

# Who takes the medicine? Adherence to antiretroviral therapy in Southern Ethiopia

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**Background:** Treatment adherence is critical for the success of antiretroviral therapy (ART) for people living with HIV. There is limited representative information on ART drug adherence and its associated factors from Southern Ethiopia. We aimed at estimating the level of adherence to ART among people living with HIV and factors associated with it in 20 randomly selected ART clinics of Southern Ethiopia.

**Methods:** In this cross-sectional study, we interviewed consecutive HIV patients on first-line antiretroviral regimen attending the clinics in June 2014 using a pretested and structured questionnaire. For measuring adherence, we used 4-day recall method based on “The AIDS Clinical Trial Group adherence assessment tool”. Patients were classified as “Incomplete adherence” if they missed any of the doses in the last 4 days. Data were singly entered using EpiData and descriptive analysis, and unadjusted odds ratios were calculated using EpiDataStat software. Multivariate logistic regression analysis was performed using Stata v12.0.

**Results:** Of 974 patients interviewed, 539 (56%) were females, and mean age was 35 years. The proportion of patients with incomplete adherence was 13% (95% confidence interval: 11%–15%). In multivariate analysis, factors significantly associated with incomplete adherence included young age, being Protestant Christian, consuming alcohol, being single, and being a member of an HIV association. Psychosocial factors like stigma, depression, and satisfaction to care were not associated with incomplete adherence in the current context.

**Conclusion:** The overall adherence to ART was good. However, there were certain subgroups with incomplete adherence who need special attention. The health care providers (especially counselors) need to be aware of these subgroups and tailor their counseling to improve adherence among these groups. Exploratory qualitative studies may help uncover the exact reasons for incomplete adherence.

**Keywords:** operational research, SORT IT, treatment compliance

## Background

Globally, there were an estimated 12.9 million people living with HIV on antiretroviral therapy (ART) in 2013, and of these, 9.1 million (71%) were in Africa.<sup>1</sup> Access to ART has expanded significantly in the last decade and has saved hundreds of thousands of lives. The impact of ART on HIV disease progression and transmission depends on many factors, one of which is adherence to ART. Adherence assessment has been included as one of the five early warning indicators for HIV drug resistance in countries scaling up ART program.<sup>2</sup> Studies on the benefits of treatment adherence have found that more than 95% adherence is required for effective and sustained viral suppression.<sup>3,4</sup> Systematic reviews have reported that adherence to ART ranged from 55% (95% CI [confidence interval]: 49%–62%) in developed countries to 77% (95% CI: 68%–85%) in developing countries. This indicates better adherence in developing countries than developed ones.<sup>5</sup> Use of fixed dose combinations,<sup>3</sup> as well as factors

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such as sex, depression, social support, pill burden, payment for drugs, adverse drug effects, malnutrition have been shown influence the adherence.<sup>5,6</sup>

In Ethiopia, HIV/AIDS has been and still is a big challenge to the health system, as elsewhere in most sub-Saharan African countries. With an estimated HIV prevalence of 1.2% (95% CI: 1.1%–1.4%), HIV/AIDS is one of the major causes of deaths.<sup>7</sup> Previous studies from Ethiopia have reported ART adherence levels ranging from 73% to 96%.<sup>6,8–11</sup> Most of these were conducted in urban areas, had small sample size, were limited to one or two facilities, and were mostly reported from Northern Ethiopia. There is limited representative information from Southern Ethiopia. While each study focused on selected factors affecting adherence, no single study examined all the factors (like demographic, behavioral and clinical characteristics, social support, access to health facilities, depression, stigma, and knowledge on ART) comprehensively together. Therefore, we aimed at determining the level of adherence to first-line ART among HIV infected patients enrolled into HIV care in Southern Ethiopia and to identify various factors associated with adherence to first-line ART.

## Methods

### Study design

This was a cross-sectional study involving a structured interview of HIV patients attending ART clinics (exit interview).

