

AN EXPLORATION OF APPROACHES EMPLOYED TO IMPROVE ART ADHERENCE AMONG PEOPLE LIVING WITH HIV IN NIGERIA

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An Exploration Of Approaches Employed To Improve ART Adherence Among People Living With HIV in Nigeria

A thesis submitted in partial fulfilment of the requirement for the degree of Master of Science in Public Health

by


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LIST OF ABBREVIATIONS

ACTG	AIDS Clinical Trials Group adherence questionnaire
AIDS	Acquired Immunodeficiency Syndrome
ALWHIV	Adolescents Living with HIV
AOR	Adjusted Odds Ratio
ARV	Antiretroviral
ART	Antiretroviral Therapy
CBO	Community-Based Organisation
CSO	Civil Society Organisation
CD4	Cluster of Differentiation 4 (a type of immune cell)
DOT	Directly Observed Therapy
EAMD	Electronic Adherence Monitoring Device
FDC	Fixed-Dose Combination
FMOH	Federal Ministry of Health
FSW	Female Sex Workers
HAART	Highly Active Antiretroviral Therapy
HCP	Healthcare Provider
HIV	Human Immunodeficiency Virus
HR	Hazard Ratio
LMIC	Low- and Middle-Income Countries
LTFU	Loss to Follow-Up
MPR	Medication Possession Ratio
MI	Motivational Interviewing
MSM	Men who sleep with Men
OR	Odds Ratio
PN	Peer Navigator
PLHIV	People Living with HIV
PWID	People who inject drugs
RR	Relative Risk
SAT	Self-Administered Therapy
SMS	Short Message Service (text messaging)

SOC	Standard of Care
TP/TS	Treatment Partner/Treatment Supporter
TWOT	Twice Weekly Observation Therapy
UNAIDS	Joint United Nations Programme on HIV/AIDS
WHO	World Health Organization
WOT	Weekly Observation Therapy
YLWHIV	Youths living with HIV

Table 1: MEANING OF ADHERENCE TERMS
CD4 count: CD4 count is a measure of immune system health, indicating the number of CD4 cells per cubic millimetre (cells/mm ³) of blood. It is crucial for monitoring HIV treatment progress and assessing treatment response (1).
Medication Possession Ratio (MPR): is a measure used to assess a patient's adherence to a medication regimen. It calculates the ratio of the total number of days' supply of medication obtained by the patient over a specified period to the number of days within that period. An MPR value of ≥90% indicates good adherence, while <90% suggests poor adherence to the prescribed medication regimen (2).
Pharmacy Refill Record: is a method used to monitor a patient's adherence to medication by tracking the dates and frequency of their prescription refills at the pharmacy. It helps healthcare providers assess how consistently the patient follows their medication schedule (1,3).
Pharmacy refill rates as a measure of adherence: indicate how regularly a patient refills their prescribed medication at the pharmacy. It helps assess how well the patient follows their treatment plan and if they are adhering to their medication schedule. Higher refill rates usually indicate better adherence to the prescribed treatment (4).
Pill Count %: A method of assessing adherence by calculating the percentage of total medication doses taken compared to the total expected doses (1,5).
Pillbox/Wise-pill: A pill box is an adherence aid used to organize and store medications, improving adherence by helping patients keep track of their daily doses conveniently and discreetly. Wise-pill is its electronic counterpart, serving a similar purpose(6)
Self-Reported Adherence: Self-reported adherence refers to patients reporting their own medication adherence using methods like pill counts, charts, self-assessment forms, or questionnaires. It is a convenient and cost-effective way to monitor adherence, commonly used in clinical settings, but may be influenced by recall bias (1,7,8).
Standard of Care (SOC): Standard of care refers to the established and accepted medical practices used for treating a specific condition, such as routine clinical care provided for HIV treatment (1,9).
Viral Load: Commonly measured in (copies/ml), is a measure of HIV RNA copies in the blood, Treatment failure is typified by detectable viral load (1).

ABSTRACT

Introduction: Antiretroviral therapy (ART) has transformed the management of HIV/AIDS, but optimal treatment outcomes depend on high adherence rates. In Nigeria, achieving consistent adherence remains a challenge due to diverse barriers faced by people living with HIV (PLHIV). This thesis aims to explore the factors influencing ART adherence, identify successful interventions, and provide recommendations to improve adherence rates among PLHIV.

Methodology: A review of existing literature was conducted, encompassing studies from Nigeria and other low- and middle-income countries (LMICs) focusing on ART adherence barriers, enablers and interventions. The conceptual model for factors contributing to medication adherence was adapted to guide the analysis and identify key domains for informing interventions.

Results: Forgetfulness, internalized stigma, and medication-related factors were prominent barriers to adherence. Interventions, such as individualized counselling, text message reminders, alarm reminders, peer support groups, and treatment partners, demonstrated positive outcomes in promoting adherence.

Discussion and Conclusions: The study highlights the need for a tailored and multifaceted approach to address diverse adherence barriers effectively. Strengthening adherence counselling services, promoting peer support groups, and conducting qualitative research on key populations are compelling recommendations. National health ministries, community-based organizations, and researchers should collaborate to implement these recommendations and improve ART adherence outcomes.

Key words: HIV/AIDS, ART adherence, Interventions, Nigeria

Word Count: 11,536

CHAPTER 1

1.0 INTRODUCTION/BACKGROUND

1.1 CURRENT EPIDEMIOLOGY OF HIV/AIDS

The Human Immunodeficiency virus (HIV) continues to be a major global public health challenge, with an estimated 40.1 million fatalities attributed to the disease (10). As at 2021, there were about 38.4 million people living with HIV (PLHIV) (10,11). Roughly 95% of these falls within 15 years of age and older, an estimated 5% are younger and 54% of PLHIV are also noted to be women and children (10). Number of estimated new cases globally in 2021 were about 1.5 million people; 75% of them had commenced Anti-retroviral treatment, however over 650,000 PLHIV died from HIV related causes (11,12). HIV has been studied to compromise the immune system by infecting and replicating within CD4 cells thereby making individuals susceptible to infections and cancers. It is primarily transmitted through unprotected sexual contact, but also through needle sharing, and transmission from mother to child during pregnancy, childbirth or breastfeeding (13).

Sub-Saharan Africa remains the hardest hit by HIV, with an estimated 3.4% of adults (or almost 1 in 25) living with the virus (14). This region also comprises approximately two-thirds of the total number of people worldwide living with HIV. In 2021, an estimated 25.6 million people in sub-Saharan Africa were living with HIV (14). Within West Africa, the HIV epidemic is more severe among key populations such as sex workers, men who have sex with men, injection drug users, transgender women who have sex with men and prisoners (15).

Since 2003, there has been a decline of the prevalence of HIV in Nigeria however as at 2019, Nigeria ranked 4th globally in terms of burden of infection and had a current national prevalence as at 2021, of 1.4%, with Akwa Ibom state (5.6%) having the highest prevalence among all the states (16).

1.2 ADHERENCE TO ART

The World Health Organization (WHO) defines Adherence as “the extent to which a person’s behaviour taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider”(17). Antiretroviral therapy (ART) is the use of anti-HIV drugs for treatment of people infected with Human Immunodeficiency Virus (HIV) and it involves the combination of different classes of drugs to increase the effectiveness and reduce the risk of viral resistance. Transmission is disrupted through viral suppression (18). According to UNAIDS, from 2010 to December 2021, there was an estimated 400% increase in uptake of ART and approximately 25% of people living with HIV (PLHIV) were receiving treatment globally (10).

Combination therapy, also known as Highly Active Antiretroviral Therapy (HAART), Antiretroviral (ARV) or Antiretroviral Therapy (ART), is a powerful treatment for HIV/AIDS. It involves using a combination of multiple antiretroviral medications to effectively control the virus in the body, reduce mortality and morbidity, and improve quality of life among infected individuals (19,20). These terms, HAART, ARV and ART, are often used interchangeably to describe this potent therapy. High levels of adherence to ART can radically provide better outcomes for PLHIV and prevent transmission (21). The standard for adherence; though it

seems to vary depending on newer ART medications, is generally accepted at 95%, at least (22). The implication is that near perfect adherence is required to achieve viral suppression in HIV cases. Adherence has been described as: compliance and sustenance of the intake of certain medications based on medical prescriptions (17,23). Adherence has also been described in three major phases namely; initiation, discontinuation and implementation (24). Initiation describes the point when the patient takes the first dose of a prescribed medication. When he stops taking it, it falls under the discontinuation phase while the extent to which the client or patient's dosing tallies with the prescribed regimen is what is termed 'implementation'. It is strongly believed that in addition to the comprehension and willingness of the patient, the selected ARV drug, the devotion of the healthcare provider and the family/support system of the patient are major factors that generally influence ART adherence (24).

1.3 NIGERIA'S PROFILE

The country is located on the Western coast of Africa. Nigeria is bordered to the north by Niger, to the east by Chad and Cameroon, to the south by the Gulf of Guinea of the Atlantic Ocean, and to the west by Benin. It covers an area of 923,769 square kilometres (356,669 sq. mi). Based on the latest United Nation's projected data, Nigeria has a population of over 221 million people and is the world's sixth most populous country (25).

Its culture is shaped by multiple ethnic groups. The three largest ethnic groups are the Hausas that are predominantly in the north, the Yorubas who predominate in the southwest, and the Igbos in the southeast.



FIGURE 1: MAP OF NIGERIA (26)

1.4 NIGERIA'S HEALTH SYSTEM STRUCTURE

It exists at 3 levels namely; the federal, state and local government level. It involves both private and public sector and engages modern and traditional methods. The Federal Government is responsible for policy formulation through the Federal Ministry of Health (FMOH), and offers specialized care through Teaching Hospitals and Federal Medical Centres. The states provide secondary health care through general hospitals and specialized care through state owned Teaching Hospitals while coordinating primary healthcare activities through the State Primary Healthcare Development Agency. They also implement public health programs formulated at the Federal level from an operational perspective. The local government area supervises the primary health centres, villages and ward health committees as well as traditional/alternative healthcare providers (27).

1.5 ART SERVICES IN NIGERIA

The Federal Ministry of Health designed the first National Policy on tackling the HIV/AIDS epidemic of Nigeria in 1997. It was closely followed by a revised policy in 2001 which emphasized intersectoral collaboration in controlling the infection. Subsequently further updates were made in 2009, 2014 and more recently in 2020 (28). Finally in 2020, The National guidelines for HIV prevention and care was released to provide evidence-based recommendations to further improve efficiency and effectiveness of previous policies.

Various studies have identified the role of different adherence improvement techniques applied in developed and developing countries. There exists discrepancy in certain approaches depending on the level of technology available as some interventions are not feasible in a resource constrained setting.

The guidelines outline various ways of monitoring adherence such as viral load monitoring, pharmacy refill methods, self-reporting and pill counts. Also several techniques for improving adherence are mentioned within the document guidelines, and they include treatment education for patients and treatment supporters, peer health education/peer counsellors, fixed-dose combination (FDC) and drugs with lower dosing frequency, reminders from (alarm clock, calendars, social media platforms etc.), adequately managed adverse drug reactions, adapting therapy to the client's lifestyle, encourage participation in support groups, improved social support, directly observed therapy and others (1).

CHAPTER 2

PROBLEM STATEMENT, JUSTIFICATION AND METHODOLOGY

2.1 Problem Statement and Justification

Nigeria is currently facing a critical public health challenge due to the HIV/AIDS epidemic, with an estimated 1.9 million individuals living with HIV as of 2021. Among adults aged 15-49 years, the prevalence rate is 1.4% (29). This places Nigeria as the world's second-largest HIV epidemic, highlighting the urgent need for effective interventions with a high prevalence rate of 1.4% among adults aged 15-49 years. Additionally, key populations such as men who have sex with men (MSMs), sex workers, and drug users experience a disproportionate burden of HIV infection (29).

In Nigeria, although there is a high ART coverage of 90% [84 - >98] for PLHIV (29), evidence reveals that the ART adherence level is still sub-optimal especially in some parts of Nigeria (30–32). Major reasons why 95% adherence was not achieved by most people was due to forgetfulness, drug side effects, feeling of stigma, non-disclosure, limited access to health care and others (31–33). Current trends in Nigeria may slow the achievement of the 3rd part of the 95-95-95 target by 2030 i.e. that 95% of those on ART achieve suppression level (34). Various interventions have been implemented to improve adherence to HAART among PLHIV in Nigeria, including education and counseling, reminder systems, peer support and the use of mobile phone technology. However, the success of these interventions is yet unclear for all PLHIV, and there is a need to explore the most common approaches to improving HAART adherence in Nigeria in order to focus limited resources on their cost-effective implementation.

