Title: Depression is associated with poor self-reported adherence to antiretroviral therapy among people living with HIV attending an HIV clinic in the UK: results from a cross-sectional study

Abstract

Contemporary evidence is needed to assess whether the prevalence of depression remains high among people living with HIV in the United Kingdom despite recent efforts to improve patients' mental health, and if depression is negatively associated with individuals' adherence to antiretroviral therapy. In a secondary analysis of a cross-sectional clinic-based survey of alcohol consumption and associated health behaviour among people living with HIV in London, of the 221 respondents, 106 (48%) had poor self-reported adherence to antiretroviral therapy (CASE Index) and 69 (31%) screened positive for depression (PHQ-9). Poor self-reported adherence to ART was 72% higher among participants who screened positive for depression in comparison with participants who screened negative. Respondents who were younger, unemployed, and reported problematic drug use were more likely to screen positive for depression. Screening and management of depression as a part of routine HIV care may support adherence to antiretroviral therapy.

Keywords: Adherence, Antiretrovirals, Cross-sectional, Depression, HIV, Mental health, Men who have sex with men, Substance use

Introduction

Adherence to antiretroviral therapy (ART) is fundamental in achieving and sustaining viral suppression and in avoiding the development of resistance by the virus. Public health authorities and healthcare providers need to identify factors that may affect patients’ adherence to ART and develop strategies and systems that address these factors to support patient adherence (UNAIDS Joint United Nations Programme on HIV/AIDS, 2017).

Previous studies suggest that depression can negatively affect adherence to ART, leading to a failure to achieve viral suppression. A systematic review of studies conducted in low-, middle- and high-income countries reported that people living with HIV with depressive symptoms are 42% less likely to sustain optimal adherence to ART (Uthman et al., 2014). Furthermore, people living with HIV experiencing depression have higher baseline viral loads (possibly linked to late diagnosis), lower CD4 T-cell counts (a laboratory test used to monitor the destruction of CD4 cells and monitor the ART effectiveness), and higher all-cause mortality (Girma et al., 2021; So-Armah et al., 2019). The prevalence of depression among people living with HIV is high in many regions, with a pooled prevalence of 37% in high-income countries (Bernard et al., 2017; Uthman et al., 2014). Finally, some findings suggest that people living with HIV may have a higher risk of depression compared to HIV-negative individuals (Ciesla & Roberts, 2001).

Some studies, published earlier than 2015, have reported a prevalence of depression ranging from 27% to 47% among people living with HIV in the United Kingdom (Chaponda et al., 2018). Also, more recent studies have reported lower health-related quality of life among PLWH in comparison to the general population and that the incidence of depression among PLWH without mental health illness at baseline is around 15 per 1,000 person-years, which was higher than the incidence in the general population (Gooden et al., 2022; Miners et al., 2014).

International, and regional guidelines support the implementation of mental health services in routine HIV care (National AIDS trust, 2022; UNAIDS Joint United Nations Programme on HIV/AIDS, 2018). However, contemporary data on the prevalence of depression is needed to assess its continued burden and its potential effect on adherence to ART. Furthermore, evidence of factors associated with depression among people living with HIV is still needed to better identify individuals at a higher risk of depression, who may benefit from more focused health interventions. Using standardised validated instruments, this study aimed to analyse the association between self-reported ART adherence and screening positive for depression and to explore individual factors associated with screening positive for depression among people living with HIV attending a sexual health and HIV clinic in central London.

Materials and methods

Study design and setting

The present study was a sub-analysis of a study conducted between May 2017 and January 2018 at asexual health and HIV clinic in central London aimed to describe alcohol consumption and associated health behaviour among people living with HIV. The details on the main study design and findings have been published and included data on HIV-negative controls (Suonpera et al., 2020). Briefly, a cross-sectional clinic-based self-administered anonymous questionnaire was offered to all clinic attendees during a 9-month recruitment period. As most potential participants attended for their routine HIV care bi-annually and to avoid including the same people again, the convenience sample recruitment was stopped after 9 months. People living with HIV were included independently of their ART status.

A research assistant invited patients to complete the paper-based questionnaire in the clinic waiting area while they waited for their routine appointment. For this sub-analysis, only people living with HIV who completed the section of the questionnaire for adherence to ART and screening for depression were included.

