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Tobacco use and health-related quality of life among individuals with depression who are receiving treatment for HIV in Cape Town, South Africa

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Abstract

Background: Tobacco use is the leading cause of preventable death worldwide, and prevalence rates are high among people living with HIV (PLWH), particularly in men. Depression is also common among PLWH, especially among smokers, who may use tobacco to manage mood. Although HIV and depression have been linked to functional impairment and poor health-related quality of life (HRQOL), little research has examined the degree to which smoking impacts these relationships in low and middle-income countries with high HIV burden.

Method: Participants (N = 289) were people living with HIV (PLWH) who were being assessed for inclusion in a study targeting depression as a barrier to HIV medication adherence. Linear regression models measured the effect of gender on tobacco use (assessed by the WHO-ASSIST)

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Welfare of animals: This article does not contain any studies with animals performed by any of the authors.

and on each of the five HRQOL functional impairment domains (assessed by the SF-21). Separate multivariable regression models examined the relationships between habitual tobacco use, defined as daily, almost daily, or weekly use, and the HRQOL domains.

Results: The prevalence of habitual tobacco use was 23.9% (48.1% among men, 15.5% among women). Habitual tobacco use was associated with decreased cognitive functioning for the whole sample (B = −8.99, $p < .05$) and with lower levels of pain-related impairment for men (B = 18.1, $p < .05$). Although men reported more tobacco use (B = 8.50, $p < .001$), they reported less pain-related limitations than women (B = 8.70, $p < .05$).

Conclusions: In our sample, men reported higher rates of habitual tobacco use than women. Smoking was associated with cognitive impairment and with less pain-related impairment among men. Future smoking cessation treatments tailored to PLWH who have symptoms of depression may benefit from strategies that consider pain management as a pathway to habitual smoking and recognize that motivations for use may differ by gender.

Keywords

HIV; Health-Related Quality of Life; Tobacco use; Gender; Global Mental Health

Introduction

Tobacco use and smoking are major public health concerns, especially in persons living with HIV (PLWH), as they exert a significant impact on co-morbidities and health outcomes [1]. A factor that is relevant to these outcomes is health-related quality of life (HRQOL), a multi-dimensional construct that is commonly used to examine the impact of health status on daily functioning and overall quality of life [2]. HRQOL is usually assessed through multiple domains of self-perceived health, physical functioning, and emotional functioning to provide a comprehensive index of the burden of preventable diseases, injuries, and disabilities. In countries where both tobacco use and HIV are prevalent, the HRQOL domains that are specific to daily functioning are important to evaluate and address, as functional impairment is a critical outcome for people managing chronic medical issues.

Tobacco use rates are high in South Africa and particularly high among PLWH. In South Africa, which is home to one of the largest populations of individuals living with HIV in the world, 37% of men and 7% of women aged 15 and older report that they currently smoke tobacco [3,4]. For both men and women, the prevalence of cigarette smoking is higher in urban areas than in non-urban areas [4]. In the Western Cape province, where Cape Town is located, 31.4% of the adult population currently smokes tobacco, with rates significantly higher in men (39.6%) than in women (26.8%) [5]. Published data on smoking rates in PWLH are limited; however, a recent study found that among PLWH in Klerksdorp, a mining town in South Africa's Northwest province, more than 50% of men and 13% of women are current smokers [6]. Though these figures are likely not representative of smoking rates in all PLWH, the prevalence of tobacco use among PLWH may be even higher in the Western Province, where rates of smoking in the general population are higher than those in the Northwest Province (39.6% vs. 22.3%, respectively) [5].

Depression is common among smokers in LMICs and among PLWH in South Africa, and research has consistently demonstrated that depression both compromises smoking cessation and negatively impacts adherence to antiretroviral therapies [7–9]. In a meta-analysis that examined the relationship between tobacco use and depression in LMICs, subsyndromal depression, brief depressive episodes, and depressive episodes were all significantly associated with smoking [10–12]. Research from high income countries has found that smoking contributes to increased mortality rates among people with depression, and these relationships may be even more pronounced in LMICs, where 80% of smokers currently reside [13,14]. Importantly, rates of depression are also high in PLWH; in a South African sample, 52.1% of individuals presenting for HIV care had elevated depressive symptoms, and similar prevalence rates have been documented among pregnant women living with HIV [15,16]. Both depression and smoking exacerbate comorbidities to which PLWH in South Africa are predisposed, and these overlapping epidemics likely increase vulnerability for functional impairment and thus poor HRQOL.