This study fills a gap as the attempts to compare various methods of improving HAART adherence have only been carried out at the regional levels of the continent; that is at Sub-Saharan level and high income countries (35–37). In Nigeria the emphasis has rather always been placed on studying the prevalence and predictors of adherence. The National HIV/AIDS management guidelines also does not promote any particular approaches to improving the uptake and adherence of HAART thereby leaving a need (28). This could guide policy makers to create a more standardized path to help Nigeria attain the 95-95-95 target. This study seeks to achieve all these specifically through a literature review of relevant past studies.

Objectives

2.2 General Objectives

To explore the different approaches used to enhance ART adherence among PLHIV in Nigeria

2.2.1 Specific Objectives

1. To explore the most common barriers and enablers of ART adherence in Nigeria
2. To identify the most common interventions used to enhance ART adherence among PLHIV in Nigeria
3. To summarize the successes of the various interventions used to improve ART adherence among PLHIV
4. To compare the different interventions conducted in Nigeria and other low- and middle-income countries

5. To formulate evidence-based recommendations for designing and implementing successful interventions to enhance ART adherence among PLHIV in Nigeria

2.3 Methodology

2.3.1 Research Design: Literature Review

The methodology, employed in this thesis involves a literature review to explore the approaches employed to improve ART adherence among PLHIV in Nigeria.

2.3.2 Conceptual Framework:

The conceptual framework for factors contributing to medication adherence was adopted and modified for this research, since it aligns very closely with the objectives of this study. The original conceptual model below, was developed through a systematic review of over 102 conceptual frameworks. The data were extracted from different patient groups (38).

Conceptual Model for Factors Contributing to Medication Adherence

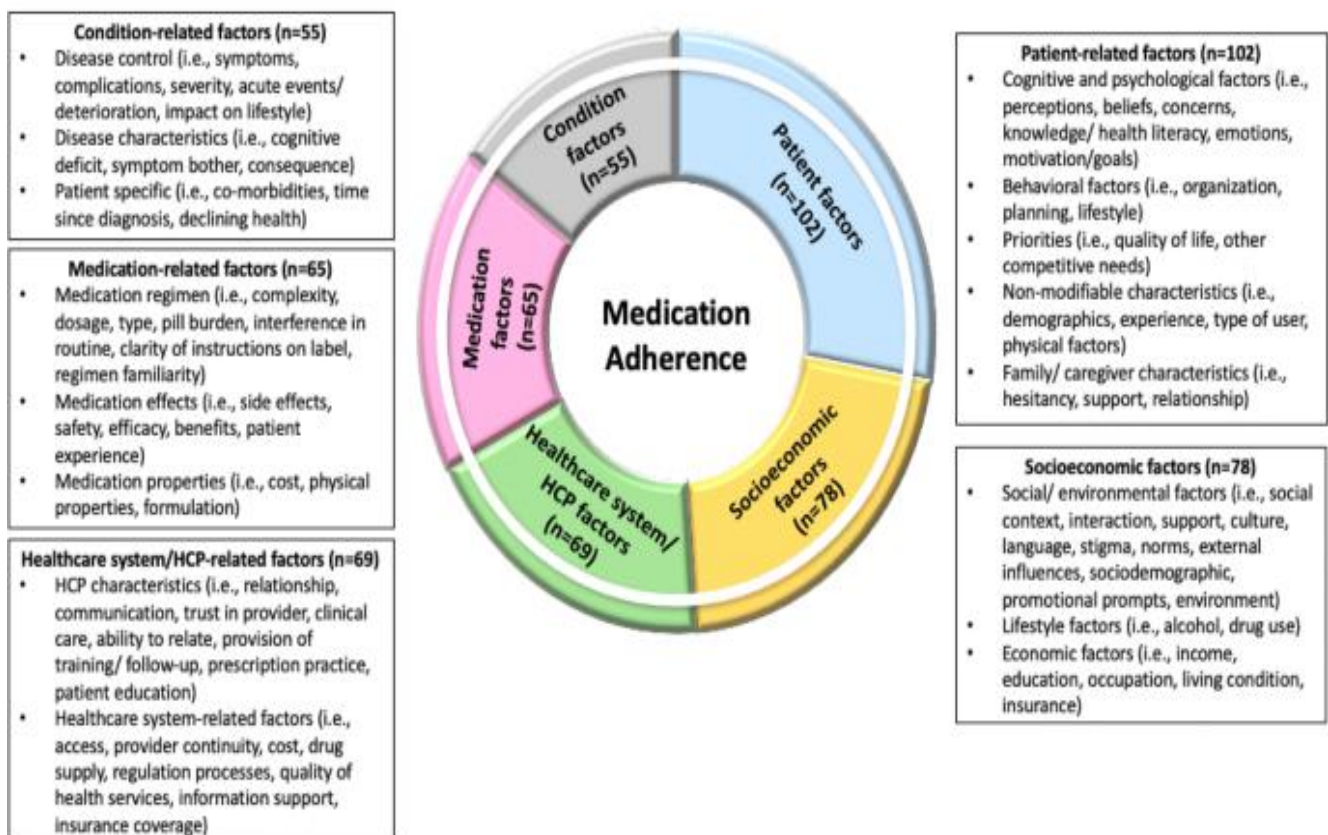


Fig 2: Conceptual Framework for Medication Adherence (Original Framework)

2.3.3 Reasons for Choosing the Conceptual Framework for Factors Contributing to Medication Adherence

The choice of the conceptual framework for factors contributing to medication adherence is driven by several reasons that make this framework well-suited for the task at hand.

Firstly, the framework offers a comprehensive representation of medication adherence by considering a wide range of influential factors such as patient, medication, condition, healthcare, and socioeconomic related factors (38).

Furthermore, the framework recognizes the diverse nature of PLHIV by categorizing them into distinct domains which allows for tailored interventions that specifically address the unique needs and challenges faced by each group.

The adaptability and flexibility of the framework further enhance its suitability for a more nuanced analysis of the common factors contributing to medication adherence in various contexts. Most importantly, this new framework builds upon the WHO five dimensions of adherence framework and/or other frameworks, and also incorporates multiple conceptual models (17).

2.3.4 Dimensions of the Conceptual Framework for Factors Contributing to Medication Adherence:

Patient Related Factors: Interventions in this dimension aim to address cognitive and psychological factors such as patients' beliefs, perceptions, and motivations. They also target behavioral factors like organization and planning, as well as patient priorities related to their quality of life and other needs. Additionally, the interventions also consider non-modifiable characteristics such as demographics and physical characteristics, as well as the characteristics of family and caregivers in terms of their support and relationship with the patient (17,38).

Socioeconomic factors: Interventions in this dimension focus on addressing social and economic barriers that impact adherence. They also include enablers that improve access to healthcare and medicines, address poverty, and establish effective social support networks (17,38).

Condition-related factors: Interventions in this dimension target the specific disease or condition of the patient as well as their impact on the patient's lifestyle. Co-morbidities are also considered. Examples include patient education, offering tailored treatment plans that address cognitive deficits or symptom bother, managing co-morbidities that may influence adherence, Screening for mental health issues and substance abuse that can impact treatment adherence (17,38).

Medication-related factors: Interventions in this dimension focus on aspects related to the ART medication itself. They aim to simplify medication regimens, address side effects, and improve patients' understanding of these adverse effects. Examples of these interventions include, simplifying medication regimens by reducing dosage frequency or pill burden, Providing clear instructions on medication labels and ensuring patients understand them, Managing side effects through education, support, and appropriate adjustments in treatment, etc. (17,38).

Healthcare system/HCP-related factors: Interventions in this dimension target healthcare providers and the healthcare system. They involve improving communication, trust, and collaboration between patients and healthcare professionals. Access to healthcare, continuity of care, and quality of health services are also important considerations (17,38).

2.4 Search Strategy

The search strategy for this study involved using various databases, including PUBMED, Google Scholar, Google, Scopus, Web of Science, and the VU library, to conduct a literature search. The search focused on identifying relevant published studies from 2000 to 2023.

To conduct the search, specific keywords and Boolean operators, such as "and" and "or," were employed to combine relevant terms related to interventions, strategies, ART adherence, and PLHIV in Nigeria. These keywords included terms like "ART adherence," "antiretroviral therapy adherence," "HAART adherence," "interventions," "strategies," "PLHIV," "Nigeria," and "sub-Saharan Africa." The Boolean operators helped to refine the search and ensure that all relevant studies were captured. In addition to the electronic database search, a manual search was conducted to explore the grey literature, which includes sources like UNAIDS, previous thesis articles, and national reports. This step aimed to ensure a comprehensive review of the available literature on ART adherence interventions in Nigeria and LMICs. Furthermore, snowballing technique was used to identify additional relevant studies.

The screening process involved evaluating articles based on predetermined inclusion and exclusion criteria (refer to Table 1). The scope of years considered for article selection was broadened to span from 2000 to 2023. This extended timeframe was chosen to capture a comprehensive view of evolving trends, and advancements in the field over the past two decades. Additionally, only articles in English language were included to ensure consistent understanding and analysis. Articles used included literatures from Nigeria and other LMIC since it relates to the objectives of this study, very few articles from outside Africa were also included to support findings. The screening process ensured that selected articles align with the study objectives, contributing to the overall quality and relevance of the research.

2.5 Inclusion and Exclusion Criteria

The eligibility criteria for inclusion in this scoping review were informed by the acronym PICOT, which considers the population, interventions, comparisons, outcomes, and time frame. Articles involving study participants that included PLHIV, including adolescents (10-19 years), youths, and pregnant women were included. The inclusion criteria encompassed any type of intervention aimed at improving ART adherence in Nigeria and LMICs, while the primary outcomes of interest were viral suppression and increased immune cells (CD4). Exclusion criteria involved studies with participants <10 years, as well as key population as their specific needs and challenges may differ from the target population of this study. Articles that did not address ART adherence or intervention were also excluded.

Table 2: Summary of Inclusion and Exclusion Criteria

Criteria	Description
Population	PLHIV including adolescents (10-19 years), youths, and women
Exclusion	Study participants <10 years, key population including transgenders, men who sleep with men (MSM), female sex workers (FSWs) and people who inject drugs (PWID)
Interventions	Any intervention to improve adherence to ART
Comparisons	Standard of care (SOC) or another intervention to improve adherence to ART
Outcomes	Viral suppression, CD4, retention in care, adherence level (measured)
Study design	Any study design

CHAPTER 3

RESULT FINDINGS

3.1 RESULT OVERVIEW

Out of the 401 articles found during the initial search, 380 were excluded based on specific criteria. After screening and applying the inclusion criteria from table 2, 20 Nigerian studies were chosen for final inclusion in the review. These results included a diverse set of studies with different study designs, such as cross-sectional studies, randomized control trials, prospective cohort studies, and interventional studies.

The primary aim of these studies was to explore various factors affecting ART adherence among PLHIV and to assess the success of different interventions in promoting adherence. The participants in these studies varied in number, with sample sizes ranging from 40 to 1676 PLHIV. The age range of the participants was wide, with some studies targeting adolescents (aged 15-24 years) and others including adults of different age ranges (e.g., ≥18 years, 20-69 years). Some studies targeted specific groups, such as peer support groups, young people living with HIV (YLHIV), or women only. The most common barriers and enablers highlighted by these articles included patient-related, socio-economic related, medication related and healthcare professionals related factors. Several interventions were employed to improve ART adherence, including, adherence counselling, text message reminders, peer support, and others which are all presented below, starting from the most frequent, according to the modified framework below.

