ORIGINAL ARTICLE

Predictors of adherence to antiretroviral therapy among Human Immunodeficiency Virus patients in Jos University Teaching Hospital, Nigeria

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ABSTRACT

Introduction: Sustained optimal adherence to antiretroviral therapy (ART) is required for long-term suppression of viral replication. However, adherence level in Jos, Nigeria has been reported to be below optimal adherence, thus this study investigates the predictors of adherence to antiretroviral therapy among Human Immunodeficiency Virus (HIV) patients there. **Methods:** A validated and pretested questionnaire was used in this cross-sectional study to collect data on sociodemographic characteristics, duration of being on ART, alcohol consumption, presence of symptoms, drug type and disclosure status from 224 randomly selected adult HIV patients. Chi-square and binary logistics regression were used for data analysis. Level of significance was set at 0.05. **Results:** Only 14.3% of the respondents had optimal adherence. Adherence to ART is significantly associated with gender ($p = 0.043$), duration of ART use ($p = 0.041$), alcohol ($p = 0.029$), drug type ($p = 0.001$), and disclosure status ($p = 0.004$). Binary logistics regression reveals that females are 2.4 times more likely to have optimal adherence than males, patients on ART for over 10 years are 2.5 times more likely to have optimal adherence than those less than 10 years, and patients with disclosed HIV status are 3.3 times more likely to have optimal adherence than those who had not. **Conclusion:** Generally, the patients had suboptimal adherence. Being female, having longer duration on ART and disclosure status are predictors for optimal adherence. Intervention with emphasis on males and new patients on ART is recommended to educate on optimal adherence and motivate patients to disclose their status.

Keywords: Predictors, Adherence, Antiretroviral therapy, Human immunodeficiency virus, Patients

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INTRODUCTION

The pandemic of Human Immunodeficiency Virus (HIV) and Acquired Immune Deficiency Syndrome (AIDS) has led to serious health and socioeconomic challenges for more than two decades. Apart from being the second country with the largest HIV epidemic in the world, Nigeria records one of the highest rates of new infections in sub-Saharan Africa (1). The advent of antiretroviral therapy (ART) propelled a significant downturn in HIV-related morbidity and mortality hence, HIV infection is currently managed as a chronic disease (2). The goal of ART is long-term suppression of viral replication and this is one of the principal considerations in lifelong HIV prognosis (3). While the importance of ART is well established and cannot be overemphasized, poor adherence to the regimens is persistent (4). Adherence to medication is defined by the World Health Organization (WHO) as "the degree to which the person's behaviour corresponds with the agreed recommendations from a health care provider." Non adherence to ART amplifies the risk of viral mutations, resulting in cross-resistance to several antiretrovirals or spread of multi resistant virus strains, consequently increasing the probability of treatment failure in subsequent naıve patients (5). Evidence of primary studies revealed how occasionally, good adherence fail to prevent multiplication of antiretroviral resistance mutation, and as such suboptimal adherence is still considered a crucial concern in HIV drug resistance (6). Adherence is essential for a guaranteed effective ART and virological suppression and is considered as the second strongest predictor (after CD4 count) of rapid progression to AIDS (7).

Suboptimal adherence to ART (<95% adherence level) can lead to inadequate suppression of HIV virus and also proliferation of drug-resistant strains of HIV-1 (8), leading to treatment failure, progression of disease, and

risk of disseminating resistant virus strains which chiefly impedes the goal ART. Thus, it is crucial to promote optimal ART adherence and appropriate treatment for maintaining viral suppression which is the goal of successful HIV treatment; as suboptimal adherence in itself is central in causing treatment failure. The World Health Organisation recommends that a minimum of 95% ART adherence which is optimal adherence level, is to be maintained as a prerequisite for successful treatment (9).

Predictors of ART adherence as reported by past studies consist of patient factors which include sociodemographic factors like age, education, income, and social status; type of treatment such as type, number of pills, complexity; characteristics of the disease such as HIV clinical stage, associated signs and symptoms, opportunistic infections associated with the disease; healthcare provider relationship factors such as patient satisfaction, therapeutic relationship, communication; and health facility factors such as accessibility, adherence programme, environment (10–12). Meanwhile common predictors of non-adherence include marital status, alcohol consumption, non-disclosure to family members, cigarette smoking, stigma, forgetfulness, side effects and being away from home (13).

Exploring the predictors of adherence is crucial for designing interventions targeted at improving optimal adherence in the community. In addition to serving as a guide for planning the management of HIV patients, this knowledge could enable health care providers and policy makers to identify barriers against adherence which interfere with treatment success. This could be achieved by designing intervention programs that will address the factors associated with suboptimal adherence, in order to improve adherence to optimal level thus thwarting viral replication and disease progression.

