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ORIGINAL PAPER

Including the Household: Individual, Community and Household Factors Affecting Antiretroviral Therapy Adherence After ART Initiation in Cape Town, South Africa

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Abstract

Antiretroviral therapy (ART) adherence is crucial for health outcomes of people living with HIV (PLHIV), influenced by a complex interplay of individual, community, and household factors. This article focuses on the influence of household factors, as well as individual and community factors, on ART adherence among PLHIV in Cape Town who have recently initiated ART. Baseline data for a cluster-randomized controlled trial were collected from 316 PLHIV in 12 districts in Cape Town between 6th May 2021 and 22nd May 2022. Zero-inflated Poisson models, with cluster-adjusted standard errors, were used to analyse the association between individual, household, and community factors and ART adherence measures. At the household-level, household support was associated with both better self-rated adherence ($\exp(\beta) = 0.81$, $z = -4.68$, $p < 0.001$) and fewer days when pills were missed ($\exp(\beta) = 0.65$, $z = -2.92$, $p = 0.003$). Psychological violence ($\exp(\beta) = 1.37$, $z = 1.97$, $p = 0.05$) and higher household asset scores ($\exp(\beta) = 1.29$, $z = -2.83$, $p = 0.05$) were weakly associated with poorer ART adherence. At the individual-level, male gender ($\exp(\beta) = 1.37$, $z = 3.95$, $p < 0.001$) and reinitiating ART ($\exp(\beta) = 1.35$, $z = 3.64$, $p < 0.001$) were associated with worse self-rated ART adherence; higher education levels ($\exp(\beta) = 0.30$ times, $z = -3.75$, $p < 0.001$) and better HIV knowledge ($\exp(\beta) = 0.28$, $z = -2.83$, $p = 0.005$) were associated with fewer days where pills were missed. At the community-level, community stigma was associated with worse self-rated ART adherence ($\exp(\beta) = 1.24$, $z = 3.01$, $p = 0.003$). When designing interventions to improve ART adherence, household, individual and community factors should all be considered, particularly in addressing gender-based disparities, reducing stigma, tackling violence, and enhancing household support.

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Keywords HIV · ART · Adherence · Household · South Africa

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Resumen

La adherencia a la terapia antirretroviral (TAR) es crucial para los resultados de salud de las personas que viven con el VIH (PLHIV), influenciada por una compleja interacción de factores individuales, comunitarios y del hogar. Este artículo se centra en la influencia de los factores del hogar, individuales y comunitarios en la adherencia al TAR entre personas que iniciaron recientemente el TAR en Ciudad del Cabo. Se recopilaron datos de referencia para un ensayo de control aleatorio por grupos de 316 PLHIV en 12 distritos de Ciudad del Cabo entre el 6 de mayo de 2021 y el 22 de mayo de 2022. Se utilizaron modelos de Poisson inflados a cero, con errores estándar ajustados por conglomerado para estudiar la asociación entre factores individuales, del hogar o comunitarios con dos medidas de adhesión al TAR: por un lado la auto declaración de adhesión, y por otro la cantidad de días en que se olvidó de tomar la medicina en los últimos 4 días. A nivel del hogar, el apoyo del hogar se asoció con una mejor adherencia auto declarada ($\exp(\beta) = 0.81$, $z = -4.68$, $p < 0.001$) y menos días en los que se omitió la medicina ($\exp(\beta) = 0.65$, $z = -2.92$, $p = 0.003$). La violencia psicológica ($\exp(\beta) = 1.37$, $z = 1.97$, $p = 0.05$) y las puntuaciones más altas de activos del hogar ($\exp(\beta) = 1.29$, $z = -2.83$, $p = 0.05$) se asociaron con una peor adherencia al TAR. A nivel individual, el sexo masculino ($\exp(\beta) = 1.37$, $z = 3.95$, $p < 0.001$) y el reinicio del TAR ($\exp(\beta) = 1.35$, $z = 3.64$, $p < 0.001$) se asociaron con una peor adherencia al TAR autodeclarada; niveles de educación más altos ($\exp(\beta) = 0.30$ times, $z = -3.75$, $p < 0.001$) y un mejor conocimiento sobre el VIH ($\exp(\beta) = 0.28$, $z = -2.83$, $p = 0.005$) se asociaron con menos días en los que se omitió la medicina. A nivel comunitario, el estigma comunitario se asoció con una peor autodelaración de adhesión del TAR ($\exp(\beta) = 1.24$, $z = 3.01$, $p = 0.003$). Para mejorar la adherencia al TAR, se deben tener en cuenta los factores del hogar, así como los individuales y comunitarios, particularmente al abordar las disparidades de género, reducir el estigma, abordar la violencia y mejorar el apoyo del hogar.