### Study setting

Ethiopia is located in East Africa (population: 88 million) and is divided into eleven administrative regions. Southern Nations, Nationalities and Peoples' Regional State (SNNPRS), with an estimated population of 16.5 million, is the third largest region and represents approximately 20% of the country's population. Approximately 93% of the populations in SNNPRS live in rural areas.<sup>12</sup> The prevalence of HIV infection among adults in the region was 0.9%, lower than the national average.<sup>7</sup>

In 2014, there were a total of 22 public hospitals, 448 public health centers, and 3,340 health posts in SNNPRS. The potential health service coverage, defined as population living within 10 km of a primary health care unit in 2010, is estimated to be 93%. In total, 22 hospitals and 141 health centers were providing ART care in the region. Most HIV-infected patients receive care from government health facilities.<sup>13</sup>

The National HIV programme has a vertical structure, and all ART clinics are staffed by trained and certified health

workers. The national guidelines for starting ART including the use of prophylactic medications like cotrimoxazole preventive therapy and isoniazid preventive therapy are based on WHO (World Health Organization) 2010 guidelines.<sup>14</sup>

Patients are started on first-line ART regimen consisting of (tenofovir or zidovudine)/lamivudine/(nevirapine or efavirenz) twice a day or once a day depending on the regimen. Patients receiving ART are expected to attend the ART clinic monthly for the first 3–6 months and once in 2 months after that (once assessed as clinically stable). All patients are counseled about the benefits of adherence to treatment and other behavioral modifications during their routine visits to the ART centers by the adherence counselors.<sup>15</sup> ART and all laboratory investigations are provided free of cost to patients at all health facilities.

### Study population

All consecutive HIV-infected adults aged 15 years and above registered for ART in selected health facilities and attending the ART clinic in June 2014. In total, 12 hospitals and 8 health centers providing ART services were randomly selected using random number generator on Excel. We included only HIV-infected adults on first-line ART regimen in these selected facilities.

### Definition of adherence

We used 4-day recall method for measuring adherence. Patients were asked whether they had taken their medications each day during the past 4 days. If none of the doses was missed during the past 4 days, adherence was considered “complete”. Patients were classified as “Incomplete adherence” if they missed any of the doses in the 4 days period.

Several methods including patient self-reporting, pill counts, audits of pharmacy refill records, drug level measurements in blood, and viral load testing have been tried to measure adherence. Each method has its own advantages and challenges.<sup>16</sup> Drug level measurements are expensive and cannot be used in routine programmatic settings. Access to viral load measurements is not yet a reality in Ethiopia. Studies using self-reported adherence have been documented to correlate with viral load.<sup>17</sup> Different periods of recall, ranging from 2 to 365 days (mode = 7 days), have been used in previous studies.<sup>17</sup> The AIDS Clinical Trials Group adherence instrument uses a 4-day recall period and has been shown to correlate well with viral load.<sup>18</sup> Other studies have also shown that brief self-report measures of antiretroviral adherence can be robust in measuring adherence to treatment.<sup>17</sup> Since the duration of recall is less, we used this method to minimize recall limitation.

## Data variables and data collection

Variables included age, sex, education, marital status, place of residence, alcohol use, type of treatment regimen and frequency of dosing, assistance to remember medication, perceived stigma, level of depression, knowledge on ART, satisfaction about care, and adherence to ART. We adapted “the Berger HIV Stigma Scale”<sup>19</sup> for assessing stigma related to HIV/AIDS. Depression was assessed using a modified version of Beck Depression Inventory.<sup>20</sup>

Interviews with study participants were conducted at ART clinics by comprehensive HIV-care-trained and certified health workers. The selected data collectors were provided 3 days training, including class sessions and pretesting the data collection formats. To avoid socially desirable responses, the patients were interviewed by health workers working in a different health facility.

## Analysis and statistics

Data were singly entered and analyzed using EpiData software (version 3.1 for data entry and version 2.2.2.182 for analysis; EpiData association, Odense, Denmark). Incomplete adherence to ART was expressed as proportion with 95% CI. Unadjusted odds ratios were calculated to assess possible association between incomplete adherence and the independent variables. Variables significant at *P*-value of less than 0.2 in unadjusted analysis were included in multivariate analysis. Adjusted odds ratios using multivariate logistic regression were calculated to assess the independent effect of factors on incomplete adherence, and a *P*-value of less than 0.05 was considered statistically significant. The multivariate regression analysis was performed using Stata v12.0 (Stata Corporation, Release 12, College Station, TX, USA).

