 102314
3 exp Acquired Immunodeficiency Syndrome/ 76887
4 exp AIDS-related opportunistic infections/ 21220
5 exp HIV infections/ 294267
6 human immunodeficiency virus*.ti,ab,kf. 91838
7 acquired immunodeficiency syndrome.ti,ab,kf. 20079
8 AIDS.ti,ab,kf. 159137
9 HIV.ti,ab,kf. 329040
10 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 465353
11 exp Antiviral agents/ 373305
12 exp Anti-HIV agents/ 71150
13 exp Antiretroviral Therapy, Highly Active/ 21988
14 exp HIV integrase inhibitors/ 2740
15 exp HIV protease inhibitors/ 13910
16 exp Reverse Transcriptase Inhibitors/ 33398
17 reverse transcriptase inhibit*.ti,ab,kf. 8626
18 antiviral*.ti,ab,kf. 101021
19 anti-HIV.ti,ab,kf. 13222
20 (antiretroviral* or anti-retro*).ti,ab,kf. 69486
21 exp Nevirapine/ 2795
22 exp Delavirdine/ 196
23 exp Zidovudine/ 9564
24 exp Lamivudine/ 6603
25 (Fosamprenavir* or Atazanavir* or Indinavir* or Nelfinavir* or Saquinavir* or Ritonavir* or Amprenavir* or Darunavir* or Lopinavir* or ritonavir* or kaletra* or Tripanavir* or tipranavir* or nevirapine* or Abacavir* or Stavudine* or Didanosine* or Lamivudine* or Zidovudine* or Zalcitabine* or Combivir* or Trizivir* or tenofovir* or efavirenz* or delavirdine*).ti,ab,kf. 35684
26 HAART.ti,ab,kf. 12298
27 cART.mp. 8331
28 ARV.mp. 3522
29 ART.mp. 126922
30 anti-HIV agents/ or Antiviral Agents/ 132191
31 Anti-Retroviral Agents/ or Antiretroviral Therapy, Highly Active/ 31883
32 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 577616
33 10 and 32 137384
34 exp Africa South of the Sahara/ 225419
35 cent* Africa*.ti,ab,kf. 4983
36 east* Africa*.ti,ab,kf. 11306
37 south* Africa*.ti,ab,kf. 51791
38 west* Africa*.ti,ab,kf. 16611
39 34 or 35 or 36 or 37 or 38 254704

40 33 and 39 14224
 41 "Treatment Adherence and Compliance"/ 762
 42 Medication Adherence/ 21370
 43 adher*.ti,ab,kf. 211179
 44 retention*.ti,ab,kf. 190213
 45 retain*.ti,ab,kf. 220493
 46 complian*.ti,ab,kf. 141300
 47 comply.ti,ab,kf. 11870
 48 complied.ti,ab,kf. 4969
 49 noncomplian*.ti,ab,kf. 8739
 50 non-complian*.ti,ab,kf. 7185
 51 non-adher*.ti,ab,kf. 9925
 52 nonadher*.ti,ab,kf. 10417
 53 loss to follow-up.ti,ab,kf. 5019
 54 lost to follow-up.ti,ab,kf. 19685
 55 attrition.ti,ab,kf. 14116
 56 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55
 781016
 57 40 and 56 3890
 58 (Angola* or Benin* or Botswana* or Burkina Faso* or Burundi* or Cameroon* or Cape Verde* or Central African Republic* or Chad* or Comoros* or Congo* or Cote d'Ivoire* or Djibouti* or Equatorial Guinea* or Eritrea* or Ethiopia* or Gabon* or Gambia* or Ghana* or Guinea* or Guinea-Bissau* or Kenya* or Lesotho* or Liberia* or Madagascar* or Malawi* or Mali* or Mauritania* or Mauritius* or Mozambique* or Namibia* or Niger* or Nigeria* or Reunion* or Rwanda* or "Sao Tome adj2 Principe*" or Senegal* or Seychelles* or Sierra Leone* or Somalia* or South Africa* or Sudan* or Swaziland* or Tanzania* or Togo* or Uganda* or Western Sahara* or Zambia* or Zimbabwe*).ti,ab,kf. 1016228
 59 39 or 58 1078865
 60 33 and 59 18347
 61 56 and 60 4589
 62 ("26927422" or "27042024" or "23573232" or "25477050" or "30691425" or "31852741" or "34134738" or "33222633" or "33125587").ui. 9
 63 61 and 62 7
 64 62 not 63 2
 65 limit 61 to yr="2010 -Current" 4113

Appendix 4: Joanna Briggs Institute for Meta-Analysis of Statistics Assessment and Review Instruments

1. JBI critical appraisal checklist for randomized control trials

Reviewer..... Date.....