Conceptual Framework for Factors Contributing to Medication Adherence (Modified)

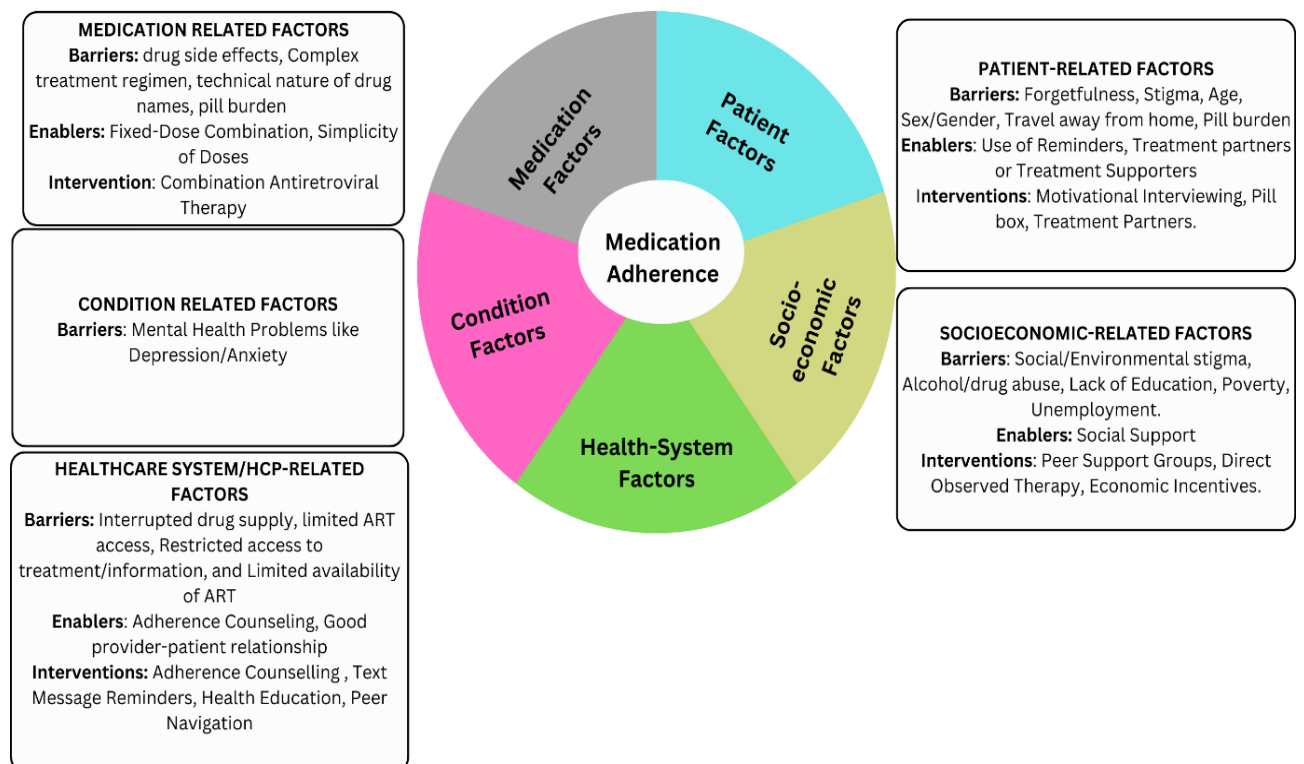


Fig 3: The conceptual framework for factors contributing to medication adherence was modified based on this research's findings. Additional interventions, identified through the study, were incorporated to fill gaps in the original framework.

3.2 MOST COMMON BARRIERS TO ART ADHERENCE

3.2.1 PATIENT RELATED BARRIERS

Forgetfulness:

Forgetfulness was consistently identified as the most prevalent barrier to ART adherence in the studies reviewed (2,5,7,8,39–43). A significant number of participants in these studies reported that as the primary reason for their challenges in adhering to antiretroviral medications. According to Igweagu et al. (44) in southeastern Nigeria, over 65% of the intervention group and nearly 70% of the control group identified forgetfulness as the major cause of poor adherence. The demands of their work (employment status) and home life can make them busy, increasing the likelihood of forgetting to take their medications (39,43). A study indicated that the lack of reminders, such as alarm devices or stickers, could contribute to this forgetfulness (43).

Internalized Stigma:

Internalized stigma and fear of disclosing positive HIV status, was observed as the second most common obstacle after forgetfulness (39,45–48). Some patients reported hiding while taking their medication or delaying medication intake in unfavourable locations due to the fear of discrimination if their HIV status became known (5). "According to Ekama et al (49), a study participant expressed their experience with adherence, stating, "I sometimes get stuck in traffic on my way home from work, and it makes me uncomfortable to carry or take my drugs in public". This highlights a practical barrier to ART adherence faced by some individuals due to negative feelings attributed to HIV positive status or fear of disclosure. Non-disclosure or fear of disclosure due to internalized stigma is associated with this adverse self-perception because of HIV-positive status (50). This trend was consistently observed across multiple studies.

Age as a Barrier and Enabler to ART Adherence:

From the studies reviewed, there was no consistent trend regarding age as a barrier to ART adherence. Some studies identified younger age groups (18-24 years) (4) and (16 - 30 years) (3) as a possible barrier citing reasons like fear of disclosure and reduced likelihood to participate in support groups. However, other studies did not find age to have a significant impact on adherence levels (6,39,51). On the contrary, some studies viewed age (30-34 years) as an enabler of adherence, showing a positive association with viral suppression and high adherence levels (4). Furthermore, older age groups (61-80 years) were also found to have higher adherence rates and better viral suppression, suggesting age could be an enabler in promoting ART adherence (3). Overall, the relationship between age and ART adherence appears to be mixed, with some studies indicating age as a barrier and others highlighting age as an enabler. This suggests that age alone may not be a major determinant of ART adherence.

Sex/Gender:

In the reviewed studies, sex was identified as a barrier to ART adherence in some cases. Several studies reported that non-adherence was more prevalent among women compared to men, suggesting a significant impact of gender on ART adherence (40,52,53). Sociocultural factors, such as male dominance in society and fear of disclosure, particularly to an HIV-negative

partner, were potential reasons for this discrepancy. Women, often assuming caregiving roles, may prioritize the care of others over their own health, leading to lower adherence rates (53). However, not all studies found a significant association between sex and adherence levels or viral suppression (6,32,51). Overall, the relationship between sex and ART adherence appears to be complex, with some studies indicating sex-related barriers and others finding no significant impact. Therefore, while sex might play a role in adherence in certain cases, its influence may vary in different populations and contexts.

Travelling or being away from home and pill fatigue:

Other less common barriers mentioned across studies under patient related included travelling away from home and pill fatigue. However, travelling away from home was also attributed to forgetfulness (5,39,44). The feeling of fatigue was attributed to a decrease in adherence to treatment plan, and as a result, led to treatment failure (54).

3.2.2 MEDICATION RELATED BARRIERS:

Drug Side Effects:

According to the articles reviewed, drug side effects was also identified as a common barrier to ART adherence among study participants after forgetfulness and stigma from several reviewed articles (5,6,39,42,43,45). Many PLHIV/AIDS reported missing their medications due to concerns about experiencing side effects from the ART drugs. The trend observed across the included articles indicated that adverse drug reactions discouraged most people from taking their medications consistently. In one study by Anyaike et al. (31), out of 72 respondents, (27) 38% reported missing their medications to avoid discomfort.

Complex treatment regimen, technical nature of drug names and pill burden

While these factors were not commonly cited as the primary barriers to ART adherence, a few articles still recognized their significant influence on medication adherence (6,42,44). Patients who knew the names of their drugs tended to have better adherence compared to those who did not (5). Moreover, regimens requiring multiple pills, instead of a fixed dose combination, can have complex scheduling requirements, leading some patients to forget doses, like afternoon pills (55). Studies also found that higher pill burden was linked to lower adherence rates. Many participants in these studies were taking 5-7 pills per dose, but reducing the number of pills taken per day improved adherence. For instance, in one study, 92% of the participants preferred a reduction in the number of pills taken per day, and this preference was associated with improved adherence (43,56).

3.2.3 SOCIO-ECONOMIC BARRIERS

Social/Environmental Stigma:

Stigmatization also led some PLHIV to avoid healthcare services and hide their antiretroviral drugs (4,57). The impact of stigma on ART adherence was consistently highlighted across multiple studies (2,4,5,8,9,42,43,45,46,48). In a study in rural Nigeria, the data shows that people who experience low levels of stigmatization and discrimination have better adherence to ART, with 92% showing good adherence and only 7.6% having poor adherence. In contrast, those facing high levels of stigmatization and discrimination have lower ART adherence, with 38% showing good adherence and 63% having poor adherence. The statistical analysis

indicates a significant association between stigmatization and discrimination and ART adherence, with a p-value of 0.001 (58).

Alcohol and Drug Abuse:

The general trend observed across the included articles regarding alcohol abuse or intake and adherence to ART was that alcohol consumption was consistently associated with low adherence to medications (8,45). Respondents who did not consume alcohol were about three times more likely to adhere to their medications compared to those who consumed alcohol (95% CI: 2.1–9.4, $p < 0.001$) (5). Two articles acknowledged that alcohol and drug use by adolescents acted as barriers, as these substances affected their ability to consistently take their medications as prescribed (8,45). Another study found that non-intake of alcohol was associated with good adherence to ART (OR: 0.3, CI 95%:(0.1305–0.5492, p-value 0.0003) (59). In addition, alcohol consumption was also associated with forgetfulness in taking medications.

Education:

Lack of or limited education emerged as potential barriers to ART adherence as some studies highlighted its possible negative impact on adherence (6,7,53). However, there were varying opinions on certain aspects. For instance, Chime et al.(5) reported that patients with lower educational status faced difficulties in understanding drug information and dosing instructions. In contrast, those who learned the names of their drugs showed better adherence. Similarly, two studies highlighted that educational status significantly influenced adherence levels and treatment outcomes and that patients who are educated are four times more likely to adhere to their ART drugs (3,60). Nevertheless, some studies did not establish a clear link between educational status and adherence (3,6,32,39,43,51,61). While educational status showed inconsistent correlation with adherence, good knowledge of ART benefits was associated with better adherence likewise positive relationships with healthcare providers and ongoing counselling contributed to good adherence (39). In summary, while some articles indicate a connection between low education and suboptimal adherence, contradictory findings exist in other studies.

Poverty, unemployment:

In the studies reviewed, poverty and unemployment emerged as potential barriers to ART adherence. Some research highlighted that financial constraints, lack of money for travel, and unemployment could negatively impact the ability to adhere to ART medications (4,5). These economic challenges may lead to difficulties in accessing health facilities regularly, resulting in missed doses and suboptimal adherence (4,62).

3.2.4 CONDITION RELATED BARRIERS

Mental Health problems:

Among the various condition-related factors that can hinder medication adherence, mental health problems stood out as the most common, specifically depression, mental distress, and poor mental health (2,8,42,43,63). These issues significantly affect a patient's motivation and ability to stick to their ART regimens. A study by Adejumo et al. (64) revealed that psychiatric disorders are prevalent among PLHIV in Nigeria. It was found that participants who missed at least one ART dose in the previous month had twice the likelihood of experiencing major depression compared to those who adhered to their prescribed doses. In simpler terms,

individuals with mental health challenges, like depression or anxiety, are more likely to struggle with taking their medication as instructed (65). The emotional burden of mental distress in PLHIV can strongly influence their attitude and behavior towards consistent non-adherence to antiretroviral medications.

3.2.5 HEALTH SYSTEM /HCP RELATED BARRIERS:

Poor Adherence Education:

Poor adherence education among healthcare professionals was identified as a significant barrier to ART adherence (7,8,54). Most of the reviewed articles reported that, without proper guidance, patients may not fully understand the importance of taking their medications consistently, the potential risks of non-adherence, and how to overcome obstacles that could hinder adherence. As a result, they may be more prone to missing doses or not adhering to their prescribed regimens, which can negatively impact their overall health outcomes and treatment success (7,8,54). Alfa et al. (7) further highlighted that individuals with inadequate knowledge are approximately four times more likely to default on ART and are at higher risk of experiencing poor health-related outcomes.

Other Health System Factors:

Most of the included articles did not focus on health system-related barriers to ART adherence. However, it was observed that factors such as interrupted drug supply, limited ART access, restricted access to treatment/information, and limited availability of ART for youth were not frequently identified as the primary barriers to ART adherence across the reviewed studies. Nevertheless, these factors can indeed impact ART adherence. For instance, interrupted drug supply and limited ART access may lead to challenges in obtaining medications regularly, potentially causing patients to miss doses. Similarly, limited access to treatment and information can result in reduced awareness about the importance of ART and its benefits, which may lead to sub-optimal adherence (43,45). While these factors were not the most commonly mentioned barriers, they are still very essential hindrances recognized to negatively influence medication adherence.