## Ethics

Permission to carry out the study was obtained from SNNPR Health Bureau. Local ethics approval was obtained from the Institutional Review Board of the SNNPR Health Bureau. The study was also approved by the Ethics Advisory Group of the International Union Against Tuberculosis and Lung Disease, Paris, France. Informed consent for the study was obtained from all participants.

## Results

A total of 1,263 patients were interviewed during the study period. Complete information was available for 974 (77%) patients, and these were included in the final analysis. Of 289 patients excluded, information on age and sex was available

for 77 patients, and there was no difference in distribution compared to those included in the analysis.

Sociodemographic and behavioral characteristics of HIV-infected patients on ART are shown in Table 1. The mean age (standard deviation) of the participants was 35 (9) years, and 539 (55.5%) were females. Most participants (61.2%) had no formal education. Fifteen percent of the participants reported that they consumed alcohol in the past 1 month.

Health facility access, social support, and treatment characteristics are described in Table 2. Fifty-two percent of the patients reached ART clinic within 30 minutes by walk, and little more than half used vehicles. Majority (86.2%) of them were on ART for more than a year, and approximately two-thirds were on a treatment regimen that requires taking the drugs twice a day.

**Table 1** Sociodemographic and behavioral characteristics of HIV-infected patients on ART and their association with treatment adherence in selected health facilities in Southern Ethiopia, 2014

Variable	Total, n	Incomplete adherence, n (%)	Crude OR (95% CI)
Total	974	122 (12.5)	–
Age in years (n=931)			
15–24	59	8 (13.6)	2.7 (0.9, 7.4)
25–34	382	50 (13.1)	2.5 (1.2, 5.5)*
35–44	347	45 (13.0)	2.5 (1.2, 5.5)*
≥45	143	8 (5.6)	Ref
Sex (n=972)			
Male	433	49 (11.3)	Ref
Female	539	73 (13.5)	1.2 (0.8, 1.8)
Place of residence (n=958)			
Urban	774	95 (12.3)	Ref
Rural	184	25 (13.6)	1.1 (0.7, 1.8)
Educational status (n=969)			
No formal education	593	65 (11.0)	Ref
Formal education	376	57 (15.2)	1.5 (1.0, 2.1)
Marital status (n=974)			
Currently single	243	36 (14.8)	1.6 (1.03, 2.6)*
Currently married	546	53 (9.7)	Ref
Not recorded	185	33 (17.8)	2.02 (1.3, 3.2)*
Religion (n=972)			
Protestant Christian	367	65 (17.7)	2.8 (1.3, 6.0)*
Non-Protestant Christian <sup>a</sup>	494	48 (9.7)	1.4 (0.6, 3.0)
Muslim	111	8 (7.2)	Ref
Current alcohol use (n=966)			
Yes	141	27 (19.1)	1.8 (1.2, 3.0)*
No	825	94 (11.4)	Ref
Chat chewing (n=931)			
Current use	45	9 (20.0)	1.8 (0.8, 3.8)
Past use	106	15 (14.2)	1.2 (0.7, 2.1)
Never use	780	96 (12.3)	Ref

**Notes:** <sup>a</sup>Includes Orthodox and Catholic Christians; \*statistically significant.

**Abbreviations:** ART, antiretroviral therapy; CI, confidence interval; n, number; OR, odds ratio; Ref, reference category.

**Table 2** Health facility access, social support, and treatment characteristics of HIV-infected patients on ART and their association with treatment adherence in selected health facilities in Southern Ethiopia, June 2014

Characteristics	Total, n	Incomplete adherence, n (%)	Crude OR (95% CI)
Time to reach health facility (n=942)			
<30 minutes	493	60 (12.2)	Ref
≥30 minutes	458	58 (12.7)	1.1 (0.7, 1.5)
Means of transport (n=960)			
Walking or animal	423	48 (11.3)	Ref
Vehicle	537	71 (13.2)	1.2 (0.7, 1.8)
Assistance to remember medication (n=940)			
Yes	701	89 (12.7)	1.0 (0.7, 1.6)
No	239	30 (12.6)	Ref
Membership in any HIV association (n=961)			
Yes	222	41 (18.5)	1.8 (1.2, 2.8)*
No	739	81 (11.0)	Ref
Treatment duration, months			
≤12	132	12 (9.1)	Ref
13–48	384	46 (12.0)	1.4 (0.7, 2.7)
≥48	443	64 (14.4)	1.7 (0.9, 3.2)
Treatment regimen			
AZT based	434	54 (12.4)	Ref
TDF based	464	61 (13.1)	1.1 (0.7, 1.6)
Others	76	7 (9.2)	0.7 (0.3, 1.6)
Treatment dose per day			
Twice daily	607	69 (11.4)	Ref
Once daily	367	53 (14.4)	1.3 (0.9, 1.9)

Note: \*Statistically significant.

