

## Factors that determine the level of non-adherence to HAART among HIV-positive pregnant women in Kaduna State

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### Abstract

Despite a decreased trend in the global HIV burden, up to 46% of fresh infections were reported in women and girls in 2022, with sub-Saharan Africa accounting for 70% of cases. One of the reasons HIV remains a major public health threat in Nigeria, the most populous country in Africa, is pregnant women's non-adherence to ART, which can lead to drug resistance resulting in the transmission of the virus to the unborn child. This study was aimed at determining the levels of non-adherence and identifying factors determining non-adherence to ART among HIV-positive pregnant women in Kaduna state.

It was a cross-sectional study using a three-stage sampling technique. It involved 318 HIV-positive pregnant women attending ANC in nine selected hospitals. Electronic questionnaires were administered over 10 weeks. Non-adherence was assessed using four validated techniques. Pill count calculation was used as an indicator of non-adherence for further analysis on account of its documented correlation with better adherence. Bivariate and multivariate analyses were done with Microsoft Excel and Epi Info software.

Levels of non-adherence ranged from 5.7% (3-day recall) to 28.6% (7-day recall) to 6.6% (Visual Analogue Scale) to 13.8% (Pill Count). Of all the factors affecting non-adherence (pill count), having a negative attitude toward ART was significantly associated with non-adherence.

The level of non-adherence, a function of the assessment method, is lower than in most similar studies. We propose that qualified staff should enhance effective ongoing triage-based interventions using a graded baseline assessment to ensure that all HIV-pregnant women on HAART attain optimal adherence.

**Keywords:** Non-adherence; Pill Count; HAART; Mother-to-child transmission; Drug resistance; Nigeria

### 1. Introduction

Despite the decline in the global burden of HIV, it remains a global public health concern having claimed about 40 million lives so far (1,2). With 39 million HIV-infected people globally, sub-Saharan Africa (SSA) accounted for 60% of AIDS-related deaths in 2022, and 70% of new infections (3–6). About 1.2 million women currently live with HIV globally with up to 46% of new infections being in girls and women (7). In Nigeria, women aged 15 – 49 years are two times more likely to be HIV-positive. The north-central geopolitical zone where Kaduna State is located has the second highest prevalence of HIV in Nigeria (2.0%) (8). Women with HIV/AIDS may transmit the infection to their children during

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pregnancy, childbirth, or breastfeeding (9,10). As of 2020, Nigeria was responsible for the highest incidence of HIV in children in the world (11). Although there is currently no cure for HIV or AIDS, the risk of mother-to-child-transmission (MTCT) of HIV may be reduced (to as low as below 1%) by the use of HIV medications known as antiretrovirals, before, during, and after pregnancy, without which, the risk of transmission is 15 – 45% (12). The WHO recorded a decrease in HIV from mother-to-child from an estimated 530,000 children born with HIV in 2000 to 130,000 in 2022 mainly due to intervention with antiretroviral therapy (ART) (13). Adherence to ART goes beyond taking antiretroviral (ARV) medications, it involves positive client's attitude and behaviour towards their health. Suitable choice of ARVs (known as highly active antiretroviral therapy, HAART), counselling, and disease monitoring are all crucial aspects of ART in enhancing and ensuring adherence (14,15).