Data collection

The following data were collected: data on gender, age, sexual orientation, employment status, ethnicity, number of sexual partners in the last 3 months, condom use in the last 3 months, problematic drug use (defined as scoring ≥6/44 for men and ≥2/44 for women in the Drug Use Disorders Identification Test (DUDIT) (Berman A, Bergman H, Palmstierna T, Schlyter F, 2003) and risky alcohol consumption (defined as scoring ≥8/40 in the Alcohol Use Disorder Identification Test (AUDIT) (Babor, Higgins-Biddle, Saunders, Monteiro, n.d.) and smoking status. Questions on sexual history were based on those utilised in a large population-based survey of sexual behaviour in the UK (Natsal 3 Questionnaire, n.d.): chemsex was defined as the use of GHB/GBL, mephedrone, crystal meth, cocaine, ketamine and/or 'legal highs' during sex in the last 3 months and information on having sex while being drunk in the last 3 months was obtained.

Adherence to ART was categorised as per standard scoring using the Centre for Adherence Support Evaluation (CASE) Adherence Index as good adherence (score ≥10) or poor adherence (score 0-9) (Mannheimer et al., 2006). Depression was categorised using the Patient Health Questionnaire-9 (PHQ-9). PHQ-9 has two potential cut-offs; ≥10 for major depression and ≥5 for screening positive for depressive symptoms (Kroenke et al., 2001). For this study, the proportions will be reported for the both cut-offs. The cut-off of ≥5 for screening positive for depressive symptoms will be used for the bivariable and multivariable analyses as the lower cut-off has clinical relevance for early intervention and follow-up. Participants screened positive for depression if they scored ≥5 and screened negative for depression if they scored <5 (Kroenke et al., 2001). Both well-validated questionnaires have been widely used among people living with HIV in varying settings (Mannheimer et al., 2006; Negeri et al., 2021).

Statistical Analysis

Continuous variables were described using medians and interquartile ranges (IQR) and percentages were used for the description of categorical variables. Prevalence ratios (PR) (analogues of Risk ratios), 95% confidence intervals (95% CI) and p-values were calculated using Generalized Linear Models with Poisson distribution and robust variances for the analysis of the association between screening positive for depression and self-reported adherence to ART and for the exploratory analyses of factors associated with screening positive for depression (Barros & Hirakata, 2003).

For the exploratory evaluation of potential confounding factors of (1) the association between screening positive for depression and self-reported adherence to ART and (2) of factors associated with screening positive for depression, two multivariable models were constructed. The first model adjusted for age and gender and the second model included other potential confounders (those with statistically significant associations, a p-value <0.05, in bivariable analysis) that were added one by one based on the change in adjusted PR by each potential confounder until no further changes in the adjusted PR of the association between self-reported adherence and screening positive for depression were found. For the exploration of the factors associated with screening positive for depression, all factors with a p-value ≤ 0.10 in bivariable analysis were included in the multivariable model. Effect modification was assessed using a likelihood ratio test for interaction between self-reported adherence and screening positive for depression for the following variables: risky alcohol consumption, problematic drug use and ethnicity. All statistical analyses were conducted using STATA v.17.

Ethical considerations

The main study was approved by the London - Bloomsbury Research Ethics Committee (Ref:). As the questionnaire was anonymous and participation voluntary a written consent was not sought; completion of the survey denoted consent. No identifiable patient data were obtained or recorded.

Results

Participant characteristics

From the 331 participants included in the main study, 69 were HIV-negative controls and 41 did not report data on adherence. A total of 221 participants were included in the analyses. Overall, most participants were, male (n=200, 91%) and from white ethnic backgrounds (n=168, 76%). Most participants were homosexual and bisexual men (n=186, 84.2%). The median age was 45 years (IQR 39-53). A total of 40 (18%) and 42 (19%) participants reported problematic drug use and risky alcohol consumption, respectively (Table 1).

Association between screening positive for depression and self-reported ART adherence

A total of 115 (52%, 95% CI 46%-58%) participants had good self-reported adherence to ART, whereas 106 (48%, 95% CI 41%-54%) reported poor adherence to ART. Furthermore, 69 (31%, 95% CI 27%-35%) participants screened positive for depression. Using the cut-off of $\geq$10, 25 (11%, 95% CI 8%-14%) had major depression.

The bivariable and multivariable analyses of the association between screening positive for depression and poor self-reported adherence to ART are presented in (Table 2).

