Multilevel of Factors Affected Optimal Adherence to Antiretroviral Therapy and Viral Suppression Amongst HIV-infected Prisoners in South Ethiopia: A Prospective Cohort Study

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Abstract

Objectives

Maintaining optimal adherence and viral suppression in people living with HIV (PLWHA) is essential to ensure both preventative and therapeutic benefits of antiretroviral therapy (ART). Prisoners bear a particularly high burden of HIV infection and are highly likely to transmit to others during and after incarceration. However, the level of treatment adherence and viral suppression in incarcerated populations in low-income countries is unknown. This study aimed to determine the prevalence of non-adherence and viral failure, and contributing factors amongst prisoners in South Ethiopia.

Methods

A prospective cohort study was conducted between June 1, 2019 and May 31, 2020 to compare the level of adherence and viral suppression between incarcerated and non-incarcerated PLWHA. The study involved 74 inmates living with HIV (ILWHA) and 296 non-incarcerated PLWHA. Background information (including sociodemographic, socioeconomic, psychosocial, behavioural, and incarceration related characteristics) was collected using a structured questionnaire. Adherence was determined based on the participants' self-report and pharmacy refill records. Plasma viral load measurements undertaken within the study period were prospectively extracted to determine viral suppression. Univariate and multivariate regression models were used to analyse data.

Results

While prisoners had a significantly higher pharmacy refill adherence compared to non-incarcerated PLWHA (89% vs 75%), they had a slightly lower dose adherence (81% vs 83%). The prevalence of viral failure (VF) was also slightly higher (6%) in ILWHA compared to non-incarcerated PLWHA (4.4%). The overall dose non-adherence (NA) was significantly associated with missing ART appointments, level of satisfaction with ART services, patient's ability to comply with a specified medication schedule and types of methods used to monitor the schedule. In ILWHA specifically, accessing ART services from a hospital compared to a health centre, an inability to always attend clinic appointments, experience of depression and a lack of social support predicted NA. VF was significantly higher in males, people of age 31to 35 years and in those who experienced social stigma, regardless of their incarceration status.

Conclusions

This study revealed that HIV-infected prisoners in South Ethiopia were more likely to be non-adherent to ART doses and to develop viral failure compared to their non-incarcerated counterparts. A multitude of factors were found to be responsible for this requiring multilevel intervention strategies focusing on the specific needs of prisoners.

Background

Antiretroviral therapy (ART) is associated with significantly reduced HIV-associated morbidities and mortality. ART is also believed to prevent HIV transmission by suppressing viral load in infected individuals [1–3]. To ensure the public health benefits, people living with HIV (PLWHA) need to have optimal treatment adherence and achieve viral suppression [4]. Prisoners are amongst the HIV key populations bearing a disproportionate burden of the epidemic accounting for more than half of all new infections worldwide [5], and have a potential of transmitting to others during incarceration and after release [5, 6]. There is a considerably higher HIV prevalence in the prisons of sub-Saharan Africa (SSA), which is much higher compared to the general population [7]. A HIV prevalence of greater than 4% has been documented in Ethiopian prisons [8], which is more than four times higher than the prevalence in the general Ethiopian population [5].

Promising outcomes have been reported amongst prisoners regarding ART adherence and viral suppression in prisons where standard HIV care is implemented [9–17]. However, the prevalence of non-adherence (NA) and viral failure (VF) remains high in prisons of many countries, with more than half of inmates living with HIV (ILWHA) having sub-optimal treatment outcomes in some settings [15, 18–25]. Several institutional, psychosocial and personal factors have previously been reported to affect optimal adherence and viral suppression in prisoners. Cooperativeness of security systems [26–32], type of ART service delivery approach (for example, provision of ART via directly observed therapy (DOT) or accessing care from external ART sites) [29, 30, 33, 34], the nature of inmate-health care provider relationships [21, 28–30, 35], and food supply insufficiency (particularly in resource limited countries) [22, 30, 31, 35] have been reported to be the main institutional circumstances to affect ART outcomes.

Psychosocial factors such as social support, stigma and depression have been found to influence ART adherence in prisoners. It has been shown that ILWHA who are able to receive social support (be it material, emotional or information support), either from inside or outside of a prison, are more likely to be adherent to ART than those who are not [18–21, 36, 37]. In contrast, social stigma perpetuated by prison staff and fellow inmates negatively affects adherence [27–30]. Further, ILWHA often have a high prevalence of depression [38] which may have substantial adverse effects on their ART adherence and viral suppression [9, 18, 19, 28, 34, 37].

With only limited data existing regarding personal factors affecting ART adherence and viral suppression in prisoners, it has been reported that self-perceptions of HIV status, the health benefits of ART as well as its potential adverse consequences have been associated with NA. For instance, ILWHA who perceive that ART is inefficient and has side-effects are less likely to adhere to ART [20, 34]. The odds of NA is higher in ILWHA who have experienced more frequent antiretroviral (ARV) side-effects [19, 28, 35, 36, 39] and other underlying disease symptoms [20, 28]; and non-adherent ILWHA are, in turn, less likely to achieve viral suppression [20]. Having a history of injecting drug use is the only major behavioural factor that has been statistically confirmed to be negatively associated with ART adherence and viral suppression in ILWHA [18, 20, 28]. Other personal characteristics reported to be associated with NA and VF are younger age (below 35 years) and being male [9, 16, 18, 22].

There have been reports showing that ILWHA in SSA prisons have limited access to HIV care [7, 31], however it remains unclear to what extent incarceration affects optimal ART adherence and viral suppression in such settings. No published studies have quantitatively investigated ART outcomes in the prison systems of Ethiopia previously, although there have been suggestions that population groups commonly referred to as 'Most at Risk Groups' (MARPS) for HIV (including prisoners) remain with restricted access to care [40]. This study therefore aimed to determine the level of adherence and viral suppression, and associated factors amongst ILWHA in South Ethiopia relative to their non-incarcerated counterparts.

Methods

Study design, setting and participants

A prospective cohort study was conducted between June 1, 2019 and May 31, 2020 to compare the outcomes of ART between HIV-infected incarcerated and non-incarcerated individuals in South Ethiopia. We have provided a detailed description of the study setting elsewhere (available as a preprint) [41]. In brief, approximately one quarter of the correctional facilities (six of 23 prisons) in South Ethiopia and their respective public health care facilities offering ART services for the prisoners were involved in the study. To increase the generalisability of study findings, the prisons were chosen based on the number of inmates they house and sociocultural diversity amongst their prisoner populations. The prisons are located in the central part of Ethiopia and accommodate people originating from diverse areas of the region and the country, including rural areas.