3.3 MOST COMMON ENABLERS TO ART ADHERENCE

3.3.1 HEALTH SYSTEM /HCP RELATED ENABLERS:

Adherence Counselling: Adherence counselling consistently stood out as a vital facilitator of ART adherence across the included articles (5,8,40,42,44,46). Counselling provided by healthcare professionals or trained adherence counsellors played a central role in improving adherence by providing knowledge and needed support to HIV patients (41,66). Effective counselling, both before initiating ART and during follow-up sessions, proved crucial in addressing patients' beliefs, attitudes, and concerns related to treatment, leading to significant improvements in ART adherence (66–68). Chime et al (5) also acknowledged the positive influence of counselling on self-rating of adherence, which further contributed to better medication adherence among the study participants. In summary, adherence counselling delivered by healthcare professionals played a pivotal role in supporting patients to adhere to their ART regimens and overcome any barriers they might encounter during treatment.

Good relationship and communication with healthcare providers: Under the health system and healthcare provider-related factors, the second most mentioned enabler of ART adherence in

the reviewed articles was a good provider-patient relationship (2,7,39,43,62,63). Participants reported having a positive and supportive connection with their healthcare providers, which played a crucial role in successful medication adherence. Additionally, a majority of respondents (84.1%) demonstrated a good understanding of the importance of adhering to their medication, and 83.9% acknowledged being informed about the potential resistance to ARV drugs due to non-adherence (63). Moreover, patients' positive attitude towards ART and their perception of healthcare providers contributed significantly to the success of medication adherence. The studies emphasized that a good therapeutic relationship with healthcare providers positively impacted patients' knowledge, self-efficacy, and confidence in the healthcare system (63,39,44,2). This high level of knowledge was attributed to the positive interpersonal relationships patients had with their healthcare providers, as well as the ongoing counselling and education they received regarding adherence to ART (39,63).

3.3.2 SOCIO-ECONOMIC RELATED ENABLERS:

Social Support: Social support, like psychosocial support, support groups, and peer assistance, significantly enables ART adherence. Several studies frequently reported support group as a strong enabler of good adherence showing higher adherence among those in peer support groups (2,4,5,9,39,40,42,46,51). Social support helps PLHIV cope with chronic health conditions like HIV/AIDS and stick to their medications. In Nigeria, PLHIV support groups are common for offering counselling, ART guidance, and peer support for HIV-related needs, along with education on HIV/AIDS management. Numerous studies highlight the protective benefits of social support for PLHIV, including reduced HIV-related stigma, increased disclosure, safer behaviors, group psychotherapy and improved ART adherence. Social support consistently proves to be a robust enabler of ART adherence across studies(2,4,46).

3.3.3 PATIENT-RELATED ENABLERS:

Use of Reminders Using reminders has been recognized highly as a valuable strategy to overcome the common barrier of forgetfulness to ART adherence among PLHIV (2,7–9,41–43). These Reminder systems can take various forms, such as pill boxes, alarms, mobile phone text messages, pager messages, (6,69). Studies have shown that the use of reminder systems, such as alarm reminders, timers, pill boxes, stickers, and reminder cards, can significantly promote good adherence (6,43,70). In a study by Ekop and Okechukwu (70), findings from 145 participants revealed that over 50% of them utilized reminder systems, with the alarm system being the most preferred method to maintain medication adherence. Since forgetfulness has been commonly attributed to Non-adherence to ARV drugs, this underscores the importance of reminder systems in improving adherence (2,44,63). Moreover, considering the stigma associated with HIV, a well-designed reminder system was found to safeguard confidentiality and minimize drawing unnecessary attention from others (70). The relationship between the use of reminder systems and adherence was also statistically significant, from client's self-reported adherence. Ultimately, reminder systems emerged as a practical and effective enabler of ART adherence, addressing forgetfulness and positively influencing medication adherence among PLHIV.

Treatment Partners: Having a treatment partner or treatment supporter, which is a friend or family member responsible for reminding and observing daily adherence to ARVs, has been recognized as a significant facilitator of ART adherence. Few of the reviewed studies have shown that having a treatment supporter is strongly linked to good

adherence.(4,39,40,45,49,54). For example, in the study by Ekama et al (49), there was a positive association between having a treatment partner and good adherence, with a p-value of 0.002 and an OR of 2.5 (95%CI: 1.3–6.7). Similar positive impacts of treatment partners on medication pick-up from the pharmacy and improvement in viral load have been reported in a few other articles (40,54). Further confirming their importance in promoting good adherence to ART.

3.3.4 MEDICATION RELATED ENABLERS

Fixed-Dose Combination and Simplicity of Doses: Few of the reviewed articles highlighted the significance of the simplicity of doses as a key enabler of good adherence(7,41,42). Patients expressed a preference for fixed-dose combinations because of the ease of following the treatment regimen and few side effects, which positively influenced their adherence to ART (7,42). Alfa et al. (7) further explained that patients were prescribed two different fixed dose combinations of antiretroviral drugs: one containing zidovudine, lamivudine, and nevirapine, taken twice daily, and the other containing tenofovir, lamivudine, and efavirenz, taken once daily. The simplicity of these dosing regimens, with specific drugs combined into a single pill, likely played a vital role in promoting adherence to the treatment. Patients found it easier to follow the medication schedule since they only needed to take a limited number of pills per day, either once or twice, instead of multiple separate medications. This simplified dosing approach is believed to have significantly contributed to better adherence among the patients. Ultimately, simplicity of doses through fixed-dose combinations emerged as an important facilitator of good adherence to ART as patients appreciated the convenience of managing their treatment with fewer pills, leading to improved adherence and better treatment outcomes (5,7,41,42).

3.4 MOST COMMON INTERVENTIONS EMPLOYED TO IMPROVE ART ADHERENCE IN NIGERIA

3.4.1 HEALTH SYSTEM/HEALTHCARE PROVIDER RELATED INTERVENTIONS

Adherence Counselling and Text Message Reminder

The most common intervention employed to improve ART adherence among PLHIV in Nigeria was the combination of adherence counselling and text message reminders sent by healthcare providers (7,8,41). Thereby categorizing this intervention under the healthcare provider domain in the framework. This intervention aimed to help patients understand their medications, overcome barriers to adherence, and build confidence in sticking to their treatment schedule. Three studies conducted in different regions of Nigeria examined the impact of this combined intervention on ART adherence among PLHIV aged 20 years and above. Adherence levels were measured using CD4 count, viral load levels, and self-reported adherence (7,8,41).

The combination of adherence counselling and text message reminders led to significant improvements in adherence rates, CD4 count, and viral load levels (36,37,39). Participants who received both counselling and text reminders demonstrated higher adherence rates and increased CD4 count compared to control groups. For instance, Maduka and Tobin-West study (41), demonstrated a significantly higher adherence rates of $\geq 95\%$ (77%) compared to the control group (55.8%), ($\chi^2 = 5.211$, $P = 0.022$). This improvement was accompanied by a noteworthy increase in median CD4 count, from 193 cells/ml to 575 cells/ml in the intervention group compared to the control group 131 cells/ml to 362 cells/ml (p-value 0.007). Similarly,

Alfa et al. (7), also showed a significant increase in the mean CD4 count (37%) compared to the control group (19%). However, these studies had no substantial difference in self-reported adherence between the control and intervention groups, probably due to recall bias. Moreover, Abiodun et al.'s study (8), reported a significant difference in the mean viral load (11,678 copies/ml) for the intervention group compared to the control group (42,677copies/ml). Although self-reported adherence did not differ significantly between the groups. A study in Kenya also reported similar findings, of improved self-reported adherence and viral suppression after intervention. Those in the intervention group had a relative risk (RR) of 0.81, indicating a lower risk of non-adherence (71). These findings indicate that the combined intervention of adherence counselling and text message reminders was associated with improved adherence rates, although there were variations in the impact on self-reported adherence across the Nigerian studies.

Adherence Counselling:

Adherence counselling was widespread in most studies, delivered through methods such as mobile phone-based, face-to-face sessions, or in combination with other approaches. It also served as the standard of care (SOC) for control groups. It involved providing knowledge, guidance, and emotional support to help individuals manage their treatment effectively (42). A descriptive cross sectional study, measured adherence using viral load and pharmacy refill data. After enhanced adherence counselling for virally unsuppressed patients for 13 weeks, 266 participants (67%) demonstrated good adherence, and 135(51%) achieved viral suppression (<1000 copies/ml). Surprisingly, despite 134 participants (34%) having poor adherence, 69 of them (52%) still achieved viral suppression. Both first and second-line HAART regimens showed good adherence and viral suppression rates, with slightly higher rates in the second-line regimen group. However, not all participants achieved viral suppression despite good adherence, indicating other factors at play. The study's limitations included reliance on pharmacy refill for adherence assessment, which may have overestimated adherence rates, and the absence of a control group to compare intervention effectiveness (3).

Another study had participants in the intervention group receive combined counselling and text messaging, while the control group received counselling alone. The intervention group showed a higher increase in mean CD4 count (37%) compared to the control group (19%), and over 74% of participants who received counselling alone achieved good adherence based on self-report, similar to 75% in the intervention group, indicating an improved immune system, even for the control group (7). Comparatively, In Uganda, counselling at ART initiation reduced poor adherence and treatment failure risk by 29% and 59% for control and intervention groups respectively, sustaining positive effects throughout 18-months follow-up, thus enhancing adherence and biological outcomes (72). Both Nigerian and Ugandan studies demonstrated the positive effects of counselling on ART adherence and treatment outcomes.

Adherence Counselling with Other Reminder Systems:

Few studies utilized enhanced adherence counselling with a combination of other approaches to improve good adherence. This includes counselling combined with reminder systems and with group education (27,33,40). In a three-arm randomized controlled field trial study, researchers aimed to improve ART adherence using enhanced adherence counselling and reminder tools. Participants were divided into three groups: one received alarm clocks and

counselling, another received stickers and counselling, and the third group received counselling alone. The intervention outcome is represented in the table 3 below:

Table 3: Intervention outcome for adherence counselling with other reminder systems

Intervention	Pre-Intervention adherence (%)	Post-intervention adherence level increased to (%)
Alarm clock + Counselling	79	98 (p<0.05)
Sticker + Reminder Card + Counselling	80	87 (p>0.05)
Counselling Only	84	86 (p>0.05)

From the above findings, the study concluded that stickers and reminder cards with counselling and counselling only showed improvements, but not statistically significant. However, combining counselling with alarm clocks was the most effective in improving adherence. In Cameroon, electronic devices like alarm clocks, phones, or watches helped maintain good adherence (73). On the other hand, a Ugandan study showed no significant difference with alarm devices, as participants encountered issues like alarm malfunction and loss (72). Combining counselling with practical reminders appears to be crucial for effective ART adherence.

Adherence Counselling and Health Education

Two studies utilized a combination of adherence counselling with group education. The interventions included group health education sessions, individual counselling, and distribution of educational materials. Knowledge of adherence factors significantly increased in the study group compared to the control group (p<0.001) (44). In these study, Igweagu et al. (44), reported that the intervention group received intensive health education training and adherence counselling for 13 weeks. Post-intervention, the intervention group (82%) showed a significant improvement in the percentage of adherent participants compared to the control group (32%). Notably, adherence level was ≥95% for adherent participants. Whereas, in the study by Agu et al.(39), participants received group education and individual counselling for 24 weeks. A significant proportion (70% - 85%) of participants showed improved adherence to both medication schedule and prescribed doses of medication, with 70% reporting >75% adherence to the medication schedule and 85% reporting >80% adherence to prescribed medication doses. However, the overall self-reported adherence was relatively poor at 79% (± 14.4%), which did not meet the desired value of >95%. Considering the study's limitations, the absence of a control group made it challenging to compare the effectiveness of the adherence intervention (39). In Uganda, a one-group pre- and post-intervention study with counselling, group education, leaflets, late attendee tracing, and adherence diaries showed a significant improvement in self-reported mean adherence levels from 97% to 99%. The intervention resulted in a 7% increase in the proportion of participants achieving optimal adherence (≥95%). Among those initially adherent, 97% remained adherent, while 95% of those with suboptimal

adherence achieved optimal adherence after the interventions. Which is consistent with the findings in Nigeria.

Reminder Text Messaging and Peer Navigation

In a pilot study by Taiwo et al.(2), a combination of text messaging (SMS) and peer navigation (PN) was employed to enhance ART outcomes among young people living with HIV in Nigeria. The intervention included daily, two-way text message reminders and support from trained peer navigators. After 48 weeks, positive outcomes were observed in the study. The proportion of participants achieving viral suppression (<1000 copies/ml) increased significantly to 60%, showing a 71% improvement from baseline. Self-reported ART adherence also increased, reaching 68% with adherence $\geq 90\%$, compared to the baseline of 43%, indicating better medication adherence. However, self-reported adherence did not show a significant correlation with viral suppression at both 24 and 48 weeks.