The employment of ART remains an available avenue offering the possibility of improving the status of people living with HIV/AIDS, ultimately reducing morbidity and mortality. Options recommended by WHO for PMTCT, include the provision of ARVs to mothers and infants during pregnancy, labour, and the post-natal period, and offering life-long treatment to HIV-positive pregnant women regardless of their CD4 count; option B+ (16–19). However, to realize the treatment benefits, strict adherence to treatment instructions is pivotal due to the rapid replication and mutation rates of the virus. The adherence rate of ART must approach and exceed 95% to achieve extended suppression of viral load and enhance CD4+ and T-cell recovery (20,21,21–25). A study conducted in the Southeast geopolitical region of Nigeria reported a 43.8% non-adherence rate among HIV-positive pregnant women due to challenges with transportation and logistics, poor health workers' attitude, and lack of family support (26). Generally, it is a great challenge for patients to maintain strict adherence to treatment therapies, especially in cases of long-term illnesses such as HIV/AIDS. Non-adherence to HAART by pregnant women can lead to (primary or transmitted) drug resistance resulting in limited therapeutic options and subsequent transmission of the infection to others including their offspring (27–32). HIV infection remains a major public health concern in Nigeria, owing to diverse reasons. Kasumu and Boateng posited that adherence to an ART is chiefly influenced by the patient's knowledge and belief about the disease in question as well as its treatment (33,34). Stigma and discrimination, family structure, lack of a support system, educational status, logistics, and geographical location are only a few of the factors previously implicated for non-adherence to ART in pregnant women (35–38). Recent reports indicate that Kaduna State with at least 8000 HIV-positive pregnant women (HIV-positivity in pregnant women of about 2.4%) has up to a minimum of 6000 newborns at risk of HIV transmission (39,40). To achieve the target of eliminating new HIV in sSA and the world by 2030, it is crucial to understand the mechanism of non-adherence in HIV-positive pregnant women (41,42). The study aimed to identify the factors that determine the level of non-adherence and adherence to HAART among pregnant women who are HIV-positive in Kaduna State

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## 2. Methods

### 2.1. Study setting

Kaduna State is a state in the north-west geopolitical zone of Nigeria and its capital is Kaduna. This study was conducted across Kaduna state's three senatorial districts (SDs). Kaduna State has a projected population of 10.4 million people (from the 2006 Population Census) spread across 23 LGAs and 255 wards (43). Kaduna State is Nigeria's twelfth largest state, covering 5% of the country's total land area. Most residents of the state are farmers and/or traders. Nearly two million people live in the two towns of Kaduna and Zaria.

Available data shows that as of 2015, Kaduna State had about 8,707 HIV-positive pregnant women with only 3388 (38.9%) commenced on HAART. This study was hospital-based research in Kaduna State. Although Kaduna State has transitioned from offering PMTCT to eliminating MTCT (eMTCT) services since 2012, only 56% of antenatal care (ANC) facilities offer dedicated eMTCT services as of 2018. Free ART services are offered at these exclusive eMTCT sites (usually part of a comprehensive ART clinic) and the ANC clinics (40) Currently, Kaduna State renders the option B+ services whereby all pregnant HIV-positive clients are commenced on HAART as soon as the baseline investigations are available, and the client is stable, in-between three adherence counselling sessions are carried out (if the client is not already on ART). Also, the child(ren) are commenced on nevirapine prophylaxis for six weeks after birth.

### 2.2. Study design

This was a cross-sectional study of HIV-positive women attending ART clinics in Kaduna State.

### 2.3. Study population

The study population for the survey was the HIV-positive pregnant women attending the ANC and ART clinics.

Inclusion criteria: HIV-positive pregnant women older than 15 years attending clinic (ANC, HAART, eMTCT) for at least three months and have had at least two adherence sessions before HAART's commencement.

Exclusion criteria: HIV-positive pregnant women with debilitating disease or cognitive impairment e.g., comorbidities. Since adherence may be compromised for those with cognitive impairment and immunity further compromised for those with comorbidities (drug-drug interaction for instance), these categories of clients were excluded from the study.

### 2.4. Sample Size Calculation

The sample size was calculated using the *Leslie Fischer* formula.

$$n = \frac{Z\alpha^2 pq}{d^2}$$

p = Proportion of HIV-positive women with non-adherence = 21.7% (44)

q = 1 - p

d = Margin of error/level of precision: 0.05 (5%)