MATERIALS AND METHODS

Study Design and Samples

This was a cross-sectional study involving 224 HIV patients who had viral load greater than 1000 copies/mL and receiving ART at AIDS Prevention Initiative in Nigeria (APIN) clinic of JUTH, Plateau State, Nigeria. This treatment centre is renowned for its provision of clinical services on HIV/AIDS ranging from prevention, care and treatment comprising of free drugs, diagnostics, and clinical services. Sample size calculated 224 was using formula for comparing two means and based on CD4 count variable by a pilot study of food supplementation to improve adherence to antiretroviral therapy among food-insecure adults in Lusaka, Zambia (14). Then simple random sampling was used to select from a list of patients who had viral load above 1000 copies/mL. Inclusion criteria into the study included all HIV positive patients on ART aged 18 years and above, with viral load greater than 1000 copies/mL on ART for at least 6 months, irrespective of CD4 count and yet to undergo enhanced adherence counselling. Patients excluded from the study were non-ambulatory or hospitalised patients, pregnant women, patients restarting their ART due to prior default, patients with psychological disorders, patients with comorbidities, and patients on second-line regimens.

Ethical Clearance

The ethical approval of UPM Ethics committee for human research (JKEUPM) with ref. no UPM/TNCPI/RMC/JKEUPM/1.4.18.2 and the Jos University Teaching Hospital (JUTH) Review and Ethics Committee with ref. no. JUTH/DCS/ADM/127/XXVII/631 were sought for review and approval. The trial was also registered with the Pan African Clinical Trial Registry (PACTR) with ref. no PACTR201811482580522. Written informed consent was also obtained from each respondent before data collection.

Data collection and analysis

Data was collected using The Adult AIDS Clinical Trial Group (AACTG) questionnaire. AACTG was adapted from previous clinical research (15) and it was pretested and revalidated for data collection in this study, with Cronbach $\alpha > 0.7$. Questionnaires were interviewer administered and was obtained from all 224 respondents.

The instrument

The questionnaire contained sub-sections ranging from patient's demographic profile, history of alcohol use, review of symptoms, and questions on the regimens taken.

Patient's demographic profile includes age, gender, residence, occupation, marital status, State of origin, educational level, disclosure status, and duration of known HIV status.

History of alcohol use (past and present) with frequency of alcohol intake in the last 30 days on a 7-point Likert scale was obtained ranging from "Daily", "Nearly Every day", "3 or 4 Times a week", "Once or Twice a week", "2 or 3 Times a month", "Once A Month" and "Never". In the chi-square bivariate analysis, the options "Daily" and "Nearly every day" were categorised as "heavy" alcohol users, "3 or 4 Times a week" and "Once or Twice a week" were categorised as "moderate" alcohol users, "2 or 3 Times a month" and "Once A Month" were categorised as "light" alcohol users, while "never" was classified as "none". For the binary logistics regression model, history of alcohol consumption was later categorised to "low" or "high" alcohol user.

Symptoms the patient experienced in the past four weeks were graded on a 5-point scale ranging from "none" to "I have this symptom" and…"it doesn't bother me", "it bothers me a little", "it bothers me a lot" and "it bothers me terribly" was obtained. It was later categorised to

"yes" or "no".

Data on drug combination, dosage, number of pills each dose, dose per day, and duration on ART was also taken. A '4-day recall of pills missed' with options "Yesterday", "two days ago", "three days ago", and "4 days ago" was obtained.

Self-reported adherence was measured based on a 4-day recall of ART medication taken by the respondent in the last four days. A 4-day recall was used because shorter time frame has been reported to have better potential for more accurate recall. It was calculated by the adapted formula from a previous prospective cohort study on HIV patients (15). Formula is as shown below,

$$\text{Adherence (\%)} = \frac{\text{Total Prescribed pills}_{(30\ \text{days})} - \text{Total pills missed}_{(4\text{days})}}{\text{Total pills Prescribed}_{(30\ \text{days})}} * 100$$

Therefore the adherence of a patient who missed;

(a) 1 day medication is 97%,
(b) 2 days medication is 93%
(c) 3 days medication is 90%
(d) 4 days medication is 87%

Hence, an adherence ≥95% by a respondent is termed "optimal adherence" while adherence <95% is termed "suboptimal adherence".

Content and face validity testing were carried out on the questionnaire and reliability testing on 30 respondents showed Cronbach's alpha ranging from 0.505 to 0.938.

