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Research Article

Correlates of missed HIV appointments in low-resource settings: a study from Uganda

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Aims: Alarming reports of antiretroviral treatment failure have recently emerged in sub-Saharan Africa. The onset of virologic failure has multiple causes but suboptimal treatment adherence is one of the leading causes. This study aimed to explore correlates of adherence to HIV appointments in community care patients living with HIV/AIDS in Uganda.
Methods: Two hundred and ninety-five people living with HIV (median age 37.0 years; interquartile range 16.0; female 67.8% [*n* = 200]) reported whether they had missed any of their four-weekly appointments during the past 24 weeks. They also completed the Internalized AIDS-Related Stigma Scale, Generalized Anxiety Disorder-7, the Patient Health Questionnaire-9, the Alcohol-Use Disorders Identification Test, and the Physical Activity Vital Sign.
Results: Thirty-three (11.2%) patients missed at least one of their six scheduled appointments in the 24-week period. The adjusted odds ratio for missing at least one of six appointments was 3.03 (95% CI: 1.21–8.43, *p* = 0.01) for those who were physically inactive, and 2.29 (95% CI: 0.93–5.63, *p* = 0.046) for those with depression.
Conclusions: Targeting future rehabilitation studies for PLHIV around feelings of depression and around physical inactivity could be important in achieving optimal HIV treatment adherence.

Keywords: adherence, alcohol, anxiety, depression, physical activity

Introduction

The burden of the global HIV epidemic is disproportionately concentrated in sub-Saharan Africa (SSA). Three out of four HIV-related deaths occurred here in 2017, alongside 65% of new infections; and more than 70% of those residing here were living with HIV (PLHIV) (James et al., 2018; Naghavi et al., 2017). Recently, alarming reports about antiretroviral treatment failure have emerged in this part of the world (Gupta et al., 2018). Moreover, there are reports of increasing virologic failure rates among adults here, ranging from 5% to 31% after 12 months, and up to 38% after 48 months of treatment (Boender et al., 2015). This onset of virologic failure has multiple causes but suboptimal treatment adherence is a leading one in SSA (Assemie et al., 2019). Suboptimal adherence to HIV treatment leads to increased risk of opportunistic infections (San-Andrés et al., 2003) and premature mortality (Lima et al., 2009).

A significant body of literature exists on effective adherence-promoting interventions among PLHIV, including viral load monitoring (Bonner et al., 2013), directly observed therapy (Hart et al., 2010), motivational interviewing (Hill & Kavookjian, 2012), cognitive behavioural interventions, education, treatment supporters, active adherence reminder devices (such as mobile phone text messages) (Chaiyachati et al., 2014; Charania et al., 2014; Mbuagbaw et al., 2015), and household-focused interventions (Mukumbang et al., 2019). However, the evidence is inconsistent and only a few studies focused on adherence in low- and middle income countries in general and in SSA in particular (Bärnighausen et al., 2011). The lack of specific information from SSA underscores the need for more knowledge in this area in order to create evidence-based, adherence-promoting interventions. This is important because HIV patients in low- and lower-middle-income countries have a higher risk of suboptimal adherence

(OR = 1.6, 95% CI: 1.3–2.0, $p < 0.001$), compared to those in upper-middle or high-income countries. Suboptimal adherence is particularly strongly associated with virologic failure in SSA (OR = 5.8, 95% CI: 4.3–7.7, $p < 0.001$) (Bijker et al., 2017).