All ILWHA who remained imprisoned for at least one month in the selected prisons, and were on ART or newly initiated on the therapy within the first six months of the study period were eligible for participation in the study as a risk group. Those with a recorded history of NA and/or VF before incarceration were excluded. The comparison group included HIV-infected and non-incarcerated people who were receiving care from the same ART clinics as the prisoners and had undertaken comparable durations of ART treatment. This group of participants were required to have no previous history of imprisonment. All participants were aged 18 years and above and had the mental and physical capacity to provide written informed consent and complete information. Figure 1 shows the process of participant recruitment. As the population pool for non-incarcerated people was much larger than incarcerated people, a simple random sampling technique [42] was used to recruit a sample of non-incarcerated participants that quadrupled the number of prisoner participants. To assist in this, a list of patients in ART registers served as a sampling frame to select potential participants using a table of random numbers.

Sample size determination

The smallest difference in the proportion of NA between incarcerated and non-incarcerated people was considered to determine the minimum sample size required to identify an estimated prevalence ratio. A formula for independent cohort studies [42]; assuming 95% of level of confidence, 80% power, a 5% level

of significance and unexposed to exposed group sample ratio of four was used to calculate the sample size. Considering a proportion of 24.4% NA in the general population in Ethiopia [43], and a prevalence ratio of 1.67 in NA in the incarcerated population [22], a minimum sample of 74 inmates was required. As four times the number of incarcerated participants was required compared to the non-incarcerated group, a final sample size of 370 participants was recruited from both populations.

Data collection procedure

ART service providers at the participating public health care facilities invited potential participants to see a trained research assistant in a separate room. The invitation occurred when PLWHA made their regular clinic visit. The research assistants were certified HIV counsellors who had a tertiary qualification in health-related disciplines. Participants underwent Paper and Pencil Interviewing (PAPI) once they gave consent for participation to the research assistant.

To minimise the effect of the language barrier on the accuracy of PAPI data, the questionnaire, which was initially prepared in English language, was translated into Amharic, a commonly spoken language in the study area. Completed questionnaires were then translated back into English at the end of the data collection process. Pre-testing was conducted to ensure context validity (i.e. clarity, meaningfulness and difficulty) of questionnaire items with a group of participants representing five percent of the study sample size; using incarcerated and non-incarcerated PLWHA at ART clinics remote to the study sites. As lay experts [44], one ART service provider from each study health facility evaluated the face validity of the questionnaire. To perform this, the ART service providers were provided with the questionnaire ahead of the data collection process. Although some items of the questionnaire were obtained from previously validated instruments (as described below), newly developed items were tested for internal consistency using Cronbach's α [45], and corrections were made by removing less consistent items based on the 'α' values of the pre-test data.

Variables and measurements

Background information: In the questionnaire, participants were asked about their sociodemographic, socioeconomic, psychosocial (social support, stigma and depression), behavioural, and incarceration related characteristics. The core components of social support including emotional, informational, tangible, comradeship and positive social interactions [46] were assessed using nine items, part of which were adapted from a multi-item scale developed by White et al [47], which had internal consistency (α) of 0.79. The items were further checked for contextual reliability and showed an acceptable Cronbach's α value (α=0.66). The four manifestations of HIV-related social stigma: internalised (negative self-image), enacted (personalised), perceived (concern with public attitude) and concerns with status disclosure [48] were measured using a shortened version [49] of the 40-item scale by Berger et al [48] (α>0.7). Non-specific psychological distress was assessed using a six-item scale developed by Kessler et al [50] (α= 0.89). Participant responses were graded using a five-point Likert scale ranging from 1, "Strongly

disagree" to 5, "Strongly agree" for social support and stigma measurements, and a four-category scale (most of the time, some of the time, a little of the time, none of the time) for depression.

Knowledge and attitudes of HIV and ART, as well as self-efficacy in medication use were assessed using items generated from the literature review. The knowledge scale consisted of eight items, and the attitude and self-efficacy scales each consisted of three-item questions. The scales showed sufficient Cronbach's α values; 0.78 and 0.65 for the knowledge and attitude constructs, respectively. Whereas responses for the knowledge items were scored by assigning one point for every correct response and zero for an incorrect answer, a five-point response scale was used for the attitude and self-efficacy items. In each measurement scale, scores were summed to determine the overall score, and the interquartile range was calculated to categorise results.

Adherence to ART: Adherence was measured using the participants' self-report and pharmacy refill records, as one method was assumed to offset the limitations of the other [51-53]. Participants were assessed once for six-monthly ART adherence within 12 months of the follow up period. Self-reported adherence was determined by calculating the proportion of pills taken of the number of pills prescribed in the previous four days, an ideal time interval to minimise possible recall and social desirability bias [53]. Variation in the medication possession ratio (MPR) was determined by dividing the number of days a patient was late for pharmacy refills by the total days on ART, and then subtracting this proportion from 100% [54, 55]. i.e.

$$Self-reported\ adherence\ = \frac{number\ of\ pills\ taken\ in\ the\ last\ four\ days}{number\ of\ pills\ prescribed\ for\ the\ last\ four\ days} x100$$

Whereas,

$$MPR = 1 - \frac{number\ of\ days\ late\ for\ ARV\ pick-up}{Total\ number\ of\ days\ between\ the\ two\ most\ recent\ ARV\ pick-ups} x100$$

For both methods, the adherence threshold was defined as ≥95% [56, 57]. Participants were also asked to self-report on their adherence to dose schedules and medication instructions in the previous four days or more and complete a brief survey on potential risk factors for NA.

Viral suppression: **The South Ethiopian Regional Public Health Laboratory (RPHL) performs a viral load measurement for patients after six months from ART initiation and every 12 months thereafter. Results of these investigations undertaken within 12 months of the study period were prospectively extracted from the laboratory registers using patient medication identification numbers. Virological failure (VF) in this study was defined as viral load above 1000 copies/mL after six months or longer duration of ART, which is partly adapted from World Health Organization (WHO) definitions for VF in adults [52].**

Data analysis

Data were entered into an EpiData (version 4.6) template, manually checked for completeness, consistency and cleanness and then exported to Stata (StataCorp. 2019. Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC.) for analysis [58]. Participant characteristics were initially described in terms of frequencies and percentages for categorical variables, while summary statistics such as means, medians, standard deviations and quartiles were calculated for continuous variables.