$Z\alpha^2$  = Normal deviate for two-tailed alternative hypothesis at 5% level of significance: 1.96

n = Minimum sample size: 264

Assuming the non-response rate is 10%,

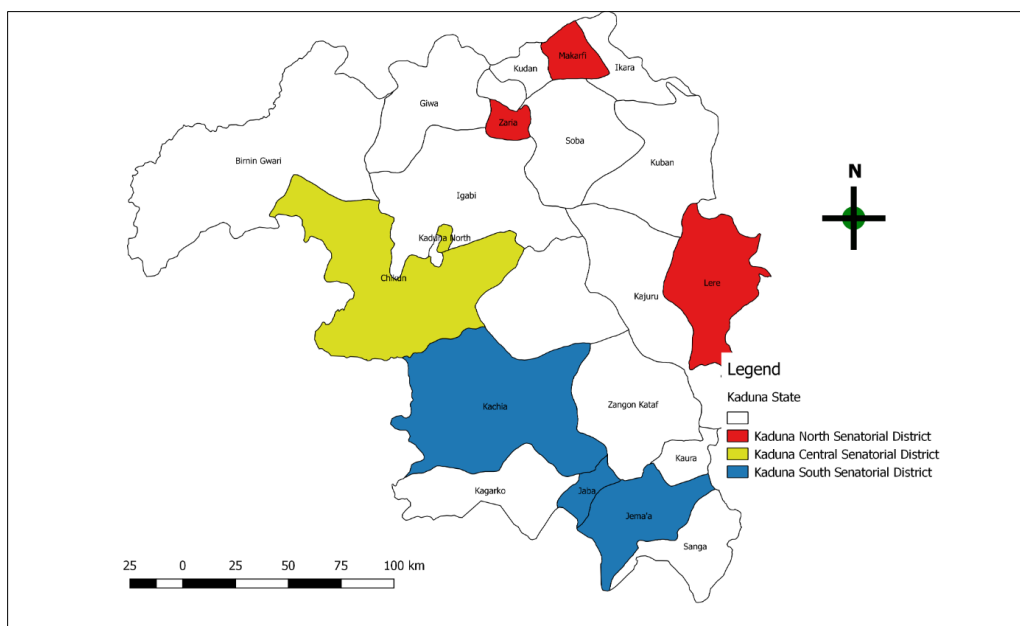
Using the formula

$$n \text{ multiplied by } \frac{1}{1-NR}$$

This brought the minimum sample size to 293.

There was a pretest at Kujama Rural Hospital in Kaduna State (not part of the sample). The tool was standardised from the pretest study. Eventually, data was collected from 318 respondents for higher precision.

### 2.5. Sampling method



**Figure 1** Map of Kaduna State showing the nine LGAs where the study was conducted

A multistage sampling procedure was used: simple random sampling for stages one and two and systematic random sampling for stage three. In stage one, the state stratified into its three senatorial districts (SDs): three local government areas (LGAs) were selected by balloting from each SD giving a total of nine LGAs. In stage two, one health facility (HF) that provides PMTCT services from each LGA was selected at random. Stage three involved systematic random sampling on clinic days via balloting, with proportionate sampling based on weekly attendance. Finally, 318 HIV-positive pregnant women attending clinics were included from the nine selected hospitals over 10 weeks. See Figure 1 for the selected LGAs.

## 2.6. Data collection

The study was carried out in three HFs each from each of the three SDs: making a total of nine HFs. Each hospital rendered HIV counselling and testing HCT/HIV testing services, eMTCT, ART, and treatment of opportunistic infection. A written informed consent was obtained, and patients were interviewed using an interviewer-administered questionnaire (Open Data Kit, ODK). After a pretest to validate instruments at Kujama Rural Hospital, the questionnaire (ODK) was thoroughly reviewed to detect errors. Then, data was collected and processed by cleaning, sorting, and coding of the scores. A coding guide was used to assign the code. The data collected was kept in a secure place to ensure confidentiality.

## 2.7. Data management

Frequencies and percentages were used to describe the characteristics of respondents, logistic regression to identify factors associated with uptake and continuation of ART, and to control for possible confounders. Data was analyzed using Epi Info 7.1 (US-CDC) and SPSS v.27 (IBM) after cleaning with Microsoft Excel 2010.