Among participants who screened positive for depression, 75% reported poor self-reported adherence to ART compared to 52% among those who did not screen positive for depression. In the bivariable analysis, those that screened positive for depression were 82% more likely (crude PR 1.82, 95% CI 1.44-2.29) to have poor self-reported adherence to ART compared to those that screened negative for depression.

Although gender and ethnicity were associated with poor self-reported adherence in the bivariable analysis, these factors did not change the PR of the association between screening positive for depression and poor self-reported adherence to ART, and thus were not included in the final model.

After adjusting for risky alcohol consumption, the prevalence of poor self-reported adherence to ART among those who screened positive for depression was 75% higher (adjusted PR 1.75, 95% CI 1.38-2.21) compared to those who screened negative for depression. In the final model, after adjusting for risky alcohol consumption and problematic drug use, the prevalence of poor self-reported adherence to ART was 72% higher (adjusted PR 1.72, 95% CI 1.35-2.18) among participants who screened positive for depression compared to those who screened negative for depression. Both risky alcohol consumption and problematic drug use were positive confounders of the association between self-reported adherence to ART and screening positive for depression.

There was no evidence that risky alcohol consumption (p=0.288), problematic drug use (p=0.897) and ethnicity (p=0.668) were effect modifiers of the association between screening positive for depression and poor self-reported adherence to ART.

Factors associated with depression among people living with HIV

The bivariable and multivariable analyses for the association between screening positive for depression and potential explanatory variables are presented in (Table 3). In bivariable analysis, gender, sexual orientation, ethnicity and chemsex in the last 3 months were associated with screening positive for depression. Sexual orientation and chemsex were not included in the multivariable analysis since they were collinear with the other variables. The associations between screening positive for depression and gender and screening positive for depression and ethnicity were attenuated in the multivariable analysis.

After multivariable analysis, the factors associated with the screening positive for depression were employment status, problematic drug use, and age. Unemployed participants were five times more likely to screen positive for depression compared to those in employment or full-time students (adjusted PR 5.41, 95% CI 2.63-11.14). Those with problematic drug use were almost three times more likely to screen positive for depression compared to participants without problematic drug use (adjusted PR 2.82, 95% CI 1.72-4.63). After the multivariable analysis, the prevalence of screening positive for depression was inversely associated with increasing age in years (adjusted PR 0.95, 95% CI 0.92-0.98).

Discussion

In this study, screening positive for depression was associated with poor self-reported adherence to ART among people living with HIV attending a sexual health and HIV clinic in the UK. Furthermore, age, employment status, and problematic drug use were associated with screening positive for depression.

A systematic review, published in 2018, that described the burden of psychiatric illnesses among people living with HIV in the UK reported a prevalence of depression ranging between 27% and 47%, which is similar to the prevalence reported in our study (33%) (Chaponda et al., 2018). Although, varying assessment instruments and cut-offs used hinder direct comparison. In our study, age, employment status and problematic drug use were associated with screening positive for depression. Among people living with HIV, being employed has been previously associated with a decrease in the odds of being depressed (Amiri, 2021). Some possible unmeasured confounding factors may have contributed to this association, such as the severity of HIV-infection at the time of the survey which could impact individual's psychological and physical health and their ability to work.

Furthermore, in our study problematic drug use was associated with screening positive for depression. Studies suggest that problematic drug use may co-occur with depression (and other mental health issues such as anxiety) among people living with HIV (Bing et al., 2001). UK guidelines for HIV care indicate that people living with HIV should be enquired about their drug use and offered support to control it, if desired (Ahmed, Angus, Boffito, Bower, Churchill, Dunn, et. al., (2015), n.d.). In addition to these guidelines, this study further supports the active screening of even lower levels of depressive symptoms among people living with HIV with problematic drug use and vice versa.