On the other hand, medication pick-up adherence measured by medication pickup ratio (MPR) showed consistent prescription pick-ups with $\geq 90\%$ adherence. While MPR was not significantly correlated with viral suppression at 24 weeks, it became significantly correlated at 48 weeks, suggesting a connection between consistent prescription pick-ups and better viral suppression outcomes at that point. Overall, the intervention had a positive impact on achieving viral suppression at 48 weeks. Similar intervention was reported during a randomized controlled trial in Malaysia, a combination of text messaging, telephone reminders, and peer counselling significantly increased the average adherence to ART in the intervention group (96%) compared to the control group (88%). The intervention group also had a significantly higher proportion of participants with good adherence ($>95\%$) (92.2%), compared to the control group (54.6%). Additionally, the intervention group had fewer missed appointments (14.0% vs. 35.5%), lower viral load, and a higher increase in CD4 count (74). The results indicate a positive correlation between the intervention and improved linkage to care and adherence, showing a similar trend to the findings observed in the Nigerian study.

3.4.2 SOCIO-ECONOMIC RELATED INTERVENTIONS

Peer Support Groups:

Peer support groups are formal associations where PLHIV gather to address health-related concerns and engage in activities focused on managing HIV/AIDS (5,51). From the reviewed articles, It was one of the most common interventions employed to improve good adherence (5,46,51). Therefore, categorized under the Socio-economic related factors. Participating in PLHIV support group activities offered individual and group benefits, including ART adherence support and addressing HIV-related needs (51). These groups are reported to be widely recognized and effective in improving adherence among PLHIV, with positive outcomes such as reduced stigma, increased disclosure, safer sexual behaviors, and improved ART adherence (5,51).

Two cross-sectional studies conducted among adults (≥ 18 years) in Nigeria consistently showed that participation in support groups positively influenced ART adherence (5,51). These studies stated that, those in support groups reported achieving good adherence ($\geq 95\%$) compared to those in non-support groups (5,46). In Chime et al.'s study (5), those in support group had a significantly higher adjusted odds ratio (AOR) of 5.8 (95% CI: 2.7–12.2, $p < 0.001$), to adhere to treatment indicating a strong association with ART adherence. Similarly, A

randomized controlled trial among adolescents (10-17 years) further supported these findings, showing that those enrolled in support groups had very high viral load suppression (<1000 copies/ml) compared to those not enrolled. The enrolled support group had 92% viral load suppression, while the non-enrolled group had only 48.3% viral load suppression (51). Overall, these studies highlight the effectiveness of support groups in improving ART adherence among PLHIV in different regions of Nigeria, leading to better health outcomes. Comparatively, in a systematic review on social support for PLWHA in LMIC, those with moderate or poor social support were 3 times more likely to report non-adherence, and those with poor social support were almost 9 times more likely to report low adherence in LMIC (75). In contrast, the second systematic review showed that a combination of peer supporter and telephone calls was significantly more effective in improving ART adherence in LMIC (OR=4.83, 95% CI: 1.88, 13.55) compared to standard care (76). However, peer intervention alone did not lead to significant adherence improvement. These findings highlight the importance of strong social support and the effectiveness of combining peer support with routine care interventions for better ART adherence in low-resource settings (77).

Social Media-Based Support Group:

Social media-based support groups were not commonly used to improve ART adherence from articles reviewed. However, a randomized controlled trial focused on young people living with HIV (aged 15-24 years). The intervention called smart connection, had the intervention group (n=177) receiving standard care along with secret Facebook group sessions, providing HIV-related knowledge, social support, and treatment literacy for 22 weeks. Facilitators, who were community-based and living with HIV themselves, were trained and provided smartphones and data allowance. The control group (n=172) received standard care, including clinical services, viral load tests, and adherence counselling. At the study's end, 76% of the intervention group and 83% of the control group remained active on treatment, but no significant difference in ART adherence between the groups was found (p=0.57). Adherence was self-reported using the ACTG adherence questionnaire, but challenges in measurement were noted due to underreported gaps and limited viral load testing availability (9). The use of social media groups for improving ART adherence in sub-Saharan countries is not widely studied. However, a pilot study in Kenya examined the impact of a mobile intervention on mental health and ART adherence among adults living with HIV. The results showed significant improvements in adherence, with only 1 participant reporting missing a dose in the past 30 days, compared to 7 at the start of the study (78). During six months of monitoring, 59% of participants were considered adherent, taking their prescribed doses on over 90% of days. About 40% of participants attributed their improved adherence to the WhatsApp intervention, which included reminders and support from friends in the group (78). Unlike the Nigerian study, that lacked a reliable means of measuring adherence, the Kenyan research utilized the electronic Medication Event Monitoring dose technique, making its findings more reliable.

Direct Observation Therapy (DOT):

Although this intervention is categorized into the socio-economic domain, it still does fall under the patient related and healthcare provider domain of the framework as its include a combination of all three which is shown in the intervention description below. This intervention was employed by one study, thus, not a common intervention for improving ART adherence. DOT involves observing patients as they take a portion of their ART regimen, while they self-administer the remaining medication (45). The study conducted in Plateau state,

northern Nigeria, explored the role of community members, such as family members or relatives, in implementing community-based DOT for HIV treatment. Treatment partners were trained to observe medication intake, conduct pill counts, and provide support to patients. Treatment supervisors maintained records and conducted monthly follow-ups. Adherence was measured using viral load and CD4 count. The study included 145 study participants divided into four intervention groups: Daily Observed Therapy (DOT), Twice Weekly Observed Therapy (TWOT), Weekly Observed Therapy (WOT), and Self-Administered Therapy (SAT, control group). The results at baseline and after 48 weeks showed the following outcomes represented in the table 4 below:

Table 4: Intervention outcome for Direct Observed Therapy

Intervention Group	Median CD4 count at baseline (cells/mm3)	Median CD4 Count at 48 Weeks (cells/mm3)	Percentage of Participants Achieving Viral Suppression (<400 copies) after 48 Weeks
DOT	138	352	91%
TWOT	138	315	88%
WOT	100	360	84%
SAT	134	326	79%

The study demonstrated the success of DOT in promoting ART adherence. The intervention groups that were observed daily (DOT), twice weekly (TWOT), and weekly (WOT), achieved higher viral suppression rates compared to the self-administered therapy group. This indicates higher medication adherence among the observed groups. The findings highlight the positive impact of DOT on ART adherence, as evidenced by the most improved viral suppression rates (45). Comparatively, A south African Study also assessed the effect of DOT on ART adherence among 274 patients. In this study, two groups of patients (DOT-ART and Self-ART group) receiving different treatment support methods were compared. The DOT-ART group, which used a network inventory instrument to select treatment supporters, had a significant increase in CD4 cell count compared to the Self-ART group at 6 months (148 cells/ μ L vs. 111 cells/ μ L, pvalue-0.02). The instrument helped identify supportive individuals who knew about the patients' HIV diagnosis and could assist with adherence. However, there were no statistically significant differences between the two groups at 12 months, 18 months, and 24 months. Overall, the study suggests that the DOT-ART approach led to a more positive improvement in CD4 cell count at 6 months, but there were no notable differences in the long-term. This correlates with the previously cited Nigerian study regarding the positive effects of DOTs on adherence (79)

Economic Incentives and Motivational interviewing

Intervention involving provision of incentives for study participants was implemented by one study among all articles reviewed thereby categorizing this intervention under socio-economic domain even though it also falls under the patient-related domain due to the motivational interviewing which was also combined in this study. This intervention was implemented in

Anambra State, Nigeria for adolescents living with HIV (aged 10-19). Adolescents with unsuppressed viral loads received conditional economic incentives and attended mandatory motivational interviewing sessions. Monetary rewards were provided for achieving and maintaining viral load suppression: US\$ 5.6 for the first three months, US\$ 2.8 for the next three and six months, and an additional US\$ 5.6 for maintaining suppression for 12 months. The intervention motivated adherence, leading to a significant proportion of adolescents achieving viral load suppression. The positive impact was also observed among participants' attitudes and perceptions of the disease. The intervention's effectiveness was evaluated in a cluster-randomized trial (N = 246). At baseline, 21.8% in the intervention group and 42.5% in the control group had undetected viral loads. After 12 months, the proportions were 31.9% and 40.9%, respectively, indicating improved virologic outcomes associated with adherence to ART. The findings suggest that the incentive scheme and motivational interviewing effectively improved adherence and viral suppression in adolescents living with HIV (48). A family-based economic empowerment (EE) intervention was tested in a five-year cluster trial in Uganda to support families of adolescents living with HIV (ALWHIV) aged 10-16 years. The intervention provided incentivized savings accounts to the adolescents to invest in their health and education needs. Along with the bolstered standard of care (SOC) that included adherence information sessions, this intervention positively improved viral suppression (adj. hazard ratio: HR = 1.446, CI: 1.073-1.949, p = 0.015). It proved to be effective in enhancing treatment outcomes for ALWHIV in achieving viral suppression (<40 copies/ml)(80).

3.4.3 PATIENT-RELATED INTERVENTIONS

Motivational interviewing (MI):

Motivational interviewing was not frequently utilized as an intervention in the Nigerian studies, despite its demonstrated success in improving ART adherence outcomes. Motivational Interviewing is a counselling approach used to address ambivalence and build motivation for behavior change (53). Motivational interviewing techniques were utilized among women alone due to the observed high non-adherence reported due to their gender roles (40,52). The intervention aimed to improve self-confidence, knowledge about HIV, the belief in positive outcomes, and establish personal goals related to ART adherence and safer sexual practices. The quasi experimental study on HIV-positive women reported a positive outcome on MI on the adherence level. Intervention outcome for this MI group showed better adherence compared to the health promotion program (HPP) group (100% vs. 61%). All 26 MI respondents reported taking 100% of their HIV drugs, while only 11 out of 18 HPP respondents (61%) took 90% or more of their HIV drugs (p<0.001) showing a positive impact of MI on ART adherence level (40). Similarly, in a research study conducted in India, two groups were compared: an intervention group receiving motivational interviews and interactive sessions, and a control group receiving standard care. After 12 months of follow-up visits, the intervention group showed significantly better results in terms of viral load suppression (53% vs. 41%, p=0.017) (81). Participants in the intervention group were twice as likely to achieve viral suppression (AOR = 1.98-95% CI 1.2-3.23) as well as high adherence rates of ≥95% (AOR = 1.86, 95% CI 1.09-3.15). They also reported successfully overcoming individual adherence barriers (AOR = 2.33, 95% CI 1.51-3.62) and clinic attendance barriers (AOR = 2.01, 95% CI 1.20-3.38) compared to the control group (81).

Pill box

The use of an adherence aid like pill box was not a common intervention identified among reviewed studies, although reported to have a strong correlation with ART Adherence ($r= 0.22$, $p<0.001$, $\beta=8.3\%$) (6). According to a prospective/observational study in South-eastern Nigeria among 299 participants of (16->45) years, showed that, around 70% of participants who used pill box as adherence aid, reported adhering to their HIV medication, while 30% did not meet the adherence threshold. The median CD4 count increased over time, with adherent individuals showing a slightly higher median change (Adherent 25 cells/ μ L and non-adherent 20 cells/ μ L). On average, % Self-reported Adherence Level was $86\% \pm 30$. that is, participants reported taking about 86% of their prescribed medication (6). The use of pill box actually showed improvement in adherence level, even though it was $<95\%$. Also, self-reported adherence may not always reflect actual medication intake. In South Africa, a study looked at the impact of a real-time electronic adherence monitoring device (EAMD) called Wise-pill. Participants were divided into two groups: one receiving standard care and the other receiving reminder text messages linked to non-opening of the device. After 48 weeks, the study found that adherence levels were 82% in the group with the electronic device and 80% in the standard care group (AOR:1.08; 95% CI: 0.77-1.52), showing a non-statistical significance. However, the use of electronic device did help reduce the number of treatment interruptions of >72 hours (adjusted incident rate ratio, 0.84; 95% CI: 0.75 to 0.94) but, it did not have a positive effect on overall adherence or viral suppression (82).