In South Africa, tobacco use may exert a negative effect on HRQOL above and beyond the effects of HIV and depression, which are both independently associated with poor HRQOL [17–20]. Though there is little data on these relationships in LMICs, the impact of tobacco use on different domains of HRQOL among PLWH has been assessed in high-income countries (HICs), such as the United States [21,22] and Canada [23]. In a review of factors impacting HRQOL in PLWH [24], DeGrotte and colleagues' identified a couple of studies that demonstrated the negative influence of smoking on HRQOL in general [21] and specifically on the mental health HRQOL domain [23]. One additional study assessed HRQOL among gay and bisexual men living with HIV in the US; current smoking was associated with significantly lower scores on several of the HRQOL domains, including physical functioning, functioning without pain, role functioning, and cognitive functioning [22]. Though the mechanisms driving the relationship between smoking and compromised HRQOL in PLWH have not been thoroughly explored in HICs or LMICs, it is likely that smoking-related illnesses and HIV-associated infections, which are more common in smokers relative to non-smokers, play a significant role [25]. If tobacco use has wide-ranging negative effects on HRQOL in HICs, then the impacts of use on HRQOL among PLWH with depression in LMICs may be even greater.

The overlapping epidemics of nicotine dependence, HIV, and depression may result in greater functional impairment in resource-limited settings like South Africa that have fewer treatment providers and service options than HICs. Though South Africa has the largest antiretroviral therapy program in the world (ART), with coverage for those eligible for ART increasing annually, access to mental health and smoking cessation treatments is limited, particularly for Black South Africans who remain disproportionally disconnected from government funded health services [26–30]. Depressive disorders contribute to more "years lived with a disability" than any other mental health issue and are a major public health issue in South Africa; less than a quarter of those with a major depressive disorder have received care within the past month and depression is associated with functional impairment and disability among PLWH [31–34]. Access to smoking cessation services is even more limited. There is only one dedicated smoking cessation clinic in South Africa, and, due to government restrictions, the clinic does not offer pharmacotherapy [35]. Given these

constraints and the increased risk of HIV-associated infections that is associated with smoking, tobacco use may exacerbate the functional impairments that are already linked to HIV and untreated depression [25].

Importantly, the effects of tobacco use on daily functioning among PLWH may differ by gender. In South Africa, smoking is significantly more common among men than women, and this pattern extends to PLWH [6,36]. It is possible that motivations for use differ between men and women, and cultural factors may also play a role. In the South African context and in other African countries, male social power may be expressed in greater restrictions on women's behavior, including social prohibitions against women's smoking [37]. Smokers in South Africa reported that 50% of their work colleagues and 91% of their closest friends also smoke; employment and social contexts likely differ between men and women, as women only accounted for 43.8% of total employment in 2018 [36,38]. Given these differences, adequate consideration of gender will allow for important gender-based comparisons that could inform the development of tailored smoking cessation interventions for PLWH.

The purpose of this study was to examine the relationship between tobacco use and HRQOL among adults with depression who were receiving ART for HIV, and, relatedly, to assess the relative impact of habitual tobacco use (i.e., daily, almost daily, or weekly use) on the specific HRQOL domains that pertain to functioning. We hypothesized that smoking would be associated with compromised functioning in all five HRQOL domains relevant to functional impairment, after controlling for demographics, psychological factors that are known to impact quality of life in South Africa (e.g., alcohol use), and HIV RNA viral load [39]. We also hypothesized that these associations would be moderated by gender. Exploring the effects of tobacco use on these functional impairment domains among PLWH in South Africa could inform the inclusion of relevant quality of life outcomes in smoking cessation interventions, which may ultimately reduce the burden of tobacco use among PLWH and depression.

Material and Methods

Participants and Procedure.

Participants in the present study completed the baseline assessment of a trial to treat clinical depression and ultimately improve ART adherence.[40] Briefly, participants were eligible to complete the baseline assessment if they (1) were HIV-positive; (2) screened positive for current major depressive disorder (MDD) on the MDD module of the MINI [41]; (3) received care from one of six public HIV clinics in Khayelitsha, a peri-urban settlement in Cape Town; (4) were currently prescribed antiretroviral therapy (ART) and had failed first-line ART; (5) were aged 18 years or older; (6) were fluent in either English or isiXhosa; and (7) did not have current untreated psychosis or psychotic disorders. Importantly, data for the current study are derived from pre-randomization assessments and therefore include all participants who completed a baseline visit, regardless of their participation in the subsequent parent study.

Potentially eligible individuals were recruited by study staff while waiting for their clinic appointments. Interested individuals met with a study recruiter in a private setting to complete preliminary screening items, and potential participants who met the study inclusion criteria were scheduled for a baseline assessment. All procedures performed were approved by the Institutional Review Boards at the University of Miami and the University of Cape Town. Prior to engaging in the baseline assessment, all participants provided informed consent. Participants were reimbursed 50 South African Rand (~$4) for the study visit.