Abbreviations

ACTG	AIDS Clinical trials group
AIC	Akaike information criterion
ART	Antiretroviral therapy
BIC	Bayesian information criterion
CI	Confidence interval
CFA	Confirmatory factor analysis
CHW	Community health workers
DHS	Demographic health survey
HIV	Human immune deficiency virus
ICC	Intracluster correlation coefficient
MCA	Multiple correspondence analysis
PLHIV	People living with HIV
SES	Socio-economic status
UNAIDS	The Joint United Nations Programme on HIV/AIDS
UTT	Universal Test and Treat
WHO	World Health Organization
WLSMV	Weighted least square mean and variance adjusted

Introduction

Following the 2015 recommendations of the World Health Organisation (WHO), South Africa adopted a Universal Test and Treat (UTT) strategy in 2016: UTT strategies aim to maximise the impact of HIV treatment and prevention by promoting ART initiation rapidly after diagnosis, regardless of CD4 count [1, 2]. By initiating ART as soon as possible, viral suppression may be achieved more rapidly, thereby improving health outcomes and reducing transmission risk for a greater period of time than if ART were introduced at a later stage [2]. As a nation with the largest population of people living with HIV (PLHIV) globally, an estimated 5.7 million PLHIV were therefore receiving antiretroviral therapy (ART) by 2022 in South Africa [2–5].

Simply initiating ART is not enough, however: consistent adherence—commonly defined at ≥ 95%—is crucial [6–11]. Adhering to ART suppresses replication of HIV, thereby lowering viral load and decreasing the likelihood of onward transmission [12–14]. ART adherence may also prevent the development of drug resistance, ensuring that medications remain effective over time [15]. Importantly, ART adherence shortly after initiation has been indicated to predict long-term adherence and virological suppression [16, 17]. Ensuring good ART adherence at therapy initiation is, therefore, a vital component of UTT and key for achieving long-term public health goals for HIV, notably the 95-95-95 goals to end HIV as a global public health threat by 2030 [18–20]. It is therefore important to gain comprehensive insights into the determinants influencing early ART adherence.

Drawing on insights from the socio-ecological model, it is evident that factors affecting ART adherence at initiation span individual, interpersonal, community, and structural levels, involving multiple interrelated levels of influence [21, 22]. Factors previously identified at the individual-level include adequate knowledge of HIV and ART, adapting to the complexity of medication regimes, adhering to timing and dietary requirements, and managing a range of ART side effects [23–28]. Interpersonal factors include

intimate partner violence, or social and household support [23, 29–37]. The community-level is defined by the physical and social environments where social relationships occur; the elements influencing ART adherence at this level may include factors such as community stigma, neighbourhood poverty, or the presence of health services [37–41]. Structural factors include health system issues, such as laws, policies, transport and access to care [34, 37–41].

While interpersonal factors such as social support are widely documented, the impact of the micro-social environment of the household on the health of PLHIV has long been neglected in HIV research, a research gap signalled by the individual-family-community (IFC) model, which underlined the importance of this intermediate level (between individual and community levels) in maintaining high levels of ART adherence [42]. The household is increasingly recognised as a complex system of interpersonal relationships that can either support or undercut ART adherence [25, 43–45]. Extending the concept developed by Campbell et al. [46] of an AIDS competent community to that of the household, Masquillier et al. [47] state that AIDS competent households can foster health-enhancing practices and thereby offer a "context in which more effective HIV/AIDS management is possible by making prevention and treatment part of daily life in the household" [47]. Household environments that are not supportive, or are stigmatising, may hamper ART adherence. Research into the role of the household as micro-social environment in ART adherence is therefore a clear research priority.

Household factors cannot, however, be explored in isolation from those at individual and community levels. To support policy makers and health professionals in their efforts to assist PLHIV, greater understanding is needed of the household, individual and community factors linked with ART adherence at ART initiation. This article therefore examines the individual, community and household factors associated with ART adherence in a sample of PLHIV who have recently initiated ART in Cape Town, South Africa.

Methods

Study Design and Ethics

This study used baseline data from trial participants of "SINAKO" ('we can' in isiXhosa), a cluster-randomised controlled trial based in the Cape Metro area, South Africa. Fieldworkers interviewed 316 PLHIV from 12 clinics (136 PLHIV assigned to the control arm, 180 PLHIV assigned to the intervention arm) in English, Afrikaans and isiXhosa between 6th May 2021 and 22nd May 2022, during which time the country moved between the government's COVID-19 adjusted alert level 1 to level 4, before returning to level 1 [48]. The trial protocol specified a sample size of 180 individuals per arm, obtained by sampling 12 clusters in total with 90% power (to ascertain an increase in ART adherence from 68 to 83% over a period of 12 months): the full trial protocol has been detailed elsewhere [49]. PLHIV are enrolled in the trial via their health facility: a standard ART adherence support service is delivered in both trial arms, with the addition of the SINAKO intervention in the intervention arm. The SINAKO intervention is delivered by community health workers (CHWs) during monthly visits, either at the health facility or in the home of the PLHIV. CHWs are linked to health facilities: twelve facilities were therefore randomly selected, stratified on size of clinic (small and large), resulting in six facilities per trial arm.

The study was approved by the ethics committee of the University of the Western Cape (BM19/4/6, June 2019) and the ethical committee for the Social Sciences and Humanities of the University of Antwerp (SHW_17_64, September 2018). The City of Cape Town and the Western Cape Department of Health granted permission for all facilities by December 2019.[1] All participants provided written informed consent at baseline in their chosen language. Participants were informed that they would receive a shopping voucher following participation at baseline and endline.