Characterising and understanding correlates of treatment adherence in low-resourced settings in SSA will be critical to attaining the targets set by the Joint United Nations Programme on HIV/AIDS (UNAIDS) that, by 2030, 95% of people living with HIV should know their HIV status, 95% of people who know their status should be on treatment, and 95% of people on treatment should be on treatment with suppressed viral loads (United Nations General Assembly, 2016). Factors that can impair HIV treatment adherence include lower socio-economic status (Arnsten et al., 2007), substance abuse (Escobar et al., 2003; Glass et al., 2010; Halkitis et al., 2008), alcohol abuse (Azar et al., 2010; Glass et al., 2010), perceived stigma (Duggan et al., 2009; Li et al., 2011), the presence of neurocognitive disorders (Anand et al., 2010), and/or mental disorders (Tegger et al., 2008). Also, in SSA, men have worse HIV-treatment adherence compared to women (Cornell et al. 2011; Shand et al., 2014). However, evidence on correlates of HIV-treatment adherence here is limited and relies on short-term data. The largest study to date in SSA (Bijker et al., 2017) investigated adults starting first-line antiretroviral treatment and evaluated patient-reported adherence at follow-up clinic visits in the past 30 days. Patient-reported adherence barriers included scheduling demands, drug stock-outs, forgetfulness, sickness or adverse events, stigma or depression, regimen complexity, and pill burden (Bijker et al., 2017).

Our study aimed to explore correlates of HIV-treatment adherence in community care patients in Uganda. We examined the association between HIV-treatment adherence during the past 24 weeks with demographic (age and gender), socio-economic (education and employment status), social (stigma), physical (chronic somatic condition, physical inactivity) and mental health factors (anxiety, depression, alcohol use disorder).

Methods
Participants and procedure
We conducted a cross-sectional study in two community health care centres in the Buikwe district of central Uganda. The HIV-prevalence in the district was 3.8% in 2018 (Buikwe Districal Local Government, 2015). All people with a registered diagnosis of HIV who were visiting the two selected health care centres and had been receiving antiretroviral therapy (ART) for at least six months were invited to take part in the study and were interviewed by a trained clinical officer. The two facilities were selected because they were located within the catchment area of a local non-governmental organisation, Africa Social Development and Health Initiatives, which provides HIV-prevention and lifestyle counselling, social support services, and emergency food distribution in rural communities. The key monthly services at the health centre include ART refill, HIV counselling and basic health monitoring. The study was approved by the ethics committee of Mengo Hospital. All participants gave their written informed consent. Participants who could not read

discussed the consent form first with the clinical officer and a relative before providing consent with a finger print.

Missed appointments
A missed HIV-care appointment was measured by the participant's response to the question, "In the last 24 weeks, in which you had 6 appointments with the health centre, did you miss any scheduled HIV-care appointment? By this, I mean you did not go for a scheduled appointment and did not re-schedule". Participants provided a dichotomous "yes" (0) or "no" (1) response to this question.

Socio-demographic and clinical variables
Patients were asked whether they had a paid job (yes/no), whether they received education (yes/no) and whether they smoked (yes/no). Age, gender (male/female), and the presence of chronic somatic comorbidities (yes/no) were obtained from the medical files. Age was dichotomous at the median value, i.e. 18–37 years was given a score of zero and 38–65 years a score of one.

Internalised AIDS-Related Stigma Scale (IARSS)
This six-item scale was designed to measure the construct of internalised stigma (Kalichman et al., 2009). Each item offers a binary (yes/no) response, and the total scale score is computed as the sum of the items (yes = 1, no = 0). Higher scores indicate more internalised stigma. Internalised stigma represents the outcome of a process through which PLHIV accept a discredited status (imposed by the majority group) as valid and develop self-defacing internal representations of themselves (Steward et al., 2008). The IARSS is a reliable and valid instrument for research in rural Uganda (Tsai et al., 2013). In agreement with previous research (Chan et al., 2017), we dichotomised IARSS at the median value, i.e., 0 to 3 as 0, and 4 to 6 as 1.

Patient Health Questionnaire-9 (PHQ-9)
The PHQ-9 (Spitzer et al., 1999) is a widely used and validated instrument that performs well in HIV patients both as a dichotomous diagnosis of depression and a continuous severity score. In Ugandan patients with HIV, the PHQ-9 has a very high sensitivity and specificity, and can be considered useful for screening HIV-positive patients for depression (Nakku et al., 2016). A cut-off of ≥10 has been shown to be the optimum cut-off for major depression (Spitzer et al., 1999), also in this patient group (Nakku et al., 2016).

