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# Adherence to antiretroviral therapy among HIV-1 patients from sub-Saharan Africa: a systematic review

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## Abstract

***More than two decades after introducing antiretroviral therapy (ART), several challenges still prevail in keeping well people living with HIV, even with "Test and Treat" and/or "Rapid Start of ART" initiatives, as well as the scale-up of ART worldwide to promote access and adherence to treatment. This review examined articles on ART adherence in Africa between 2016 and 2023, published in English and indexed in PubMed. A total of 16 articles out of 2415 were eligible and included for analyses. Overall, good ART adherence rates in sub-Saharan African (SSA) regions ranged from 43% to 84%. Rates in the center of the SSA region ranged from 58% to 80%, in the north from 50% to 83%, in the south from 77% to 84%, in the west from 43% to 60%, and in the east from 69% to 73%. Most African countries use self-reporting to assess treatment adherence, which is frequently unreliable. The main factors with negative influence on ART adherence were comorbidities, lack of motivation, socioeconomic difficulties, or side effects. Conclusion: Adherence to ART is a good indicator for controlling the spread of HIV in a given region. It is important to overcome the barriers that make it difficult to comply with ART and reinforce the factors that facilitate access to medication.***

## Keywords

***HIV-1. Antiretroviral therapy. Treatment adherence. Sub-Saharan Africa.***

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# Introduction

At present, there are still major challenges in starting and maintaining HIV-positive people on antiretroviral therapy (ART) throughout their infection, even with awareness-raising actions and initiatives that promote adherence to therapy, such as "Test and Treat" and "Rapid Start of ART" campaigns[1].

The success of ART in HIV-positive patients varies according to the patient's daily adherence to medication. This adherence is essential to ensure viral suppression, prevent the emergence of drug-resistance mutations, and minimize further HIV transmission. The previous studies reported that factors such as sex, age, residence, educational status, occupation, marital status, income, disclosure status, history of substance abuse, and clinical and medication-related factors all influence patient's medication adherence, mainly in resource-limited settings[2,3].

The WHO defines treatment adherence as the degree to which a person's behavior is consistent with standardized recommendations made by a trained health professional. The behavior consists of taking medication, adhering to a diet, and/or implementing lifestyle changes[4]. ART adherence interventions must, therefore, recognize this cultural diversity during the research development, evaluation, and implementation phases[4]. To assess adherence to ART, laboratory investigations and clinical assessments must be carried out to verify tolerance and the appearance of adverse drug effects.

Factors related to patients, health-care professionals, and the drugs themselves also have a major impact on adherence to ART. Several "patient-centered" interventions are currently in development and being implemented, however, few offer highly effective solutions, particularly for vulnerable groups such as women and children, and key populations of men and young adults[1,4]. The existence of high levels of discrimination in employment, fear of being abandoned by family members or divorce, and communication difficulties all contribute to poor ART adherence. There have been some strategies to be broken down to maximize treatment adherence[5].

Considering the scarcity of data related to factors associated with adherence to ART or its rejection, we set out to qualitatively explore and review adherence to ART among HIV-infected adults and the differences depending on the characteristics of the population studied in sub-Saharan African (SSA) countries. Based on such information, we will provide approaches that could maximize ART adherence in different regions of Africa[6].

## Systematic literature review

The bibliographic search included the PubMed database, particularly articles published in English between 2016 and 2023. The search was performed using the Boolean operators "AND," "OR," and "NOT;" and the search keywords combining the medical subject headings: (i) "Antiretroviral therapy" or (ii) "highly active antiretroviral therapy" or (iii) "antiretroviral8 or (iii) "antiretroviral agents HIV" or (iv) "ART or ARV" and (v) "treatment adherence 8 or (vi) "adherence" and (vii) "Sub-Saharan Africa." Reporting of the results of this systematic review complies with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, which provide guidelines for this type of research that allows the identification, selection, evaluation, and synthesis of studies.