Measures

Given that there is no single optimal measure of ART adherence, and self-report measures may be subject to recall bias and social desirability bias, a common recommendation is to use multiple measures when assessing adherence [50]. Furthermore, adherence is a multi-dimensional concept, and different measures may therefore capture different aspects of adherence behaviour [51]. Adherence was therefore analysed using two self-reported measures from the extensively used Adult AIDS Clinical Trials Group (ACTG) Adherence Follow Up Questionnaire [52, 53]: (1) adherence rated out of 10 over the past month (hereafter: "self-rated adherence"), and (2) the number of days in the last 4 days that the patient did not take the full complement of their medication (hereafter: "number of days of missed pills") [54]. Self-rated adherence responses ranged between 0 and 10 in answer to the question "If 0 would mean you take no pills and 10 means you take all your pills correctly, how would you rate your ART adherence in the past month?" To facilitate analysis, self-rated adherence was reversed so that 0 counted as best rated adherence, and 10 counted as worst-rated adherence [55]. The variable 'number of days of missed pills' ranged

[1] Ethical approval was updated for follow-up interviews during the COVID-19 pandemic (SHW_17_64 (wijziging), BM19/4/6, August 2020).

between 0 and 4 days in response to the question "During the past 4 days, on how many days have you missed taking ALL of your doses?" Viral load data was unavailable to measure adherence for this study.

Individual-level variables included important socio-demographic characteristics such as age (standardised), education level, and "what gender do you identify as". Individual-level characteristics also included HIV knowledge and ART (re-)initiation status which were indicated to be important factors in other studies [23, 56, 57]. Education level was recoded into a binary variable, the first category incorporating participants whose education level ranged from 'no education' to having completed 'some secondary education'; the second category incorporated those who had completed their matric (the qualification received upon completing high school) and those who had completed a degree. ART (re-)initiation status reflected whether the patient was beginning ART for the first time or had previously been on an ART regime, and was included as a binary variable (yes/no). HIV knowledge was measured using the average scores from seven questions related to HIV knowledge previously used in a cluster randomised controlled trial in the Free State Province of South Africa (see Supplementary Materials, Table S1) [58]. Possible responses include "Yes/No/Don't know"; higher average scores indicate better levels of knowledge. Distress from ART side effects was measured using standardised sum scores of nine questions from the ACTG adherence questionnaire, asking about how much PLHIV were bothered by e.g., headaches, muscle pains, fatigue, etc. [54]. Response options encompassed a five-point Likert scale ranging from "I do not have this symptom", "It doesn't bother me" to "It bothers me terribly" (see Supplementary Materials, Table S2). Higher scores indicated higher levels of distress from experiencing side effects.

Household-level variables included household social support, household asset index scores, and household violence [23, 56]. For household social support, 19 questions were drawn from the Medical Outcomes Study (MOS) social support survey [59, 60] and adapted to the household context, e.g., "How often is someone in your household available who shows you love and affection?" Response options were comprised of a five-point Likert scale ranging from "None of the time" to "All of the time" (see Supplementary Materials, Table S3). Average scores for the 19 variables were used to generate a household social support variable, with higher scores reflecting better support.

In order to assess the socio-economic status of households, an asset index was constructed following Booysen et al. [61]. Multiple correspondence analysis (MCA) was used, which is better suited to discrete and categorical variables than principal component analysis (PCA) [62]. MCA can be used to analyse a mixture of binary, categorical, discrete or continuous variables, using covariance between items to determine if an asset is either positively or negatively correlated with ownership of other assets [62]. Participants in the SINAKO trial were asked questions regarding household assets, including ownership of durable goods (radio, phones, etc.), house-build type (brick house, room, shack, etc.), sanitation (type of toilet), and access to services (electricity and water supply). If a household states that they own an asset, or have access to a service, their asset index score increases; a household's asset index score decreases if they state that they do not own an asset, have no access to services or have access to lower quality water supplies. After running the MCA, 15 dimensions were found: each of these dimensions are the weighted sum of the original variables. The first dimension in this analysis accounted for 68.2% of the variance (see Supplementary Table S4). Scores were subsequently predicted, and wealth quintiles were generated from the predicted scores. Lower scores correspond to lower asset ownership and access to services, and higher scores correspond to higher asset ownership and access to services.

Household-level variables also included questions on intimate partner violence adapted from the WHO's multi-country study [63]. Questions focused on four areas of violence: control, emotional violence, physical violence and sexual violence. Response options were adapted to ask about violence from household members and partners, as well as partners who lived outside the household. A binary composite physical and sexual violence was created, as was a composite emotional and psychological violence variable, to reflect violence experienced within the household. The composite variables only included those who experienced violence within the household, either from partners or other household members, and did not include those who experienced violence from a partner who did not live in the household.

At the community level, three questions on community stigma were included, drawn from Herek et al. [64] focusing on experiences of HIV stigma in the community [64]. Response options included a five-point Likert scale ranging from 'strongly agree' to 'strongly disagree' (see Supplementary Materials, Table S5). Running a confirmatory factor analysis (CFA) on the items using the weighted least square mean and variance adjusted (WLSMV) estimator for categorical variables, the model results stated that there were 0 degrees of freedom: a just-identified model means it is difficult to assess model fit. It was therefore decided to add external factors to the model to add further testable implications: personal stigma was included, with community stigma as a predictor of personal stigma. The confirmatory factor analysis indicated that there was an acceptable fit and factor scores were saved for inclusion in the analysis; fit indices and factor loadings for each item are noted in the Supplementary Materials, Table S5. Structural level factors were

not available for analysis, although it was considered that health system challenges would be similar across the clinics.