In a systematic review and meta-analysis of 111 studies published before 2013, patients with depressive symptoms were 42% less likely to report good adherence to ART (Uthman et al., 2014). The likelihood of poor adherence among people living with HIV with depressive symptoms decreased with the year of publication. This may be due to improved management of depression and better strategies for supporting adherence to ART, since simpler antiretroviral regimens (e.g., with less tablets), may improve adherence to ART. These changes in time of the association between depression and adherence to ART, highlight the need for generating contemporary evidence to assess whether depression is still common among people living with HIV and to evaluate whether it is still associated with adherence to ART. Depression may affect adherence to ART in multiple ways. First, depression may lead to hopelessness and uncertainty about the future impairing patients' motivation or interest to adhere to their medication. Also, depression may impair the cognitive capacity of patients, limit their understanding of treatment indications and it can affect patients' memory, leading to poor patient adherence to medication (Foley et al., 2021). Reverse causality is possible since some ART (such as Efavirenz-based regimens) are strongly associated with mental health disorders such as depression (Checa et al., 2020). In the last 10 years guidelines for 1st and 2nd line preferred ART have changed to combinations with less impact on mental health which can help explain why contemporary data are more relevant as they are less impactful. Information on ART was not collected in this study.

In our study, increasing age was associated with a decrease in the prevalence of depression, similar to a finding of a large-scale study in the UK that enrolled over 3,000 people living with HIV (McGowan et al., 2014). Younger people living with HIV may have a more recent diagnosis, and the higher rates of depression in this population may be partially explained by individual's adjustment to their diagnosis, the stress associated with disclosure of HIV-status, and the presence of somatic symptoms.

Future studies could further explore the associations between depression and employment status, problematic drug use, age, gender, and their possible explanations. Active screening for depressive symptoms and early support could be emphasised in people living with HIV who are unemployed, young and who report problematic drug use.

In fact, in 2018, UNAIDS recognised the need for addressing depression among people living with HIV and recommended integrating its screening and treatment in routine HIV care (UNAIDS Joint United Nations Programme on HIV/AIDS, 2018). A systematic review of over 10,000 people living with HIV reported that psychosocial interventions were strongly associated with improvement in mental health outcomes (van Luenen et al., 2018). In the UK, interventions have tried to improve the mental health of people living with HIV such as a program called “Improving Access to Psychological Therapies” which was implemented already in 2008 (National AIDS trust, 2022). However, by 2020, only 37% of people living with HIV who participated in a national survey reported that their clinic had in-house psychological support, and concerns regarding the understanding of the association between HIV and mental health among healthcare providers were raised. These findings, in addition to the relatively large proportion of people living with HIV who screened positive for depression in our study, highlight the continued need to evaluate existing programs of mental health support for people living with HIV, assess new interventions for the implementation of mental health services in routine HIV care, and estimate the effect of those interventions on other important outcomes, such as adherence to ART.

Limitations

This study should be interpreted considering its limitations. Firstly, our study was a sub-analysis of an anonymous self-completed cross-sectional survey that assessed risky alcohol consumption among people living with HIV. Also, around 16% of participants had missing data for self-reported adherence, and they might have had poorer adherence than those included. The study design may have led to measurement and/or selection biases since adherence to ART was self-reported and there was no data on treatment refills and/or viral suppression. Furthermore, given the limited sample size, the study might have been underpowered to find associations, especially in the multivariable analysis. The prevalence of poor self-reported adherence to ART in this study was higher than previous estimates in the UK of less than 30% (Brook et al., 2001). Also, depression was assessed using the PHQ-9 questionnaire and was not clinically confirmed. However, PHQ-9 has been widely used for the screening of depression among people living with HIV worldwide (Edwards et al., 2014; Kaggwa et al., 2022). Selection bias is also possible since those who decided to complete the survey may have felt more comfortable answering questions on alcohol consumption and mental health in comparison with those who declined participation. One key factor that was not recorded in the main study was the time since HIV diagnosis which could potentially be associated with screening positive for depression and with poor adherence to ART. Especially, since almost 70% of newly diagnosed people living with HIV in the UK in 2019 were 25-49 years of age (National AIDS trust, 2022). Despite these limitations, the findings of this study are important as they reinforce an association between depression and ART adherence and a large burden of depression among people living with HIV, despite implementation of strategies to address mental health. It is unclear whether those who screened positive for depression in this study had a previous mental health diagnosis or had previously been screened for mental health symptoms. Finally, as discussed above, this cross-sectional study cannot establish temporality. Poor adherence to ART could have been present prior to screening positive of depression, or both factors could have been caused by a third unmeasured factor. Without routine screening as part of HIV care, depression may remain undiagnosed.

Conclusion

Among people living with HIV attending a sexual health and HIV clinic in the UK, screening positive for depression was associated with poor self-reported adherence to ART. People living with HIV who were younger, unemployed, and reported problematic drug use were more likely to screen positive for depression. The detection and treatment of depression as a part of HIV care may support adherence to antiretroviral therapy. This study suggests that routine screening for depression should be incorporated in the clinical assessment of people living with HIV.