## Study selection

This review involved studies evaluating adherence to ART in adults from the SSA region. The definition of adherence in this review was operationally restricted to adherence to ART, which implied the degree of antiretroviral (ARV) intake by HIV-positive patients, as recommended by their health-care providers. Studies related to the different concepts of adherence, such as attendance or consultation and retention, were also included. There was no restriction on measures to assess adherence to ART. Information on the year of publication, type of intervention, the country where the study was conducted, and health-care setting was obtained from each study. Subjective and objective measures of adherence were recorded, including biological correlates of adherence, for example, viral load and CD4 count. The guide used for inclusion criteria covered the population, intervention, comparison, outcome, and time. Studies conducted in the SSA region, involving HIV-positive adults on adult correlates of adherence, were included in the study. On the other hand, meta-analysis and systematic review studies involving children and/or adolescents were excluded from the study. Studies were reviewed based on strict adherence to ART appointments and medication as scheduled by health-care professionals. In sequence, (i) articles were selected according to title, (ii) abstract, and (iii) full-text access to verify their inclusion (Fig. 1).

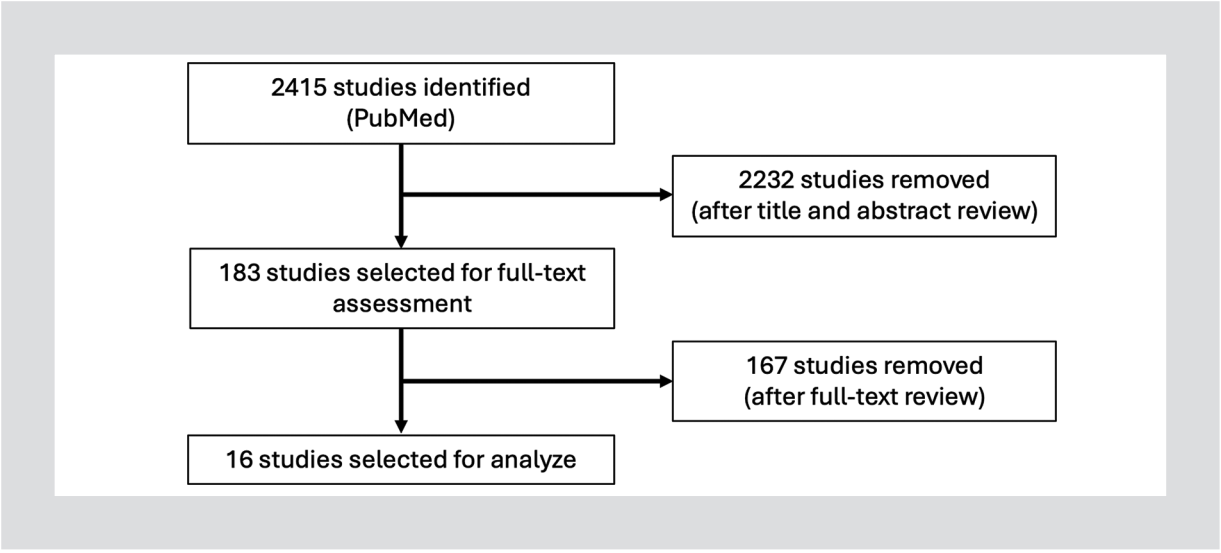


**Figure 1**. *Study selection flowchart. All articles were identified through an electronic literature search on PubMed between 2016 and 2023.*

## Quality assessment

The studies selected and included in the review were subjected to a systematic bias assessment using the Cochrane criteria, with the risk of bias being assessed as "low risk," "high risk," or "uncertain risk" and analyzed in seven domains. Low risk indicates information reported with evidence of little or no possible bias, whereas high risk implies evidence of possible bias. Unclear risk denotes a paucity of information or scepticism about possible biases (38). The author's PRSA was involved in the search for scientific articles as well as the evaluation of the inclusion criteria. Authors CSS, VP, and JM were involved in evaluating the selected manuscripts, validating, and writing the first draft of the manuscript. The authors CACR and ABA were involved in reviewing the text.

## Results

A total of 2415 articles were identified in PubMed. Of these 2232 were excluded based on the content of their titles and abstracts that did not meet the inclusion criteria defined for the present study. Then, 183 articles met the inclusion criteria and full-text were further analyzed. After evaluating the full text, 170 articles were removed as they did not represent the context of the present study. In the end, 13 studies met all inclusion criteria and were selected for analysis and interpretation of the rate and determinants of ART adherence in the SSA region between 2016 and 2023. Table 1 presents the characteristics of the selected articles, which include the authors' summary, study design, population, variables of interest, country of the study, African region, location, outcome, adherence measure, time, and study findings. The studies selected for this review included patients undergoing treatment in Angola, Uganda, Ethiopia, Zimbabwe, Zambia, South Africa, Nigeria, Ghana, and Mozambique. Overall, ART adherence rates in different SSA regions ranged from 43% to 84%. Rates in the center of the SSA region ranged from 58% to 80%, in the north from 50% to 83%, in the south from 77% to 84%, in the west from 43% to 60%, and in the east from 69% to 73% (Table 2).