Abbreviations: ART, antiretroviral therapy; AZT, zidovudine; CI, confidence interval; OR, odds ratio; Ref, reference category; TDF, tenofovir.

Psychosocial characteristics and level of knowledge of HIV-infected patients on ART are described in Table 3. Forty-nine percent of the study participants had expressed experience of stigma due to their disease status. Only 25% had complete knowledge on ART.

The proportion of patients with incomplete adherence was 13% (95% CI: 11%–15%). Of them, 68%, 16%, and 16% missed one, two, and three or more doses, respectively. Age group 25–44 years, currently single, Protestant Christian, alcohol use in the past 1 month, and being a member of the HIV/AIDS association were associated with incomplete adherence in unadjusted analysis (Tables 1–3). In multivariate analysis, being in the age group 25–44 years, being a Protestant Christian, being a member of HIV/AIDS association, consuming alcohol, and being single were associated with incomplete adherence (Table 4).

## Discussion

This study, involving a large number of health facilities from the southern region of Ethiopia, showed that a majority of

**Table 3** Psychosocial characteristics and level of knowledge of HIV-infected patients on ART and their association with treatment adherence in selected health facilities in Southern Ethiopia, June 2014

Characteristics	Total, n	Incomplete adherence, n (%)	Crude OR (95% CI)
Stigma (n=971)			
Yes	477	54 (11.3)	Ref
No	466	64 (13.7)	1.3 (0.9, 1.8)
Depression (n=921)			
No or minor depression	252	39 (15.5)	2.0 (0.9, 4.7)
Low depression	585	70 (12.0)	1.5 (0.7, 3.4)
High depression	84	7 (8.3)	Ref
Satisfaction to care (n=956)			
Not satisfied or neutral	125	15 (12.0)	Ref
Satisfied	831	105 (12.6)	1.1 (0.6, 1.9)
ART knowledge (n=954)			
Incomplete knowledge	716	87 (12.2)	Ref
Complete knowledge	238	32 (13.4)	1.1 (0.7, 1.7)

Abbreviations: ART, antiretroviral therapy; CI, confidence interval; n, number; OR, odds ratio; Ref, reference category.

the patients were adherent to the ART medications. Factors associated with incomplete adherence were young age, being a Protestant Christian, membership in HIV/AIDS association, alcohol consumption, and being single.

**Table 4** Multivariate logistic regression analysis of factors associated with incomplete treatment adherence among HIV-infected patients on ART in selected health facilities in Southern Ethiopia, June 2014

Variables	AOR (95% CI)
Age in years	
15–24	2.1 (0.7, 6.3)
25–34	2.3 (1.1, 5.1)*
35–44	2.2 (1.1, 5.0)*
≥45	Ref
Educational status	
No formal education	Ref
Formal education	1.4 (1.0, 2.2)
Religion	
Protestant Christian	3.1 (1.4, 4.1)*
Non-Protestant Christian <sup>a</sup>	1.5 (0.7, 3.3)
Muslim	Ref
Membership in any HIV association	
Yes	1.8 (1.2, 2.8)*
No	Ref
Alcohol drinking	
Yes	1.9 (1.2, 3.2)*
No	Ref
Marital status	
Currently single	1.7 (1.03, 2.7)*
Currently married	Ref
Unknown	1.9 (1.2, 3.2)*
Treatment dose	
Once per day	1.4 (0.9, 2.0)
Twice per day	Ref

Notes: <sup>a</sup>Includes Orthodox and Catholic Christians; \*statistically significant.

Abbreviations: ART, antiretroviral therapy; AOR, adjusted OR; CI, confidence interval; OR, odds ratio; Ref, reference category.

