REVIEW PAPER

Factors influencing non-adherence to antiretroviral therapy in South Africa: a systematic review

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Abstract

This systematic review was conducted based on the available data on antiretroviral therapy adherence among human immunodeficiency virus (HIV)-infected individuals in South Africa and identified factors that were outlined by different studies. In order to identify said factors, the review question was: "What are the factors influencing non-adherence to antiretroviral therapy (ART) in South Africa?".

The search was conducted on four databases: PubMed (9), Google Scholar (5340), EBSCOhost (9), and South African national EDT (10) using the keywords: "non-adherence"/"non-compliance", "antiretroviral therapy", "HAART", "ARVs", and "South Africa". The search yielded seven studies that met the inclusion criteria.

From the results, six themes and 14 sub-themes emerged of factors influencing non-adherence to antiretroviral therapy in South Africa, inclusive of: patient-related factors, economic factors, social factors, health system and health team factors, therapy-related factors, and cultural and belief factors.

It is believed that from the information provided in this review, interventions can be drawn which will help patients achieve the benefits of ART, while at the same time helping South Africa to achieve its aim of reducing high mortality and morbidity rates.

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Key words: non-adherence, antiretroviral therapy, people living with HIV, South Africa.

Introduction

Acquired immunodeficiency syndrome (AIDS) has emerged as a global crisis. South Africa is amongst the countries with the greatest burden, and antiretroviral therapy (ART) is very important in achieving optimal treatment outcomes [1]. Despite the tremendous benefits of ART use in human immunodeficiency virus (HIV) progression and survival benefits, non-adherence to this ART still remains a strong predictor of high mortality and morbidity rates in South Africa [2]. There are many reported factors that influence non-adherence to ART, so the researcher found it crucial to embark on this topic.

By the year 2017, it was estimated that the number of people infected with HIV globally would have been 36.9 million, and it is further indicated that this syndrome was responsible for 0.9 million deaths in said year [3]. Although the syndrome is incurable, 21.7 million people were receiving ART by the end of 2017, which is indicated for suppression of the HIV [4-6]. ART is defined as a drug indicated to treat and supress the HIV virus by blocking the enzymes used by said virus from replicating [7, 8].

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South Africa is amongst the countries in Sub-Saharan Africa, which has an estimated 7,200,000 people living with HIV/AIDS with 61% of ART coverage in 2017 [3]. ART was introduced in South Africa in 2004 and statistics have shown a decline in morbidity and mortality rates since. Effective ART outcomes still depend on adherence, which means patients should take 95% or more of their prescribed treatment in order to obtain survival benefits [9]. According to Azia *et al.* [10], South Africa runs the largest public ART programme, which makes the treatment easily accessible to all infected people.

Even with the survival benefits and accessibility of ART, there are individuals who fail to take their treatment [11]. Kagee *et al.* [5] highlighted that non-adherence to ART is a major problem in South Africa because it leads to many problems, e.g. treatment failure, which will need a second-line regimen, which is expensive. Non-adherence is not only defined as the inability of a patient to follow treatment plans but also the inability to follow restrictions regarding lifestyle, food, and other medication [10].

Multiple studies have been conducted in different provinces in South Africa to identify factors influencing adherence to ART, for example in KwaZulu-Natal [4], Limpopo [12], Western Cape [10], and Eastern Cape [13]. The aforementioned articles/mentions found that non-adherence is still a problem in South Africa, and there are specific factors that give rise to the problem. The purpose of this systematic review is to provide a clear or comprehensive picture of factors that have been identified to influence non-adherence to ART, specifically in scholarly articles of studies conducted in South Africa.

To the best of our knowledge, no systematic review has been published to summarise the developing knowledge of research regarding this topic, and specifically in South Africa; therefore, we conducted this systematic review of available data on ART adherence among HIV-infected individuals in South Africa and identified factors that were outline by the mentioned studies.

The review question was: "What are the factors influencing non-adherence to ART in South Africa?".