Data Analysis

Data was analysed using Statistical Package for Social Sciences (IBM SPSS) version 25; descriptive analysis was achieved using frequency and percentages, mean and standard deviation, to determine the respondent's characteristics. Bivariate analysis was done using chi-square, in order to determine statistically significant associations between the independent variables and the outcome variable. Multivariate analysis was done using binary logistics regression, to identify predictors of adherence. Level of significance in the preliminary model of simple logistics regression was set at $p<0.25$. Confounders were controlled while adjusting for covariates in the exp. (β) (adjusted odds ratio) from simple logistics regression to multiple logistics regression. Thereafter, all the significant variables were analysed using the 'ENTER' method and the level of significance was set at $p<0.05$.

RESULTS

Distribution of respondents

The results revealed that a majority of the respondents had suboptimal adherence to ART (85.7%) while only 14.3% had optimal adherence (Table I). Furthermore, the mean ART adherence of the respondents is 90.34% (3.315%) implying that the overall ART adherence of the respondents was suboptimal.

Table I: Adherence score and level of ART adherence (N=224)

Variable	n	%	Mean	SD
Adherence score			90.34	3.315
Suboptimal adherence	192	85.7		
Optimal adherence	32	14.3		

Demographic Distribution of the respondents

The findings of this study showed that a majority of the respondents were between the ages of 41 to 50 years (37.9%), more than half were females (59.8%), were urban dwellers (63.8%), and mostly married (67.7%). Furthermore, the results showed that the majority of respondents (48.2%) had been on ART for a longer duration (11-20 years). Also, majority were non-consumers of alcohol (80.8%) while more than half of the respondents (67%) had presence of symptoms. Quite an appreciable proportion (85.7%) were on the AZT/3TC/NVP regimen, and slightly more than half of the respondents (54.5%) had undisclosed HIV status (Table II).

Factors associated with ART adherence

The results in table III show that gender was significantly associated with ART adherence ($p=0.043$); with 17.9% of females having optimal adherence while only 8.9% of males were optimally adherent, implying that females were more optimally adherent than males. The duration on ART was also found to be associated with ART adherence ($p = 0.012$); with 20.4% of those on ART for over 10 years having optimal adherence compared to only 8.6% of those on ART for less than 10 years. Furthermore, alcohol consumption was found to be significantly associated with ART adherence ($p = 0.049$); with 15.8% of low consumers having optimal adherence while no high consumer (0%) was optimally adherent. Similarly, type of regimen was found to be associated with ART adherence ($p = 0.001$); with 26.2% of those on AZT/3TC/NVP regimen being optimally adherent while none (0%) of those on TDF/3TC/EFV was found to have optimal adherence. Disclosure status was significantly associated with ART adherence ($p = 0.004$); with 21.9% of those with disclosed HIV status having optimal adherence while only 7.6% of those with undisclosed HIV status were optimally adherent.

Predictors of ART adherence

Binary logistic regression was done to obtain factors predicting ART adherence in HIV patients. Six variables were included in the preliminary model of simple logistics regression, after which four variables were found to be significant at $p<0.25$, these variables were; gender, presence of symptoms, duration on ART, and HIV disclosure status. Thereafter, all the four variables were analysed using the 'ENTER' method and three variables were found to be significant at $p<0.05$. Multicollinearity

Table II: Characteristics of the respondents (N=224)

Variables	n	%
Age		
20-30	15	6.7
31-40	74	33
41-50	85	37.9
51 above	50	22.3
Gender		
Male	90	40.2
Female	134	59.8
Residence		
Urban	143	63.8
Rural	81	36.2
Occupation		
Student	8	3.6
Civil service	94	42
Business	96	42.9
Unemployment	26	11.6
Marital status		
Single	17	7.6
Married	152	67.9
Divorced	17	7.6
Widowed	38	17
Education		
None	15	6.7
Primary	52	23.2
Secondary	63	28.1
Tertiary	94	42
Duration on ART		
<5 years	41	18.3
5-10 years	75	33.5
11-20 years	108	48.2
Alcohol consumption		
None	181	80.8
Light	22	9.8
Moderate	11	4.9
Heavy	10	4.5
Presence of symptoms		
Yes	150	67
No	74	33
Drug type		
AZT/3TC/NVP	192	85.7
TDF/3TC/EFV	32	14.3
HIV Disclosure status		
Yes	102	45.5
No	122	54.5

Table III: Factors associated with level ART adherence (N=224)

