Patterns of mental health symptoms among women living with HIV aged 45-60 in England: associations with demographic and clinical factors

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Abstract

Objective: We aimed to describe the prevalence of various mental health symptoms according to menopausal status (pre, peri, post) among women living with HIV aged 45-60 in England, and to identify groups of women with similar general and menopause-related mental health symptoms. We then investigated demographic predictors of group-membership, and group differences in HIV-related care outcomes (antiretroviral therapy [ART] adherence, HIV clinic attendance, CD4-count and last HIV viral load).

Methods: An analysis of cross-sectional data from the PRIME (Positive Transition through Menopause) study, an observational study of the health and well-being impacts of menopause on 869 women with HIV aged 45-60 years. Self-reported data on eight mental health indicators were collected from women in pre-, peri- and post-menopausal state using validated measures. Groups (termed "classes") of women with similar mental health symptoms were derived via latent class analysis. Class membership was linked to demographic factors using nominal logistic regression, and clinical outcomes using Wald's tests.

Results: We identified five classes: 1) few mental health symptoms (*n*=501, 57.8%); 2) high current anxiety/depression (*n*=120, 13.8%); 3) history of depression, with elevated current substance use (*n*=40, 4.6%); 4) history of depression with current psychological menopause symptoms (*n*=81, 9.3%); and 5) high previous and concurrent mental health problems (*n*=125, 14.4%). University attendance, ethnicity and longer time since HIV diagnosis predicted class membership. ART adherence was lower in classes 3 (11%), 4 (19%) and 5 (24%) compared to class 1 (4%; all $p<.001$). Members of class 5 were more likely to have missed ≥1 HIV clinic appointment in the past year than those in class 1 (34% vs. 17%, $p=.005$).

Conclusions: Women with a history of depression, current anxiety/depression, and current menopause – related mental health symptoms were more likely to have poorer clinical outcomes. Although we cannot comment on causality, our findings highlight the importance of assessing and managing menopausal symptoms and mental health in order to improve wellbeing and engagement in HIV care.

Keywords: HIV; women; menopause; mental health; depression

Introduction

Due to therapeutic advances, especially the widespread availability of antiretroviral therapy (ART), the life expectancy of people living with HIV has improved substantially [1]. Over 40% of individuals accessing HIV care in 2019 in the United Kingdom were aged 50 years or older [2], highlighting the importance of investigating the effects of ageing in this population. One group of interest is women living with HIV who reach menopausal age, a time of substantial hormonal and psychological changes. This group of women has so far been understudied, but may face specific challenges and needs in terms of their mental health. People living with HIV are more likely than the general population to be diagnosed with mental illness or substance use disorders [3]. Women living with HIV are at particular risk of mental health difficulties, reporting poorer quality of life [4,5], higher levels depression [6], and more relationship and sex - related difficulties [7] than men with HIV. Many of these differences are driven by structural factors such as poverty, stigma and gender - based violence [8].

In general, women can experience a range of somatic, urogenital and psychological symptoms during menopause [9]. Their mental health may decline during this period, due to biological effects of oestrogen depletion on the brain, and in response to menopausal symptoms such as sleep disturbance and pain, as well as co - existent social stressors, including relationship breakdown or caring responsibilities [10,11]. Studies on menopause in women living with HIV are limited in number but suggest a high prevalence of vasomotor and psychological symptoms [12,13]. Furthermore, women living with HIV aged 45 and above are more likely to suffer from anxiety, major depressive disorder (MDD) and menopause - associated psychological symptoms [14] than those under age 45, suggesting that menopause and/or ageing could adversely affect psychological well - being.

Importantly, mental health difficulties have been shown to negatively impact clinical outcomes among people living with HIV, including ART adherence, HIV viral load, clinic attendance and health seeking behaviours [15,16]. Poor adherence and self - care could ultimately lead to higher rates of HIV - related morbidity and poorer quality of life [17,18], as well as increasing the risk of onward transmission if someone is not virologically suppressed on ART [19]. Deriving classes with similar profiles of mental health, i.e. groupings of women suffering from similar types of mental health difficulties, and determining their association with sociodemographic factors and clinical outcomes may help to identify women at highest risk of poor mental health during the menopause transition, ultimately supporting appropriate prevention and management strategies.

Using cross - sectional data from the PRIME (Positive Transition through Menopause) study of women living with HIV aged 45-60, we aimed to: 1) describe the prevalence of various mental health symptoms in women living with HIV aged 45-60, 2) derive classes with different profiles of mental health difficulties, and 3) study potential demographic factors associated with class membership, as well as associations with HIV - related care outcomes (ART adherence, HIV clinic attendance, latest HIV viral load and CD4 count).