Adherence was analysed in two ways: as a continuous outcome restricted to the interval between 0 and 1, and a binary outcome categorised as adherence and non-adherence (NA). In the first case, as the data included the upper and lower bounds [0, 1], a fractional regression model was used to estimate the results with logit as a link function [59]. Covariates of NA and VF were determined using a logistic regression model [60]. Significance of associations between covariates and the outcome variables was determined at $P<0.05$ with 95% confidence intervals. Goodness-of-fit for the logistic regression models was assessed using Hosmer and Lemeshow Chi^2 test [60] whereas that of the fractional regression analyses was checked using a generalised linear model applying logit as a link function [61, 62]. In all cases, the models fit the data well.

Missing values were observed within several dependent and independent variables in the dataset. For variables included in the analysis models, Little's test was used to check whether the missingness occurred completely at random (MCAR), independent of observed and unobserved values [63]. The test identified that the pattern of missingness varied across the variables and violated the assumption of MCAR. Thus, the multiple imputation technique (m=20) was applied to take into account the effect of missing values, in which the results obtained from each completed-data analysis were combined to produce a single multiple-imputation result. The fit of the imputation models was checked using a graphical method [64]. The distribution of the observed and completed values appeared to be comparable.

Results

Participant characteristics

One hundred and twenty-two ILWHA were identified in the six selected correctional facilities. Of these, 24 (19.7%) ILWHA did not participate due to their release from prison ahead of their clinic appointment at which the consenting process would have been conducted. Ten ILWHA (8.2%) failed to meet the study eligibility criteria. Of the remaining 88 ILWHA, 74 agreed to participate in the study, which gives a response rate of 84.1%. During the study period, there was a total of 3806 non-incarcerated adult PLWHA who were receiving ART services at the six selected public health care facilities; of whom, 296 were randomly selected for participation in this cohort study as comparators.

Characteristics of participants are described in Table 1. The majority (89%) of ILWHA participants were male, as were only 47% of non-incarcerated PLWHA participants. Both groups were of comparable age; the median age of ILWHA was 34 years whereas that of non-incarcerated PLWHA was 35 years.

Significantly more non-incarcerated PLWHA participants reported having completed high school and college education compared to ILWHA participants. ILWHA were significantly more likely to be farmers or daily labourers prior to incarceration relative to their comparators. Half of the ILWHA reported urban areas as their last residence before incarceration whereas 69% of non-incarcerated PLWHA were urban residents. A history of homelessness was significantly more common in ILWHA than non-incarcerated PLWHA.

Table 1
Characteristics of incarcerated and non-incarcerated people living with HIV in South Ethiopia (N = 370)

Characteristic		Incarcerated (N = 74), n (%)	Non-incarcerated (N = 296), n (%)	*P*-value (Ch^2)
Gender	Male	66 (89.2)	139 (47.0)	0.000
	Female	8 (10.8)	157 (53.0)	
Age in years	18–25	13 (17.6)	30 (10.1)	0.213
	26–30	18 (24.3)	62 (21.9)	
	31–35	14 (18.9)	57 (19.3)	
	> 35	29 (39.2)	147 (49.7)	
Current marital status	Have partner	35 (47.3)	169 (57.1)	0.130
	Have no partner	39 (52.7)	127 (42.9)	
Highest level of education completed	No school	24 (32.4)	82 (27.7)	0.047
	Elementary school	37 (50.0)	116 (39.2)	
	High school	11(14.9)	66 (22.3)	
	College graduate	2 (2.7)	32 (10.8)	
Employment status	Unemployed	4 (5.4)	19 (6.4)	0.000
	Government employee	7 (9.4)	60 (20.3)	
	Home duties	2 (2.7)	67 (22.6)	
	Farmer	19 (25.7)	46 (15.5)	
	Daily labourer	19 (25.7)	55 (18.6)	
	Other	23 (31.1)	49 (16.6)	
Monthly income in USD	≤ 13.5	22 (31.0)	110 (37.4)	0.497
	13.6–22.8	8 (11.3)	24 (8.2)	

ART: antiretroviral therapy; MPR-NA: non-adherence based on medication possession ratio (pharmacy refill); SR-NA: self-reported non-adherence; VF: virological failure; USD: United States dollars

* Residence, employment status and monthly income for incarcerated people refer to the last circumstances before incarceration.

* Sum of 'monthly income', 'length of current sentence' and 'viral failure' categories may not give the total sample due to missing data (1.3%, 10.5% and 3% respectively)

Characteristic		Incarcerated (N = 74), n (%)	Non-incarcerated (N = 296), n (%)	*P*-value (Ch^2)
	> 22.8	41 (57.7)	160 (54.4)	
Residence	Urban	37 (50.0)	204 (68.9)	0.019
	Rural	27 (36.5)	68 (23.0)	
	Both	10 (13.5)	23 (7.8)	
	Unknown	0 (0.0)	1 (0.3)	
History of homelessness	No	61 (82.4)	284 (96.0)	0.000
	Yes	13 (17.6)	12 (4.0)	
Length of current incarceration in months	< 12	28 (37.8)	–	–
	≥ 12	46 (62.2)	–	
Length of current sentence in months	< 12	2 (3.0)	–	–
	12–59	24 (36.4)	–	
	60–119	16 (24.2)	–	
	≥ 120	24 (36.4)	–	
Number of incarcerations	1	61 (82.4)	–	–
	> 1	13 (17.6)	–	
Dissatisfaction with ART services		65 (87.7)	234 (79.1)	0.086
ART adherence and VF	SR-NA	14 (18.9)	50 (16.9)	0.680
	MPR-NA	8 (10.8)	74 (25.0)	0.009
	VF	4 (6.0)	13 (4.4)	0.598

ART: antiretroviral therapy; MPR-NA: non-adherence based on medication possession ratio (pharmacy refill); SR-NA: self-reported non-adherence; VF: virological failure; USD: United States dollars

* Residence, employment status and monthly income for incarcerated people refer to the last circumstances before incarceration.