Study materials (informed consent forms, measures, etc.) were available in both English and isiXhosa. The self-report psychosocial assessment battery was conducted via interview by trained research assistants in the participants' preferred language (English or isiXhosa) to facilitate accurate understanding of the measures and to aid in data collection. Study data were collected and managed using Research Electronic Data Capture (REDCap) tools hosted at The University of Miami [42,43]. REDCap is a secure, web-based software platform designed to support data capture for research studies. All measures were translated into isiXhosa following Brislin's back-translation method [44]. Participants completed the measures below, as well as additional measures not included in the present study, during the baseline assessment. As these data were collected at a baseline visit, some individuals did not meet criteria for inclusion in the longitudinal trial.

Setting

The study was conducted in Khayelitsha, Cape Town's largest peri-urban settlement. Cape Town is the capital of South Africa's Western Province, where about a third of the country's current smokers reside [5]. The prevalence of HIV in Khayelitsha is high relative to other regions in South Africa; in 2012, 34.3% of pregnant women in Khayelitsha were living with HIV, compared to 29.5% nationally [45]. Khayelitsha has an estimated unemployment rate of 38%, and only 45% of Khayelitsha's population lives in formal low-cost housing [46]. The first government-run services in South Africa to routinely provide ARTs to PLWH began in Khayelitsha in 1999 [47].

Measures

Tobacco use.—Tobacco use was measured in two ways. First, tobacco use was assessed via seven items of the WHO-ASSIST [48]. The WHO-ASSIST measures lifetime tobacco use as well as frequency of use, urges, and problematic use in the past 3 months via Likert-type scales, with one item ranging in score 0 to 3 and six items ranging in score from 0 to 6. The measure designates three categories of risk (low, moderate, high); scores that fall between 0 and 3 indicate low risk for tobacco addiction, scores between 4 and 26 indicate moderate risk for addiction, and scores of 27 or greater indicate high risk for addiction. Participants' total scores for the tobacco use items ranged from 0–39; these scores were used as a continuous measure of tobacco addiction severity when assessing for gender differences.

Second, a dichotomous variable for habitual tobacco use was created. Habitual tobacco use was defined as daily, almost daily, or weekly use. Participants who indicated daily or weekly

tobacco use in the past 3 months were coded as 1, and non-users or those who used tobacco less frequently than weekly in the past 3 months were coded as 0. This variable was used in the multivariate regression models predicting the five different HRQOL domains that pertain to functioning.

We chose to measure both tobacco addiction severity risk and habitual tobacco use because these assessments serve different functions. The WHO-ASSIST offers important information about addiction severity that is meaningful in a research context, whereas the categorical measure of habitual tobacco use may have the most public health utility, as the assessment of smoking and tobacco use does not routinely occur in South African HIV primary care settings.[49] Very brief (i.e., single item) measures of tobacco use have been linked to important HIV treatment and disease outcomes [1,50], are sensitive to smoking cessation interventions [1,50], and as such may be particularly appropriate for HIV primary care clinics in LMICs.

Health-related quality of life.—Health-related quality of life was measured by the 22-item AIDS Clinical Trial Group Quality of Life Measure Short Form-21 (ACTG SF-21) [51]. The ACTG SF-21 measures nine areas of HRQOL over the past four weeks. Because the aim of this study was to examine the effects of smoking on the functional domains of HRQOL, only five of the nine HRQOL domains were included: physical functioning, role functioning, social functioning, cognitive functioning, and functioning without pain. The other four domains assessed by the ACTG SF-21 (overall health, general health perceptions, mental health, energy) do not directly measure self-reported function.

The SF-21 physical functioning dimension has four items that assess physical limitations (e.g., different levels and kinds of limitations experienced when lifting heavy objects or climbing several flights of stairs), ranging from severe to minor. The role functioning domain assesses how participants' health affects their ability to perform their jobs; the social functioning domain measures the extent to which health limits social activities; the cognitive functioning domain assesses recent difficulties with reasoning or problem-solving, forgetfulness, and challenges concentrating or remaining attentive; and pain domain gauges the intensity of bodily pain and the degree to which pain has interfered with normal activities. Participants indicated responses on Likert-type scales for each of the five domains such that higher scores reflected better HRQOL for each subscale. Each of the relevant subscales were analyzed as continuous variables on a scale from 0 to 100.

The ACTG-SF-21 has been used to assess HRQOL among PLWH in South Africa [52]. Though this measure does not have established South African norms, there are published means for each of the relevant functioning domains; they are as follows: 88.4 for physical functioning, 88.3 for role functioning, 94.9 for social functioning, 91.9 for cognitive functioning, and 85.2 for functioning without pain [52].

HIV RNA viral load.—Recent HIV RNA viral load data (within 1 month of baseline) were accessed via chart extraction. If no recent HIV RNA viral load data were available for a given participant, viral load was assayed via blood draw using COBAS AmpliPrep/TaqMan HIV-1 Test [53]. All HIV RNA viral load data were log-transformed for analyses.