Data Analysis

Confirmatory factor analysis (CFA) was undertaken in MPlus 8.7, descriptive and further analysis was undertaken using Stata v.17.0. Descriptive analysis examined demographic and adherence characteristics as percentages and as mean or median values. Due to the health clinic being used as the unit of randomisation, participants are nested within geographical districts. The primary implication of this multilevel structure is that the fundamental independence assumption is violated. If the clustered nature of the data is ignored, then analysis may produce incorrect parameter estimates and standard errors, as well as incorrect conclusions on model fit [65, 66]. The analysis therefore adjusted the standard errors for clustering within districts. The intraclass correlations for the variables used in the analysis were however low, ranging between 0.005 and 0.02, indicating that between 0.5% and 2% of the total individual differences in adherence are at the cluster level.

A high proportion of zeros were noted for both the number of days that pills were missed and for self-rated adherence (where 'zero' is perfect adherence). The analytic strategy for this study followed Saberi et al., who used zero-inflated negative binomial models as well as hurdle models to analyse highly skewed (continuous and count) ART adherence variables. First, zero-inflated negative binomial models were compared to generalised Poisson and zero-inflated Poisson models to assess issues with dispersion [55]: zero-inflated Poisson models were the preferred of these three models (and results varied little between these models). These results were subsequently compared with hurdle models, comprising a combination of binary logistic regression as well as generalised linear models for > 0% adherence using a gamma distribution (see Supplementary Tables S6 and S7) [55]. Conclusions were not changed after running the hurdle models.

In Poisson regression, the regression coefficient represents the change in the difference in the logs of the expected counts for a one-unit change in the independent variable (with all other variables in the model held constant). The coefficients from these models are exponentiated for ease of interpretation: in count models, exponentiated coefficients from the Poisson model are interpretable as incidence rate ratios [67]; for the purposes of this baseline analysis, the exponentiated coefficients for self-rated adherence are interpretable as representing the association between a unit increase in the independent variable and decreasing scores for the self-rated adherence variable, or an increase in the number of days where all pills were missed, so that for example, an exponentiated coefficient of 1.50 for 'days where all pills were missed' would mean that a unit increase in the predictor was associated with a 50% increase in the expected number of days where all pills are missed.

Bivariate and then multivariable analysis were conducted to assess the association between correlates and both ART adherence measures: following bivariate analysis, a base model was run that included the outcome and variables of a priori interest (age, gender, education, and size of clinic). Individual-level variables such as HIV knowledge, disclosure, and ART (re-)initiation status were then added simultaneously to the base model. Household-level and then community-level variables were subsequently added. Model validity was assessed using the Akaike information criterion (AIC) and Bayesian information criterion (BIC). Given concerns regarding data sparsity, variable selection was subsequently undertaken to ensure a parsimonious model: variables were removed from the adjusted model if the AIC/BIC indicated that the inclusion of the variable did not improve the model, and the final model was run. The same procedure was followed for both measures of adherence, and the base and final models were run using hurdle models. Further sensitivity analysis was undertaken by re-running the models without adjusting for clustering.

Results

Descriptive Statistics

Demographic characteristics of participants are summarised in Tables 1 and 2. Of the 316 participants who enrolled in the SINAKO trial and completed the baseline questionnaire, 224 (71%) rated their ART adherence over the past month at 90% or higher. In the previous 4 days, 270 (85%) participants had taken all their doses every day. The two measures of adherence were strongly associated with each other (exp(β): 1.25, $z = 9.82$, $p < 0.001$), after controlling for gender, education and age. The majority of the participants identified as female (262, 83%), with 54 identifying as male (17%). The median age was 34 (IQR 28–42, min–max 18–65) and the majority of participants (247, 78%) stated that their education level was either none, primary school or some secondary school. Almost a third of participants (91, 29%) stated that they were experiencing violence within the household, either from a partner that they lived with or from other household members. 23 (7%) had not disclosed their HIV status to another household member. For just over half of participants (175, 55%), this was their first time on an ART regime: the rest of the participants had previously been on an ART regime. Just over a third of participants (86, 34%) stated that their household income was very low: between nothing and 1000 ZAR a month (approx. 53 US$).