* Sum of 'monthly income', 'length of current sentence' and 'viral failure' categories may not give the total sample due to missing data (1.3%, 10.5% and 3% respectively)

Adherence to ART and viral suppression

The median duration of ART use was 44 months for prisoners and 48 months for non-incarcerated clients. The overall prevalence of non-adherence (NA) was 17% by self-report and 22% using MPR. While prisoners had a significantly higher MPR adherence compared to non-incarcerated clients (89% vs 75%),

they had a slightly lower dose adherence. Both populations had comparable median values of plasma viral load (0 copies/mL). The total prevalence of virological failure (VF) was 4.7%, with a slightly higher occurrence in prisoners (see Table 1).

Factors associated with ART non-adherence

Various factors were identified as determinants of overall dose-NA in a multivariate logistic regression analysis (see Table 2). The analysis indicated that missing a clinic appointment increases the risk of dose-NA. For instance, missing a single ART appointment increased the risk by 94% (AOR: 0.06; 95%CI: 0.02–0.22). As shown in Fig. 2, ART clients missed their clinic appointments for various reasons. Prisoners often missed appointments due to a lack of cooperativeness by prison staff and/or forgetting. Being away from usual residence, being occupied by daily routines, forgetting ART appointments, a lack of transport or a combination of two or more of these factors played a role in the case of non-incarcerated clients. Some prisoners reported missing their ART appointment due to a fear of being socially stigmatised, having a sense of hopelessness and lacking interest in the medication. A small number of non-incarcerated clients missed appointments being too ill to attend a health care facility.

Figure 2: Reasons for missing clinic appointments amongst incarcerated and non-incarcerated antiretroviral therapy clients in South Ethiopia

* Reasons reported by non-incarcerated ART clients such as ‘being busy in daily routines’ and ‘a lack of transport’ are included under ‘Others’ category.

The ability to strictly adhere to a specific medication schedule was a determinant of dose adherence in incarcerated and non-incarcerated clients. Accordingly, the odds of dose adherence was 99% lower in those who were able to keep their medication schedule most of the time rather than all of the time (AOR: 0.01; 95%CI: 0.002–0.13) and 99.8% lower in those who never followed their medication schedule (AOR: 0.002; 95%CI: 0.0001-0.05). Methods that participants used to manage their medication schedule also appeared to affect dose adherence. Clients who used news time on radio/TV or other social cues, such as sunlight or departure time to school/church/mosque were less likely to comply with doses relative to those who were able to use one or more time monitoring devices such as a mobile phone, wristwatch, etc. (AOR: 0.08; 95%CI: 0.01–0.53 vs AOR: 0.07; 95%CI: 0.01–0.67). In addition, the risk of dose-NA was more than seven times higher in clients who had poor satisfaction with ART services (AOR: 0.14; 95%CI: 0.03–0.63), which was higher in incarcerated ART clients than their non-incarcerated counterparts (see Table 2).

Table 2
Logistic regression model of factors associated with self-reported ART non-adherence amongst incarcerated and non-incarcerated ART clients in South Ethiopia (incarcerated = 74; non-incarcerated = 296)

Variable		Adherence		COR (95% CI)	AOR (95% CI)
		Adherent, n (%)	**Non-adherent, n (%)**		
Relationship with a person to whom HIV status disclosed	Spouse	48 (92.3)	4 (7.7)	3.07 (1.03–9.12)*	1.71 (0.38–7.71)
	Offspring	11 (64.7)	6 (35.3)	0.47 (0.16–1.36)	0.58 (0.11–3.02)
	Parent	10 (71.4)	4 (28.6)	0.64(0.19–2.17)	0.98 (0.13–7.23)
	More than one of the above	129 (79.6)	33 (20.4)	1	1
Adherence to specific medication schedule in the last four days	Never	6 (75.0)	2 (25.0)	0.08 (0.01–0.51)*	0.002 (0.0001-0.05)*
	Some	6 (54.5)	5 (45.5)	0.03 (0.01–0.15)*	0.03 (0.002–0.52)*
	Half	20 (57.1)	15 (42.9)	0.04 (0.01–0.12)*	0.002 (0.0001-0.02)*
	Most	120 (75.9)	38 (24.1)	0.08 (0.03–0.24)*	0.01(0.002–0.13)*
	All of the time	154 (97.5)	4 (2.5)	1	1
Aids used to manage medication schedule	Mobile phone	33 (80.5)	8 (19.5)	0.67 (0.28–1.61)	0.35 (0.07–1.72)
	Watch	24 (72.7)	9 (27.3)	0.43 (0.18–1.03)	0.23 (0.04–1.26)

COR: crude odds ratio; AOR: adjusted odds ratio; CI: confidence interval; ART: antiretroviral therapy; TV: television; * statistically significant association at $P < 0.05$

	Radio/TV	19 (63.3)	11(36.7)	0.28 (0.12–0.66)*	0.08 (0.01–0.53)*
	Others	26 (74.3)	9 (25.7)	0.47 (0.20–1.11)	0.07 (0.01–0.67)*
	More than one aid	166 (86.0)	27 (14.0)	1	1
Number of clinic appointments missed in the last 12-months	None	210 (93.8)	14 (6.3)	1	1
	One	83 (65.3)	44 (34.7)	0.13 (0.07–0.24)*	0.06 (0.02–0.22)*
	Two and more	13 (68.4)	6 (31.6)	0.14 (0.05–0.44)*	0.16 (0.03–0.97)*
Satisfaction with ART services	Poor	242 (80.9)	57 (19.1)	0.46 (0.20–1.06)	0.14 (0.03–0.63)*
	Good	64 (90.1)	7 (9.9)	1	1

COR: crude odds ratio; AOR: adjusted odds ratio; CI: confidence interval; ART: antiretroviral therapy; TV: television; * statistically significant association at $P < 0.05$

- Sum of categories of 'relationship with a person to whom HIV status disclosed' and 'aids used to manage medication schedule' may not give the total sample as some categories were not considered in the analysis due to an insufficient number of observations.