Depression severity.—Depressive symptom severity was measured via the 20-item Center for Epidemiologic Studies-Depression (CES-D) Scale [54]. The CES-D assesses the frequency of depressive symptoms over the past week using a Likert-type scale on which participants rate the frequency with which they experienced a symptom from 0 (*rarely or none of the time – less than 1 day)* to 3 (*most or all the time – 5–7 days*), though some items are reverse-scored. Higher total scores on this measure are associated with greater symptom severity, and the total score was calculated and used as a continuous measure of depressive symptoms. The CES-D has been psychometrically validated in Black South Africans and has been used among individuals receiving HIV care in Cape Town [55,56]. Scores of at least 20 yielded high sensitivity and specificity for detecting major depressive disorder on the Mini-International Neuropsychiatric Interview among PLWH in South Africa [56].

Alcohol use disorder.—Alcohol use disorder (AUD) was assessed via the AUD module of the MINI 7.0 [41]. The MINI 7.0 utilizes yes or no items to determine whether an individual is likely to meet criteria for AUD, as defined by the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) [57]. Whether a participant met criteria for AUD was retained as a dichotomous variable. The AUDIT was developed by the World Health Organization for global use, and it has been validated in samples across Southern Africa and used among PLWH in Cape Town [56,58–60].

All analyses were conducted using SPSS software version 25 [61]. Descriptive statistics were calculated and presented as frequencies (%) or means (SD; see Table 1), and distributions were assessed for each continuous variable. To determine if there were significant effects of gender on both tobacco use and HRQOL across the five specified functioning domains, six linear regression models were run.

Next, to assess the relationship among habitual tobacco use and perceived functional impairment, five multiple linear regression models were fit, one for each HRQOL domain (physical functioning, role functioning, functioning without pain, social functioning, and cognitive functioning). Six covariates were included in each of the five models. Demographic variables (age and gender) controlled for gender-based differences in tobacco use behavior that have been observed among South African adults [5], and depression symptom severity (CES-D total score) was included to account for the nature of the data set and the parent study. The log transformation of HIV RNA viral load was used to control for any effects of HIV disease progression on HRQOL, and a dichotomous variable indicating the presence or absence of an alcohol use disorder (AUD) was also included, as AUD is common among PLWH in South Africa [56] and may also influence HRQOL. Gender moderated effects of habitual tobacco use on HRQOL were also assessed with the inclusion of an interaction term. For all analyses, unstandardized estimates are reported.

Results

The demographic and HIV-related disease profile of the study participants is presented in Table 1. Most participants were women (72.0%), and all women were cisgender, but two male participants were transgender (0.7%). The average age of the sample was 31.1 years (SD = 8.3); the majority of participants were Black African (99.3%) and exclusively

attracted to opposite sex partners (93.3%). Unemployment was high (77.9%), and levels of education varied, with most of the sample indicating that they completed up to grades 9–11 (56.8%, cumulative). On average, participants had a monthly income of $138.20 (SD = 164.9). With respect to HIV disease, 77.2% of participants had detectable plasma HIV viral load, with a sample mean of 3.4 log copies/mL (SD = 1.6 log copies/mL, max = 6.1 log copies/mL). Participants rated how often they adhered to their prescribed HIV medication regimens over the past two weeks; on average, self-reported adherence across the sample was almost 70%.

Descriptive statistics for tobacco use and tobacco addiction risk are presented in Table 1. About 35% of participants reported lifetime tobacco use; among those who currently use tobacco or have a history of tobacco use, 22.7% reported no use of tobacco products over the past three months, whereas 71.2% reported habitual use, defined as daily, almost daily, or weekly use. Therefore, out of the total sample, 23.9% of participants were habitual tobacco users; 48.1% of men reported habitual tobacco use, whereas the corresponding figure for women was 15.3%. Among the individuals who reported lifetime tobacco use, risk for tobacco addiction over the past three months was moderate (M = 6.6, SD = 10.8). The mean depression symptom severity score for the sample was 33.1 (SD = 13.5), ranging from 0 to 60 (scores of at least 20 are indicative of mild major depressive disorder in South African PLWH) [56]. With respect to alcohol use, 37.3% of the sample met criteria for alcohol use disorder, and there was a significant positive correlation between the presence of an alcohol use disorder and tobacco use severity, $r(273) = .35$, $p < .01$. Tables 2 and 3 present the Pearson correlation coefficients among all study variables by gender.

Gender difference in tobacco addiction risk.

Tobacco addiction risk was significantly greater among men than women (B = 8.50, $p < .001$, 95% CI: 5.81–11.19); that is, male gender was associated with an 8.50 unit increase in risk for tobacco addiction.

Physical functioning.