Table 1 Socio-demographic characteristics of the sample

Item	Category	Freq	(%)
Age	18–34	163	51.58
	34–65	153	48.42
Gender	Male	54	17.09
	Female	262	82.91
Language	Afrikaans	24	7.59
	English	153	48.42
	Xhosa	139	43.99
Education	None-Secondary	247	78.16
	Matric-Diploma	69	21.84
Disclosed HIV status	No	23	7.28
	Yes	293	92.72
First time on ART/treatment re-initiation	First time on ART	175	55.38
	Reinitiating ART	141	44.62
Emotional violence (household)	None reported	281	88.92
	At least one incident reported	35	11.08
Psychological violence (household)	None reported	281	88.92
	At least one incident reported	35	11.08
Physical violence (household)	None reported	291	92.09
	At least one incident reported	25	7.91
Sexual violence (household)	None reported	312	98.73
	At least one incident reported	4	1.27
Any reported violence in the household	None reported	239	71.20
	At least one incident reported	77	28.80
Household income (ZAR per month)	Nothing-1 k	86	33.86
	1 k-2 k	55	21.65
	2-4 k	83	32.68
	4 k +	30	11.81
ART clinic[a]	1	23	7.28
	2	42	13.29
	3	21	6.65
	4	37	11.71
	5	52	16.46
	6	5	1.58
	7	17	5.38
	8	29	9.18
	9	8	2.53
	10	24	7.59
	11	13	4.11
	12	45	14.24

[a]Unit of randomisation

Generating the asset index revealed that the most important indicators of wealth were items such as cars, dishwashers, tumble dryers, and computers. Public sources of tap water and no access to electricity were the principal indicators of poverty for this sample.

Self-Rated Adherence

Table 3 depicts the bivariate and multivariable associations between the outcome variable "self-rated adherence in the last month" and individual, household and community factors. At the individual level, male participants estimate their adherence consistently worse than female participants ($\exp(\beta) = 1.37$, $z = 3.95$, $p < 0.001$), while holding all other variables in the model constant. Participants who were

Table 2 Adherence measures

Item	Category	Freq.	(%)
How would you rate your ART adherence in the PAST MONTH?	10/10	204	64.56
	9/10	20	6.33
	8/10	36	11.39
	7/10	20	6.33
	6/10	7	2.22
	5/10	18	5.70
	4/10	4	1.27
	3/10	3	0.95
	2/10	1	0.32
	1/10	1	0.32
	0/10	2	0.63
	Total	316	100
During the past 4 days, on how many days have you missed taking ALL of your doses?	0	270	85.44
	1	26	8.23
	2	14	4.43
	3	1	0.32
	4	5	1.58
	Total	316	100

re-initiating ART reported lower adherence scores when compared to those who were beginning ART for the first time (exp(β): 1.35, z = 3.64, p < 0.001). In the inflation part of the model, a one-unit increase in experiencing side effects decreased the log odds of belonging to the 'perfect adherence' group by a factor of 0.58 (exp(− 0.54), z = − 2.76, p = 0.006).

At the household-level, there was weak evidence that those experiencing psychological and emotional violence at the hands of their household members reported lower adherence scores (exp(β) = 1.37, z = 1.97, p = 0.05) than those who reported no psychological and emotional violence: those who did not experience violence in the household therefore had better adherence. Conversely, those who experienced higher levels of household support reported better ART adherence (exp(β) = 0.81, z = − 4.68, p < 0.001) than those who experienced lower levels of household support, holding all other variables in the model constant. At the community level, for participants who experienced higher levels of stigma in their communities, the expected scores of poor ART adherence would increase by a factor of 1.24 (z = 3.01, p = 0.03) while holding all other variables in the model constant: experiencing less community stigma means better ART adherence. Patients attending larger health facilities also reported better adherence (exp(β) = 0.73, z = − 2.83, p = 0.005).

The Number of Days, in the last 4 Days, When ALL Pills were Missed

The bivariate and multivariable associations between individual, household, and community factors and 'number of days that all pills were missed in the last 4 days' are described in Table 4. At the individual level, a participant's level of education was important: the expected number of days that pills were missed for a participant with a high level of education was lower than that of participants with a lower level of education (exp(β) = 0.30, z = − 3.75, p < 0.001): the more educated they were, the better their adherence over the past 4 days. Similarly, for every point increase in HIV knowledge, the expected number of days where pills were missed would decrease by a factor of 0.28 (z = − 2.83, p = 0.005), holding all other variables constant. In the inflation part of the model, there was fairly strong evidence that being male increased the log odds of saying that they had missed their pills on 'zero days' in the last four days by a factor of 4.56 (exp.(1.52), z = 2.51, p = 0.01), although this association was attenuated in analysis with hurdle models (Table S7).

At the household level, household support was once again associated with improved adherence: for every point increase in household support, the expected number of days of missed pills decreased by a factor of 0.65 (z = − 2.92, p = 0.003). Conversely, there was weak evidence that for every point increase in household asset index scores the expected number of days of missed pills would increase by a factor of 1.29 (z = 2.01, p = 0.05); which meant that higher socioeconomic status was associated with poorer adherence over the

Table 3 Bivariate (crude) and final adjusted correlates of self-reported ART adherence