Treatment Partners (TP) or Treatment Supporters (TS)

Use of treatment partners or supporters have been implemented either as a single intervention or in combination with other interventions. Few of the reviewed articles investigated the use of treatment partners to improve adherence either as a single intervention or combined with other interventions. Treatment partners can be categorized under either patient or socio-economic related according to the framework, since a treatment partner can either be a family relative or trusted community member. In one study, clients had a chosen treatment partner who helped them with medication intake, side effects, and reminders for drug pickup. This group showed better adherence at 48 weeks 80% (199/248) compared to the standard care group 67% (169/251)(AOR: 1.77 CI 95% (1.15-2.73) Pvalue-0.01). Their viral load also improved at 24 weeks, but the improvement didn't last till 48 weeks, possibly because all patients with detectable virus received extra support (54). The second study, combined treatment partners with alarm reminders, follow-up calls, and peer support. They found that participants with adherence rates of $\geq 95\%$ based on medication refill had a viral load suppression rate of 58%, while those with lower adherence rates had a suppression rate of 41%. Poor self-reported adherence and medication refill rates $< 95\%$ were negatively associated with viral load suppression (4). Both studies had limitations, such as difficulties accurately measuring adherence, and one study experienced a high rate of participants loss to follow-up, which could have influenced the results (4,54). Similar findings was demonstrated in a Ugandan study, a higher proportion of TS participants (96%) achieved at least 95% adherence compared to non-TS participants (86%)(83). The odds of achieving this level of adherence were higher in the TS group (OR = 4.51, 95% CI: 1.22–16.62, exact Pvalue-0.027). Overall, evidence shows that using treatment partners and other support measures can help improve adherence and viral load outcomes for PLHIV.

3.4.3 MEDICATION-RELATED INTERVENTION

Fixed Dose Combination Antiretroviral Pills

According to a 5-year retrospective cohort study at a Teaching hospital in Lagos, despite significant adverse effects associated with the drug, newer fixed dose combinations have improved adherence to ART (84). Fixed-dose combinations (FDCs) are preferred because they are easy to use, have distribution advantages (procurement and stock management) which result in improved adherence (85).

A qualitative study at three community health centres in South Africa reviewed the experiences of 15 HIV patients within age 23 to 56years who had been on the FDCs for at least a year (86). Participants in this study indicated that since they converted from triple pill to FDC they had seen life as being simpler and they adhered better to treatment without confusing treatment and forgetting. They indicated that using FDC had given them a sense of relief from taking too many tablets at once. They also mentioned that this made their lives much easier. On the other hand, participants who only suffered the HIV infection also mentioned that taking three tablets twice a day was a burden. Now that they had been moved to the FDC pill they felt relieved that the number of tablets had been reduced (86).

CHAPTER 4

4.1 DISCUSSION

The discussion provides a concise analysis of the main findings, exploring factors influencing ART adherence and the successes of interventions employed to address common barriers and improve adherence. It covers healthcare provider-related factors, socio-economic conditions, patients, and medications, highlighting from the most frequently mentioned factors and interventions and their implications for ART adherence.

Forgetfulness emerged as the most prevalent barrier to ART adherence, with many participants struggling to remember to take their medications amidst busy work and home life. To address this challenge, various interventions have been employed, including reminder text messaging, reminder cards, alarms, and pill boxes. These interventions have shown promising results in promoting adherence.

One of the most common interventions to address forgetfulness is the combination of adherence counselling and text message reminders sent by healthcare providers. This approach has shown positive outcomes in multiple studies, with participants receiving counselling and text reminders demonstrating higher adherence rates and increased CD4 counts compared to control groups. The use of text messages as reminders is particularly effective in Nigeria due to the widespread use of mobile phones, and similar findings have been observed in other LMICs like Kenya.

Adherence counselling alone is also a frequently employed intervention to improve adherence. While counselling alone can be effective in tackling diverse barriers, such as drug/alcohol abuse, mental distress like depression, and stigma, combining counselling with other interventions has shown even better results. Two studies from Nigeria and Uganda, combined counselling with practical reminders like alarm clocks, stickers and reminder cards. The combination of counselling with alarm reminders proved to be the most effective in improving adherence. However, the combination of counselling with stickers and reminder cards did not show statistically significant improvements. The successes of such combinations may vary based on individual preferences and circumstances, which was evident in the Ugandan study as most of the participants' alarms were faulty or lost leading to non-statistical significant outcome.

Internalized stigma and fear of disclosing HIV status were identified as significant barriers to ART adherence. counselling and group education were employed in most studies to tackle these barriers, providing emotional support, addressing negative feelings, and improving self-confidence. These interventions also offered knowledge about HIV and allowed individuals to discuss their fears openly, resulting in better understanding and management of HIV.

Age-related barriers to ART adherence were addressed through interventions such as peer navigation and social media-based support groups. Young individuals' engagement with social media made it a viable platform to provide HIV-related knowledge, treatment literacy, and adherence support. Though the findings from social media-based support group interventions were mixed and had difficulties with adherence monitoring, retention in care was considerably high. Further studies with emphasis on adherence monitoring are needed to assess the long-term impact of these interventions.

Alcohol and drug abuse, were also identified as barriers to ART adherence among PLHIV. Peer support groups, counselling, and DOT have shown promise in addressing these challenges and improving adherence rates. Participation in peer support groups has been effective in improving adherence rates among PLHIV, providing a safe space to share experiences and receive encouragement from others facing similar struggles. Social support in these groups fostered a sense of belonging and understanding, helping individuals overcome barriers to adherence. This finding was consistent with a systematic review from LMICs, highlighting the positive impact of support groups on adherence outcomes.

Sex/gender was identified as a barrier, with non-adherence more prevalent among women. Motivational interviewing (MI) emerged as a promising intervention for HIV-positive women, addressing specific challenges related to gender roles. MI helped build motivation for behavior change and showed a statistically significant impact, with >95% adherence for the intervention group.

Adherence aids, such as pill boxes, have shown a positive correlation with ART adherence, with around 70% adherence reported by participants who used them. While not reaching the optimal threshold of 95%, pill boxes provided an organized reminder of medication schedules. However, it is important to note that self-reporting used for adherence measurement in this study, may not always reflect actual medication intake accurately. Electronic adherence monitoring devices like Wise-pill (a smart pillbox) employed in a South African study did not also show statistical significance in improving overall adherence. However, Wise-pill was effective in reducing treatment interruptions of over 72 hours. These devices may probably be more suitable when combined with other interventions to achieve better results.

Medication-related barriers, such as drug side effects and depression, were addressed through interventions involving treatment partners. Having a chosen treatment partner who provided support with medication intake, reminders, and side effects was associated with better adherence and viral suppression rates. Treatment partners played a crucial role in improving adherence through monitoring, encouragement, and emotional support, while also assisting in managing depression symptoms by providing active listening, offering emotional support, and facilitating access to mental health resources. They create a supportive environment where individuals can openly discuss their feelings and fears related to depression, leading to improved coping strategies and mental well-being, ultimately enhancing adherence to ART medications. Similar findings of improved adherence with treatment partners were reported in studies from Uganda, where over 96% of study participants with a treatment supporter achieved $\geq 95\%$ adherence.

DOT has also demonstrated promising results in promoting ART adherence. By involving trusted community members to observe medication intake, DOT achieved higher viral suppression rates compared to self-administered therapy. The intervention addresses patient-related, healthcare provider, and socio-economic factors, making it a comprehensive approach to adherence improvement. However, it is essential to consider the sustainability and scalability of the DOT approach, especially in resource-limited settings. Comparing findings from other countries, such as South Africa, supports the effectiveness of DOT in improving adherence rates in the short term.

Poverty and unemployment were identified as potential barriers to ART adherence, impacting access to health facilities and leading to missed doses. To address these barriers, economic

incentives and motivational interviewing were employed in Nigeria, showing promising results. Similar interventions in Uganda have also demonstrated positive outcomes. The provision of monetary rewards and economic empowerment motivated PLHIV, particularly adolescents, to adhere to their treatment regimens, leading to improved viral suppression rates and treatment outcomes. However, the effectiveness of these interventions may vary based on cultural differences, healthcare infrastructure, and the level of poverty or unemployment in the population.

A tailored and comprehensive approach is necessary to address the diverse barriers to ART adherence effectively. It is crucial to consider individual differences and preferences when implementing these interventions. While text message reminders, alarm clocks, and treatment partners may be effective for some, others may benefit more from counselling or peer support groups. Providing a range of options and tailoring interventions to individual circumstances can increase their effectiveness.

The findings from the reviewed studies are essential not only for the context of Nigeria but also for similar settings and countries facing challenges in HIV/AIDS management and ART adherence. However, it is important to recognize that interventions may yield varying results based on the context and population being studied. Factors such as cultural differences, healthcare infrastructure, and the level of poverty or unemployment in the population may influence the outcomes of such interventions. In the pursuit of enhancing adherence, it is crucial to continue exploring and evaluating various interventions, taking into account individual differences and contexts.

This study has two significant limitations. Firstly, it did not include specific groups like key populations and individuals from diverse backgrounds, which could have offered valuable insights. Future research should address this gap by encompassing a broader and more representative sample. Secondly, the study predominantly used quantitative designs, limiting the understanding of complexities related to ART adherence. Expanding methodological approaches to include mixed and qualitative methods would provide a more comprehensive and holistic perspective. This study also had significant strengths including its ability to highlight the most common and successful interventions to improve ART adherence.

Finally, the original conceptual framework proved highly relevant and beneficial in addressing the research questions. Its adaptability and flexibility allowed for a comprehensive exploration of the barriers, enablers, and interventions employed to improve ART adherence, showcasing another significant strength of this study. The framework, developed to categorize factors affecting adherence, provided constructs that were adeptly utilized to categorize the various interventions implemented to enhance adherence. Incorporating additional findings from the study rendered the framework more comprehensive and context-specific, thereby deepening the understanding of adherence challenges and enabling the identification of tailored interventions for PLHIV and LMICs. The diverse domains in the modified framework effectively highlighted areas where interventions were initially underrepresented in the original version. Overall, the modified framework significantly contributed to the study's success in exploring factors influencing ART adherence and the corresponding strategies employed to bolster medication adherence rates among PLHIV in Nigeria and LMICs.

4.2 CONCLUSION AND RECOMMENDATIONS

In this study, various approaches to enhance ART adherence among PLHIV were explored. The study identified forgetfulness, internalized stigma, and medication-related factors as prominent barriers, while counselling, peer support groups, and reminder systems emerged as key enablers. The most common interventions used to improve adherence were highlighted, including individualized adherence counselling, counselling combined with text message, counselling combined with other reminders like alarm, peer support groups, and treatment partners. These interventions demonstrated positive outcomes in enhancing adherence rates. By comparing interventions in Nigeria with those in other LMICs, valuable insights into their successes were obtained. Ultimately, a tailored, multifaceted approach that considers individual preferences is essential in enhancing ART adherence in Nigeria. Continued research is needed to assess the long-term impact and sustainability of these interventions.

4.3 RECOMMENDATIONS

Recommendations to enhance ART adherence in Nigeria should involve a collaborative effort from various stakeholders, including the FMOH, state governments, HCPs, CMOs, and CSOs. The following feasible recommendations that can be accomplished to address the identified barriers and improve adherence.

- 1. Strengthen Adherence Counseling Services:** HCPs should receive quarterly training to provide effective counseling services to PLHIV. This should include counseling tailored to address specific barriers, such as internalized stigma and depression, and equip HCPs with MI techniques to promote behavioural change and eliminate negative perceptions regarding HIV. The FMOH and state governments should prioritize funding these capacity building programs in healthcare facilities across the country.
- 2. Support and Expand the Utilization of Reminder Systems:** The FMOH, in collaboration with the National Primary Healthcare Development Agency (NPHCDA) should invest in making reminder systems more operational within ART services. HCPs at all levels of healthcare should be assisted with logistics to issue regular and timely text message reminders and phone calls based on the need. This can be sustained by partnership with private telecommunication companies to activate automated coded text messages for PLHIV on treatment. Additionally, clients should be adequately counselled on the use of cost-effective measures such as the alarm clocks and in the case of married couples, partners should be involved in reminding their spouses.
- 3. Promote and Strengthen Peer Support Groups:** CBOs and CSOs should continue to support and expand peer support groups for PLHIV. Special attention should be given to reaching out to young people and leveraging social media platforms to create online support groups.
- 4. Conduct Qualitative Studies on Key Populations:** Researchers from NGO partners and the FMOH should prioritize qualitative studies to understand unique adherence barriers among key populations. Research findings should be properly disseminated to the Legislature and to the FMOH in order to inform targeted interventions and policies.
- 5. Integrate Mental Health Services:** Mental health problems, such as depression, can significantly impact ART adherence. The National Primary Healthcare Development Agency and its state counterparts should support the integration of mental health services into HIV care and treatment programs. This integration should involve task shifting through development of Standard Operating Procedures (SOPs) to enable community health workers provide these services at a basic level.