We specifically assessed predictors of non-adherence to doses and pharmacy refill in prisoners using a multivariate fractional regression analysis (see Tables 3 & 4). Prisoners who were accessing ART services from a hospital were 75% less likely to comply with scheduled doses (AOR: 0.25; 95%CI: 0.07–0.90) compared to prisoners who were accessing the services from a health centre. The risk of dose-NA increased by 93% when prisoners missed a single ART appointment (AOR: 0.07; 95%CI: 0.01–0.67) and by 99% when they missed two or more appointments (AOR: 0.01; 95%CI: 0.002–0.08). Depressed inmates had a 74% lower likelihood of dose adherence than non-depressed inmates (AOR: 0.26; 95%CI: 0.07–0.88) (see Table 3).

Table 3
Fractional regression model of factors associated with self-reported dose adherence amongst incarcerated people living with HIV in South Ethiopia (N = 74)

Variable		COR (95% CI)	AOR (95% CI)
Employment status	Unemployed	1.20 (0.07-20.00)	0.09 (0.004–2.03)
	Government employee	1	1
	Farmer	3.40 (0.37–31.12)	2.46 (0.81–7.44)
	Daily labourer	0.867 (0.13–5.89)	0.69 (0.28–1.72)
	Others	2.67 (0.34–20.79)	0.70 (0.34–1.44)
Depression	Non-depressed	1	1
	Depressed	0.28 (0.08–0.95)*	0.26 (0.07–0.88)*
Type of health facility	Health centre	1	1
	Hospital	0.89 (0.26–3.02)	0.25 (0.07–0.90)*
Number of clinic appointments missed in the last 12-months	None	1	1
	1	0.04 (0.01–0.19)*	0.07 (0.01–0.67)*
	≥ 2	0.02 (0.001–0.33)*	0.01 (0.002–0.08)*

COR: crude odds ratio; AOR: adjusted odds ratio; CI: confidence interval; ART: antiretroviral therapy; * statistically significant association at $P < 0.05$

- Employment status refers to the last occupation before incarceration.
- Sum of categories of 'employment status' may not give the total sample as some categories were not considered in the analysis due to an insufficient number of observations.

Similar to dose adherence, accessing ART services from a hospital decreased the inmates' pharmacy refill adherence by 95% compared to accessing the services from a health centre (AOR: 0.05; 95%CI: 0.02–0.13). Prisoners who developed a viral failure were more than two times less likely to comply with pharmacy refill (AOR: 0.38; 95%CI: 0.20–0.73). Moreover, the likelihood of pharmacy refill adherence was 86% lower in inmates who reported lacking ILWHA-roommates (AOR: 0.14; 95%CI: 0.05–0.40) (see Table 4).

Table 4
Fractional regression model of factors associated with pharmacy refill adherence amongst incarcerated people living with HIV in South Ethiopia (N = 74)

Variable		COR (95% CI)	AOR (95% CI)
Length of time on ART in months	-----	1.01 (1.001–1.02)*	1.01 (0.99–1.03)
ART use before incarceration	No	2.54 (0.88–7.35)	2.78 (0.99–7.79)
	Yes	1	1
Presence of anyone living with HIV in a cell	No	0.26 (0.08–0.79)*	0.14 (0.05–0.40)*
	Yes	1	1
Type of health facility	Health centre	1	1
	Hospital	0.28 (0.10–0.82)*	0.05 (0.02–0.13)*
Viral failure[m]	No	1	1
	Yes	0.12 (0.02–0.64)*	0.38 (0.20–0.73)*

COR: crude odds ratio; AOR: adjusted odds ratio; CI: confidence interval; ART: antiretroviral therapy; MPR: medication possession ratio (pharmacy refill); [m] variable with missing value; * statistically significant association at $P < 0.05$; -----: not applicable

The effect of missingness in this particular dataset is negligible as the complete case analysis and multiple imputation gave exactly the same AORs (results not displayed).

Factors associated with virological failure

A multivariate logistic regression identified predictors of an overall virological failure (VF) in incarcerated and non-incarcerated ART clients. The estimation was made based on a complete case analysis and multiple imputation of variables with missing values (see Table 5). Sociodemographic factors such as gender, age and social stigma appeared to be determinants of VF in both analyses. In the complete case analysis, the risk of VF was 97% higher in males than females (AOR: 0.03; 95%CI: 0.003–0.41) whereas 96% higher in multiple imputation (AOR: 0.04; 95%CI: 0.003–0.41). ART clients in the age group of 31 to 35 years had more than fourteen times the risk of developing VF relative to those who were > 35 years old in the complete case analysis (AOR: 14.10; 95%CI: 2.35–84.57) and about thirteen times higher risk in the multiple imputation (AOR: 13.05; 95%CI: 2.10-81.16). Experiencing social stigma increased the risk of VF more than tenfold both in the complete case analysis and multiple imputation (AOR: 10.59; 95%CI: 1.81–62.03 vs AOR: 10.19; 95%CI: 1.77–58.57).

Table 5
Logistic regression model of factors associated with virological failure amongst incarcerated and non-incarcerated ART clients in South Ethiopia

Variable		Virological failure		COR (95% CI)	AOR (95% CI), Complete case analysis (N = 279)	AOR (95% CI), Multiple imputation (N = 370)
		Yes, n (%)	No, n (%)			
Gender	Male	16 (8.0)	183 (92.0)	1	1	1
	Female	1 (0.4)	156 (99.4)	0.07 (0.01–0.55)*	0.03 (0.003–0.41)*	0.04 (0.003–0.41)*
Age in years	26–30	3 (3.9)	74 (96.1)	1.12 (0.27–4.61)	5.37 (0.62–46.34)	4.89 (0.54–44.32)
	31–35	8 (11.4)	62 (88.6)	3.57 (1.19–10.70)*	14.10 (2.35–84.57)*	13.05 (2.10-81.16)*
	> 35	6 (3.5)	166 (96.5)	1	1	1
Social stigma	Non-stigmatised	9 (3.3)	262 (96.7)	1	1	1
	Stigmatised	8 (9.1)	80 (90.9)	2.91 (1.09–7.79)*	10.59 (1.81–62.03)*	10.19 (1.77–58.57)*
Follow up CD4 count[m]	-----	-----	-----	1.00 (0.99-1.00)	0.998 (0.995-1.000)	0.998 (0.995-1.00)

COR: crude odds ratio; AOR: adjusted odds ratio; CI: confidence interval; ART: antiretroviral therapy; [m] variable with missing value; [*] statistically significant association at $P < 0.05$; -----: not applicable

- Sum of the age categories may not give the total sample as a category '18–25 years' was not considered in the analysis due to an insufficient number of observations.