Variable	Category	Crude exp(β)	z & p-value	95% CI	Adjust. exp(β)*	z & p-value	95% CI
Base model							
Age	(std.)	0.65	−1.45, 0.31	0.52, 0.15	0.85	−0.68, 0.49	0.53, 1.36
Gender	Female (ref)	–	–	–	–	–	–
	Male	1.11	0.75, 0.45	0.85, 1.44	1.37	3.95, < 0.001	1.17, 1.61
Education level	None—secondary	–	–	–	–	–	–
	Matric—degree	0.88	−0.68, 0.50	0.62, 1.26	1.005	0.04, 0.97	0.79, 1.28
Clinic size	Small clinics	–	–	–	–	–	–
	Large clinics	0.78	−1.91, 0.06	0.60, 1.006	0.73	−2.83, 0.005	0.59, 0.91
Individual variables							
Disclosed	Yes (ref)	–	–	–	–	–	–
	No	1.12	0.81, 0.42	0.85, 1.49	–	–	–
Treatment (re)initiation	Initiating ART (ref)	–	–	–	–	–	–
	Reinitiating ART	1.43	3.63, < 0.001	1.18, 1.73	1.35	3.64, < 0.001	1.15, 1.58
ART side effects	(std.)	0.99	−0.21, 0.83	0.87, 1.12	0.93	−1.66, 0.10	0.85, 1.01
HIV knowledge	(std.)	0.89	−0.43,0.67	0.52, 1.52	–	–	–
Household variables							
Physical and/or sexual violence	No reported violence (ref)	–	–	–	–	–	–
	At least one reported instance	1.49	1.89, 0.06	0.99, 2.26	–	–	–
Psychological violence	No reported violence (ref)	–	–	–	–	–	–
	At least one reported instance	1.49	2.08, 0.04	1.01, 2.02	1.37	1.97, 0.05	1.001, 1.87
Asset index scores		1.08	0.94, 0.35	0.92, 1.25	–	–	–
Household support	(std.)	0.81	−3.29, 0.001	0.71, 0.92	0.81	−4.68, < 0.001	0.75, 0.89
Structural variables							
Community stigma					1.24	3.01, 0.003	1.08, 1.43
Inflation model for final model				ART side effects	−0.54	−2.76, 0.006	−0.92, −0.16

*Adjusted for age, gender, education level, treatment (re)initiation, ART side effects, psychological violence, household support and community stigma

preceding 4 days. Higher asset scores were associated with higher levels of education ($\beta = 0.48$, $z = 3.39$, $p = 0.006$) and the number of household members in the household ($\beta = 0.18$, $z = 6.42$, $p < 0.001$) after controlling for age, gender and strata.

Discussion

This study examined data from PLHIV enrolled in the SINAKO study based in Cape Town who had recently initiated ART. The study focused on household factors, as well as individual and community factors, that may affect ART adherence, utilising two measures of ART adherence. The results have indicated that factors at all levels are indeed associated with ART adherence; furthermore, household support was associated with both measures of adherence, underlining the importance of the household level in adherence support.

Household-Level

Household-level factors played a crucial role in shaping ART adherence outcomes for PLHIV. Participants who

Table 4 Crude and adjusted correlates of 'the number of days that pills were missed in the last 4 days'

Variable	Category	Crude exp(β)	z & p-value	95% CI	Adjust. exp(β)*	z & p-value	95% CI
Base model							
Age	(Std.)	0.22	−2.01, 0.05	0.05, 0.97	0.47	−1.06, 0.29	0.12, 1.89
Gender	Female (ref)	–	–	–	–	–	–
	Male	4.01	3.57, < 0.001	1.87, 8.58	2.51	1.50, 0.13	0.76, 8.35
Education	Low—secondary	–	–	–	–	–	–
level	Matric—degree	0.41	−1.26, 0.21	0.11, 1.63	0.30	−3.75, < 0.001	0.16, 0.56
Clinic size	Small clinics	–	–	–	–	–	–
	Large clinics	0.53	−2.12, 0.034	0.30, 0.95	0.62	−1.49, 0.14	0.33, 1.16
Individual variables							
Disclosure	Disclosed	–	–	–	–	–	–
	Not disclosed	1.11	0.25, 0.80	0.51, 2.43	–	–	–
Treatment re-initiation	initiating ART (ref)	–	–	–	–	–	–
	Reinitiating ART	0.64	−0.90, 0.37	0.25, 1.67	–	–	–
ART side effects	(Std.)	0.84	−1.27, 0.20	0.65, 1.10	–	–	–
HIV knowledge	(Std.)	0.95	−0.06, 0.95	0.17, 5.33	0.28	−2.83, 0.005	0.11, 0.67
Household variables							
Physical and/or sexual violence	No reported violence (ref)	–	–	–	–	–	–
	At least one reported instance	1.52	1.03, 0.30	0.69, 3.36	–	–	–
Psychological violence	No reported violence (ref)	–	–	–	–	–	–
	At least one reported instance	1.08	0.94, 0.35	0.78, 2.03	–	–	–
Asset index scores		1.242	1.94, 0.05	1.00, 1.55	1.29	−2.83, 0.05	1.01, 1.65
Household support		0.74	−2.64, 0.008	0.59, 0.93	0.65	−2.92, 0.003	0.48, 0.86
Structural variables							
Community stigma		1.35	1.81, 0.07	0.98, 1.87	–	–	–
Inflation model				Gender: female (ref) Male	−1.52	−2.51, 0.01	−0.33, 2.71