Generalized Anxiety Disorder-7 (GAD-7)
The GAD-7 (Spitzer et al., 2006) is a seven-item instrument that is used to measure or assess the severity of generalized anxiety disorder (GAD). Each item asks the individual to rate the severity of their symptoms over the past two weeks. Each item is scored on a Likert scale with symptoms rated as 0 (not at all), 1 (several days), 2 (more than half the days), and 3 (nearly every day). The optimal cut-off for the presence of GAD is ≥10 (Spitzer et al., 2006).

Alcohol Use Disorders Identification Test (AUDIT)
To assess the presence of alcohol-use disorders in this study, we used the AUDIT (Babor et al., 2001), which was developed by the World Health Organization (WHO) as a

simple method of screening for alcohol-use disorders. The AUDIT comprises three domains: (1) hazardous alcohol use (frequency of drinking, typical quantity, and frequency of heavy drinking); (2) dependence symptoms (impaired control over drinking, increased salience of drinking, and morning drinking); and (3) harmful alcohol use (guilt after drinking, blackouts, alcohol-related injuries, and other concerns about drinking). The AUDIT was adapted for local use through the use of pictures and local terms for standard alcohol units. In accordance with previous research in Uganda, a score of ≥8 was considered to be a positive screening result (Nalwadda et al., 2018).

Physical Activity Vital Sign (PAVS)

Physical activity was assessed using the PAVS, comprising of two simple questions (Greenwood et al., 2010): (1) "On average how many days per week do you engage in moderate to vigorous physical activity like a brisk walk?" It was explained to patients by the clinical officer that this meant that due to the physical activity their heart rate increased and they breathed more deeply and faster than normal, with some experiencing sweating; (2) "On those days, how many minutes do you engage on average in physical activity at this level?"

Next the research assistant multiplied the two responses together to calculate the minutes per week of self-reported moderate to vigorous physical activity and verified whether the patient was achieving the recommended target of 150 minutes per week of moderate to vigorous physical activity (yes = 1; no = 0) (Coleman et al., 2012; Sallis et al., 2015; Vancampfort et al., 2012).

Statistical analyses

Continuous data were tested for normality using the Shapiro–Wilks test and found not to be normally distributed. Therefore, these data are presented as median (interquartile range). Bivariate analyses were conducted using chi-square tests to assess for potential differences in demographic, socio-economic, social, physical and mental variables on missing HIV treatment appointments. Odds ratios were calculated via binary logistic regression analyses. In the multivariable model (i.e. adjusted odds ratios), only variables which were significant at the bivariate level were included. The level of significance was set at $p < 0.05$. Statistical analyses were performed with IBM SPSS Statistics, version 26.

Results
Participants

All 295 eligible patients (median age = 37.0 years, IQR = 16.0; 67.8% [n = 200] female) agreed to participate. Thirty-three patients (11.2%) missed at least one of their six scheduled appointments. Forty-four patients (14.9%) had received no formal education, and 97 patients (32.9%) did not currently have a job. Fifteen patients (5.1%) smoked; the median number of cigarettes smoked per day was 5.5 (interquartile range = 18). Thirty-six patients (12.2%) had a chronic somatic condition such as ulcers (n = 7), hypertension (n = 6), lower back pain (n = 6), and cardiovascular disease (n = 4). In total, 27 (9.1%) of the 295 participants had a GAD-7 score ≥10. The prevalence of major depressive disorder was 10.2% (30/295), while the prevalence of alcohol use disorder was 3.4% (10/295). Sixty patients (20.3%) did not comply with the physical activity guidelines.