Variables	Level of ART adherence				χ^2	p value
	Optimal		Suboptimal			
	n	%	n	%		
Age					1.276	0.735
20-30	1	6.7	14	93.3		
31-40	11	14.9	63	85.1		
41-50	14	16.5	71	83.5		
51 above	6	12.0	44	88.0		
Gender					3.579	0.043*
Male	8	8.9	82	91.1		
Female	24	17.9	110	82.1		
Residence					0.570	0.352
Urban	19	13.3	124	86.7		
Rural	13	16	68	84		
Occupation					0.933	0.817
Student	2	25	6	75		
Civil service	13	13.8	81	86.2		
Business	14	14.6	82	85.4		
Unemployment	3	11.5	23	88.5		
Marital status					0.934	0.817
Single	2	11.8	15	88.2		
Married	20	13.2	132	86.8		
Divorced	3	17.6	14	82.4		
Widowed	7	18.4	31	81.6		
Education					3.650	0.302
None	1	6.7	14	93.3		
Primary	4	7.7	18	92.3		
Secondary	11	17.5	52	82.5		
Tertiary	16	17	78	83		
Duration on ART					6.306	0.012*
<10 years	10	8.6	106	91.4		
>10 years	22	20.4	86	79.6		
Alcohol consumption					3.862	0.049*
Low	32	15.8	171	84.2		
High	0	0	21	100		
Presence of symptoms					0.164	0.222
Yes	18	12	132	88.0		
No	14	18.9	60	81.1		
Drug type					31.213	0.001*
AZT/3TC/NVP	32	26.2	90	73.8		
TDF/3TC/EFV	0	0	102	100		
HIV Disclosure status					9.370	0.004*
Yes	23	21.9	82	78.1		
No	9	7.6	110	92.4		

Note: (*) – significant $p < 0.05$

was not detected; neither was significant interactions between variables. The model fits the sample as p = 0.382 for Hosmer-Lomeshow. The Negelkerke's R squared showed that only about 16.7% of the variation in optimal adherence to ART is explained by this logistic model. As such, there was likelihood that other predictors of ART adherence other than those included in this study exist. From the results on table IV, it was deduced that females were 2.413 times more likely to have optimal adherence than males, patients taking ART for more than 10 years were 2.537 times more likely to be optimally adherent than those on ART for less than

Table IV: Predictors of ART adherence among HIV positive patients (N=224)

Variable	B	S.E	Wald	df	p value	Exp (B)	95% CI Lower	95% CI Upper
Gender								
Male						1.000		
Female	0.881	0.467	3.564	1	0.049*	2.413	1.007	6.020
Duration on ART								
<10 years						1.000		
>10 years	0.931	0.472	4.752	1	0.029*	2.537	1.099	5.859
Symptoms								
No						1.000		
Yes	-0.395	0.433	0.835	1	0.361	0.673	0.288	1.573
Disclosure status								
No						1.000		
Yes	1.221	0.444	7.581	1	0.006*	3.391	1.422	8.090
Constant	-7.261	1.696	18.329	1	0.001	0.001		

Note: (*) – significant $p < 0.05$

10 years, and patients that had disclosed their HIV status were 3.391 times more likely to be optimally adherent than those with undisclosed HIV status.

DISCUSSION

Adherence to antiretroviral therapy which entails judiciously taking the recommended prescription, was categorised in this study as either optimal (95% and above) or suboptimal (below 95%). According to the findings of this study, adherence level of the respondents was found to be suboptimal. Although treatment-experienced, these respondents had viral load above 1000 copies/mL implying virologic failure. As suggested by previous literature, suboptimal adherence is a major factor contributing to virologic failure and treatment discontinuations (17). Suboptimal adherence was reported to be robustly associated with virologic failure (18) and can take the form of treatment defaulting and treatment interruption, incomplete dosing and inaccurate observance of medication time, frequency and dosage . A defaulter was defined as an HIV positive patient on ART, who had missed one monthly clinic appointment while treatment interruption referred to defaulted patients who have returned to care. Missing appointment schedules has been reported to be associated with missed doses (19), while missing pharmacy refills, missed doses and missed clinic appointment are causes of nonadherence (20). This finding is akin to the findings of some studies (21,22) which reported poor adherence. Contrarily, the findings of a study (22) reported 73.7% of respondents having optimal ART adherence, other studies have also reported a higher optimal adherence (8,24,25). Suboptimal adherence is one of the most common reasons for treatment failure which poses a risk for developing drug resistance through suboptimal viral suppression, with resulting poor health outcomes and increasing healthcare costs (26).

Gender was found to have a significant association with ART adherence in this study, and more females were observed to have optimal adherence (17.9%) than males (8.9%). This is consistent with findings of some studies (27,28), while other studies have reported contrary findings (15,29). The finding of the present study could be attributed to poor health-seeking behaviour in males compared to females (30,31). It is expected that people with good health-seeking behaviour will exhibit good health behaviour such as adherence to regimens and scheduled clinic appointments. This is because, adherence information is sought in the course of health-seeking activities and as knowledge is increased, so to is adherence to regimens. Furthermore, it is reported that health seeking behaviour may lead to an increase in medication self-efficacy thereby leading to adherence (32). In viewing gender from a socio-cultural perspective, it has been asserted that both women and men seek care from informal and formal institutions however, their motives differ which results to dissimilar health-seeking outcomes. While women's role in conserving socio-cultural norms steers them to centre on long discussions with socio-cultural traits which evades social and economic consequences, men on the other hand seek fast and absolute recovery in order to prevent financial pressure (33). Gender in this study was found to be a predictor of optimal adherence in this study, and female patients were two times more likely to have optimal adherence than males.