Methods

Sample

The PRIME study is a mixed-methods observational study of menopause in 869 women living with HIV in England aged 45-60 (for detailed methodology, see Tariq and colleagues [20]). Our analysis is based on the available quantitative data only, which were collected between February 2016 and June 2017. Participants completed self-administered paper-based questionnaires, which included questions on demographics, general health including mental health, HIV medical history, women's health including menstrual pattern and menopausal symptoms, and sexual well-being. Data on CD4 count and HIV viral load were obtained from

clinical records where possible. All participants with data on psychological measures were eligible for the current analysis (further details on missing data are provided below).

Measures

Anxiety and depression. The Patient Health Questionnaire 4 (PHQ - 4) [21] is an ultra-brief screening tool for depression and anxiety. Presence of symptoms of depression and anxiety over the past two weeks are assessed via two items each, with response options ranging from 0 = *"not at all"* to 3 = *"nearly every day".* Total scores for the anxiety and depression subscales range from 0-6 and for the overall measure from 0-12, with cut - offs of $\geq$3 on the anxiety and depression subscales indicating high symptom levels [22].

Alcohol |use. The Alcohol Use Disorders Identification Test-C (AUDIT-C) [23] was used to screen for problematic alcohol use. This measure comprises three items, assessing frequency of drinking (0 = *"never"* to 4= *"4 or more times per week*"), number of drinks consumed on a standard day of drinking (0 = *"1 or 2*" to 4 = *"10 or more")* and the frequency of the participant having 6 or more drinks on one occasion (0 = *"never*" to 4 = *"daily or almost daily"*). A cut-off score of $\geq$6 on the overall scale was used to indicate risky drinking in the current analyses.

Psychological Symptoms on the Menopause Rating Scale. The "Psychological Symptoms" subscale of the Menopause Rating Scale (MRS) [24] was used to ascertain whether participants had reported any psychological symptoms commonly associated with menopause. Participants completed three items indicating the presence of symptoms of anxiety, depression and irritability during the past two weeks on a scale from 0 = *"no symptoms"* to *4 = "severe symptoms".* A total score $\geq$ 7 was considered to reflect "severe psychological symptoms". Since items were more detailed than for the PHQ-4 (they captured an additional dimension of well-being (irritability)), were asked in the context of assessing other menopause-related symptoms, and rates of overlap with other markers of mental health

difficulties were modest, we decided to include this score as an additional measure of mental health potentially more related to menopause.

Prior diagnosis of depression. Participants completed a standard screening question assessing prior diagnosis of depression: "Have you ever been diagnosed with depression?", with answering options *"yes"* and *"no"*. If participants answered affirmatively, they were also asked whether they were currently taking any antidepressants.

Smoking. Participants were asked whether they smoked cigarettes regularly (i.e., at least once per day) and subsequently categorised as current smokers, ex - smokers and those who had never smoked. For the purpose of the current analyses, answers were binary-coded into 0 = "*never smoked or ex - smoker"* and 1 = "*current smoker"*.

Recreational drug use. Participants were asked whether they had used any recreational drugs (excluding those prescribed by doctors) during the past three months, with answering options *"yes"* and *"no".*

Sleep quality. One item from the Pittsburgh Sleep Quality Index (PSQI) [25] was used to screen for sleep disturbances. Participants were asked to rate their sleep quality during the past month on a scale from 0 = *"very good*" to 3 = *"very bad*". For the purpose of the current analyses, scores of *"good"* and *"fairly good"* were combined into a *"good sleep"* category, while *"fairly bad"* and *"very bad*" were combined into a *"bad sleep"* category.

Covariates. Several covariates that have been found to predict mental health outcomes in previous studies were included in the current analyses. These were poverty (not having enough money to afford basic necessities), years since HIV diagnosis, education (having a University education, as compared to having completed secondary education or not having completed school), and ethnicity (Black African, White [including White British and other White ethnicities], Black Other [including Black Caribbean and Black Other], Other [comprising the pre-defined categories of Mixed, Asian, Hispanic/Latino ethnicities, and

Any Other- not specified by respondent, which were grouped for the purpose of the current analysis]). Menopausal status (pre– vs. peri- and post-menopausal) was also included as a covariate, assessed from menstrual history alone, according to STRAW +10 criteria [26].