Older age (B = −0.42, $p = .006$, 95% CI: 0.12–0.76), depression symptom severity (B = −0.56, p < .001, 95% CI: 0.34–0.78), and higher HIV RNA viral load (B = −2.00, $p = .03$, 95% CI: 0.13–3.80) were negatively associated with physical functioning. That is, each year older was associated with a 0.45 unit decrease in physical functioning; similarly, a one unit increase in depression severity was associated with a 0.56 unit decrease in physical functioning, and one unit increase in HIV RNA viral load was associated with about a two unit decrease in physical functioning. Habitual tobacco use was not significantly associated with self-reported physical impairments.

Role functioning.

Depression symptom severity (B = −0.74, $p < .001$, 95% CI: 0.52–0.96) was the only variable that was negatively associated with participants' self-reported ability to perform their professional jobs or domestic tasks. A one unit increase in depression severity was associated with a 0.74 unit decrease in role functioning.

Social functioning.

In the model predicting self-reported social functioning, greater depression symptom severity (B = −1.04, p < .001, 95% CI = 0.80–1.28) was negatively associated with functioning in social settings. That is, a 1.04 unit increase in depression severity was associated with a single unit decrease in social functioning. Habitual tobacco use was not linked to social difficulties.

Cognitive functioning.

Two predictor variables were negatively associated with cognitive function: depression symptom severity (B = −.91, p < .001, 95% CI: 0.71–1.11) and habitual tobacco use (B = −8.99, p = .04, 95% CI: 0.52–18.03). A one unit increase in depression severity was associated with 0.91 unit decrease in self-reported cognitive functioning, and endorsing habitual tobacco use (daily or weekly use, yes/no) was associated with almost a nine unit decrease in cognitive function for both men and women. A post hoc analysis revealed that the addition of the smoking variables significantly increased the total variance explained by the model (p < .05).

Functioning without pain.

Depression symptom severity (B = −0.91, p < .001, 95% CI: 0.69–1.14) was negatively associated with pain-related functioning; each unit increase in depression severity was associated with approximately a one unit decrease in ability to function without pain. The interaction of gender and habitual tobacco use (B = 18.06, p = .019, 95% CI: 2.95–33.18) was also significantly related to pain-related impairment. To determine the direction of the effect, two follow-up analyses were conducted. Separate linear regression models, one for men and one for women, assessed the association between habitual tobacco use and functioning without pain. Among men, habitual tobacco use was positively associated with pain-related functioning (B = 15.44, p = .02, 95% CI: 2.62–28.27), such that habitual smoking was related to a 15.44 unit increase in the ability to function without pain. The relationship between habitual smoking and pain-related functional impairment was not significant in women.

Results for all five multivariate regression models are presented in Table 4.

Gender difference in HRQOL.

Men had significantly less difficulties functioning without pain compared to their female counterparts, (B = 8.70, p = .02, 95% CI: 1.26–16.15), such that male gender was associated with an 8.70 unit increase in ability to function without pain. Gender did not significantly affect the other four HRQOL domains.

Discussion

This was the first study to identify a significant relationship between habitual tobacco use and specific domains of functional impairment among PLWH with depression in South Africa, where rates of cigarette smoking and HIV are particularly high [5]. This sample was more functionally impaired—across all five domains—than a previous sample of South

African PLWH who completed the same measure, which may have been due to the high level of depression severity that was documented in this study [52]. Over a third of participants reported lifetime tobacco use. When asked about the frequency of tobacco use over the past three months, about 24% of the sample reported current habitual (i.e., daily or weekly) tobacco use, with higher rates of habitual use among men (48.1%) than women (15.5%) and with significantly greater tobacco use severity among men than among women. Habitual tobacco was significantly related both to self-reported decreased cognitive functioning in men and women and to decreased pain-related functional impairment in men.

In this sample, the prevalence of habitual tobacco use was high relative to one study that assessed smoking rates among PLWH in Johannesburg [62] and slightly low relative rates among PLWH in Klerksdorp [6]. Waweru and colleagues [62] found an overall smoking prevalence of 15% among PLWH in Johannesburg, again with higher rates in men (23.3%) than women (7.4%), whereas 52% of men living with HIV in the Klerksdorp sample were defined as current smokers. It is possible that sociodemographic factors and regional differences help account for these discrepancies, as rates of cigarette smoking differ greatly by province, with the highest rates among men reported in the Northern Cape and the highest rates among women reported in the Western Cape [4]. Importantly, the depression severity documented in this sample likely contributed to these differences: individuals with depression are more likely to smoke, smoke more cigarettes per day, and are less likely to quit that those who do not have depression [63]. An assessment of depression severity among PLWH in South Africa reported that over 35% of participants met criteria for moderate depression [64], and depression is known to be a significant barrier to smoking cessation [65,66]. The parent study for which these participants were recruited sought to treat clinical depression in the context of HIV care to increase adherence to antiretroviral therapies (ART), and the tobacco use severity findings should be interpreted within this context.