Material and methods

Information sources and search strategy

This review was conducted using a systematic review and meta-analysis guidelines [14]. The search was conducted on four databases: PubMed (n = 9), Google Scholar (n = 5340), EBSCOhost (n = 9), and South African national EDT (n = 10) (refer to Diagram 1). The keywords that were used were as follows: "non-adherence/non-compliance", "antiretroviral therapy", "HAART", "ARVs", and "South Africa".

Eligibility criteria

The eligibility criteria were based on the type of the study and the types of participants, namely:

Type of study: the review included only studies assessing adherence in South Africa. The authors only included articles written in English, published between 2014 and 2018 (5 years).

Types of participants: HIV infected individuals, specifically in South Africa, on ART.

Study selection

The authors independently reviewed all titles and abstracts of each and every article to assess their potential relevance to this systematic review. They also scanned full texts of articles and an agreement was reached as to which articles were relevant. Seven articles were selected based on their relevance and meeting the eligibility criteria as indicated in Figure 1.

Data abstraction

The authors independently extracted data and compared the information that was collected. With all the studies that met the inclusion criteria, details were retrieved about where the study was conducted, the study design, the objectives of the study, the study population, documented outcomes, and limitations. Refer to Table 1 for the characteristics of the included studies.

Appraisal of the included studies

The included articles were carefully and systematically examined using CASP (critical appraisal skills programme) to assess the trustworthiness, value, and relevance of those articles. Refer to Table 2 for results.

Results

From the articles included in this study, six themes and 14 sub-themes emerged regarding factors influencing non-adherence to ART in South Africa. The following themes emerged: patient-related factors, economic factors, social factors, health system and health team factors, therapy-related factors, and cultural and belief factors. Table 3 provides themes and subthemes that emerged from data analysis.

Patient-related factors

Substance abuse, forgetfulness, and stress were identified to be the factors influencing non-adherence to ART in South Africa under *patient-related* factors. In this theme, substance abuse was the main factor (n = 4, 57%), and participants within the included studies explained that they abuse substances while taking their treatment – that was why their viral load was high and their CD4 count was low [8, 10, 13, 16]. Substance abuse is regarded as a health problem that affects an individual's health in totality [17], and a systematic review was done to evaluate the impact of alcohol use disorders on ART.