HIV care-related outcomes. Current CD4 count and HIV viral load were extracted from routine clinical data or completed from self-report if missing. Such data were available for 89.0% and 95.6% of participants respectively. To measure ART adherence, participants were asked how frequently they took their pills during the past seven days, with answers comprising *"none of my pills", "very few", "about one - half", "most"* and *"all"* (Terry Beirn Community Programs for Clinical Research on AIDS (CPCRA) Antiretroviral Medication Adherence Self - Report Form [27]). For the purpose of the current analyses, those with less than 100% adherence over the past seven days were classified as exhibiting *"suboptimal adherence".* Attendance for HIV care was ascertained via the question "In the past 12 months, have you missed any appointments at this clinic?". Responses were binary coded as *"complete attendance"* (100%) and *"incomplete attendance"* (<100%).

Statistical analysis

Statistical analyses were performed using Stata, V. 16 SE (Stata Corp, College Station, Texas) and MPlus V. 8.1 (Muthén & Muthén, 1998-2017). As a first step, descriptive information on the frequency of mental health conditions in the PRIME sample was obtained. χ^2 analyses were used to compare women at different menopausal stages (pre -, peri -, post -) on key variables. In a second step, latent class analysis was undertaken, using all the eight binary mental health indicators available in the dataset: prior diagnosis of MDD, current MDD, current anxiety, recreational drug use, risky drinking, smoking, severe menopause - related mental health symptoms and sleep quality. A manual 3 - step procedure [28,29] was used to first estimate an unconditional model of class membership. Selection of the final number of classes was undertaken using the Bayesian Information criterion (BIC), as well as the Lo -

Mendell - Rubin (LMR) Likelihood Ratio Test (LRT), Bootstrap LRT and interpretability. As a sensitivity analysis, class estimation was repeated controlling for menopausal stage (i.e., pre-, peri- and post-) instead of using it as a demographic predictor variable. This yielded similar class profiles, and only very slight variations in the number of participants assigned to each class. In the following step, class membership was related to demographic covariates (poverty, education status, years since HIV diagnosis, Black African ethnicity, menopause status) using multinomial logistic regression. Effects of these covariates on class memberships are presented as odds - ratios as compared to a base class with little or no mental health symptoms. Wald's tests were used to compare estimated thresholds in each class for binary HIV-related outcomes (current CD4 count $\leq$200 cells/mm^3, last HIV viral load detectable, ART adherence and HIV clinic appointments missed).

Ethical approval

Ethical approval was obtained from the South East Coast - Surrey Research Ethics Committee (REF 15/0735) on behalf of all National Health Service (NHS) sites. Written consent was obtained from all participants before participation

Results

Sample characteristics

For the overall sample (N = 869), availability on mental health indicators ranged from n=789 for anxiety to n=854 for sleep quality. Under full-information maximum likelihood assumptions, data from n=867 participants were included in the initial latent class estimation (step 1), which was reduced to n=723 for the third step including covariates and outcomes because of missing data in the latter two variables. Those without full data on the covariates and thus excluded from the analyses were less likely to show suboptimal ART adherence (4.9 versus 10.8%, $\chi2 = 4.52$, p = .03) and to have been born in the UK (10.0 versus 15.7 %, χ^2 = 3.03, p = .08) and more likely to be unemployed (41.0 % versus 32.2%, χ^2 = 5.34, p = .07).

No differences were found on other demographic factors (age, number of medical conditions) and our HIV care outcome variables (all p >.29). Due to varying numbers, descriptive data in the following are presented for all participants who had data available for a specific measure. Median age for the overall sample was 49 years (IQR: 47-52). Most participants were of Black African ethnicity (72.1%; see Table 1 for additional descriptive statistics). One-fifth (20.9%, *n* = 177) of women were pre-menopausal, 44.0% (*n* = 373) peri-menopausal and 35.1% (*n* = 297) were post-menopausal. Almost all women (97.6%, *n*= 840) were on ART; most had a CD4 count of >200 cells/mm^3 (93.5%) and an undetectable most recent HIV viral load (88.1%).

Mental health according to menopausal stage

Overall, current anxiety and depression, as measured by the PHQ-4, were the most commonly reported mental health difficulties, with 20.4% (*n*=157) scoring above the cut-off for *both* depression *and* anxiety; a further 7.9% (*n*= 61) and 4.4% (*n*= 34), scored above the cut-off for anxiety or depression alone respectively. Approximately one-third (*n*= 277) of participants reported a previous diagnosis of MDD. Risky drinking (8.6%), current smoking (8.6%) and recreational drug use over the past three months (2.5%) were less frequently reported. Approximately one-quarter of participants (*n*= 226) reported sleep problems over the past month, and 28.6% reported severe menopause-related psychological problems. The prevalence of previous diagnosis of depression, psychological symptoms on the MRS and current sleep problems were each higher in the peri- and post-menopausal groups compared to those who were pre-menopausal, with a trend towards a higher prevalence of current anxiety in the peri-menopausal group (see Table 1). Of note, we found no evidence of a direct association between menopausal stage and any of the HIV-related outcomes.