Furthermore, respondents who had been on ART for a period of more than 10 years were found to have more optimal adherence compared to those who had been on it for a period of less than 10years (8.6%). While an explanation to this could be that patients get accustomed to the medication after a long period of time and integrate it into their daily routine resulting in lifestyle changes; treatment fatigue on the other hand is inextricably linked to ART adherence and is identified as a consequence of long-term regimen (34). However, treatment-experienced patients who have

longer duration on ART are said to have understood the concept of long-term therapies hence present with less suboptimal adherence problems. Patients who have been on ART for a very long time must have had quite appreciable sessions of adherence counselling which increase their knowledge and understanding of ART thus improving adherence. However some studies reported no significant association between duration on ART and adherence to ART (35). Duration on ART was found to be a predictor of optimal adherence in this study, and patients who were on ART for more than 10 years were two times more likely to have optimal adherence than those who were on ART for less than 10 years.

Alcohol consumption was found to be significantly associated with ART adherence in this study. While 15.8% respondents who were low consumers of alcohol were found to have optimal adherence, no high consumer of alcohol recorded optimal adherence. This finding agrees with the findings of other studies (36,37). Alcohol use has been reported to be one of the strongest predictors of non-adherence to ART (38), this is because many HIV patients often use alcohol to cope with perceived stress experienced by most HIV patients (39). Besides interactive toxicity beliefs linked to alcohol consumption while on ART, treatment interruption has been strongly associated with alcohol consumption thus resulting in poor adherence. Heavy drinkers have been reported to have even higher rates of nonadherence. Identifying the cause of the nonadherence among HIV positive alcohol users has been suggested to increase their adherence (40). Additionally, interventions to improve ART adherence and routine counselling sessions in clinics should include alcohol counselling content in their programs according to the level of understanding of each patient.

The type of ART regimen the respondents were taking was found to be significantly associated with ART adherence, a few of those on AZT/3TC/NVP (26.2%) had optimal adherence while those on TDF/3TC/EFV recorded no optimal adherence. While it is a bit unusual for multiple-tablet regimens such as AZT/3TC/NVP to have higher adherence rates than single-tablet regimens such as TDF/3TC/EFV due to pill burden, it is noteworthy to state that pill burden which leads to treatment fatigue may not be a significant reason for non-adherence in treatment-experienced patients. This could be the explanation for the finding of the present study, because the respondents of this study were all treatment-experienced. Furthermore, AZT/3TC/NVP combination was introduced to the clinic before TDF/3TC/EFV combination, which explains why pill burden and treatment fatigue may not affect both groups of patients. It is expected that respondents on AZT/3TC/NVP would be more experienced than those on TDF/3TC/EFV, and would have understood adherence to life-long regimens better thereby incorporating it into their routine. Generally, compared to multiple-tablet regimens, single-tablet regimens have demonstrated higher adherence rates, and improved viral suppression due to their lower pill burdens (41). Nonetheless, most of these findings are reports from studies involving treatment-naïve patients.

Disclosure of HIV status by the respondents was found to be significantly associated with ART adherence, respondents who disclosed their HIV status (21.9%) were more optimally adherent than those who had not disclosed (7.6%). The finding is similar to the findings of other studies (36,42). Disclosure of HIV status by the patient enables patients to seek social support and lessens the burden of self-discrimination and pressure of consistent medication intake. Non-disclosure is reported to be associated with low social support (43), poor adherence rates and depression (42). Some studies on the contrary found no significant association between disclosure status and ART adherence (22). Disclosure status was found to be a predictor of optimal adherence in this study, patients who had disclosed their HIV status were three times more likely to be optimally adherent than patients who had not.

CONCLUSION

The respondents in this study had suboptimal adherence. Factors such as gender, duration on ART, and disclosure status were found to be the predictors of optimal adherence although, alcohol consumption and type of ART were also associated with ART adherence. Interventions to improve optimal adherence is recommended with more emphasis on males, patients starting ART and patients with undisclosed HIV status. Interventions to address the needs of male patients related to ART adherence is requisite to improve optimal adherence.

In addition, theory-based interventions such as the information-motivation-behavioural skills (IMB) model intervention should be designed and implemented for improving ART adherence. The behavioural skills content of the IMB-based intervention should be targeted at treatment-naïve patients in order to prevent any future occurrence of treatment failure. Behavioural skills related to ART adherence will include incorporating medication schedule into activities of daily living, utilizing reminder cues such as pill boxes, medication diaries and associating meal times with medication timing.