## 2.8. Scoring system

Tools from the *Development of a Multi-Method Tool to Measure ART Adherence in Resource-Constrained Settings* by USAID were adapted (45). To determine whether there would be differences in distinct means of measurement of adherence, four validated methods were employed: the first was by a 3-day recall and the second was 7-day recalls (self-report). The visual analogue scale is then used, asking respondents to rate their level of adherence over the last four weeks on a scale of zero to ten. Lastly was the *pill count*. This was by calculating the number of pills brought back for a follow-up visit by the client:

Percentage adherence (pill count)

$$\% \text{ Adherence} = \frac{\text{Dispensed} - \text{Returned}}{\text{Expected to be taken}} \times 100$$

Pill count calculation was used as an indicator of non-adherence for further analysis on account of its preferred correlation with better adherence (46–50).

## 2.9. Ethical consideration

Ethical clearance was obtained from Kaduna State Ministry of Health Ethical Review Board (MOH/ADM/744/VOL.1/487) and BDTH Health Research Ethical Committee (Kaduna State University Teaching Hospital with reference number 17-0010).

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## 3. Results

The dominant ethnic groups included Hausa 26.7 % (85), Jabba 11.0 % (35), and Bajju 7.9% (25). The average age of respondents is 31.4 years (SD=5.6). Most respondents are in the 30 – 39-year age range. Most (96.9%) of the respondents were married. None of the 318 respondents smoke cigarettes. However, up to 6.6% of the respondents consume alcohol with 57.1% (12) of them consuming beer, 38.1% (8) taking locally brewed alcohol, and 4.8% (1) consuming spirit. A few of them 18.9 (60%) were on other medications: ranging from antihypertensives to antimalarials, haematinics, anti-Kochs, moringa, and traditional herbs against typhoid and malaria.

**Table 1** Sociodemographic characteristics of HIV-positive pregnant women on HAART in Kaduna State.

n=318

Variable	Frequency	%
Age (years)		
15 - 20	10	3.1
20 - 29	100	31.4
30-39 years	184	57.9
40-49 years	24	7.5
Locality		
Urban	183	57.5
Rural	135	42.5
Education (formal)		
Yes	288	90.6
No	30	9.4
Highest education		
None	21	6.6
Quranic	17	5.4
Primary	98	30.8
Secondary	116	36.4
Tertiary	66	20.8
Currently in school		
Yes	36	11.3
No	281	88.4
Religion		
Christian	214	67.3
Islam	104	32.7
Marital status		
Single	8	2.5
Co-habiting	1	0.3
Married	308	96.9
Separated	1	0.3
Family type		
Monogamous	221	71.3
Polygamous	89	28.7
Alcohol		
Yes	21	6.6
No	297	93.4
Alcohol types		

Spirit	1	4.8
Beer	12	57.1
Locally brewed	8	38.1
Other medications		
Yes	60	18.9
No	258	81.1

The outcome of non-adherence assessment using different validated methods is in Table 2. Non-adherence in the study ranged from 5.7% and 28.6% using three- and seven-day recalls, respectively, to 13.8% employing pill count and 6.6% using a visual analogue scale.

**Table 2** Assessment of non-adherence of HIV-positive pregnant women on HAART in Kaduna State. n=318

Assessment	Frequency	Proportion
7-days recall		
Adherent	227	71.4
Not adherent	91	28.6
3-day assessment		
Not adherent	18	5.7
Adherent	300	94.3
Pill count		
Not adherent	44	13.8
Adherent	274	86.2
Visual Analogue Scale		
Not adherent	21	6.6
Adherent	297	93.4

Table 3 shows some factors affecting non-adherence to ART in HIV-positive pregnant women. Although, religion (Christianity), attitude to ART (poor attitude), and family type (monogamous) were all factors related to non-adherence to ART in HIV-positive pregnant women in Kaduna State, only poor attitude to ART was significantly related to non-adherence (logistic regression: good attitude to ART [aOR= 13.6, CI= 1.6 – 119.7] as a predictor to adherence). Table 4.