Determining latent classes of mental health

The data were clustered into 1-6 classes, ultimately favouring a five-class solution based on LMR-LRF, Bootstrap LRT and interpretability, despite a slightly lower BIC for a four - class solution (Table 2). Figure 1 provides a radar plot of the five classes and their associated mental health item loadings. Class 1 (*n*=501, 57.8%; posterior probability: 56.4%) showed overall *"few mental health symptoms"*. Class 2 (*n*=120, 13.8%; posterior probability: 13.4%) was termed the *"high current anxiety and depression class"* for the purpose of the current analyses, and captures individuals reporting high levels of symptoms of both conditions, with a medium-sized loading on current psychological symptoms on the MRS. Class 3 (*n*=40, 4.6%; posterior probability: 4.8%) was termed *"history of MDD with elevated current substance use"*, with members frequently reporting histories of MDD and high rates of smoking, as well as showing higher rates of alcohol and recreational drug use than the other classes. Class 4 captured those with a *"history of MDD with current psychological symptoms on MRS"* (*n*=81, 9.3%; posterior probability: 12.6%). Finally, members of class 5, *"high previous and concurrent problems"* (*n*=125, 14.4%; posterior probability: 12.8%), showed high loadings for a history of MDD, as well as current smoking, anxiety, depression, psychological symptoms on the MRS and sleep problems, but not recreational drug use or substance use.

Class covariate characteristics

Results of a multinomial regression with class 1 as a baseline comparison group are presented in Table 3. Those who had enough money to cover their basic needs had lower odds of being in classes 3, 4, or 5. Individuals in classes 4 and 5 had been diagnosed with HIV for a longer period of time and were less likely to have a university education. Women in peri- and post-menopausal stages (compared to those who were pre-menopausal) had higher odds of being in class 5. Compared to the White baseline group, Black African women had lower odds of being in classes 3, 4 and 5. Follow-up analyses comparing mental health symptoms between

different ethnicity groups using $\chi 2$ tests to understand drivers of class assignment indicated that Black African women were less likely than White women to have received a prior diagnosis of depression, and to report substance use and/or psychological symptoms on MRS. Women of Black Other ethnicity were less likely to be in group 3, again due to lower rates of reported substance use. Of note, confidence intervals for ethnicity predictions for class 2 were large, with follow-up analyses using posterior probabilities for class assignment suggesting that this may be due to comparisons with the White baseline group, with a very small number of White women being assigned to class 2.

Associations of latent class membership with HIV - related outcomes

We found no evidence of differences between classes in terms of last HIV viral load or CD4 count (Table 4). Suboptimal ART-adherence appeared to be higher in all symptomatic groups and was particularly high in groups 4 and 5 (19 and 24% respectively, as compared to 4% in the reference group (group 1)). Standard errors were large for comparisons between groups 1 and 2, reducing the reliability of the results. Missed appointments were particularly common among women in classes 2 (29%), 4 (24%) and 5 (34%), however this difference was only statistically significant for class 5 compared to the baseline class 1 (17%, p <.001).

Discussion

In this novel analysis of data from a representative sample of women living with HIV aged between 45 and 60 years old in England, who were accessing clinical care, we identified five classes with distinct mental health profiles: class 1 “few mental health symptoms”; class 2 “high current anxiety and depression”; class 3 “history of MDD with elevated current substance use”; class 4 “history of MDD with current psychological symptoms on the MRS”; and class 5 “high previous and concurrent mental health problems”. Although nearly 60% of women in this analysis were classified as having “few mental health problems”, it is notable that two-in-five reported some degree of historic and/or concurrent mental health issues. The

most common mental health difficulty was current symptoms of depression and anxiety (as measured by PHQ-4), with 20.4% scoring above the cut-off. Almost a quarter of women were in classes 4 and 5, which included potentially menopausal-related psychological symptoms. Women living with HIV bear a high burden of poor mental health, affecting well-being and quality of life, as well as HIV clinical outcomes including adherence and engagement in care [16,17]. Despite this, the mental health needs of these women are often under-recognised and unmet [30]. White ethnicity, not having enough money to meet basic needs, having been diagnosed with HIV for longer, and non-university education were all associated with having a history of and/or concurrent mental health problems in our analysis. Women from racially minoritized groups were more likely to report *current* symptoms of depression and anxiety (although this finding was not statistically significant), but not a history of previous MDD or substance use. This may reflect findings in the general population that people from racially minoritized groups face barriers to accessing mental health services, so may not have been given a mental health diagnosis, despite having symptoms [31]. It is also possible that Black women may under-report substance use because of cultural factors and/or stigma [32]. Of interest, being peri- or post-menopausal predicted membership of class 5, the class comprising a range of mental health conditions. This may be partially driven by the higher reporting of menopause-related psychological symptoms and sleep disturbance among women this group, but could also reflect previous findings of increased overall psychological distress during menopause [14].