Our study findings on adherence levels are comparable with other studies from Ethiopia.<sup>21,22</sup> A recent study from Northern Ethiopia reported adherence of 96% among HIV-infected patients on ART, higher than this study.<sup>23</sup> The difference might be due to the use of a 30-day recall method for measuring adherence; also the sample population was only from referral hospitals in the previous study. WHO recommends that adherence to ART less than 90% among HIV-infected persons is an early warning indicator for monitoring emergence and transmission of HIV drug resistance.<sup>2</sup> However, studies conducted using newer NNRTI (nonnucleoside reverse transcriptase inhibitor) regimens (eg, rilpivirine, etravirine), though unavailable in the current setting, indicated adherence level as low as 85% could achieve successful viral suppression.<sup>24</sup> This study with adherence levels marginally less than 90% without newer nonnucleoside reverse transcriptase inhibitor calls for measures to improve adherence to prevent drug resistance.

In our study, relatively younger age (25–44 years) individuals were more nonadherent to treatment compared with older age group (more than 44 years). Exact reasons for poor adherence were not explored. Previous studies have reported reasons for poor adherence among young people, including denial and fear of HIV infection, low self-esteem, and unstructured and chaotic life styles.<sup>25–27</sup> Also, a few studies have documented high levels of risky sexual behavior among young age groups on ART.<sup>28,29</sup> Poor adherence to ART and high-risk sexual behavior among young individuals may increase the spread of drug resistant HIV viruses. Incomplete treatment adherence may also affect future drug choice for such patients for managing treatment failure. The health system should recognize such complex needs of the young age group to design a targeted counseling and support for this high-risk group.

Regarding the association between marital status and adherence, the findings were not consistent across the studies.<sup>30</sup> In our study, we found an increased risk of incomplete adherence among individuals who were single or not married. Surprisingly, being member of an HIV association was associated with incomplete adherence to treatment. This might have happened because patients with poor adherence were usually advised to be part of such association and this study, being a cross-sectional one, could not establish temporal relations between the two variables.

Studies have reported a statistically significant association between religion and antiretroviral drug adherence.<sup>31–35</sup> Our study showed that Protestant Christians were more likely

to be nonadherent compared to other religions. Qualitative studies may help in finding the contextual reasons behind this difference.

Similar to other studies, alcohol use was associated with incomplete adherence. Previous literature showed that alcohol interacts with ART treatment through both behavioral and physiological pathways. Behaviorally, alcohol use is linked to risky sexual behavior, apart from the poor adherence observed in our study.<sup>36</sup>

We did not find association between psychosocial factors like perceived stigma and depression and knowledge on ART with adherence. Literature reviews also indicated inconsistent findings on the association between these variables, though most publications tend to show the presence of associations.<sup>37–40</sup>

There are few implications for the HIV program. First, the health care providers, especially counselors, should be informed about the high-risk groups for incomplete adherence and appropriately trained to guide these patients. During routine counseling sessions, they can recognize/identify the high-risk groups and provide focused counseling after exploring the barriers to adherence. Second, existing support systems, like associations for HIV patients, can be strengthened. Innovative approaches like creating medication adherence clubs and mobile phone reminders for the selected high-risk groups can be tried to improve adherence. Third, involving the community leaders, especially religious leaders, may help to reduce this problem.

This study has several strengths. First, the study had a large sample size involving patients from several health facilities. Second, the recall period was shorter than similar studies in Ethiopia, minimizing recall bias, and data collection by a trained health worker from a different health facility may have reduced potential social desirability bias. Third, we comprehensively assessed the factors associated with incomplete adherence including psychosocial and health access factors. There are also a few limitations. The cross-sectional nature of the design does not allow us to establish true cause–effect relations. Furthermore, the level of adherence may be an overestimate because of self-reporting, and we could not validate it using other methods like viral load testing. The response rate in our study is 77%, though those excluded were similar in age and sex distribution. The reasons for providing incomplete questionnaire responses could be withdrawal from the interview after consenting to participate in the study and workload from data collectors, among others. This might still have resulted in over- or underestimation of overall level of adherence.

In conclusion, around nine out of ten patients on ART adhered to the medication. However, there were certain subgroups with incomplete adherence. Innovative approaches including mobile phone reminders and forming medication adherence clubs could be tried to help improve adherence for patients with the identified risk factors.

## Open-access statement

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## Disclosure

The authors report no conflicts of interest in this work.

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