Discussion

This study aimed to identify factors contributing to ART non-adherence and viral failure in prisoners in South Ethiopia. Prisoners had a level of viral suppression (94%) which is close to the third goal of the Joint United Nations Programme on HIV/AIDS (UNAIDS), i.e. achieving viral suppression in 95% of treated individuals by 2030 [65]. They also had a lower prevalence of NA and VF than that commonly reported in SSA general populations [66, 67] including that of Ethiopia [68, 69], as well as in prison populations internationally [9–11, 15, 16, 19, 20, 22, 70]. However, NA and VF prevalence amongst prisoners in this

study was higher relative to the local non-incarcerated population. The recent and rapid expansion of ART services in Ethiopia might have contributed to the positive treatment outcomes in this study [4, 71], but the discrepancy between incarcerated and non-incarcerated individuals may suggest an inequitable access to standard HIV care between community- and correctional facility-based populations. The findings also indicate the importance of a patient's compliance with specified doses for achieving viral suppression [72, 73], which predicts HIV-related morbidities and mortality, as well as further transmission [1–3].

Various structural, psychosocial, individual and clinical factors were identified to influence ART adherence and viral suppression in ILWHA relative to non-incarcerated PLWHA. While missing ART appointments was an important factor affecting adherence in both incarcerated and non-incarcerated populations, it appeared to be more critical in ILWHA. Regular clinic visits are essential for ART clients in order to receive ongoing adherence counselling and support services, as well as clinical assessment and further prescription of ART [52]. Omission of such appointments, therefore, subsequently leads to sub-optimal adherence and facilitation of community transmission [6, 52, 57, 74–78]. Prisoners in low-income countries often access ART services from external public health care facilities, which presents serious of institutional barriers (e.g. a lack of transport facilities and uncooperative security system) [30, 32]. We recommend implementation of standard HIV care package in the prison system as supported by international guidelines [38, 79, 80].

A significantly lower level of satisfaction with ART services was observed in ILWHA than non-incarcerated PLWHA. This is important because the results revealed an 86% lower likelihood of dose adherence in clients who had low satisfaction. Furthermore, the odds of dose adherence were 75% lower in ILWHA who had received ART services from a hospital compared to those who were receiving ART services from a health centre. The importance of good health care provider-patient relationships for enhancing adherence is well recognised both in prison [21, 28, 29] and community-based populations [74, 81]. It is also known that when patients believe that health care providers are uncaring and unsympathetic, their ability to conform to medication instructions will be negatively affected [35, 82]. However, health care provider- and health facility-related issues are amongst the most frequently reported barriers to ART adherence in SSA [83]. Health care facilities in SSA, particularly hospitals, often serve a large volume of patients, which leads to a long waiting time, overcrowding and loss of patient privacy [83]. The findings therefore suggest a need for decentralisation of ART services to primary health care facilities including prison clinics. Training of health care providers in HIV care provision is pivotal to achieve this, in addition to reinforcing collaboration between prison and community healthcare systems [84].

Our study showed a significant decrease in the odds of adherence in depressed prisoners and in those who lacked social support. Although depression strongly predicts NA in the community-based populations as well [82, 85, 86], ILWHA often feel depressed due to concerns related to imprisonment [38] and HIV infection itself [87]. Global and local studies identified depression as one of the main predictors of NA in prison populations [18, 28, 34]. The positive impact of social support on prisoners' ART adherence and the likely increase in the risk of NA when ILWHA suffer from social isolation is well

recognised [18, 20, 21, 36, 88, 89]. Thus, in addition to enhancing peer support programs in prison settings [18, 20, 21, 36], integration of HIV care and treatment of medically diagnosed depression is likely to be essential for maintaining ART adherence in prisoners.

Among the individual level factors assessed in this study, the ability to comply with a specified medication schedule determined dose adherence in incarcerated and non-incarcerated ART clients. Our study also signified that the type of methods clients used to manage their medication schedule affected dose adherence. For example, dose adherence significantly decreased in clients who used news time on radio/TV or other social cues compared to those who used more direct methods, such as mobile phones and/or wristwatches. Research shows that patients' ability to comply with medication instructions generally increases when they perceive good efficacy and safety of ART [20, 34, 81]. In addition, the use of reminder devices such as telephone reminders, clocks and alarms has been associated with a significant increase in ART adherence [90–92]. Adapting such interventions to prison context and the specific needs of prisoners is required.

In the current study, ILWHA who experienced viral failure had a significantly lower MPR adherence. Prior studies have shown that having NA lessens the likelihood of viral suppression in both prison- [20] and community-based populations [43, 93–95]. However, the current study provided no evidence regarding such a relationship, which might be due to the small number of participants who had developed the clinical outcomes. Nonetheless, people with a higher plasma viral load [96–98] and other disease symptoms [20, 28] often find it challenging to consistently use their medication. This could be related to a high pill burden and potential drug interactions that are likely to occur during the advanced stages of HIV infection due to opportunistic infections [66, 99, 100]. The finding underscores the importance of early HIV treatment for achieving optimal adherence in prisoners.

This study identified a significantly higher likelihood of VF in males, people in the age group of 31 to 35 years and in those who encountered or perceived social stigma, irrespective of their incarceration status. Prior studies also showed higher odds of viral suppression in female prisoners than male prisoners [101]. With limited evidence available regarding the mechanism of how gender influences viral suppression, females often conform better to ART in the community settings [66, 68, 97], which might have also facilitated their adherence during incarceration.

Younger age (below 35 years) has been frequently reported to be associated with a higher risk of NA and VF in both incarcerated [18, 22] and non-incarcerated populations [66–68, 95, 102]. People in this age group are generally more likely to adopt substance misuse behaviours and often encounter social stigma and discrimination [103]. They are also more likely to initiate ART late [104–107], which may lead to subsequent NA and VF [95–98, 108]. Young adult males predominate prison populations in South Ethiopia [109] and around the world [110, 111], and they have a high prevalence of HIV infection compared to other age groups [112, 113]. Group specific HIV care intervention strategies including provision of adequate educational information about HIV and the importance of a consistent use of ART, are highly recommended.