## Discussion

ART is the best successful strategy in the fight against HIV. Data identifying the main reasons and associated factors causing poor ART adherence is scarce in HIV-positive patients living in African countries, where several interventions have been developed. This review allowed for exploring multiple contexts, exploring relevant information about the different approaches applied, and also enabling a critical analysis of the results obtained. There are different ways to measure adherence to ART among populations affected by HIV, highlighting self-report as the predominant measure of adherence used[7], pill counts, pharmacy refills, electronic adherence monitoring devices, plasma viral load, medication possession rate, and appointment scheduling[8-10]. On the other hand, among the many

**Table 1. List of scientific articles selected to analyze ART adherence in sub-Saharan countries, 2016-2023**

| No. | Author | Study design | Population | Variables of interest | Country of study | Africa region | Local | Result | Measuring adherence | Time | Adherence results and comments |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Tariku et al. (2023) | Transversal | Men and women | Associated factors | Ethiopia | Sub-Saharan East | Community-based | Accession | Self-report<br>Pill Count<br>CD4 count | 1 month | Around 50% of those interviewed in the study scenarios have perfect ART adherence |
| 2 | Ângelo and Alemayehu (2021) | Transversal | Men and women | Associated factors | Ethiopia | Sub-Saharan East | Hospital (outpatient) | Accession | Attendance at the clinic<br>Pill Count<br>Self-report | 1 month | Patients' adherence to ART was 83% |
| 3 | Nyamayaro et al. (2020) | Case series | Men and women | Problem-solving therapeutic intervention for depression and barriers to adherence to antiretroviral therapy | Zimbabwe | Sub-Saharan South | Hospital (outpatient) | Accession | Self-report | 6 months | Studies in the country reveal an ART adherence rate of around 80% |
| 4 | Abdu and Walelgn (2021) | Case-control | Men and women | Determinant factors | Ethiopia | Sub-Saharan East | Hospital (outpatient) | Accession | Pill Count<br>CD4 count | 1 month | Adherence to ART was 82.3% in the studied population (29) |
| 5 | Agala et al. (2020) | Quasi-experimental | Women | Reliability, validity, and measurement invariance of the Simplified Medication Adherence Questionnaire | Ethiopia | Sub-Saharan East | Hospital (outpatient) | Accession | Self-report | 18 months | The ART adherence rate was 50-77% |
| 6 | Asrat et al. (2020) | Transversal | Men and women | Major depressive disorder | Ethiopia (North) | Sub-Saharan North | Hospital | Accession | Pill Count | 3 months | Membership to ART found in this study was 81.9% of the interviewees. |

(*Continues*)

**Table 1. List of scientific articles selected to analyze ART adherence in sub-Saharan countries, 2016-2023 (*continued*)**

| No. | Author | Study design | Population | Variables of interest | Country of study | Africa region | Local | Result | Measuring adherence | Time | Adherence results and comments |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 7 | Izudi et al. (2021) | Quasi-randomized | Men and women | Effect of disclosing HIV status | Uganda (East) | Sub-Saharan center | Hospital outpatient | Accession | Attend the clinic on the scheduled date or within seven days before or after the scheduled date | 12 months | It is estimated that the ART adherence rate is around 80% |
| 8 | Jones et al. (2020) | Randomized clinical trial | Men and women | Stigma | Zambia and South Africa | Sub-Saharan South | Community-based | Accession | Self-report | 17 months | The membership fee to ART fee is estimated at 84.2% |
| 9 | Safren et al. (2021) | Randomized clinical trial | Men and women | Depression treatment | South Africa | Sub-Saharan South | Hospital (outpatient) | Accession | Self-report, Wisepill, Hamilton Depression Scale, Viral load, and CD4 | 36 months | ART adherence is estimated at 77% |
| 10 | Eze et al. (2023) | Transversal | Men and women | Belief in medicine | Nigeria | Sub-Saharan West | Community-based | Accession | Self-report | 13 months | ART adherence is estimated at 54% |
| 11 | Sefah et al. (2022) | Transversal | Men and women | Barriers and facilitators | Ghana | Sub-Saharan West | Hospital (outpatient) | Accession | Self-report | 3 months | Adherence to ART among patients living with HIV was 42.9% |
| 12 | Pires et al. (2017) | Transversal | Men and women | Clinical and Socioeconomic Factors | Mozambique | Sub-Saharan South | Hospital (outpatient) | Accession | Self-report | 30 months | The ART adherence rate was 69% |
| 13 | Baptista (2016) | Transversal | Men and women | Associated factors | Angola | Sub-Saharan South | Hospital outpatient | Accession | Self-report | 120 months | The fee of Adherence to ART was 58% |