**Table 3** Factors related to non-adherence (pill count) to HAART in HIV-positive pregnant women in Kaduna State. n= 318

Variable	Not adherent	Adherent	Chi sq.	p-value
Education (formal)				
Yes	42 (95.4)	246 (89.8)	1.4	0.232
No	2 (4.6)	28 (10.2)		
Currently in school				
Yes	3 (6.8)	33 (12.0)	1.2	0.546
No	41 (93.2)	240 (88.0)		
Religion				

Christian	38 (86.4)	176 (64.2)	8.4	0.004
Islam	6 (13.6)	98 (35.8)		
Married	42 (95.5)	266 (97.1)	1.2	0.761
Family type				
Monogamous	36 (85.7)	185 (69.0)	4.9	0.026
Polygamous	5 (11.9)	75 (28.0)		
Alcohol use				
Yes	3 (6.8)	18 (6.6)	0.0	0.951
No	41 (93.2)	256 (93.4)		
Counselled				
Yes	39 (88.6)	257 (94.8)	8.8	0.117
No	4 (9.1)	11 (4.1)		
Counsel times				
0-1	8 (18.2)	35 (13.1)	0.8	0.361
2-3	36 (81.8)	233 (86.9)		
Support group				
Yes	4 (9.1)	13 (4.8)	1.7	0.422
No	34 (77.3)	228 (84.1)		
Privacy				
Yes	41 (95.3)	260 (97.4)	2.4	0.662
No	2 (4.6)	4 (1.5)		
Attitude to ART				
Poor	2 (5.3)	2 (0.8)	4.9	0.027
Good	36 (94.7)	251 (99.2)		
ARV knowledge				
Poor	2 (4.6)	2 (0.7)	4.4	0.108
Fair	23 (52.3)	150 (54.7)		
Good	19 (43.2)	122 (44.5)		
HIV knowledge				
Poor	-	7 (2.7)	3.1	0.217
Fair	13 (30.9)	54 (20.8)		
Good	29 (69.1)	198 (76.5)		

**Table 4** Logistic regression analysis of predictors of adherence to HAART among HIV-positive pregnant women in Kaduna State. n=318

Variable	OR	aOR	p-value	95% CI
Religion	3.5	2.3	0.182	0.7 – 7.8
Family type	2.7	1.9	0.317	0.5 – 6.7
Attitude to ART	7.0	13.6	0.018	1.6 – 119.7
HIV Knowledge	1.2	0.8	0.667	0.4 – 1.8
ARV Knowledge	1.2	1.6	0.214	0.8 – 3.3

#### 4. Discussion

Non-adherence assessment was measured using four different previously validated means. The reported level of non-adherence reported depends on the method of evaluation. In a systematic review in SSA, the pooled adherence to option B+ ART using various methods was 27.7% (51). The study revealed a non-adherence level of 5.7% via the use of three-day recall, table 2. This is quite lower than those of two cross-sectional studies utilising similar techniques: Iroha et al. in a study in the paediatric age group in a donor-funded clinic at a tertiary hospital that got a non-adherence rate of 14% and that of Ekama, a study among HIV-positive pregnant women in LUTH that got a non-adherence rate of 19.4% (52,53). However, on a regional and global scale, there have been reports of higher levels of non-adherence in this group. Kadima *et al.* reported a three-day non-adherence rate of 7.5% in Lesotho in pregnant HIV-positive women in a prospective cohort study while Yadav et al. in Eastern Nepal got a non-adherence level of 8% (a cross-sectional study in measuring adherence in PLWHA though he used four-day recall) (54,55). Possible reasons for getting a lower adherence rate in this study include: two of these studies were older studies when there were fewer HAART combinations, hence pill burden, as of 2010, access to HAART was not as much as now, also there is more ART awareness now. Using the seven-day recall, the study reported a non-adherence rate of 28.6%. in Bayelsa State, Nigeria involving two tertiary hospitals (2016), with a non-adherence rate of 26.6%, but higher than another study in Tigray, Northern Ethiopia, with a non-adherence rate of 12.9%. Both were conducted on HIV-positive pregnant women using self-report (seven and fourteen days) (56,57). The use of a three-day report results in lower rates of adherence because clients tend to forget over a longer period, leading to recall bias. This trend was noticed in this study with levels of non-adherence using visual analogue scale yielding 6.6% and pill count non-adherence of 13.8%. Two studies that assessed adherence with the use of pill count (the first in PLWHA, the second in HIV-positive women on HAART) got higher non-adherence levels: 41.9% and 56.9% (24,25). Both studies were, however, prospective cohort studies (58,59).