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Table 1 Participant characteristics

	Number of participants (%) N=221
Self-reported adherence to ART	
Good	106 (48.0)
Poor	115 (52.0)
Screened positive for depression	
Yes	69 (31.2)
No	152 (68.8)
Median age (in years) (IQR)	46 (40-53)
Gender	
Male	200 (90.5)
Female	21 (9.5)
Sexual orientation (n=216)	
Homosexual and bisexual men	186 (86.1)
Heterosexual male	11 (5.1)
Heterosexual women	18 (8.3)
Gay and bisexual women	1 (0.5)
Employment status	
Employed or full-time student	185 (83.7)
Unemployed	36 (16.3)
Ethnicity	
White	168 (76.4)
Black African	20 (9.1)
Other	32 (14.6)
Problematic drug use (n=182)	
Yes	40 (22.0)
No	142 (78.0)
Alcohol consumption (n=161)	
Risky alcohol consumption	42 (26.1)
Sensible drinking	119 (73.9)
Smoking status	
Current smoker	45 (20.6)
Ex-smoker	60 (27.4)
Never smoked	114 (52.1)
Chemsex in the last 3 months (n=214)	
Yes	48 (22.4)
No	166 (77.6)
Had sex while being drunk in the last 3 months (n=214)	
Yes	28 (13.1)
No	186 (86.9)

Poor adherence was defined as having a score of having a score <10 in the Centre for Adherence Support Evaluation (CASE) Adherence Index. Depressive symptoms was defined as having a score of ≥5 in the Patient Health Questionnaire-9 (PHQ-9). Problematic drug use was defined as scoring ≥6/44 for men and ≥2/44 for women in the Drug Use Disorders Identification Test. Risky alcohol consumption was defined as scoring ≥8/40 in the Alcohol Use Disorder Identification Test. Chemsex was defined as the use of GHB/GBL, mephedrone, crystal meth, cocaine, ketamine and/or 'legal highs' during sex. IQR= Interquartile range

Table 2 Bivariable and multivariable analysis of the association between self-reported adherence to ART and screening positive for depression among people living with HIV attending a sexual health and HIV clinic

	Poor self-reported ART adherence [a] (n=115)	PR (95% CI)	Adjusted for age and gender and sexual orientation PR (95% CI) [d]	Multivariable analysis PR (95% CI) [e]
Screened positive for depression				
No	63 (51.5)	1	1	1
Yes	52 (75.4)	1.82 (1.44-2.29) [c]	1.82 (1.44-2.30) [c]	1.69 (1.27-2.25) [c]
Age in years (continuous)		1.00 (0.99-1.01)	1.00 (0.99-1.01)	-
Sexual orientation and gender				
Homosexual or bisexual male	93 (50.0)	1	1	-
Heterosexual male	4 (36.4)	0.73 (0.33-1.61)	0.73 (0.33-1.61)	0.44 (0.16-1.19)
Homosexual/bisexual/heterosexual female	18 (75.0)	1.50 (1.14-1.97) [c]	1.50 (1.15-1.97)	1.15 (0.82-1.61)
Employment status				
Employed/full time student	95 (51.4)	1	1	-
Unemployed	20 (55.6)	1.08 (0.78-1.50)	1.03 (0.73-1.47)	-
Ethnicity				
White	47 (28.0)	1	1	
Black-African	10 (50.0)	1.79 (1.08-2.95) [c]	1.01 (0.99-1.01)	
Other	12 (37.5)	1.34 (0.80-2.23)	1.30 (0.76-2.21)	
Number of sexual partners (continuous)		1.00 (0.99-1.00)	0.99 (0.96-1.01)	-
Problematic drug use and chemsex [f]				
No	57 (46.7)	1	1	1
Problematic drug use but not chemsex	10 (76.9)	1.64 (1.16-2.35) [c]	1.69 (1.21-2.37)	1.16 (0.83-1.62)
Problematic drug use and chemsex	17 (62.3)	1.35 (0.95-1.91)	1.43 (1.01-2.04)	1.04 (0.71-1.53)