(*Continues*)

**Table 1. List of scientific articles selected to analyze ART adherence in sub-Saharan countries, 2016-2023 (*continued*)**

| No. | Author | Study design | Population | Variables of interest | Country of study | Africa region | Local | Result | Measuring adherence | Time | Adherence results and comments |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 14 | Isika et al. (2022) | Transversal | Men and women | Increased survival and quality of life of people with good adherence to ART | Nigeria | Sub-Saharan West Africa | Hospital outpatient | Accession | Respondents were recruited via a multi-stage technique. Data were obtained by a pre-tested interviewer-administered questionnaire | 6 months | The self-reported adherence rate was 60.1% |
| 15 | Eyassu et al. (2016) | Transversal | Men and women | Factors that hinder adherence to ART among HIV and AIDS patients at Kwa-Thema clinic. Determination of prevalence rate of ART adherence among HIV/AIDS patients at Kwa-Thema clinic. | South Africa | Southern the sub the sub-Saharan Africa | Hospital outpatient | Accession | The researchers obtained data for this study through a structured questionnaire administered with open and closed questions | 3 months | The study found that ART adherence at the Kwa-Thema clinic was suboptimal (< 95%) at 77% |
| 16 | Macovela (2016) | Transversal | Men and women | Clinical and Socio-Econ Factorsomics | Mozambique | Sub-Saharan South | Hospital Outpatient | Accession | Self-report | 30 months | The adherence rate obtained in the study was 72.6% |

ART: antiretroviral therapy.

**Table 2. Estimated adherence to ART in several Sub-Saharan African countries**

| Countries | Sub-Saharian region | ART adherence rate (%) | References |
|---|---|---|---|
| Angola | Central | 58 | Baptista, 2016 |
| Uganda | Central | 80 | Izudi et al., 2021 |
| Ethiopia | North | 50-83 | Tariku et al., 2023<br>Ângelo et al., 2021<br>Abdu et al., 2021<br>Agala et al., 2020 |
| Zimbabwe | South | 80 | Nyamayaro et al., 2020 |
| Zambia | South | 84 | Jones et al., 2020 |
| South Africa | South | 77 | Safren et al., 2021 |
| Nigeria | West | 54-60 | Eze et al., 2023<br>Isika et al., 2022 |
| Ghana | West | 43 | Sefah et al., 2022 |
| Mozambique | East | 69-73 | Pires et al., 2017<br>Macovela et al., 2016 |

ART: antiretroviral therapy.

factors responsible for low adherence to ART in African countries, we highlight stigmatization, fear of seeking and denying health care, social isolation, difficult access to health services, and depression[11,12].

The lack of a "gold standard" method to measure adherence makes the choice of the evaluation method highly dependent on the economic scenario of the location where the study is taking place[13]. The association of methods such as interviews with self-report, questionnaire structured with a verbal assessment of understanding with a small group of patients (e.g.: CEAT-VIH), an electronic questionnaire with questions aimed at people living with HIV (e.g., WebAd-Q), when properly applied, can help measure adherence with more precision[14]. Although some methods of evaluation processes may consume financial resources, such as the Medication Event Monitoring System (MEMS), they could be used periodically in clinical studies and influence the application of interventions.

The selection of measures of adherence has become a major challenge in many African countries, due to the economic vulnerability of the populations. Self-reports were the method most commonly used in HIV/AIDS hospital settings, whereas the MEMS was used above all in studies intervention clinics[12,13,15]. Due to its ease of use and access, self-reporting has been the most frequently used method in environments where resources are limited, such as in low- and middle-income countries, consistent with data obtained from the present review, which reveals that 81% of the selected studies used self-reporting[16]. There are many advantages associated with self-reporting, making it the most commonly applied measure of ART adherence. In addition to being valid and easy to use, self-reporting is consistent with objective methods of measuring adherence, such as plasma viral load monitoring and the MEMS. Other advantages of self-reports in resource-limited settings include accessibility and low dependence on the use of distinct personnel. It is also considered a robust method and an adequate indicator of adherence[16,17]. However, the biggest demerit of self-report is the overestimation of adherence due to its memory bias and social desirability, which arises, in most cases, from the patient's fear of being judged by health professionals or the consequences of providing negative feedback, which forces you to inaccurate reporting of membership. Despite these facts, in most studies in Africa, especially in resource-limited environments such as Angola, Mozambique, Nigeria, Ghana, Zambia, and Ethiopia, self-reporting is the most widely used method to record ART adherence[17].