Since pill count calculation has a stronger correlation with adherence, we employed it as an index for further analysis of non-adherence. We found out that of all the factors related to non-adherence to ART (bivariate analysis, logistic regression shows that) poor attitude to ART shows statistically significant result in non-adherence i.e. showing that clients that have a positive attitude to ART are 13 times more likely to adhere to ART, Tables 3 and 4. To have a positive attitude to ART, a client must score  $\geq 50\%$  in ten standardised questions (see supplementary material 1). It has been documented that a negative attitude toward ART is an obstacle to medical adherence (60).

Surprisingly, up to 6.6% of the respondents agree to the use of alcohol and up to 18% make use of other drugs, Table 1. The use of alcohol, moringa, and other herbs, as evident in this study, especially in the first trimester by pregnant women can form the basis for future research in this region. This reveals potential drug-drug interactions that could improve or reduce the efficacy of HAART and result in teratogenicity. More research will be required to understand the relationship between the use of alcohol, and ART in HIV-positive pregnant women in this clime. The respondents using alcohol were however counselled on the possible effects of both alcohol use in pregnancy and the use of alcohol in combination with the use of medications generally (which is alcohol can lead to a decrease in adherence with attendant increased morbidity and mortality) (61). Although the use of alcohol in HIV-positive pregnant women has not been documented locally, it is not unusual in most of the settings. In other locations, in a prospective study carried out in the same study population (HIV-positive pregnant women on ART), up to 11% used alcohol while up to 16% reported the use of alcohol in another group of pregnant women about to be initiated into ART in Cape Town(62,63).

#### Study Limitations

Recall bias for self-report means of measuring non-adherence. This was compensated for using other validated means to measure non-adherence.



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## 5. Conclusion

According to the findings of this study, the level of non-adherence is determined by the evaluation approach. Pill count non-adherence (13.8%) was used as an index for analysis of predictors of non-adherence and it is lower than those found in the literature using the same method. This indicates hope for better PMTCT outcomes, reduced resistance in mothers, and transmitted drug resistance (TDR). We propose a differentiated, client-targeted intervention in Kaduna State at baseline based on identified risk factors for non-adherence. Based on our findings we propose a conceptual framework to screen for factors affecting non-adherence before ART initiation (during counselling). (See Supplementary Material 2 for the framework). These could be scored and graded to classify clients (64,65). Clients identified as having a high risk for non-adherence would benefit from established, tailored support to overcome recognised barriers via the provision of specialised psychological, counselling, additional knowledge, buddy support, use of electronic reminders, etc. on a case-by-case basis.

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## Compliance with ethical standards

### *Acknowledgments*

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### *Disclosure of conflict of interest*

We have no competing interests to declare.

### *Statement of informed consent*

Written informed consent was obtained from all individual participants included in the study.

### *Supporting Information*

The following supplementary information are attached.

- Attitude to ART score
- Conceptual framework for factors affecting non-adherence