Furthermore, the motivation content of the IMB-based intervention will address the attitude and beliefs of patients relating to HIV as well as dispelling negative social norms regarding HIV. This will include counselling patients to allay any fear of discrimination and stigmatization. In addition, this will encourage patients to disclose their status and improve patient-social support relationship and participation, thereby

improving optimal adherence. Lastly, other determinants of ART adherence which were not included in this study should be further researched.

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REFERENCES

1. UNAIDS 'AIDSinfo' [Accessed October 2018] https://www.avert.org/professionals/hiv-around-world/sub-saharan-africa/nigeria
2. Deeks SG, Lewin SR, Havlir DV. The end of AIDS: HIV infection as a chronic disease. The Lancet. 2013 Nov 2;382(9903):1525-33. DOI:10.1016/S0140-6736(13)61809-7
3. Meintjes G, Moorhouse MA, Carmona S, Davies N, Dlamini S, Van Vuuren C, Manzini T, Mathe M, Moosa Y, Nash J, Nel J. Adult antiretroviral therapy guidelines 2017. Southern African journal of HIV medicine. 2017;18(1). DOI: 10.4102/sajhivmed.v18i1.776
4. Huang L, Li L, Zhang Y, Li H, Li X, Wang H. Self-efficacy, medication adherence, and quality of life among people living with HIV in Hunan Province of China: a questionnaire survey. Journal of the Association of Nurses in AIDS Care. 2013 Mar 1;24(2):145-53. DOI:10.1016/j.jana.2012.04.006
5. Johnston V, Cohen K, Wiesner L, Morris L, Ledwaba J, Fielding KL, Charalambous S, Churchyard G, Phillips A, Grant AD. Viral suppression following switch to second-line antiretroviral therapy: associations with nucleoside reverse transcriptase inhibitor resistance and subtherapeutic drug concentrations prior to switch. The Journal of infectious diseases. 2013 Aug 13;209(5):711-20. DOI: https://doi.org/10.1093/infdis/jit41
6. Schultze AT. The Epidemiology and Consequences of HIV Drug Resistance: Analyses of resistance data from European cohort studies (Doctoral dissertation, UCL (University College London)) 2017.
7. Basti BD, Mahesh V, Bant DD, Bathija GV. Factors affecting antiretroviral treatment adherence among people living with human immunodeficiency virus/acquired immunodeficiency syndrome: A prospective study. Journal of family medicine and primary care. 2017 Jul;6(3):482. DOI: 10.4103/2249-4863.222014
8. Bezabhe WM, Chalmers L, Bereznicki LR, Peterson GM. Adherence to antiretroviral therapy and virologic failure: a meta-analysis. Medicine. 2016 Apr;95(15). DOI:10.1097/MD.0000000000003361
9. Hardon A, Davey S, Gerrits T, Hodgkin C, Irunde H, Kgatlwane J, Kinsman J, Nakiyemba A, Laing R, World Health Organization. From access to adherence: The challenges of antiretroviral treatment: Studies from Botswana, Tanzania and Uganda 2006. http://archives.who.int/prduc2004/Book/MULTICOUNTRY.pdf
10. Ahmed S, Autrey J, Katz IT, Fox MP, Rosen S, Onoya D, BΔrnighausen T, Mayer KH, Bor J. Why do people living with HIV not initiate treatment? A systematic review of qualitative evidence from low- and middle-income countries. Social Science & Medicine. 2018 Sep 1;213:72-84. DOI: 10.1016/j.socscimed.2018.05.048
11. Shigdel R, Klouman E, Bhandari A, Ahmed LA. Factors associated with adherence to antiretroviral therapy in HIV-infected patients in Kathmandu District, Nepal. HIV/AIDS (Auckland, NZ). 2014;6:109. DOI:10.2147/HIV.S55816
12. Suleiman IA, Momo A. Adherence to antiretroviral therapy and its determinants among persons living with HIV/AIDS in Bayelsa state, Nigeria. Pharmacy Practice (Granada). 2016 Mar;14(1):0-0. DOI:10.18549/PharmPract.2016.01.631
13. Adeniyi OV, Ajayi AI, Ter Goon D, Owolabi EO, Eboh A, Lambert J. Factors affecting adherence to antiretroviral therapy among pregnant women in the Eastern Cape, South Africa. BMC infectious diseases. 2018 Dec;18(1):175. DOI:10.1186/s12879-018-3087-8
14. Cantrell RA, Sinkala M, Megazinni K, Lawson-Marriott S, Washington S, Chi BH. et al. A pilot study of food supplementation to improve adherence to antiretroviral therapy among food-insecure adults in Lusaka, Zambia. Journal of acquired immune deficiency syndromes (1999), 2008) 49(2), 190–195. doi:10.1097/QAI.0b013e31818455d2).
15. Chesney MA, Ickovics JR, Chambers DB, Gifford AL, Neidig J, Zwickl B, Wu AW, Patient Care Committee & Adherence Working Group of the Outcomes Committee of the Adult AIDS Clinical Trials Group (AACTG). Self-reported adherence to antiretroviral medications among participants in HIV clinical trials: the AACTG adherence instruments. AIDS care. 2000 Jun 1;12(3):255-66.
16. Olowookere SA, Fatiregun AA, Ladipo MM, Abioye-Kuteyi EA, Adewole IF. Effects of adherence to antiretroviral therapy on body mass index, immunological and virological status of Nigerians living with HIV/AIDS. Alexandria Journal of Medicine. 2016;52(1):51-4.
17. McCluskey SM, Musinguzi N, Haberer JE, Martin JN, Hunt PW, Marconi VC, Bangsberg DR, Siedner MJ. Brief Report: Appraising Viral Load Thresholds and Adherence Support Recommendations in the World Health Organization Guidelines for Detection and Management of Virologic Failure. Journal of acquired immune deficiency syndromes