Scheduling appointments, considered an early warning indicator or proxy of ART adherence, is also considered subjective, although access to the results is possible in clinic attendance records and, therefore, enables a more objective analysis, being considered similar to the self-report assessment. Although the assessment clinic is prone to manipulation by clinical staff, pill counts and pharmaceutical refills remain commonly used objective measures due to their relatively inexpensive nature and ease using. Pharmacy refills are a validated measure of adherence to ART that has the advantage of being related to viral load, which allows measuring adherence or non-adherence to medication. However, disadvantages of pharmacy refills include dumping or sharing of pills, the need for a closed pharmacy system, its dependence on accurate and reliable records, and its inability to predict or detect viral rebound in patients. The disadvantages of pill counts, also an early warning indicator, include pill procurement and limited availability. Difficulty in keeping records of pharmacy appointments and refills when patients obtain their medications from different pharmacies is another disadvantage that impacts measurement closer to reality, although most patients with limited resources return to their primary care providers for free treatment. This makes pharmacy refills a relatively good and reliable adherence measure[16-18].

The real-time adherence monitoring devices that have been proven are automated medication vials that have long-lasting battery half-lives capable of holding medication supplies for 30 days. Although adherence information can be examined in real-time, allowing for rapid intervention in ART adherence, an internet connection is required for this task, making this measure less feasible, especially in resource-limited settings, such as in several SSA countries. Other disadvantages of this measure would be the inability to confirm medication intake and the lack of privacy, as patients may have to move around with the device. Finally, there are more precise, although expensive, measurements that include direct methods such as measuring levels of the drug or its metabolite in urine or blood, detecting a biomarker added to the drug formulation, and targeting observed therapy[16,18].

Validating the measure of adherence against viral load is beneficial, and achieving undetectable viral load is also considered one of the most common measures of ART adherence. Adherence rates in SSA countries are between 43% and 84%, which may indicate that many patients do not achieve viral suppression. Indeed, a high level of ART adherence of 95% or above has previously been associated with undetectable viral load, equating viral suppression with adherence[19]. At present, adherence levels between 80 and 85% are sufficient for viral suppression, making undetectable viral load an unsatisfactory intermediate method for estimating maximal adherence. This is consistent with other studies that have highlighted that treatment adherence levels must be between 80% and 95%[19,20].

## Conclusions

ART adherence in the SSA region ranges from 43% to 84%. Most African countries use self-reporting to assess treatment adherence, which is largely unreliable. Complementary assessment methods, such as clinical response, monitoring of dispensing records, and counting and refilling of ARV tablets, are more objective ways of measuring ART adherence, although they are more expensive and difficult to implement. They should be considered at least for a subset of a representative group of patients in SSA, to monitor more accurately the benefit of ART and the risk of drug resistance.

## Authors' contribution

Conceptualization: PRSA, ABA, CSS, and JM; methodology: PRSA, ABA, CSS, and JM; validation: PRSA and CSS; formal analysis: PRSA, VP, CSS, and JM; investigation: PRSA, CACR, VP, ABA, CSS, and JM; resources: CSS and JM; data curation: PRSA, VP, CSS, and JM; writing – original draft preparation: PRSA, CACR, CSS, and JM; writing – review and editing: PRSA, CACR, VP, ABA, CSS, and JM; supervision: CSS and JM; project administration: ABA and JM. All authors have read and agreed to the published version of the manuscript.

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## Conflicts of interest

None.

## Ethical disclosures

**Protection of human and animal subjects.** The authors declare that no experiments were performed on humans or animals for this study.

**Confidentiality of data.** The authors declare that no patient data appear in this article. Furthermore, they have acknowledged and followed the recommendations as per the SAGER guidelines depending on the type and nature of the study.

**Right to privacy and informed consent.** The authors declare that no patient data appear in this article.

**Use of artificial intelligence for generating text.** The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript nor for the creation of images, graphics, tables, or their corresponding captions.

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