The models relating habitual tobacco use on each of the five HRQOL functioning domains revealed strong relationships between tobacco use and self-reported cognitive function. In other words, smoking negatively impacts cognitive functioning above and beyond the effects of HIV disease and depression. Evidence from numerous studies suggest that objective markers of cognitive function are compromised among smokers living with HIV. Some of these decrements include reduced learning memory [25] and deficits in verbal learning and processing speed [67]. Individuals living with HIV may suffer from HIV-associated neurocognitive disorders (HAND), which are acquired impairments in cognitive functioning that can be compounded by smoking. In a recent study, treatment-seeking smokers living with HIV performed significantly worse on measures of working memory and processing speed compared to smokers who were not living with HIV [68]. Depression is also independently associated with cognitive impairments in episodic memory, executive function, and processing speed [69]. Providers who are treating PLWH and depression, who are already at elevated risk for cognitive impairment, should be aware of the additional negative effects of tobacco use on cognitive functioning. Indeed, these effects may compromise ART adherence and complicate efforts to manage depressive symptoms. Though there are limited smoking cessation treatment options available in South Africa, brief but consistent cognitive screening for PLWH who report habitual smoking may enable

providers to offer a clear rationale for cessation, educate their patients on the potential benefits of cessation, and offer support for those who are seeking to quit. Additional ART adherence-related support for smokers living with HIV and depression may also be warranted. The emergence of recent treatment models addressing both of the overlapping epidemics of depression and cigarette smoking [70,71] await adaptation to LIMCs.

Men who were habitual smokers reported significantly less pain related impairment. Although women reported greater pain-related impairment than men, these differences were not related to habitual tobacco use. Though preliminary, these findings suggest that tobacco use may be a pain-related coping strategy for men living with HIV and depression in South Africa and potentially among PLWH and depression in other LMICs. Higher rates of tobacco use have been observed among individuals with chronic pain compared to those without pain [72,73]. Recent research conducted in the United States indicated that PLWH with pain may use tobacco to cope, posing a barrier to cessation [74], but also that pain in the presence of substance use can interfere with full engagement in HIV care [75]. However, the relationship between tobacco use and pain may be bidirectional. Pain is believed to motivate smoking, and pain is highly prevalent among PLWH [76], so some smokers may perceive smoking as a means of coping with pain [77]; however, chronic smoking can also exacerbate pain [72], which then may complicate and compromise attempts to quit.

If tobacco use is indeed a pain-related coping strategy, it is unclear why men more so than women would use tobacco, especially given that women in this study had significantly greater pain-related impairment. These findings may be attributable to gender differences in pain-related coping strategies; women coping with pain rely more on social support, positive self-statements, and emotion-focused techniques, whereas men tend to engage in behavioral distraction (for a review, see Bartley and Fillinghim [78]). Tobacco use may facilitate distraction from painful stimuli and/or bodily pain that occurs during daily tasks, particularly for men. Indeed, pain sensitivity in men has been demonstrated to be lower under conditions of distraction, but this is not the case for women [79]. Another possible explanation is cultural; tobacco use is believed to be more socially acceptable among men than women in many South African communities, and men often have more disposable income than women [80]. Indeed, among women in South Africa, smoking cigarettes correlates with wealth, with the prevalence increasing from 3% among women in the lowest income bracket to 10% among women in the highest two income brackets [4]. The same is not true for men, for whom smoking prevalence rates vary little across wealth distributions [4]. Though these differences may help explain the gender-moderated effects of tobacco use on functioning without pain, additional psychological and environmental factors that impact on pain-related coping in South Africa and are unique to PLWH in LMICs also need to be explored.

Notably, we hypothesized that smoking would be associated with impairments in all HRQOL functioning domains, which was not the case. There are several possible explanations for this finding. There may be no systematic relationships among habitual tobacco use and physical functioning, role functioning, and social functioning in this population. It is also possible that the effects of depression overshadowed the impact of tobacco use on these areas, particularly as depression has been shown to impact functional impairment across multiple domains in diverse samples of PLWH [81,82]. Finally, the

WHO-ASSIST, the tobacco use measure included in this study, may not have provided the information needed to isolate the impact of smoking on the other functional domains. For example, the WHO-ASSIST does not assess length of time spent smoking or “pack years”, which may be critical to these relationships.