(1999). 2017 Oct;76(2):183-7.
18. Das M, Angeli F, Krumeich AJ, van Schayck OC. The gendered experience with respect to health-seeking behaviour in an urban slum of Kolkata, India. International journal for equity in health. 2018 Dec;17(1):24.
19. Shumba C, Atuhaire L, Imakit R, Atukunda R, Memiah P. Missed doses and missed appointments: adherence to ART among adult patients in Uganda. ISRN AIDS. 2013 Jan 14;2013.
20. Mills EJ, Nachega JB, Buchan I, Orbinski J, Attaran A, Singh S, Rachlis B, Wu P, Cooper C, Thabane L, Wilson K. Adherence to antiretroviral therapy in sub-Saharan Africa and North America: a meta-analysis. Jama. 2006 Aug 9;296(6):679-90.
21. Cauldbeck MB, O'Connor C, O'Connor MB, Saunders JA, Rao B, Mallesh VG, Kumar NK, Mamtha G, McGoldrick C, Laing RB, Satish KS. Adherence to anti-retroviral therapy among HIV patients in Bangalore, India. AIDS research and therapy. 2009 Dec;6(1):7. DOI: 10.1186/1742-6405-6-7
22. Obirikorang C, Selleh PK, Abledu JK, Fofie CO. Predictors of adherence to antiretroviral therapy among HIV/AIDS patients in the upper west region of Ghana. Isrn Aids. 2013 Dec 10;2013. http://dx.doi.org/10.1155/2013/873939
23. Pasternak AO, De Bruin M, Bakker M, Berkhout B, Prins JM. High current CD4+ T cell count predicts suboptimal adherence to antiretroviral therapy. PloS one. 2015 Oct 15;10(10):e0140791. https://doi.org/10.1371/journal.pone.0140791
24. Do HM, Dunne MP, Kato M, Pham CV, Nguyen KV. Factors associated with suboptimal adherence to antiretroviral therapy in Viet Nam: a cross-sectional study using audio computer-assisted self-interview (ACASI). BMC Infectious Diseases. 2013 Dec;13(1):154. DOI:10.1186/1471-2334-13-154
25. Siefried KJ, Mao L, Kerr S, Cysique LA, Gates TM, McAllister J, Maynard A, de Wit J, Carr A, PAART study investigators. Socioeconomic factors explain suboptimal adherence to antiretroviral therapy among HIV-infected Australian adults with viral suppression. PLoS One. 2017 Apr 3;12(4):e0174613. https://doi.org/10.1371/journal.pone.0174613
26. Heestermans T, Browne JL, Aitken SC, Vervoort SC, Klipstein-Grobusch K. Determinants of adherence to antiretroviral therapy among HIV-positive adults in sub-Saharan Africa: a systematic review. BMJ global health. 2016 Dec 1;1(4):e000125. http://dx.doi.org/10.1136/bmjgh-2016-000125
27. Maqutu D, Zewotir T, North D, Naidoo K, Grobler A. Determinants of optimal adherence over time to antiretroviral therapy amongst HIV positive adults in South Africa: a longitudinal study. AIDS and Behavior. 2011 Oct 1;15(7):1465-74. DOI: 10.1080/09540121.2011.565028
28. Wasti SP, Simkhada P, Randall J, Freeman JV, Van Teijlingen E. Factors influencing adherence to antiretroviral treatment in Nepal: a mixed-methods study. PloS one. 2012 May 1;7(5):e35547. https://doi.org/10.1371/journal.pone.0035547
29. Tapp C, Milloy MJ, Kerr T, Zhang R, Guillemi S, Hogg RS, Montaner J, Wood E. Female gender predicts lower access and adherence to antiretroviral therapy in a setting of free healthcare. BMC infectious diseases. 2011 Dec;11(1):86. https://doi.org/10.1186/1471-2334-11-86
30. Thompson AE, Anisimowicz Y, Miedema B, Hogg W, Wodchis WP, Aubrey-Bassler K. The influence of gender and other patient characteristics on health care-seeking behaviour: a QUALICOPC study. BMC family practice. 2016 Dec;17(1):38.
31. Wang Y, Hunt K, Nazareth I, et al. Do men consult less than women? An analysis of routinely collected UK general practice data. BMJ Open 2013; 3:e003320.doi: 10.1136/bmjopen-2013-003320
32. Samal L, Saha S, Chander G, Korthuis PT, Sharma RK, Sharp V, Cohn J, Moore RD, Beach MC. Internet health information seeking behavior and antiretroviral adherence in persons living with HIV/AIDS. AIDS Patient Care and STDs. 2011 Jul 1;25(7):445-9.
33. Das M, Angeli F, Krumeich AJ, van Schayck OC. The gendered experience with respect to health-seeking behaviour in an urban slum of Kolkata, India. International journal for equity in health. 2018 Dec;17(1):24.
34. Claborn KR, Meier E, Miller MB, Leffingwell TR. A systematic review of treatment fatigue among HIV-infected patients prescribed antiretroviral therapy. Psychology, health & medicine. 2015 Apr 3;20(3):255-65. https://doi.org/10.1080/13548506.2014.945601
35. Okafor UB. Antiretroviral Treatment Adherence Among Patients in Selected Health Facilities in East London, South Africa: A Cross-Sectional Study. Online Journal of Health and Allied Sciences. 2018 Jul 25;17(2). https://www.ojhas.org/issue66/2018-2-1.html
36. Yaya I, Landoh DE, Saka B, Wasswa P, Aboubakari AS, N'Dri MK, Patassi AA, Kombatй K, Pitche P. Predictors of adherence to antiretroviral therapy among people living with HIV and AIDS at the regional hospital of Sokodй, Togo. BMC public health. 2014 Dec;14(1):1308. DOI:10.1186/1471-2458-14-1308
37. Sileo KM, Simbayi LC, Abrams A, Cloete A, Kiene SM. The role of alcohol use in antiretroviral adherence among individuals living with HIV in South Africa: Event-level findings from a daily diary study. Drug and alcohol dependence. 2016 Oct 1;167:103-11. DOI:10.1016/j.drugalcdep.2016.07.028
38. Shubber Z, Mills EJ, Nachega JB, Vreeman R, Freitas M, Bock P, Nsanzimana S, Penazzato M, Appolo T, Doherty M, Ford N. Patient-reported barriers to adherence to antiretroviral therapy: a systematic