6. **Increased Public Awareness and Sensitization against Stigma:** Increased awareness about the negative effects of stigma on adherence, among religious and traditional leaders is required as they are a powerful and influential group of stakeholders within the community. This will lead to re-orientation of other members of the community to refrain from stigmatizing people receiving ART services.
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REFERENCES

1. National Guidelines for HIV prevention, treatment and care 2020 [Internet]. [cited 2023 Jun 19]. Available from: https://www.google.com/url?sa=t&source=web&rct=j&opi=89978449&url=https://nascp.gov.ng/resources/get_resource_doc/17&ved=2ahUKEwih4ankyMqAAxWVhFwKHdbcACkQFnoECBEQAQ&usg=AOvVaw38h7ekwJ-UgQPdb_Jdv3ym
2. Taiwo BO, Kuti KM, Kuhns LM, Omigbodun O, Awolude O, Adetunji A, et al. Effect of Text Messaging Plus Peer Navigation on Viral Suppression Among Youth With HIV in the iCARE Nigeria Pilot Study. *J Acquir Immune Defic Syndr*. 2021 Aug 1;87(4):1086–92.
3. Awolude OA, Olaniyi O, Moradeyo M, Abiolu J. Virologic Outcomes Following Enhanced Adherence Counselling among Treatment Experienced HIV Positive Patients at University College Hospital, Ibadan, Nigeria. *I-SRR*. 2021 Mar 2;53–65.
4. Coker M, Etiebet MA, Chang H, Awwal G, Jumare J, Musa BM, et al. Socio-Demographic and Adherence Factors Associated with Viral Load Suppression in HIV-Infected Adults Initiating Therapy in Northern Nigeria: A Randomized Controlled Trial of a Peer Support Intervention. *Curr HIV Res*. 2015;13(4):279–85.
5. Chime OH, Arinze-Onyia SU, Obionu CN. Do peer support groups have an effect on medication adherence? A study among people living with HIV/AIDS in Enugu State, Nigeria. *Proceedings of Singapore Healthcare*. 2018 Dec 1;27(4):256–64.
6. Ukwe CV, Ekwunife OI, Udeogaranya PO, Iwuamadi UI. Self-reported adherence to HAART in South-Eastern Nigeria is related to patients' use of pill box. *SAHARA-J: Journal of Social Aspects of HIV/AIDS*. 2010 Jul 1;7(1):10–5.
7. Alfa MA, Zezi AU, Gyang SS, Yusuf H, Aliyu IM. Effect of Counselling and Reminder Text Messages Follow-Up on Adherence to Antiretroviral Therapy in Hajiya Gambo Sawaba General Hospital, Zaria, Nigeria. *J App Pharm Sci*. 2016 Sep 26;6(9):174–8.
8. Abiodun O, Ladi-Akinyemi B, Olu-Abiodun O, Sotunsa J, Bamidele F, Adepoju A, et al. A Single-Blind, Parallel Design RCT to Assess the Effectiveness of SMS Reminders in Improving ART Adherence Among Adolescents Living with HIV (STARTA Trial). *Journal of Adolescent Health*. 2021 Apr;68(4):728–36.
9. Dulli L, Ridgeway K, Packer C, Murray KR, Mumuni T, Plourde KF, et al. A Social Media-Based Support Group for Youth Living With HIV in Nigeria (SMART Connections): Randomized Controlled Trial. *J Med Internet Res*. 2020 Jun 2;22(6):e18343.
10. UNAIDS_FactSheet_en.pdf [Internet]. [cited 2023 Jun 19]. Available from: https://www.unaids.org/sites/default/files/media_asset/UNAIDS_FactSheet_en.pdf
11. HIV and AIDS [Internet]. [cited 2023 May 3]. Available from: <https://www.who.int/news-room/fact-sheets/detail/hiv-aids>
12. HIV data and statistics [Internet]. [cited 2023 Jun 19]. Available from: <https://www.who.int/teams/global-hiv-hepatitis-and-stis-programmes/hiv/strategic-information/hiv-data-and-statistics>
13. WHO | Regional Office for Africa [Internet]. 2023 [cited 2023 May 3]. HIV/AIDS. Available from: <https://www.afro.who.int/health-topics/hiv/aids>

14. Estimated number of people (all ages) living with HIV [Internet]. [cited 2023 Mar 1]. Available from: <https://www.who.int/data/gho/data/indicators/indicator-details/GHO/estimated-number-of-people--living-with-hiv>
15. Jin H, Restar A, Beyrer C. Overview of the epidemiological conditions of HIV among key populations in Africa. *Journal of the International AIDS Society*. 2021;24(S3):e25716.
16. Thirty-five years (1986–2021) of HIV/AIDS in Nigeria: bibliometric and scoping analysis | *AIDS Research and Therapy* | Full Text [Internet]. [cited 2023 Jun 19]. Available from: <https://aidsrestherapy.biomedcentral.com/articles/10.1186/s12981-022-00489-6>
17. Sabaté E, World Health Organization, editors. *Adherence to long-term therapies: evidence for action*. Geneva: World Health Organization; 2003. 198 p.
18. Antiretroviral Therapy - PAHO/WHO | Pan American Health Organization [Internet]. [cited 2023 Jun 19]. Available from: <https://www.paho.org/en/topics/antiretroviral-therapy>
19. International Association of Providers of AIDS Care [Internet]. [cited 2023 Jun 19]. *Antiretroviral Therapy (ART)*. Available from: <https://www.iapac.org/fact-sheet/antiretroviral-therapy-art/>
20. Eggleton JS, Nagalli S. Highly Active Antiretroviral Therapy (HAART). In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 [cited 2023 May 3]. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK554533/>
21. Quinn KG, Voisin DR. ART adherence among men who have sex with men living with HIV: key challenges and opportunities. *Curr HIV/AIDS Rep*. 2020 Aug;17(4):290–300.
22. Byrd KK, Hou JG, Hazen R, Kirkham H, Suzuki S, Clay PG, et al. Antiretroviral Adherence Level Necessary for HIV Viral Suppression Using Real-World Data. *J Acquir Immune Defic Syndr*. 2019 Nov 1;82(3):245–51.
23. Delamater AM. Improving Patient Adherence. *Clinical Diabetes*. 2006 Apr 1;24(2):71–7.
24. Iacob SA, Iacob DG, Jugulete G. Improving the Adherence to Antiretroviral Therapy, a Difficult but Essential Task for a Successful HIV Treatment—Clinical Points of View and Practical Considerations. *Front Pharmacol*. 2017 Nov 23;8:831.
25. Nigeria Population (2023) - Worldometer [Internet]. [cited 2023 Jun 20]. Available from: <https://www.worldometers.info/world-population/nigeria-population/>
26. Administrative Map of Nigeria - Nations Online Project [Internet]. [cited 2023 Jun 20]. Available from: <https://www.nationsonline.org/oneworld/map/nigeria-administrative-map.htm>
27. Severe Malaria Observatory [Internet]. [cited 2023 Jun 20]. Nigeria health system. Available from: <https://www.severemalaria.org/countries/nigeria/nigeria-health-system>
28. NATIONAL-POLICY-ON-HIV-AND-AIDS-2020-1.pdf [Internet]. [cited 2023 Jun 20]. Available from: <https://naca.gov.ng/wp-content/uploads/2022/03/NATIONAL-POLICY-ON-HIV-AND-AIDS-2020-1.pdf>
29. Nigeria [Internet]. [cited 2023 May 3]. Available from: <https://www.unaids.org/en/regionscountries/countries/nigeria>
30. Ibezim M, Ogbodo U, Ndie J, Kanu-Oji O, Oji N, Dada M, et al. Factors Affecting Level of Adherence Among People Living with HIV Attending Antiretroviral Care at Nnamdi Azikiwe University Teaching Hospital, Nnewi, Anambra State. *Central African Journal of Public Health*. 2020 Jan 1;6:80.

31. Anyaike C, Atoyebi OA, Musa OI, Bolarinwa OA, Durowade KA, Ogundiran A, et al. Adherence to combined Antiretroviral therapy (cART) among people living with HIV/AIDS in a Tertiary Hospital in Ilorin, Nigeria. *Pan African Medical Journal* [Internet]. 2019 Jan 7 [cited 2023 Feb 27];32(1). Available from: <https://www.ajol.info/index.php/pamj/article/view/207962>
32. Oku AO, Owoaje ET, Ige OK, Oyo-ita A. Prevalence and determinants of adherence to HAART amongst PLHIV in a tertiary health facility in south-south Nigeria. *BMC Infect Dis*. 2013 Aug 30;13(1):401.
33. Usman SA, Shehu A, Ajumobi O, Gidado S, Dalhatu I, Balogun M, et al. Predictors of non-adherence to antiretroviral therapy among HIV patients in secondary health care facilities in Kano State- Nigeria: a case-control study. *Pan Afr Med J*. 2019 Jan 21;32(Suppl 1):3.
34. UNAIDS-Putting people at the centre brings good results in Nigeria [Internet]. [cited 2023 May 6]. Available from: https://www.unaids.org/en/resources/presscentre/featurestories/2021/march/20210305_people-at-the-centre-nigeria
35. Mbuagbaw L, Mertz D, Lawson DO, Smieja M, Benoit AC, Alvarez E, et al. Strategies to improve adherence to antiretroviral therapy and retention in care for people living with HIV in high-income countries: a protocol for an overview of systematic reviews. *BMJ Open*. 2018 Sep 1;8(9):e022982.
36. Enriquez M, McKinsey DS. Strategies to improve HIV treatment adherence in developed countries: clinical management at the individual level. *HIV/AIDS - Research and Palliative Care*. 2011 Dec 31;3:45–51.
37. Bijker R, Jiamsakul A, Kityo C, Kiertiburanakul S, Siwale M, Phanuphak P, et al. Adherence to antiretroviral therapy for HIV in sub-Saharan Africa and Asia: a comparative analysis of two regional cohorts. *Journal of the International AIDS Society*. 2017;20(1):21218.
38. Peh E, Kwan YH, Goh H, Ramchandani H, Phang J, Lim Z, et al. An Adaptable Framework for Factors Contributing to Medication Adherence: Results from a Systematic Review of 102 Conceptual Frameworks. *Journal of General Internal Medicine*. 2021 Mar 1;36:1–12.
39. Agu KA, Okojie O, Oqua D, King RC, Omonaiye O, Onuoha C, Isah MA, Iyaji PG. Medication Adherence and Risk factors for Non-adherence among Patients taking Highly Active Antiretroviral Therapy. 2011. 22(1):19–26.
40. Holstad MM, Essien JE, Ekong E, Higgins M, Teplinskiy I, Adewuyi MF. Motivational Groups Support Adherence to Antiretroviral Therapy and use of Risk Reduction Behaviors in HIV Positive Nigerian Women: A Pilot Study. *Afr J Reprod Health*. 2012 Sep;16(3):14–27.
41. Maduka O, Tobin-West CI. Adherence counseling and reminder text messages improve uptake of antiretroviral therapy in a tertiary hospital in Nigeria. *Nigerian Journal of Clinical Practice*. 2013 Sep 10;16(3):302–8.
42. Ali MW, Musa MS. The effect of mobile phone utilization for enhanced adherence counselling intervention among persons with HIV. *AIDS Care*. 2023 Feb 13;1–9.
43. Jenewari JA. Effect of Reminder Tools on Drug Adherence among Patients on Anti-retroviral Drug in Specialist Hospital Yola, Adamawa State: A Randomized Field Trial. *TIJPH*. 2021 Jun 30;9(2):45–61.
44. Igweagu C, Chime O, Onwasigwe C. Improving Adherence to Anti-retroviral Therapy among Persons Living with HIV/AIDS in Enugu State, South East Nigeria. *International Journal of TROPICAL DISEASE & Health*. 2019 Nov 6;1–9.