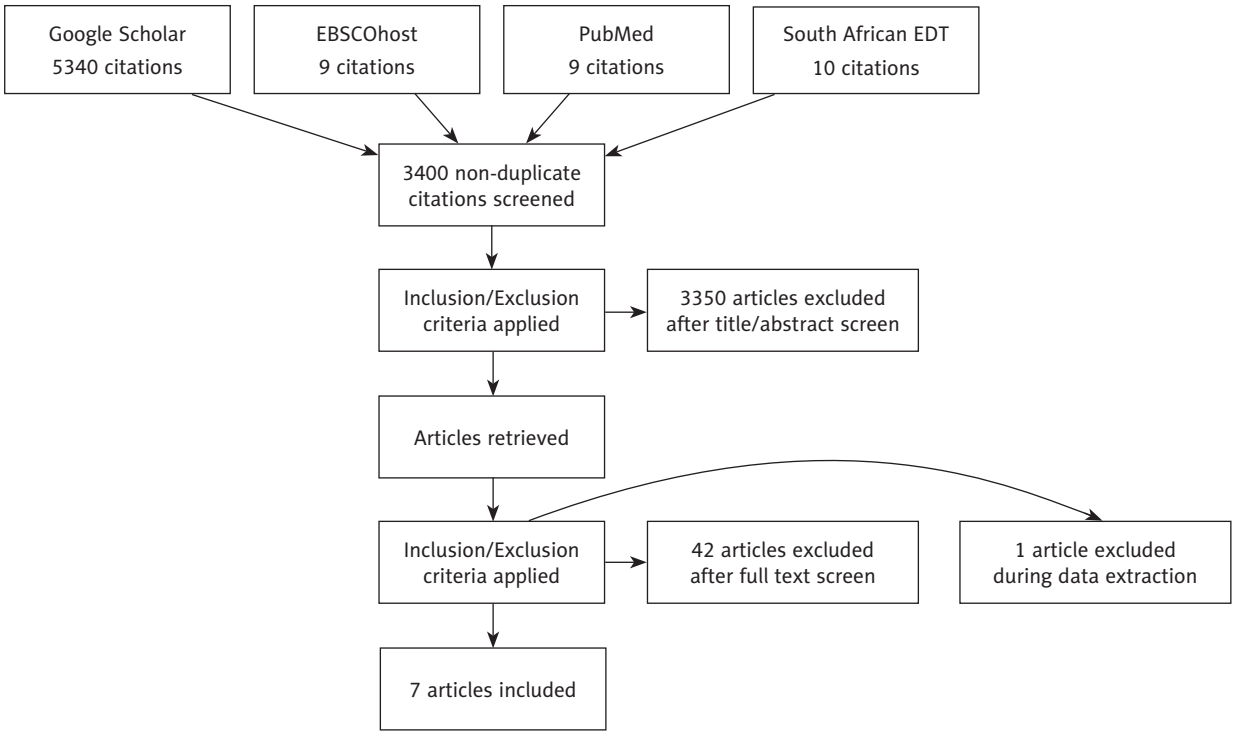

Figure 1. PRISMA flow diagram

The interaction between alcohol and ART was not favourable [18]. The other sub-themes were forgetfulness (n = 2, 28%) and stress (n = 2, 28%) – these factors are interrelated according to participants because they alluded that stressing so much about their HIV status somehow made them forget to take their ART [6, 10, 11, 13].

Economic factors

Three sub-themes emerged from the *economic factors* theme, which included: food insecurity, no finances for transportation, and disability grants. The main factor was food insecurity (n = 6, 86%) – this simply means that participants did not adhere to their ART because they did not have food to eat prior to taking their treatment [6, 8, 10, 11, 13, 16]. It was mentioned by Labadarios *et al.* [19] that South Africa is still a developing country and most people are undernourished because of the high unemployment rate; they need continuous support from the government to maintain their daily living needs. The second sub-theme under economic factors was no finances for transportation (n = 5, 71%) – participants reported that they did not have the finances for transportation to go to clinics for collection of their ART [6, 8, 10, 13, 16]. The last identified factor was disability grants (n = 3, 43%) – participants explained that they depend on their disability grants for maintenance of daily living. In South Africa, people with high viral load and low CD4 are given disability grants because it is argued that they are unable to work; these patients thus depend on that grant for maintenance of daily living, and this was also stated as a reason for not adhering to the ART [6, 13, 15].

Social factors

In this theme, the sub-themes that were identified were: fear of disclosure, stigma, and discrimination. All the included studies pointed to fear of disclosure being a major factor influencing non-adherence to ART in South Africa (n = 8, 100%) – this simply means that patients do not adhere to their ART because they are fearful of making their HIV status known. Furthermore, it was indicated that disclosure, according to patients, is very costly because it results in judgement from their families and friends [6, 8, 10, 11, 13, 15, 16]. Regarding this matter of HIV-related discrimination and stigma, participants alluded that their families and community do not see them as people when taking their ART, so they do not adhere. It had a negative impact (n = 4, 57%) according to the study reviewed. Many studies have been conducted on HIV-related stigma and discrimination, in order to prove that this is a problem, and many people do not adhere to their treatment because they are afraid of being discriminated against [20, 21].

Health team and health system factors

Poor quality and poor treatment literacy emerged as sub-themes for *health team* and *health system factors* that in-