The significant positive association between social stigma and VF in this study may reflect the adverse effect of alienation on a patient's appropriate use of medication [99, 114, 115], which is particularly profound in prison populations [27–30]. Nonetheless, there existed no statistically significant association between social stigma and self-reported or pharmacy refill adherence in this study, which may represent a lower specificity of both methods in detecting adherence relative to plasma viral load measurement [51, 53, 116, 117]. Educational interventions are required to reduce this health related social stigmatisation by improving a general understanding of HIV amongst prison staff and prisoners [118].

This study had a few limitations. Approximately one quarter of correctional facilities present in South Ethiopia were included in the study based on the size of their prison populations. While there was no variation in treatment outcomes based on the type of correctional facility, it is still possible that ILWHA who were in other prisons may have had different outcomes. A nationally representative study is required to draw conclusions that are illustrative of the prison populations in Ethiopia. Given the high turnover amongst prisoners and the high prevalence of sub-optimal ART outcomes in recidivists [119, 120], the prevalence of NA and VF might have been underestimated in incarcerated people. Factors that affect ART outcomes throughout the incarceration cycle (during arrest, stay in jail, stay in prison and after release) should be longitudinally investigated by examining individuals at each stage of incarceration.

The participants' true compliance to medication might have been over- or under-estimated as adherence in this study was measured using self-report and pharmacy refill methods [116, 117]. Self-reported adherence is likely to be threatened by recall and social desirability bias [117]. To minimise the effect of recall bias, short term (the previous four days) adherence was measured so that the participants' memories about doses would be clearer. Strategies that could reduce the participants' perceptions of the possible consequences of reporting adherence or non-adherence (such as reinforcing the importance of reporting both adherence and non-adherence for the research project, and reassurance that the information provided would not affect their care) were used to minimise social desirability bias. The pharmacy refill method of adherence measurement does not guarantee that clients could not obtain drugs from sources other than the reporting pharmacy, or provide information about when and how they take the medication [117]. Nonetheless, public health care facilities in the study area were almost exclusively providing ART services, which might have minimised an oversupply of drugs as only such institutions were involved in this study. In addition, when self-report and pharmacy refill methods are used in conjunction, the weakness of one approach could be offset by the strength of the other [117].

Conclusions

This study revealed that HIV-infected prisoners in South Ethiopia are more likely to be non-adherent to doses and to develop viral failure compared to their non-incarcerated counterparts. Structural, psychosocial, personal and clinical factors contributed to sub-optimal ART outcomes for prisoners. A discouraging institutional context hindered inmates from attending clinic visits, which increased the likelihood of dose-NA. While a lack of satisfaction with ART services predicted dose-NA in both incarcerated and non-incarcerated PLWHA, prisoners were significantly less likely to be satisfied with ART

services provided by external health care facilities. Experience of psychiatric distress and a lack of social support were found to be important psychosocial determinants of adherence in prisoners. Adherence to medication schedules, which itself was strongly influenced by the type of methods used to monitor time, predicted dose-adherence in both populations. Regardless of an incarceration status, males, people in the age group of 31 to 35 years and those who encountered social stigma were more likely to develop viral failure. The findings suggest a need for multilevel interventional approaches that focus on the specific needs of prisoners to alleviate these multiple barriers.

Abbreviations

ART
Antiretroviral therapy; ARV:Antiretroviral; AOR:Adjusted odds ratio; CD4:cluster of differentiation-4; Chi-square (Chi^2); CI:Confidence interval:COR:Crude odds ratio; DOT:Directed observed therapy; ILWHA:Inmates living with HIV; MARPS:Most at risk groups; MCAR:Missing completely at random; MPR:Medication possession ratio; NA:Non-adherence; PAPI:Paper and pencil interviewing; PLWHA:People living with HIV; RHB:Regional Health Bureau; RPHL:Regional Public Health Laboratory; SBREC:Social and Behavioural Research Ethics Committee; SNNPR:Southern Nations, Nationalities and People's Region; SR:Self-report:SSA:sub-Saharan Africa; TV:Television; UNAIDS:The Joint United Nations Programme on HIV/AIDS; USD:United States dollars; VF:Viral failure; WHO:World Health Organization

Declarations

Ethics approval and consent to participate

This study received ethical approvals from Flinders University, Social and Behavioural Research Ethics Committee (SBREC) (Project Number: 8362) and Ethical Review Board of SNNPR Health Bureau. Formal permissions were obtained from the SNNPR State Prison Administration and Regional Health Bureau (RHB), and consent was obtained from each correctional and health care facility authority. All participants gave written consent to confirm voluntary participation.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

TGF conceived and designed the study; supervised data collection; analysed and interpreted data; drafted the manuscript. GT and ERM participated in the subsequent revisions of the manuscript. All authors read and approved the final paper.