Risky alcohol use consumption [g]				
No	52 (43.7)	1	1	1
Yes	28 (66.7)	1.53 (1.13-2.05) [c]	1.53 (1.14-2.06)	1.24 (0.86-1.79) [b]
Had sex while being drunk in the last 3 months				
No	56 (30.1)	1	1	1
Yes	19 (67.9)	1.36 (0.01-1.82) [c]	1.41 (1.03-1.93)	1.33 (0.89-1.67)

Poor adherence was defined as having a score <10 in the Centre for Adherence Support Evaluation (CASE) Adherence Index. Screening positive for depression was defined as having a score of ≥5 in the Patient Health Questionnaire-9 (PHQ-9). [a] row percentages; [c] *p* value < 0.05 derived from Wald test ; [d] after controlling for Risky alcohol consumption; [e] after controlling for Risky alcohol consumption and problematic drug use; [f] problematic drug use was defined as scoring ≥6/44 for men and ≥2/44 for women in the Drug Use Disorders Identification Test; [g] risky alcohol consumption was defined as scoring ≥8/40 in the Alcohol Use Disorder Identification Test; PR= Prevalence Ratio; 95% CI = 95% Confidence Interval

Table 3 Bivariable and multivariable analysis of factors associated with screening positive for depression symptoms among people living with HIV attending a sexual health and HIV clinic

	Number (%) of participants that screened positive for depression [a, b] (n=69)	Crude PR (95% CI)	Adjusted for age and gender and sexual orientation adjusted PR (95%CI)	Adjusted PR (95% CI) [c]
Age in years (continuous)		0.98 (0.97-0.99) [g]	0.98 (0.96-0.99)	0.95 (0.92-0.98) [g]
Gender and sexual orientation				- [d]
Male, homosexual/bisexual	53 (28.3)	1	1	1
Male, heterosexual	5 (45.5)	1.60 (0.80-3.17)	1.58 (0.79-3.16)	0.75 (0.33-1.74)
Female, homosexual/bisexual/heterosexual	11 (45.8)	1.60 (0.98-2.63)	1.58 (0.79-3.16)	1.19 (0.61-2.32)
Employment status				
Employed/full time student	49 (26.5)	1	1	1
Unemployed	20 (55.6)	2.10 (1.44-3.06) [g]	3.30 (2.19-4.99)	2.30 (1.51-3.52)
Ethnicity				
White	47 (28.0)	1	1	1
Black-African	10 (50.0)	1.79 (1.08-2.95) [g]	1.47 (0.81-2.66)	1.48 (0.75-2.92)
Other	12 (37.5)	1.34 (0.80-2.23)	1.29 (0.79-2.12)	1.12 (0.75-1.85)
Number of sexual partners in the last 3 months				
Number of sexual partners (continuous)		1.00 (0.99-1.00)	1.00 (0.98-1.02)	-
Alcohol consumption [f]				
Sensible drinking	30 (25.2)	1	1	-
Risky alcohol consumption	16 (38.1)	1.51 (0.92-2.48)	1.38 (0.85-2.25)	-
Smoking status				

Never smoked	31 (27.2)	1	1	-
Current smoker / ex-smoker	37 (35.2)	1.30 (0.87-1.93)	1.39 (0.94-2.05)	-
Problematic drug use and chemsex[f]				
No	30 (24.6)	1	1	1
Problematic drug use but not chemsex	11 (84.6)	3.44 (2.33-5.08)	3.22 (2.12-4.91)	3.30 (2.17-5.01)
Problematic drug use and chemsex	12 (44.4)	1.81 (1.07-3.06)	1.73 (1.03-2.92)	2.01 (1.18-3.42)
Had sex while being drunk in the last 3 months				
No	56 (30.1)	1	1	
Yes	12 (42.9)	1.42 (0.88-2.30)	1.30 (0.80-2.13)	

[a] row percentages [b] defined as having a score of ≥5 in the Patient Health Questionnaire-9 (PHQ-9); [c] adjusted by the other variables included in the model excluding those with missing data in problematic drug use (DUDIT) and risky alcohol consumption (AUDIT); [d] omitted due to collinearity; [e] problematic drug use was defined as scoring ≥6/44 for men and ≥2/44 for women in the Drug Use Disorders Identification Test (DUDIT); [f] risky alcohol consumption was defined as score ≥8/40 in the Alcohol Use Disorder Identification Test (AUDIT); [g] p value derived from Wald test < 0.05; PR = Prevalence Ratio; 95% CI = 95% Confidence Interval