There are several limitations of the current study that warrant mention. First, as previously discussed, these data were collected during the baseline visit of a study that sought to treat depression among PLWH as a pathway to increased engagement in HIV-related care. Individuals with suspected sub-threshold or clinical levels of depression completed the baseline assessment, inflating the prevalence of depression in the sample such that it likely does not reflect the characteristics of the general population of PLWH in South Africa. However, rates of depression among PLWH in South Africa are high [64], and recent data demonstrates that, among smokers in Cape Town who are attempting to quit, moderate levels of nicotine dependence coexist with significant depression symptoms [35]. A secondary limitation of the current study is that the smoking assessment and other measures used in this study are based upon self-report and are therefore vulnerable to the biases of that methodology. Tobacco use, rather than cigarette use, was assessed; it is possible that the tobacco used by participants was consumed not only as cigarettes and in other forms such as snuff, which is primarily chewed. However, cigarettes are the most common form of tobacco in South Africa; over 21% of South Africans smoke cigarettes, whereas 7.9% of the population uses other forms of tobacco products [83]. Another limitation of the smoking measure used in this study is that it captures risk for tobacco addiction but does not assess number of cigarettes smoked per day, which would have been useful to contextualize these findings and may have helped identify relationships between tobacco use and other HRQOL domains. In addition, the gender findings should be interpreted with some caution and confirmed in future studies, as this sample was primarily women, and men comprise the majority of smokers living with HIV in South Africa [6]. Because these data are cross-sectional, causal inferences cannot be made; that is, it cannot be conclusively determined that habitual smoking led to functional impairments, especially given that HIV and depression alone have both been associated with poor HRQOL in certain domains [17–19]. However, our analyses did account for depression severity and HIV RNA viral load, suggesting that smoking significantly impacted self-reported cognitive function and ability to function without pain (in men) even after controlling for depression and HIV disease state. It is also important to acknowledge the potential effect of unmeasured variables on these analyses. For example, in the model predicting cognitive functioning, only 26% of variance in the outcome was explained by the variables included in the model. Though the addition of the smoking variables did significantly increase the total variance accounted for in the model, there are likely other factors that are contributing to cognitive functioning that were not assessed in this study. Finally, we conducted multiple statistical tests, and we did not adjust our analyses for multiple comparisons; therefore, our findings must be interpreted with caution and confirmed in future studies that are designed to examine these relationships. Despite the study’s limitations, these findings provide important information about the severity of tobacco use and the areas of functioning that are associated with tobacco use among PLWH with depression, which have not been comprehensively assessed in South Africa or in other LMICs.

Conclusion

Overall, the results of the present study demonstrate the prevalence of tobacco use in a sample of PLWH, a negative association between habitual tobacco use and self-reported cognitive function for both men and women, and a relationship between habitual tobacco use and decreased pain-related impairment in men. The association between habitual tobacco use and reduced pain-related impairment suggests that men may use tobacco to both cope with pain and to facilitate daily functioning. The relationships reported here are likely complex and should be explored further, with continued attention paid to LMICs where smoking and HIV significantly increase the risk for TB and other pulmonary comorbidities [84]. Information on the detrimental effects of tobacco use on HRQOL and other functional outcomes should catalyze the development of policy and practice for HIV/AIDS care in South Africa. This includes the prioritization of smoking cessation intervention development for PLWH. The emergence of evidenced based treatments for depression [85,86] and smoking cessation [71] in the context of HIV infection that can be implemented and sustained in resource limited setting may be particularly relevant for addressing the overlapping epidemics of HIV, depression, and smoking in South Africa and support real improvements in self-care and daily functioning.

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Table 1.

Demographics and clinical characteristics by gender (N = 289)

	Men		Women			
	n (%)	M (SD)	n (%[b])	M (SD)	χ^2	t (df)
Age		38.2 (9.0)				−2.8 * (280)
Sexual orientation					87.7[c**]	
Exclusively opposite sex partners	64 (81)		199 (98)			
Mostly opposite sex partners	6 (7.6)		1 (0.5)			
Either opposite sex or same sex partners	1 (1.3)		1 (0.5)			
Mostly same sex partners	1 (1.3)		1 (0.5)			
Exclusively same sex partners	7 (8.9)		1 (0.5)			
Race or ethnicity					61.6[c**]	
Black African	79 (100)		201 (99)			
Colored	0		2 (1)			
Indian/Asian	0		0			
White	0		0			
Monthly household income (USD)		127.5 (194.0)		139.9 (149.3)		0.6 (280)
HIV RNA viral load (log transformed)		3.7 (1.5)		3.3 (1.6)		−1.8 (277)
HIV RNA viral suppression					3.3	
Yes		15 (19)		51 (25.1)		
No		64 (81)		152 (74.9)		
Engagement in HIV care						
Percent self-reported ART adherence (past 2 weeks)		71.1 (29.4)		68.5 (32.9)		−0.6 (273)
Percent HIV appointments attended (past year)		64.2 (31.7)		60.5 (29.5)		−0.9 (280)
Lifetime cigarette use					56.6 **	
Yes	53 (70.7)		44 (22.0%)			
No	22 (29.3)		156 (78.0%)			
Habitual tobacco use (daily, almost daily, or weekly use)					35.9 **	
Yes	38 (50.7)		31 (15.5%)			
No	37 (49.3)		169 (84.5)			
Tobacco addiction risk (WHO-ASSIST total score)		12.7 (12.2)		4.2 (9.2)		−5.5[d] ** (106.9)
Alcohol use disorder (MINI)					8.8 *	
Yes	39 (51.3)		64 (32.0)			