45. Idoko JA, Agbaji O, Agaba P, Akolo C, Inuwa B, Hassan Z, et al. Direct observation therapy-highly active antiretroviral therapy in a resource-limited setting: the use of community treatment support can be effective. *Int J STD AIDS*. 2007 Nov 1;18(11):760–3.
46. Tumwikirize S, Torpey K, Adedokun O, Badru T. The Value of Support Group Participation in Influencing Adherence to Antiretroviral Treatment among People Living with Human Immunodeficiency Virus (HIV). *World Journal of AIDS*. 2015 Oct 1;5:189–98.
47. Dulli L, Ridgeway K, Packer C, Plourde KF, Mumuni T, Idaboh T, et al. An Online Support Group Intervention for Adolescents Living with HIV in Nigeria: A Pre-Post Test Study. *JMIR Public Health Surveill*. 2018 Nov 28;4(4):e12397.
48. Ekwunife OI, Anetoh MU, Kalu SO, Ele PU, Eleje GU. Conditional economic incentives and motivational interviewing to improve adolescents' retention in HIV care and adherence to antiretroviral therapy in Southeast Nigeria: study protocol for a cluster randomised trial. *Trials*. 2018 Dec 29;19(1):710.
49. Ekama SO, Herbertson EC, Addeh EJ, Gab-Okafor CV, Onwujekwe DI, Tayo F, et al. Pattern and Determinants of Antiretroviral Drug Adherence among Nigerian Pregnant Women. *Journal of Pregnancy*. 2012;2012:1–6.
50. Olowookere SA, Fatiregun AA, Akinyemi JO, Bamgboye AE, Osagbemi GK. Prevalence and determinants of nonadherence to highly active antiretroviral therapy among people living with HIV/AIDS in Ibadan, Nigeria. *J Infect Dev Ctries*. 2008 Oct 1;2(5):369–72.
51. Chukwudi U, Olawale A. Impacts of Operation Triple Zero (OTZ) Club Support Group on Anti-Retroviral Therapy (ART) Adherence among Adolescents in Enugu State. 2022.
52. Salami AK, Fadeyi A, Ogunmodede JA, Desalu O. Factors Influencing Adherence to Antiretroviral Medication in Ilorin, Nigeria. *Journal of the International Association of Physicians in AIDS Care*. 2010 May 1;9(3):191–5.
53. Holstad MM, Dilorio C, Kelley ME, Resnicow K, Sharma S. Group Motivational Interviewing to Promote Adherence to Antiretroviral Medications and Risk Reduction Behaviors in HIV Infected Women. *AIDS Behav*. 2011 Jul;15(5):885–96.
54. Taiwo BO, Idoko JA, Welty LJ, Otoh I, Job G, Iyaji PG, et al. Assessing the Virologic and Adherence Benefits of Patient-Selected HIV Treatment Partners in a Resource-limited Setting. *JAIDS Journal of Acquired Immune Deficiency Syndromes*. 2010 May 1;54(1):85.
55. Miles CH, Shpitser I, Kanki P, Meloni S, Tchetgen Tchetgen EJ. Quantifying an Adherence Path-Specific Effect of Antiretroviral Therapy in the Nigeria PEPFAR Program. *Journal of the American Statistical Association*. 2017 Oct 2;112(520):1443–52.
56. Adeyemi A, Olaogun O, Adesola O. Challenges to adherence among HIV-positive patients on antiretroviral therapy in Lagos, Nigeria. *Journal of The International Aids Society - J Int AIDS Soc*. 2008 Nov 1;11:1–1.
57. Obidiya OM, Alali DJ. Stigma as a Challenge To Adherence To Antiretroviral Therapy Among People Living With Hiv/Aids In Nigeria – A Review. *European Scientific Journal, ESJ*. 2020 Dec 31;16(36):128–128.
58. Omosanya OE, Elegbede OT, Agboola SM, Isinkaye AO, Omopariola OA. Effects of stigmatization/discrimination on antiretroviral therapy adherence among HIV-infected patients in a rural tertiary medical center in Nigeria. *J Int Assoc Provid AIDS Care*. 2014;13(3):260–3.

59. Falang KD, Akubaka P, Jimam NS. Patient factors impacting antiretroviral drug adherence in a Nigerian tertiary hospital. *J Pharmacol Pharmacother*. 2012;3(2):138–42.
60. Iliyasu Z, Kabir M, Abubakar IS, Babashani M, Zubair ZA. Compliance to antiretroviral therapy among AIDS patients in Aminu Kano Teaching Hospital, Kano, Nigeria. *Niger J Med*. 2005;14(3):290–4.
61. Nwauche C, Erhabor O, Ejele O, Akani C. Adherence to antiretroviral therapy among HIV-infected subjects in a resource - limited setting in the Niger Delta of Nigeria. *African Journal of Health Sciences* [Internet]. 2008 Jun 18 [cited 2023 Jul 18];13(3). Available from: <http://www.ajol.info/index.php/ajhs/article/view/30831>
62. Ekwunife OI, Ofomata CJ, Okafor CE, Anetoh MU, Kalu SO, Ele PU, et al. Cost-effectiveness and feasibility of conditional economic incentives and motivational interviewing to improve HIV health outcomes of adolescents living with HIV in Anambra State, Nigeria. *BMC Health Services Research*. 2021 Jul 11;21(1):685.
63. Agu K, Ochei U, Oparah A, Onoh O. Treatment outcomes in patients receiving combination antiretroviral therapy. *Retrovirology*. 2010 May 11;7(1):P54.
64. Adejumo O, Oladeji B, Akpa O, Malee K, Baiyewu O, Ogunniyi A, et al. Psychiatric disorders and adherence to antiretroviral therapy among a population of HIV-infected adults in Nigeria. *Int J STD AIDS*. 2016 Oct 1;27(11):938–49.
65. Adeoti AO, Dada M, Elebiyo T, Fadare J, Ojo O. Survey of antiretroviral therapy adherence and predictors of poor adherence among HIV patients in a tertiary institution in Nigeria. *Pan Afr Med J*. 2019 Jul 31;33:277.
66. Omonaiye O, Kusljic S, Nicholson P, Mohebbi M, Manias E. Post Option B+ implementation programme in Nigeria: Determinants of adherence of antiretroviral therapy among pregnant women with HIV. *International Journal of Infectious Diseases*. 2019 Apr 1;81:225–30.
67. Igwegbe AO, Ugboaja JO, Nwajiaku LA. Prevalence and determinants of non-adherence to antiretroviral therapy among HIV- positive pregnant women in Nnewi, Nigeria.
68. Onyeonoro UU, Ebenebe UE, Ibeh CC, Nwamoh UN, Ukegbu AU, Emelumadu OF. Adherence to antiretroviral therapy among people living with human immunodeficiency virus/acquired immunodeficiency syndrome in a tertiary health facility in South Eastern Nigeria. *Journal of HIV and Human Reproduction*. 2013 Jan 7;1(2):58.
69. Bärnighausen T, Chaiyachati K, Chimbindi N, Peoples A, Haberer J, Newell ML. Interventions to increase antiretroviral adherence in sub-Saharan Africa: a systematic review of evaluation studies. *The Lancet Infectious Diseases*. 2011 Dec 1;11(12):942–51.
70. Ekop EE, Okechukwu AA. Reminder Systems for Improving Adherence among HIV-infected Adolescents Attending a Tertiary Facility in Abuja. *Asian Journal of Pediatric Research*. 2018 Oct 22;1–10.
71. Lester RT, Ritvo P, Mills EJ, Kariri A, Karanja S, Chung MH, et al. Effects of a mobile phone short message service on antiretroviral treatment adherence in Kenya (WelTel Kenya1): a randomised trial. *The Lancet*. 2010 Nov 27;376(9755):1838–45.
72. Chung MH, Richardson BA, Tapia K, Benki-Nugent S, Kiarie JN, Simoni JM, et al. A Randomized Controlled Trial Comparing the Effects of Counseling and Alarm Device on HAART Adherence and Virologic Outcomes. *PLoS Med*. 2011 Mar 1;8(3):e1000422.
73. Roux P, Kouanfack C, Cohen J, Marcellin F, Boyer S, Delaporte E, et al. Adherence to Antiretroviral Treatment in HIV-Positive Patients in the Cameroon Context: Promoting the Use of

Medication Reminder Methods. *JAIDS Journal of Acquired Immune Deficiency Syndromes*. 2011 Jul 1;57:S40.

74. Abdulrahman SA, Rampal L, Ibrahim F, Radhakrishnan AP, Kadir Shahar H, Othman N. Mobile phone reminders and peer counseling improve adherence and treatment outcomes of patients on ART in Malaysia: A randomized clinical trial. *PLoS One*. 2017 May 16;12(5):e0177698.

75. Khamarko K, Myers JJ. *The Influence of Social Support on the Lives of HIV-Infected Individuals in Low- and Middle-Income Countries*. 2013;

76. Kanters S, Park JJ, Chan K, Ford N, Forrest J, Thorlund K, et al. Use of peers to improve adherence to antiretroviral therapy: a global network meta-analysis. *J Int AIDS Soc*. 2016 Nov 30;19(1):21141.

77. Berg RC, Page S, Øgård-Repål A. The effectiveness of peer-support for people living with HIV: A systematic review and meta-analysis. *PLOS ONE*. 2021 Jun 17;16(6):e0252623.

78. Chory A, Callen G, Nyandiko W, Njoroge T, Ashimosi C, Aluoch J, et al. A Pilot Study of a Mobile Intervention to Support Mental Health and Adherence Among Adolescents Living with HIV in Western Kenya. *AIDS Behav*. 2022;26(1):232–42.

79. Nachega JB, Chaisson RE, Goliath R, Efron A, Chaudhary MA, Ram M, et al. Randomized controlled trial of trained patient-nominated treatment supporters providing partial directly observed antiretroviral therapy. *AIDS*. 2010 Jun 1;24(9):1273–80.

80. Ssewamala FM, Dvalishvili D, Mellins CA, Geng EH, Makumbi F, Neilands TB, et al. The long-term effects of a family based economic empowerment intervention (Suubi+Adherence) on suppression of HIV viral loads among adolescents living with HIV in southern Uganda: Findings from 5-year cluster randomized trial. *PLoS One*. 2020 Feb 10;15(2):e0228370.

81. Ekstrand ML, Heylen E, Pereira M, D'Souza J, Nair S, Mazur A, et al. A behavioral adherence intervention improves rates of viral suppression among adherence-challenged people living with HIV in South India. *AIDS Behav*. 2020 Jul;24(7):2195–205.

82. Orrell C, Cohen K, Mauff K, Bangsberg DR, Maartens G, Wood R. A Randomized Controlled Trial of Real-Time Electronic Adherence Monitoring With Text Message Dosing Reminders in People Starting First-Line Antiretroviral Therapy. *JAIDS Journal of Acquired Immune Deficiency Syndromes*. 2015 Dec 15;70(5):495.

83. Kunutsor S, Walley J, Katabira E, Muchuro S, Balidawa H, Namagala E, et al. Improving Clinic Attendance and Adherence to Antiretroviral Therapy Through a Treatment Supporter Intervention in Uganda: A Randomized Controlled Trial. *AIDS Behav*. 2011 Nov 1;15(8):1795–802.

84. Oreagba L, Usman S, Olayemi S, Oshikoya K, Opanuga O, Adeyemo T, et al. Pharmacoepidemiology of antiretroviral drugs in a teaching hospital in Lagos, Nigeria. *Ghana Medical Journal*. 2015 Feb 11;48(4):194.

85. Sahay S, Reddy KS, Dhayarkar S. Optimizing adherence to antiretroviral therapy. *Indian J Med Res*. 2011 Dec;134(6):835–49.

86. Matlawe LP, Musekwa OP, Makhado TG, Makhado L. Patients' experiences of treatment migration from ART triple pill to fixed-dose combination therapy in Ngaka Modiri Molema District, North West Province, South Africa. *HIV & AIDS Review*. 2023;22(2):150–9.

ANNEX

Table 5: Combination of Keywords used in the Literature search

AND				
	Problem	Interventions and related terms	Population	Geographical Location
OR	ART Adherence	Intervention	PLHIV	Nigeria
	Antiretroviral therapy Adherence	Strategies	Adolescents	Uganda
	Adherence	Text messages	Young people	South Africa
	HAART	Text message reminder	Youths	Kenya
	Adherence	SMS reminder	Women	Ghana
	ARV	Pager messages	Men	LMIC
		Reminder device		Sub-Saharan Africa
		Alarm		
		Alarm reminder		
		Pill box		
		Peer support group		
		Peer educator		
		Peer counselling		
		Treatment partner		
		Motivational Interviewing		
		Health promotion program		
		ART adherence counselling		
		Social media based intervention		
		Education		
		Treatment supporter		

		Fixed-Dose Combination Therapy		
		Directly observed therapy		
		Cash incentives		
		Treatment supporter		
		Group Education		