Table 1. Characteristic of the included studies

Author	Year	Province	Objectives of the article	Study design	Population	Documented outcomes	Limitations
Dekeda	2014	Eastern cape	- To describe factors contributing to non-adherence of ART among HIV-positive pregnant women. - To determine the knowledge of the HIV-positive pregnant women and the use of ART - To recommend strategies that will enhance adherence to ART.	Qualitative-descriptive design.	The target population are HIV-positive pregnant women on ART, who attend the antenatal care clinic at the tertiary hospital in Buffalo City.	The findings in this research reflect that among participants (HIV-positive pregnant women on ART) who were educated and employed, disclosure and levels of knowledge of ART were good. However, some of the participants were still not adhering to ART.	The study was conducted in East London, Buffalo City Metropolitan, Amathole District, Eastern Cape. The study participants were residents of East London and surrounding villages. The study was limited to isiXhosa speaking participants who cannot read or write English. The study was basically for more research to be conducted with a larger number of participants in other places.
Mahlalela	2014	Mpumalanga	- To determine the problems encountered by patients regarding adherence to HAART. - To determine the support structures of people living with HIV/AIDS. - To determine if the patients are taking additional medication.	Qualitative, exploratory, descriptive.	The population in this study comprised 31 HIV/AIDS-infected patients on HAART at the Kanyamazane Clinic, Ehlanzeni District, Mpumalanga Province.	Findings indicate that factors contributing to non-adherence of patients to HAART are the patient-provider relationship and delivery of services, waiting hours and overcrowding, working hours of the facility, forgetfulness and experiencing better health, belief systems, side-effects, pill burden, migration due to employment, poverty and unemployment, as well as disclosure, stigma, and discrimination.	The results cannot be generalised to neither the entire Mpumalanga Province, nor to the other provinces in South Africa, since the study is limited to one clinic in the Mpumalanga Province.
Coetzee *et al.*	2015	Rural South Africa.	To determine how doctors, nurses, counsellors, traditional healers, and caregivers understand the barriers and facilitators to ART adherence among children residing in rural South Africa.	Qualitative-descriptive design.	Data was obtained from: 5 doctors (3 females, 2 males), 4 nurses (female), 12 counsellors (11 females, 1 male), 10 traditional healers (7 males, 3 females), and 11 caregivers (female).	Characteristics of the caregivers including absent mothers, grandmothers as caregivers and denial of HIV amongst fathers were themes related to the micro-system. Language barriers and inconsistent attendance of caregivers to monthly clinic visits were factors affecting adherence in the meso-system. Adherence counselling and training were the most problematic features in the exo-system. In the macro-system, the effects of food insecurity and the controversy surrounding the use of traditional medicines were most salient.	The study provides a broad range of perspectives expressed by the key role players in the treatment and care of children on ART. Due to the small sample size and nature of the data, the findings cannot be generalised, but may be used to inform future research.

Table 1. Cont.

Author	Year	Province	Objectives of the article	Study design	Population	Documented outcomes	Limitations
Dewing *et al.*	2015	Western Cape	To describe the frequency with which structural and individual-level barriers to adherence are experienced by people receiving antiretroviral treatment, and to determine predictors of non-adherence.	Case control study.	600 adult patients from 6 primary health care ARV clinics in the Cape Town Metropolitan area.	Information-related barriers were reported most frequently, followed by motivation and behaviour skill defects. Structural barriers were reported least frequently. Logistic regression analyses revealed that gender, behaviour skill deficit scores, SBCA scores and SBMT scores predicted non-adherence.	Limitations to this study include the use of clinic staff to refer patients for recruitment by data collectors. Another limitation to this study (and other similar studies) is that the categorisation of participants as "adherent" or "non-adherent" is somewhat arbitrary because adherence status is not necessarily stable over time.
Makua	2015	Limpopo	To explore the determining factors for reduced adherence to ART for HIV-positive patients on ART, residing in Polokwane in the Limpopo Province of South Africa.	Qualitative research design.	In-depth interviews were conducted with a purposive sample of 18 patients from the Polokwane clinics who were identified as reduced adherents.	From 18 participants interviewed, 3 themes and 6 sub-themes emerged. The themes included service delivery, socio-economic factors and family-related factors.	Not included.
Azia *et al.*	2016	Western Cape	To describe the experiences of HIV and/or AIDS patients in Vredenburg about accessing ART; the social, structural, economic, and cultural factors that influence adherence to ART in Vredenburg.	Descriptive qualitative research design.	All PLWHA who were registered in the ART programme in the Vredenburg general hospital for more than six months prior to the inception of this study, constituted the study population.	Stigma, disclosure, unemployment, lack of transport, insufficient feeding, disability grants, and alternative forms of therapy were identified as major barriers to adherence, whereas inadequate follow-ups and lack of patient confidentiality came under major criticism from the patients.	Time and financial constraints hindered the researchers from conducting all the interviews. The study did not include some of the adhering patients in the same facility of Vredenburg who may have had similar experiences as those included in the study.
Adeniyi *et al.*	2018	Eastern Cape	This study examined adherence levels and reasons for non-adherence during pregnancy in a cohort of parturient women enrolled in the PMTCT programme in the Eastern Cape province of South Africa.	Mixed-methods descriptive design.	All HIV-infected parturient women who delivered their index pregnancy at the maternity centres in Frere, Cecilia Makiwane, and Bisho hospitals between September 2015 and May 2016 were recruited into the electronic database.	Most of the study participants were single (69.5%), had completed grade 12 schooling (86.5%), were unemployed (74.5%), and were non-smokers (89.5%). The majority of the participants booked during the second trimester (73.2%), knew their HIV status before booking (80.9%), and were already on ART (58.4%).	The study used self-reporting of non-adherence, which might have introduced social desirability bias.