	Men		Women			
	n (%)	M (SD)	n (%[b])	M (SD)	χ^2	t (df)
No	37 (48.7)		136 (68.0)			
Depression symptom severity (CES-D total score)		29.8 (13.1)		34.3 (13.4)		2.5* (273)
Health-related quality of life						
Physical functioning		76.2 (24.0)		70.4 (25.1)		−1.7 (271)
Role functioning		68.0 (23.8)		66.3 (27.7)		−0.49 (273)
Social functioning		63.0 (28.9)		59.9 (30.6)		−0.76 (272)
Cognitive functioning		61.6 (24.1)		56.5 (25.9)		−1.5 (273)
Functioning without pain		54.4 (28.7)		45.7 (27.6)		−2.3* (273)

*$p<0.05$

**$p<0.001$

[a]Due to small cell sizes, this category is inclusive of transgender males (n = 2).

[b]Percentages are calculated from the total of non-missing values.

[c]Due to small cell sizes, a Fisher's Exact Test is reported.

[e]Levene's Test for Equality of Variances was statistically significant, so a correction as applied.

Table 2.

Pearson Correlation Coefficients Among All Study Variables Stratified by Gender (Women)

	Age	Tobacco use severity	Habitual smoking	Physical functioning	Role functioning	Social functioning	Cognitive functioning	Functioning without pain	Depression severity	HIV RNA viral load
Tobacco use severity	0.074									
Habitual smoking	0.092	0.923**								
Physical functioning	−0.124	−0.123	−0.122							
Role functioning	0.035	0.027	0.023	0.441**						
Social functioning	−0.009	−0.022	−0.010	0.487**	0.446**					
Cognitive functioning	−0.049	−0.158*	−0.167*	0.512**	0.421**	0.456**				
Functioning without pain	0.011	−0.053	−0.075	0.441**	0.646**	0.527**	0.495**			
Depression severity	0.056	−0.043	0.055	−0.365**	−0.391**	−0.463**	−0.483**	−0.475**		
HIV RNA viral load	−0.074	−0.028	−0.034	−0.119	−0.071	−0.090	−0.035	−0.082	−0.042	
Alcohol use disorder	−0.179*	0.356**	0.298**	−0.044	−0.053	−0.014	−0.147*	−0.103	0.047	0.051

* $p < .05$

** $p < .01$

Table 3.

Pearson Correlation Coefficients Among All Study Variables Stratified by Gender (Men[a])

	Age	Tobacco use severity	Habitual smoking	Physical functioning	Role functioning	Social functioning	Cognitive functioning	Functioning without pain	Depression severity	HIV RNA viral load
Tobacco use severity	−0.100									
Habitual smoking	−0.107	0.835**								
Physical functioning	−0.238*	−0.009	0.090							
Role functioning	−0.009	−0.068	0.018	0.480**						
Social functioning	−0.100	−0.048	0.038	0.320**	0.335**					
Cognitive functioning	−0.022	−0.182	−0.083	0.190	0.409**	0.495**				
Functioning without pain	−0.042	−0.249*	0.270*	0.530**	0.317**	0.410**	0.046			
Depression severity	−0.055	−0.011	−0.064	−0.121	−0.289*	−0.448**	−0.467**	−0.347**		
HIV RNA viral load	−0.056	−0.154	0.063	−0.076	−0.005	0.013	−0.046	−0.005	−0.092	
Alcohol use disorder	−0.019	0.235*	0.360**	−0.050	−0.038	0.286*	0.178	0.135	−0.079	0.021

*p < .05

**p < .01

[a]Transgender men (n =2) are included in this table.

Table 4.

Linear Regression Analyses Examining the Relationship Among Habitual Smoking, Gender, and their Interaction with 5 Health-Related Quality of Life Outcomes.

	Physical functioning	Role functioning	Social functioning	Cognitive functioning	Functioning without pain
	B[a]	B	B	B	B
Age	−0.42**	0.07	−0.02	−0.09	0.006
Gender[b]	2.76	−0.66	−1.60	2.91	−2.60
Depression severity	−0.56***	−0.74***	−1.04***	−0.91***	−0.91***
Alcohol use disorder	−2.00	−2.97	5.87	−0.45	−2.43
Viral load (log)	−2.00*	−1.17	−1.75	−1.01	−1.71
Habitual smoking	−5.79	3.93	0.09	−8.99*	−2.94
Habitual smoking x Gender	9.48	−2.90	−1.47	3.71	18.06*
R^2	.15	.14	.23	.26	.24
F	6.38***	6.36***	11.16***	13.09***	11.63***
df	269	271	270	271	271

[a] All B coefficients are unstandardized.

[b] The referent group is women.

* p < .05

** p < .01

*** p < .001