Author..... Year.....

		Yes	No	Unclear	Not applicable
1	Was the assignment and treatment groups truly random?				
2	Were participants blind to treatment allocation?				
3	Was the allocation to treatment groups concealed from the allocator?				
4	Were the outcomes of people who withdrew described and included in the analysis?				
5	Were those assessing outcomes blind to the treatment allocation?				
6	Were the control and treatment groups comparable at entry?				
7	Were groups treated identically other than for the named interventions?				
8	Were outcomes measured in the same way for all groups?				
9	Were outcomes measured in a reliable way?				
10	Was appropriate statistical analysis used?				

Overall appraisal: include..... exclude..... Seek further info.....

Comments (include reasons for exclusion)

2. JBI critical appraisal checklist for non-randomized control trials

Reviewer..... Date.....

Author..... Year.....

1	Was study based on random or pseudo sample?				
2	Were the criteria for inclusion in the sample clearly defined?				
3	Were confounding factors identified and strategies to deal with them stated?				
4	Were outcomes assessed using objective criteria?				
5	If comparisons are being made, was there sufficient description of the groups?				
6	Was follow up carried out over a sufficient time period?				
7	Were the outcomes of people who withdrew described and included in the analysis?				
8	Were outcomes measured in a reliable way?				
9	Was appropriate statistical analysis used?				

Overall appraisal: include..... exclude..... Seek further info.....

Comments (include reasons for exclusion)

Appendix 5: Data Extraction Form for Quantitative Research

Study Characteristics

1. **Author:**
2. **Year of publication:**
3. **Journal:**
4. **Record number:**

Study Method

1. **Study Design:**

RCT	Quasi-RCT	Longitudinal	Retrospective	Observational	Other

2. **Purpose:**

3. **Research Questions:**

Participant Characteristics

Country where the study took place	Setting	Population	Sex	Age	Sample size	Ethnicity (if applicable)	socioeconomic status (if applicable)	education level (if applicable)

ART adherence interventions

Strategy 1:

Strategy 2:

Strategy 3:

Outcome Measures

Outcome Description	Scale/measure

--	--

Study results

Dichotomous data

Outcome	Intervention () number / total number	Intervention () number / total number

Continuous data

Outcome	Intervention () mean & SD (number)	Intervention () mean & SD (number)

Authors' conclusions:

Comments:

Appendix 6: Self-reported ART non-adherence questionnaire

Dear respondent, thank you for accepting to participate in this study. The following statements are some things people say about their ART experience. Please listen attentively, keeping in mind the HIV treatment you are receiving; (We would like to know how you feel about the ART you are taking. Your answers to the questions will help us understand what works and what doesn't, and how we can develop strategies that will improve patients' adherence to ART). We are very interested in your candid opinion on your experience taking ART.

A) Socio-demographic/structural characteristics

- i) Region of residence: 0=Northwest..., 1=Southwest..., 3=Littoral....
- ii) Your Age.....years
- iii) Sex (please tick): 0 = Male..., 1 = Female.....
- iv) Marital status (select one): 0=Single...,1=Married..., 2=Divorced..., 3=Separated...,4=Never married...
- v) Level of education (select one): 0=Primary..., 1=Secondary..., 2=High school..., 3=University...
- vi) Religion: 0=Muslim..., 1=Catholic..., 2=Protestant..., 3=Pentecostal..., 4=animist....
- vii) Working status (select one): 0=no job..., 2=self-employed..., 3=government staff..., 4=private staff...
- viii) What is your estimated monthly income?
- ix) What is the distance from your house to this Centre? Kilometers
- x) How long does it take you to get to this centre? Minutes
- xi) How do you get here? 0=by foot..., 2=by bike..., 3=by car/taxi...
- xii) How many people are living with you in the same house?.....
- xiii) Who are the persons living together with you? (select all that apply)
0=spouse/partner..., 1=children..., 2=parents..., 3=relatives/friend..., 4=Nobody...
- xiv) Have you disclosed your HIV status to family or friend? 0=No..., 1=Yes...