Table 2. CASP appraisal outcome for selected studies

Reference	Study design	Assessment of studies
8	Qualitative descriptive design.	70%
11	Qualitative exploratory-descriptive design.	80%
15	Qualitative descriptive design.	70%
6	Case control study.	60%
16	Qualitative research design.	80%
10	Descriptive qualitative research design.	90%
13	Mixed-methods descriptive design	60%

fluence non-adherence to ART in South Africa. Poor quality is a major factor (n = 5, 71%). With poor quality factors, participants indicated that they do not adhere to ART because of being afraid to collect their treatment. There is no confidentiality in the clinics and again there are stigmatised rooms, whereby certain rooms in health care facilities are allocated for ART collection, so if the said room is entered, the patient's HIV status is made "public" [10, 11, 13, 15, 16]. The second factor under this theme is poor literacy (n = 3, 43%) – participants explained that they are often confused and cannot recall their treatment instructions, and they then ended up not taking their ART as prescribed [10, 11, 15].

Therapy-related factors

Two sub-themes emerged from *therapy-related* factors which are side-effects and feeling better. Side-effects were the major reported factor (n = 3, 43%) – participants alluded that they got fed up with ART side effects, which include hallucination and pruritus. They mentioned that people were regarding them as foolish and that's why they discontinued their ART [10, 11, 13]. Feeling better (n = 1, 14%) was also reported to be a factor; according to Azia *et al.* [10], the participants explained that they felt better after commencing their ART, so they decided to discontinue it.

Cultural and belief factors

Using traditional medication as HIV treatment and relying on pastors for HIV healing emerged as sub-themes for *cultural and belief* factors. Using traditional medication for the healing of HIV was a major factor (n = 3, 43%) – with this factor, participants explained that they use their traditional medication simultaneously with ART [6, 10, 11]. The second factor was relying on pastors for healing (n = 2, 29%), and with regard to this factor participants mentioned that their pastors promised that God will heal them as He promised only good things upon His children, and they then discontinued their ART [6, 8].

Discussion

In this systematic review, six major factors that influence non-adherence to ART in South Africa emerged, and these were identified as: fear of disclosure, food insecurity, poor quality, no finances for transportation, substance abuse, and stigma and discrimination, listed in ascending order. For patients to reach an optimal adherence rate, the above-mentioned factors should be addressed according to the patient's perspective. The major factor that leads to non-adherence to ART, according to the included studies, is fear of disclosure. It is believed that this factor should be addressed from the patient's point of view in the future, meaning that when a healthcare provider comes across a patient with fear of disclosure, the best solution is for them to ask the patient what his/her intentions are to address said problem (fear) as it is affecting their adherence. With the said question being asked, the healthcare provider should show understanding and support to the patient; disclosure is not an easy step to take, but with improved support from the patient's health team member, the results should be favourable.

The second leading factor is food insecurity; realistically, how can patients be expected to take their ART on an empty stomach? Research has proven that ART has side effects and will be adverse when taken while the patient is hungry [21]. It is believed that the best solution to this problem is to not discontinue disability grants when the patient's condition is stable, because patients depend on these grants for food and also transportation to clinics in order to collect their ART. The third factor is poor quality; this, according to the reviewed studies, refers to a lack of confidentiality and the use of allocated rooms for collection of ART, which automatically makes the patient's status known. According to all acts regulating nursing and training of nurses, confidentiality is stressed because failure to maintain it can lead to serious penalties. Legal measures should be taken against those who fail to abide by the rules. Facilities should not have stigmatised rooms because it discloses the status of patients indirectly.