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### Supplementary materials

#### 1. Attitude to ART score

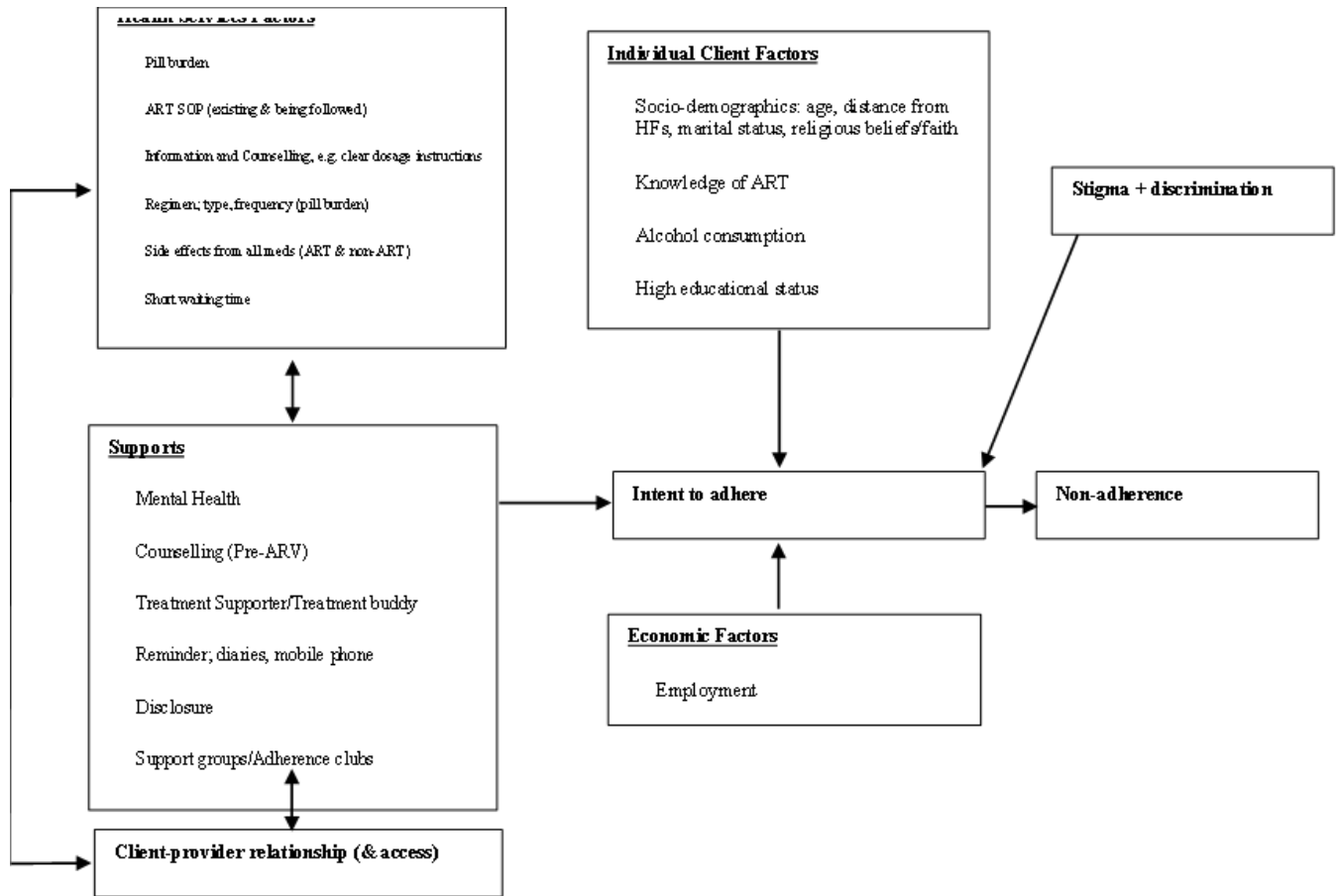
Does ART have a positive effect on health?	Yes	(1)
Does ART have more benefits than harm?	Yes	(1)
Does it reduce frequent sicknesses?	Yes	(1)
Does it assist in fulfilling family obligations?	Yes	(1)
Does it cause fewer financial difficulties?	Yes	(1)
Does it make one forced to take medications?	Yes	(1)
Does it prolong life?	Yes	(1)
Does it help to gain weight or energy?	Yes	(1)
Can its side effects lead to organ failure?	Yes	(1)
Does it enhance the quality of life?	Yes	(1)

The 10 questions, each 10% with

≥ 50% Positive attitude

< 50% Negative attitude

Adapted from Kasumu et al. (66)



2. Conceptual framework for factors affecting non-adherence

Notes: All 18 variables will be scored, and clients will be categorised. There will be an algorithm whereby clients with less than a predetermined proportion (high risk) will be followed up concerning overcoming identified barriers to adherence. This is one of the next steps inferred from this study.