*Adjusted for age, gender, education level, strata, HIV knowledge, household asset score, household support

perceived higher levels of household support reported better ART adherence. There is strong evidence in the literature that social support is important for ART adherence: for example, a meta-analysis found significant and moderate effect sizes from social support interventions in improving adherence to ART [68]. Furthermore, individual studies have also demonstrated the importance of social support for ART adherence specifically within the household [69, 70]. Household support was also the only factor to be associated with both self-rated adherence and the number of days where pills were missed. Conversely, participants who reported experiencing psychological and emotional violence within their households exhibited worse adherence than those who did not. These results are similar to those found in the literature: a scoping review in 2019 identified 29 studies exploring intimate partner violence (IPV) and ART initiation and adherence, finding that experiencing violence led to reduced ART adherence and virological suppression [71]. These findings underscore the impact of the household environment on the ability of PLHIV to adhere to ART: as explained by Wouters when describing the IFC model, adaptation to HIV and ART is shaped by a process of continual interactions between the individual and their environment, in which the family plays a key role [45]. Addressing IPV and fostering supportive household dynamics should therefore form integral components of interventions aimed at improving ART adherence.

The analysis indicated a weak association between higher asset index score and a higher number of predicted days where all pills were missed. The pathway between asset ownership and ability to adhere to ART is complex, and findings in the literature regarding the relationship

between asset scores and ART adherence are frequently mixed: for example, a systematic review of 35 studies indicated that the majority of the reviewed studies reported little to no association between a variety of economic measurements and ART adherence [72]. In this study, further analysis revealed that asset ownership was associated with the number of household members. Larger households may be able to pool resources, therefore resulting in higher asset scores, while simultaneously discouraging ART adherence as PLHIV may be pressed for privacy or space to be able to adhere to ART, especially in households where disclosure has not yet occurred [25]. Additionally, PLHIV may not have control over the distribution or use of assets and may not, therefore, be able to use these if needed to support adherence. It should furthermore be noted that, given the durability of assets, asset indices are better at indicating increases in income rather than capturing decreases; they are not, therefore, perfect representations of poverty or wealth [61]. Misreporting of assets may also be of concern, especially given sensitivity to answering questions seen as related to poverty and socio-economic status. The association between asset ownership and adherence therefore warrants further exploration in future quantitative and qualitative research to understand pathways with adherence more clearly, as well as the relationship between assets, income and decision-making power.

Individual-Level

At the individual-level, male gender was associated with poorer self-rated adherence over the previous month, and yet male participants also had higher odds of having 'zero' days of missed pills: this difference could potentially be explained by the difference in the recall periods for the two outcomes. Results in the literature regarding gender and ART adherence are mixed. A study examining adherence in six countries in Africa, including South Africa, recorded male gender as associated with suboptimal adherence [73], as did a study in South Africa that found that men living with HIV had a 20% higher risk of death at 24 months and 36 months of follow-up when compared to females [74]. A number of studies and reviews have indicated that men test, access care and treatment, and achieve viral suppression at lower rates than women; men are recorded as having higher mortality rates with greater loss to follow up after testing and treatment [75–77]. A qualitative study with health care workers in Cape Town outlined their perceptions of the barriers to adherence faced by the men living with HIV that they work with, including rigid masculine gender norms, HIV stigma and competing concerns such as obtaining employment [78]. Conversely, a meta-analysis of 207 studies based in low-, middle-, and high-income countries also found an association between male gender and better adherence, although the effect size was very small [79]. Gender differences in ART adherence therefore underscore the importance of developing context-specific gender-tailored interventions for ART adherence that look at upstream drivers of gender variations in ART adherence rates, as well as for testing and retention in care.

ART re-initiation status was found to be associated with poorer self-rated adherence. The negative impact of treatment interruption is well documented in the literature: a study in Ethiopia found that those restarting ART had higher odds of immunological failure [80], and a systematic review and meta-regression analysis indicated that "previous antiretroviral exposure" was associated with higher ART drug-resistance (specifically resistance to Non-Nucleoside Reverse Transcriptase Inhibitor-Based regimens) [7]. A South African cohort study found that for those re-initiating ART, their median CD4 count was similar to their initial CD4 count prior to starting treatment at all, indicating that immunological recovery while on ART had subsequently been lost; they furthermore found that the probability of reinitiating ART within 3 years was only 42% [57]. The fact that this article's results indicate that participants who had previously been on an ART regime already rated their adherence less well those who were starting ART for the first time highlights the importance of support for maintaining consistent adherence for individuals who have experienced previous treatment interruptions.

Higher levels of education and HIV knowledge meant fewer missed pills in the preceding four days, emphasizing the role of education and knowledge in health literacy and medication management. These findings are similar to others in the literature; for example, two cross-sectional South African studies found better adherence with higher levels of education [81, 82], and a sero-behavioural survey in South Africa also found an association between education level and the number of days pills were missed, although this was over a 30-day recall period rather than 4 days [83]. A cross-sectional study in Guinea-Bissau similarly found that a lack of HIV-related knowledge about ART and HIV was a barrier to adherence [84]. The pathways between HIV knowledge, education and ART adherence are complex: for example, a cross-sectional study with newly diagnosed HIV-positive adults at four primary health clinics in Johannesburg, South Africa, highlighted a correlation between better HIV knowledge and English literacy, indicating the importance of making HIV information available in all relevant languages [85]. There is therefore a clear need for further research on the interplay between education, HIV knowledge, and ART adherence.