Not having finances for transportation is also a leading factor in ART non-adherence. Because this adherence is a great concern in South Africa and positive ART results are desirable, it should be considered to deliver therapy to patients in need. ART decreases mortality and morbidity rates, so if patients are unable to collect their medication, measures to deliver to them should be put in place. One of which might be a mobile clinic with enough treatment, visiting areas that have a high non-adherence rate to treatment (ART), depending on the statistics of each and every clinic in South Africa. A second measure could be to not disable/discontinue grants for patients who are stable; this will also help because they can use the grant for transportation to collect their treatment.

With factors such as substance abuse and stigma and discrimination, there is limited success for recommended strategies such as health education and community outreaches whereby healthcare workers explain HIV in full detail, in order for community members to comprehend. Kagee *et al.* [5]

Table 3. Themes and sub-themes emerging from the selected studies

Patient-related factors				
Author	**Year**	**Substance abuse (4/7)**	**Stress (2/7)**	**Forgetfulness (2/7)**
Dekeda	2014	√		
Mahlalela	2014			√
Dewing *et al.*	2015		√	
Makua	2015	√		
Azia *et al.*	2016	√		√
Adeniyi *et al.*	2018	√	√	
Economic factors				
		Food insecurity (6/7)	**Transportation fare (5/7)**	**Disability grant (3/7)**
Dekeda	2014	√	√	
Mahlalela	2014	√		
Coetzee *et al.*	2015			√
Dewing *et al.*	2015	√	√	√
Makua	2015	√	√	
Azia *et al.*	2016	√	√	√
Adeniyi *et al.*	2018	√	√	
Social factors				
		Fear of disclosure (7/7)	**Stigma & discrimination (4/7)**	
Dekeda	2014	√	√	
Mahlalela	2014	√		
Coetzee *et al.*	2015	√		√
Dewing *et al.*	2015	√	√	√
Makua	2015	√	√	
Azia *et al.*	2016	√	√	√
Adeniyi *et al.*	2018	√	√	
Health team & health system factors				
		Poor treatment literacy (3/7)	**Poor quality (5/7)**	
Mahlalela	2014	√	√	
Coetzee *et al.*	2015	√	√	
Makua	2015		√	
Azia *et al.*	2016	√	√	
Adeniyi *et al.*	2018		√	
Therapy factors				
		Side effects (3/7)	**Feeling better (1/7)**	
Mahlalela	2014	√		
Azia *et al.*	2016	√	√	
Adeniyi *et al.*	2018	√		
Culture and belief factors				
		Use of traditional herbs (3/7)	**Religious beliefs (2/7)**	
Mahlalela	2014	√		
Dewing *et al.*	2015	√	√	
Azia *et al.*	2016	√		
Adeniyi *et al.*	2018		√	

suggested that research is needed to develop valid measures to reduce stigma and discrimination against people infected with HIV. With regards to substance abuse, we believe that health education about the interactions between ART and substances (alcohol and drugs) should be emphasised to the recipients of ART on a monthly basis. Research should also be conducted to develop new strategies for patient empowerment regarding substance abuse.

Conclusions

ART adherence is a very crucial issue in South Africa, in fact worldwide. Due to certain factors, optimal adherence cannot be achieved by ART recipients. This review highlights factors that influence non-adherence to ART in South Africa. The interventions that are being developed are aimed at reducing this problem and are also based on patient-reported factors that hinder their adherence. However, there still seems to be a gap with regard to the compliance required to fully curb non-adherence and promote strict adherence to ART measures. It is believed that from the information provided in this review, interventions can be drawn, and this will help patients achieve ART benefits while at the same time helping South Africa achieve its aim of reducing high mortality and morbidity rates.

Conflict of interest

The authors declare no conflict of interest with respect to the research, authorship, and/or publication of this article.

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