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Figures

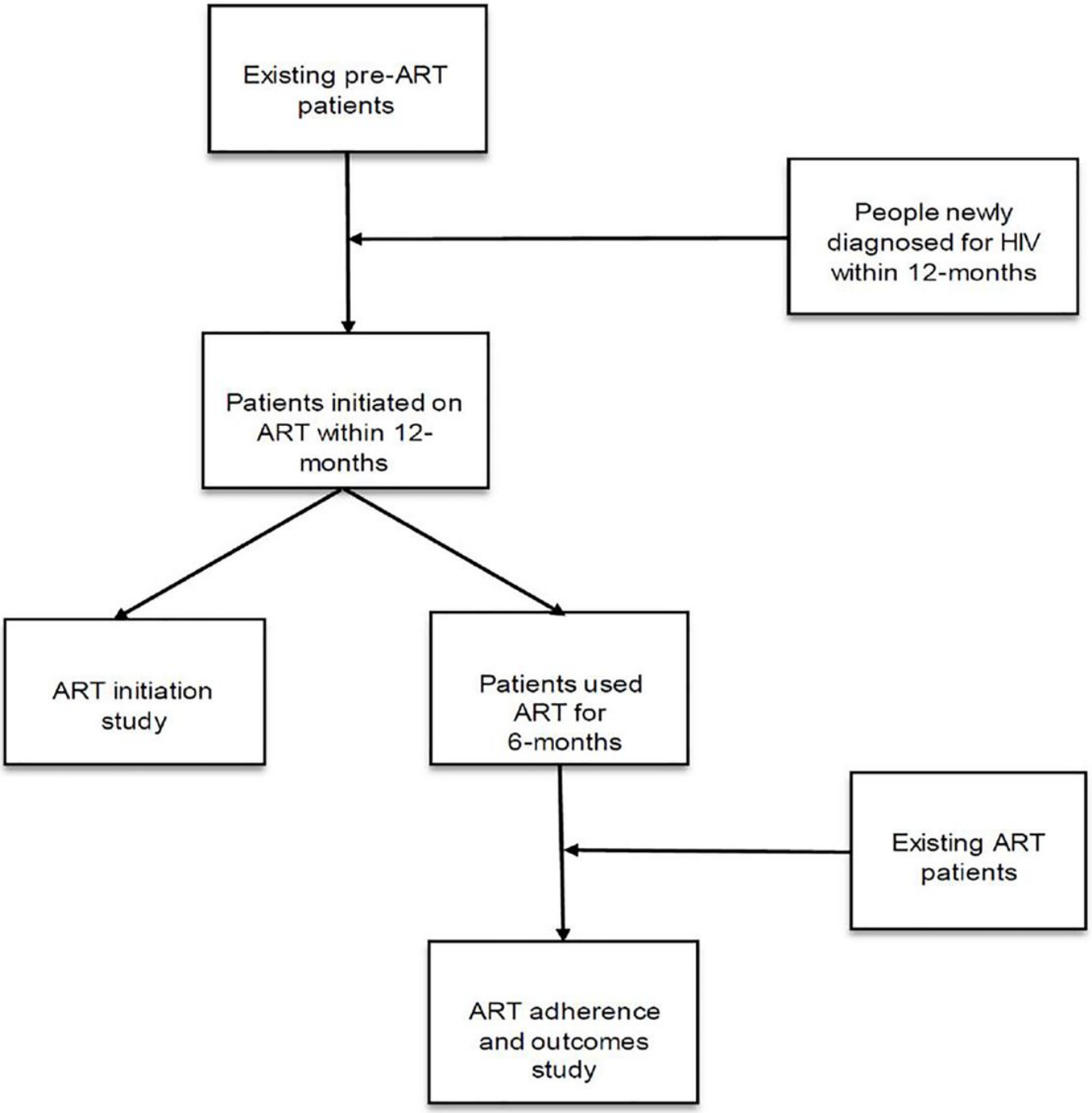

Figure 1

Participant recruitment process

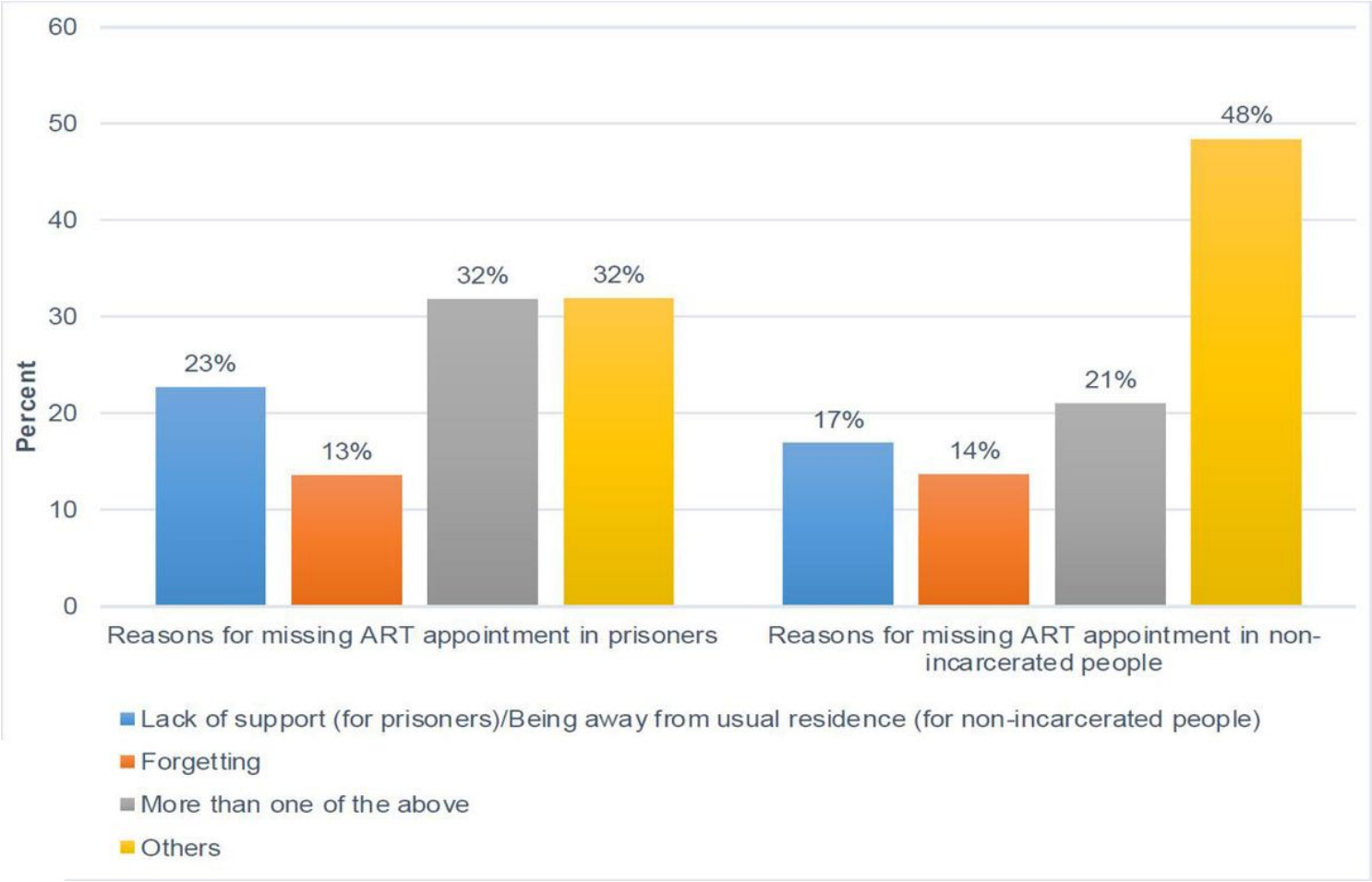

Figure 2

Reasons for missing clinic appointments amongst incarcerated and non-incarcerated antiretroviral therapy clients in South Ethiopia * Reasons reported by non-incarcerated ART clients such as ‘being busy in daily routines’ and ‘a lack of transport’ are included under ‘Others’ category.