review and meta-analysis. PLoS medicine. 2016 Nov 29;13(11):e1002183. https://doi.org/10.1371/journal.pmed.1002183
39. Kalichman SC, Amaral CM, White D, Swetsze C, Kalichman MO, Cherry C, Eaton L. Alcohol and adherence to antiretroviral medications: interactive toxicity beliefs among people living with HIV. Journal of the Association of Nurses in AIDS Care. 2012 Nov 1;23(6):511-20. https://doi.org/10.1016/j.jana.2011.11.005
40. Kim JY, Yang Y, Kim HK. The Impact of Alcohol Use on Antiretroviral Therapy Adherence in Koreans Living with HIV. Asian nursing research. 2018 Dec 1;12(4):258-64. https://doi.org/10.1016/j.anr.2018.10.002
41. Sutton SS, Ahuja D, Magagnoli J. What is the effect of pill burden on adherence to HIV antiretroviral therapy?. Journal of the American Academy of PAs. 2016 Nov 1;29(11):16-7. doi: 10.1097/01.JAA.0000502870.89587.b6
42. Yu Y, Luo D, Chen X, Huang Z, Wang M, Xiao S. Medication adherence to antiretroviral therapy among newly treated people living with HIV. BMC public health. 2018 Dec;18(1):825. doi: 10.1186/s12889-018-5731-z
43. Pichon L, Rossi K, Ogg S, Krull L, Griffin D. Social support, stigma and disclosure: Examining the relationship with HIV medication adherence among Ryan White Program clients in the Mid-South USA. International journal of environmental research and public health. 2015 Jun;12(6):7073-84. https://doi.org/10.3390/ijerph120607073