Correlates with missed appointments

Patients with HIV/AIDS missing an appointment were more physically inactive ($\chi^2 = 14.5$, $p < 0.001$), had higher depression scores ($\chi^2 = 8.0$, $p = 0.005$) and higher anxiety scores ($\chi^2 = 6.5$, $p = 0.011$). We did not find any significant association with age ($\chi^2 = 1.62$, $p = 0.20$), gender ($\chi^2 = 0.02$, $p = 0.88$), educational status ($\chi^2 = 0.23$, $p = 0.63$), employment status ($\chi^2 = 1.53$, $p = 0.22$), smoking status ($\chi^2 = 1.24$, $p = 0.27$), the presence of a chronic somatic condition ($\chi^2 = 2.81$, $p = 0.09$), the presence of alcohol use disorder ($\chi^2 = 0.81$, $p = 0.37$) and higher levels of internalized stigma ($\chi^2 = 1.80$, $p = 0.18$). Odds ratios for missing an appointment were 4.02 for being physically inactive (95% CI: 1.88–8.56); 3.49 for having depression (95% CI: 1.41–8.65); and 3.26 for having anxiety (95% CI: 1.26–7.27, $p = 0.013$). When adjusted, the odds ratios were significant for physical inactivity (AOR = 3.03, 95% CI: 1.21–8.43, $p = 0.01$, adjusted for depression and anxiety) and having depression (AOR = 2.29, 95% CI: 0.93–5.63, $p = 0.046$, adjusted for physical inactivity and anxiety), but not for anxiety (AOR = 1.87, 95% CI: 0.75–4.66, $p = 0.18$, adjusted for physical inactivity and depression).

Discussion
General findings

To the best of our knowledge, this study is the first to explore demographic, socio-economic, social, physical and mental health related variables that might be associated with HIV-treatment adherence in a low-resource setting in SSA. We found that the presence of depression and physical inactivity were important reasons for a missed HIV treatment appointment.

While our study found that the presence of depression was associated with a higher odds for a missed appointment, a study from the USA (Himelhoch et al., 2009) found that the hazard probability for discontinuation of antiretroviral drugs was significantly lower in the first year among those with depressive disorders (AOR = 0.61, 0.54–0.69) relative to those with no depression. In that study, mental health visits were associated with decreased risk of discontinuing HIV treatment, suggesting the importance of ongoing and consistent mental health treatment among HIV-positive people with co-occurring mental health conditions. However, in SSA, mental health care in rural community settings for PLHIV is often minimal or absent. For example, a survey of 95 HIV clinics in 29 low- and middle-income countries reported variable prevalence of combined screening and on-site management of depression (42%), post-traumatic stress disorder (PTSD, 14%), substance-use disorder (26%), and other mental health disorders (19%). On-site management of depression was reported significantly less often in rural (33%) versus urban settings (78%), as with PTSD (rural 24%, urban 58%; Parcesepe et al., 2018). Therefore, low-resource HIV-care settings should investigate the efficacy of integrating a holistic physical and mental health care into HIV care, and whether such care

might also improve adherence to HIV services. The mhGAP provides guidance on how to integrate holistic care into these settings (World Health Organization [WHO], 2016). Research is needed to better understand how the WHO mhGAP recommendations (2008) can be most effectively implemented into HIV-care settings in low-resourced settings. Future research should examine access to mental health care services provided at HIV-treatment programs, the quality thereof, and the extent to which such treatment protocols are evidence-based and associated with improved mental, physical and HIV-care outcomes. Research has demonstrated the efficacy and effectiveness of several collaborative care models to integrate mental health care into primary care, including in low- and middle income countries (Thornicroft et al., 2019).

Our study indicates that research into collaborative care models should also add a focus on a patient's lifestyle; not complying with the current physical activity guidelines of being active for at least 150 min per week was associated with a more than three times higher odds of missing an appointment. Although the presence of a chronic somatic condition was not related to a higher odds of missing an appointment and we adjusted for the presence of depression and anxiety, it might be that those who are sufficiently active have a better physical and mental health status and are therefore more likely to be able to reach the health centre independently. For example, there is an abundance of evidence that physical activity reduces levels of depressive symptoms (Schuch, Vancampfort, Richards et al., 2016; Schuch, Vancampfort, Rosenbaum et al., 2016), anxiety symptoms (Stubbs et al., 2017), and also helps prevent people from developing depression and anxiety (Schuch et al., 2019; Schuch et al., 2018). A recent study of Ugandan community care patients with HIV and a co-morbid mental health disorder showed large effect sizes for reductions in depressive symptoms (Cohen's $d = 1.47$) and improvements in physical health (Cohen's $d = 1.38$), psychological health (Cohen's $d = 0.95$), and social relationships. (Cohen's $d = 1.39$) following eight weekly physical activity counselling sessions (Vancampfort et al., 2020).