B) Health risk behaviours

- a. Are you currently smoking? 0=No..., 1=Yes....
- b. Do you drink alcohol? 0=No..., 1=Yes...
- c. Do you use drugs that are not prescribed for you? 0=No..., 1=Yes...
- d. Do you have multiple sex partners (more than one at a time)? 0=No..., 1=Yes...
- e. Do you carryout physical exercises? 0=No..., 1=Yes...

C) Medical history and ART adherence experience

- 1. Have you ever been admitted to hospital for HIV related issues? 0=No..., 1=Yes...

2. If yes, what were the reasons for hospital admittance? (tick all that apply): 0=chronic diarrhea..., 1=chronic herpes simplex..., 2=TB/pneumocystis..., 3=meningitis..., prolong fever..., 4=weight loss..., 5=Jaundice..., 6=other (specify).....
3. How long has it been since you were first diagnosed HIV positive?.....Months
4. What was your CD4 count at ART initiation?...../MM3
5. How long have you been taking ART? Months
6. What is your ART dosing frequency per day? times/day
7. How is your health status since ART initiation? (Select one): 0=Worse..., 1=stable..., 2=better...
8. Have you ever missed taking your ART in the last month? 0=No ..., 1=Yes ...
9. If yes to question 7, how many times have you missed taking ART in the past 4 weeks?
10. What was the reason(s) for missing to take your ART (tick all that apply): 0=Forgot ..., 1=Busy ..., 2=Too many pills/taste of medicine ..., 3=Long distance to hospital ..., 4=Run out of medicine ..., 5=Severe symptoms/difficulty to follow up ..., 6=Stigma ..., 7=Other, specify
11. Have you ever had any side effects of ARV? 0=No..., 1=Yes...
12. Have you ever missed an appointment for ART services? 0=No ..., 1=Yes ...
13. Please indicate how strongly you AGREE or DISAGREE with each of the following statements. (Tick only one, where appropriate).

		Strongly agree	Agree	Uncertain	Disagree	Strongly disagree
a	I know that ART is lifelong					
b	I do not believe in the benefits of ART					
c	Taking tablets gives me an unwanted reminder that I have HIV					
d	I am worried that in the future, my medication will stop working for me					
e	I have experienced physical adverse events in the last 12 months					
f	I have experienced health service discrimination in the last 2 years					

Thank you for your time!

Source: adapted from [30,49,68–70].

Appendix 7: In-depth interview guide for clients who have experience non-adherence with ART

Dear respondent, thank you so much for accepting to participate in this study and for your permission to have this interview on record which will enable us to transcribe appropriately for our study report. Our study aims at improving patients' adherence to ART which helps to reduce the development of drug resistant strains of HIV and HIV related mortality specifically in Cameroon. Please, be honest in your responses to the questions and give a detailed explanation as much as you can about your experiences with ART.

Questions:

A. Socio-demographic/structural characteristics

Before we talk about your experience taking ART, please, tell us about yourself by stating your:

- a. Region of residence: (Northwest, Southwest or Littoral)
- b. Age.....years
- c. Sex (Male or Female)
- d. Marital status (Single, Married, Divorced, Separated or Never married)
- e. Level of education (Primary, Secondary, High school or University)
- f. Religion: (Muslim, Catholic, Protestant, Pentecostal or animist)
- g. Occupation

B. ART experience

1. Please, tell me your views about ART (what they are and what they do)
2. Please, tell me your experience in taking ART (how long you have been on treatment and the frequency of taking the drugs daily)
3. What do you think is the hardest part for you in taking your medications?
4. What do you think are factors that could facilitate your adherence to your medication?

Probe: - interaction at the clinic and home (do healthcare providers tell you when to take your drugs).

- Knowledge of regimen and health literacy (do you struggle to understand how to take your drugs)
5. Please, tell me any other thing you would like to share about difficulties in taking your treatment or factors you think will help you adhere to your treatment.

Thank you so much for your time and for responding to our questions.

Source: adapted from [72,73].

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