Community-Level

At the community level, participants who reported experiencing higher levels of community stigma in their communities reported worse ART adherence. This finding concurs with results from other studies: a structural equation modelling study conducted using data from the US found that anticipated stigma negatively impacted ART adherence [86], as did a cross-sectional study in Zambia and South Africa [87]. A further US study indicated that HIV-related stigma in the community may result in PLHIV internalizing stigma and therefore anticipate stigmatizing experiences, resulting in suboptimal health outcomes [88]. This underscores the critical need for community-level interventions to reduce HIV-related stigma, which can have far-reaching effects on treatment outcomes.

Participants who attended larger health clinics reported better ART adherence. Differences at the facility level could be due to the quality of care offered: a longitudinal study based in South Africa found that larger health clinics offered better quality HIV care, while there was considerable variation in quality among smaller health clinics [89]. Differences in the type and quality of care that may vary between clinics may include, for example, the presence of an ART adherence club, specialised staff such as HIV counsellors, as well as type and quantity of equipment. Further qualitative research is needed to understand the link between HIV care, health clinic facilities and ART adherence.

ART Adherence Measurement

The two measurements of ART adherence were both associated with household support, whereas associations differed for other variables according to the adherence measure used. This difference could be due to the distinction in the timeframe of each outcome, namely 1-month versus 4 days: a meta-analysis of 53 studies in Latin-America and Caribbean countries similarly found differences according to timeframe, with better reported adherence for the shortest recall period and lower adherence for longer time frames [53]. It is unclear as to which time period best predicts virological suppression or failure: shorter recall periods may allow for better accuracy as the risk of recall bias may be minimized, conversely, longer time periods increase the possibility of capturing adherence issues that may not be seen within a shorter time frame [53]. A cohort study based in Uganda that asked PLHIV to recall the numbers of missed doses in the last 30-days and 7-days indicated that the 30-day period was associated with virological suppression whereas the 7-day period was not [90]. Using multiple measures of adherence may therefore be prudent to gain a fuller understanding of the multi-dimensional nature of medication adherence and to cross-validate results.

Limitations

This study is subject to several limitations. First, the main outcomes were both self-reported. These measures may therefore be subject to social desirability bias [91]. Although there is currently no gold standard for measuring adherence [92], further studies should be undertaken using other objective adherence measures and in additional populations to assess these findings. Utilising two measures for assessing adherence has nonetheless allowed for exploration of the multidimensional nature of adherence and indicated the importance of household support for both measures.

Second, the number of clusters is low when considering recommendations in the literature [93, 94]. Sensitivity analysis undertaken that ignored possible clustering returned lower p-values: accounting for clustering may be important even when intracluster correlation coefficients (ICC) are low. Future research should comprise methodological studies that focus on accounting for clustering with small numbers of clusters and small ICC's. Nevertheless, this study provides further information on the factors affecting ART adherence at treatment initiation.

Third, the IPV measure used in the analysis only included those who experienced violence within the household and did not include those who experienced violence from a partner who did not live in the household. The relationship between ART adherence and violence would therefore probably be more strongly estimated if the analysis had included partners external to the household.

Fourth, this study used baseline data from the SINAKO trial, and is therefore cross-sectional: any associations cannot therefore be stated to be causal. Further research is needed to explore changes over time. Nevertheless, this study contributes to the literature on the importance of household factors for ART adherence.

Conclusion

This study elucidates the multifaceted nature of ART adherence at therapy initiation, with household factors playing a pivotal role in ART adherence, as well as individual and community factors. These findings underscore the importance of tailoring interventions to address the unique challenges faced by various subgroups of PLHIV, at a critical moment in their therapy trajectory. Comprehensive strategies that address clinic resources, gender-based disparities, promote HIV knowledge, tackle violence, reduce stigma, and enhance household support are essential for improving

ART adherence and, consequently, the overall health and well-being of PLHIV. Further research is warranted to examine the nuanced relationships between these factors and to develop targeted interventions that optimize adherence to ART regimens – paying particular attention to the role of the household.

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Author Contributions LC was responsible for statistical analysis and interpretation of data, as well as drafting and revising the manuscript. EW, CM, LK and LC developed the manuscript concept. LK managed the trial, oversaw data acquisition, and supervised fieldwork teams. EW, LK and CM were responsible for SINAKO study design and acquisition of funding. All authors provided critical revision of the article and read and approved the final version of the manuscript.

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Data Availability The datasets analysed during the current study are available from the corresponding author on reasonable request.

Code Availability The coding used during the current study is available from the corresponding author on reasonable request.

Declarations

Competing Interests The authors declare no competing interests.

Ethical Approval The study was approved by the ethics committee of the University of the Western Cape (BM19/4/6, June 2019) and the ethical committee for the Social Sciences and Humanities of the University of Antwerp (SHW_17_64, September 2018). The City of Cape Town and the Western Cape Department of Health granted permission for all facilities by December 2019. Ethical approval was updated for the follow-up interviews (SHW_17_64 (wijziging), BM19/4/6, August 2020). All participants provided written informed consent at baseline in their chosen language, and oral informed consent during the follow-up questionnaire.

Consent to Participate Informed consent was obtained from all individual participants included in the study.

Consent for Publication Patients signed informed consent regarding publishing their anonymized data.

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