Higher levels of internalized stigma were not related to missing an appointment in the current study. This observation warrants further investigation. There is substantial empirical evidence linking stigma to adherence difficulties, but few studies provide data on psychosocial mechanisms that may account for this relationship (Sweeney & Vanable, 2016). It is very likely that the proposed mechanisms linking stigma with non-adherence are more important than stigma itself, for example, enhanced vulnerability to mental health problems and reduction in self-efficacy. Future research should also strive to assess the multiple domains of stigma, use standardized measures of adherence, and include prospective analyses. For example, in addition to internalized stigma, anticipated stigma and enacted stigma are also important to explore in PLHIV (Earnshaw et al., 2013; Nyblade, 2006). Anticipated stigma refers to expectations of discrimination, stereotyping, and/or prejudice from others because of one's HIV status. Enacted stigma refers to experiences of discrimination, stereotyping, and/or prejudice from others in the past or present due to one's HIV status.

The underlying reason why we, in contrast to other studies (Azar et al., 2010; Glass et al., 2010), did not find a relationship between alcohol-use disorder and missing an appointment might be that the prevalence of alcohol-use disorder in our study was relatively low (10/295, 3.4%) and lacked statistical power to detect any significant associations. Previous research among fishermen attending HIV clinics near Lake Victoria showed that 31% of men reported suboptimal adherence and demonstrated that hazardous drinking had a great effect on missed antiretroviral doses (AOR = 4.91, 95% CI: 1.68–14.37) (Sileo et al., 2019). However, in contrast to our population of farmers, fishermen are at increased risk for hazardous drinking, with almost 65% meeting criteria for hazardous drinking (Tumwesigye et al., 2012).

Limitations

Our findings, although promising, should be interpreted in light of some limitations. Firstly, we relied on participant self-report data instead of hospital/medical records because the latter were mostly missing and/or incomplete. Secondly, the construct validity and test-retest reliability of the PAVS are still unknown in this vulnerable population. A self-report physical activity questionnaire is less accurate than objective assessments (Soundy et al., 2014; Stubbs et al., 2016) because it may overestimate physical activity levels (Ainsworth et al., 2006). The PAVS method also does not capture light physical activity or sedentary behaviour. Thirdly, the presence of anxiety disorder, major depressive disorder, and alcohol-use disorder were based on questionnaires that were not confirmed via structural interviews. Recent research demonstrated that rates of anxiety disorder diagnoses in PLHIV were significantly higher when questionnaire-based assessments rather than diagnostic interviews were employed (Brandt et al., 2017). Fourth, the finding are from only two health care centres in rural Uganda, which may limit generalisability. Fifth, due to the cross-sectional nature of this study, causal relationships cannot be inferred. Finally, we did not measure treatment adherence, only adherence to clinic appointments, which does not necessarily reflect treatment adherence. While patients might miss an appointment, they may have the antiretroviral drugs needed to carry them through until their next appointment, or patients could have asked someone to collect their medicine.

Conclusion

Our results contribute to a larger body of knowledge on the correlates of HIV-related outcomes among adults in community settings in SSA. Targeting future intervention design around potentially important risk- and resilience-promoting factors, such as mental health care and lifestyle support, could be important to achieving optimal adherence. Our results also clearly identify the need for more rigorous research to better capture the diverse range of factors that impact on the lived experience and adherence-related behaviours of PLHIV in low-resourced settings.

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