The psychological impact of menopause on women is well-recognized [12, 33-35]. Recent studies have highlighted the association between menopausal age and/or symptoms and reduced clinic attendance and adherence to ART [36-39]. Our analysis adds to this emergent literature. We did not find evidence that mental health class membership was associated with undetectable last viral load or CD or CD4 count $\leq$200 cells/mm^3. However, both outcomes

were relatively rare, with the majority of women being on ART. Women in classes 4 and 5 (exhibiting both general and menopause-related mental health difficulties, such as sleep disturbance and irritability) were more likely to report sub-optimal ART adherence, with the latter group also being more likely to have missed one or more HIV clinic appointment in the past year. This suggests potential syndemic effects between menopause-related symptoms and mental health difficulties, leading to worse engagement in HIV care. Overall, our analyses thus indicate that not only are mental health difficulties common and wide-ranging in midlife women living with HIV, but also that those with pre-existing mental health difficulties who experience psychological symptoms commonly associated with menopause may be at particular risk of poorer engagement in HIV care. Furthermore, in establishing classes with different mental health profiles, we highlight the syndemic effects of substance use, current psychological symptoms, and menopause in women living with HIV [40]. We recommend further qualitative work to examine the mechanisms by which menopausal symptoms impact engagement in HIV care, and how this is mediated by mental health difficulties. Longitudinal studies would also be of benefit to investigate how the relationship between menopausal symptoms, mental health problems and HIV clinical outcomes changes during pre-, peri- and post-menopause.

Our findings have several important clinical implications. Firstly, healthcare professionals working with women living with HIV of menopausal age should be aware that women with a history of and/or current mental health problems, as well as menopause-related psychological difficulties such as irritability and sleep disturbance, may be more likely to have poorer engagement in care. This includes missing clinic appointments and suboptimal adherence to ART, which in turn could lead to worse HIV outcomes. Women living with HIV aged ≥40 years, particularly those with a history of and/or current mental health problems, should therefore be asked regularly by their clinicians whether they are experiencing menopause-

related symptoms. If so, these should be addressed, for example by offering menopausal hormone therapy, psychological support and/or information. This may not only benefit the health and wellbeing of women, but may also improve HIV clinical outcomes by supporting them to stay engaged in care and adherent to ART.

This current analysis has several strengths. The PRIME Study is one of the largest studies set up to explore menopause in women living with HIV, with a sample that is representative of women accessing HIV care in England. Our questionnaire included validated measures of both psychological and menopause-related symptoms, and we derived classes with different profiles of mental health, thus conceptualising mental health holistically, rather than looking at single indicators. However, there are also several limitations. Firstly, PRIME is a cross-sectional study, and we therefore cannot comment on causality, directions of associations or investigate changes over time. Future studies should aim to collect longitudinal data and study temporal relations, to clarify amongst other questions whether poorer mental health and higher menopause-related symptoms predict poorer engagement in care, or vice versa, in this group of women. Secondly, whilst our sample is representative of women living with HIV in the UK, with the majority of participants being of Black African ethnicity and virologically suppressed, our findings may not be generalisable to other populations of women living with HIV. Thirdly, in recruiting solely through HIV clinics, we did not include women not engaged in HIV care, whose mental health needs and difficulties may differ. Fourth, there were slight differences between the groups included and excluded (due to missing data on covariates) in the third step of the analyses, potentially limiting the generalizability of the current findings. Finally, the small numbers in some of the groups and in a number of outcomes considered restrict the precision of some of our estimates.

Conclusion

In conclusion, our analysis reveals five classes with distinct mental health profiles in women living with HIV aged between 45 and 60. Two-fifths of women reported some degree of historic and/or concurrent mental health issues, and those with a history of depression, current anxiety/depression, *and* current menopause-related symptoms were more likely to exhibit poor engagement with HIV care. These findings highlight the importance of screening for both mental health and menopausal symptoms in mid-life women, especially those with a history of mental health issues. Addressing menopausal symptoms and offering appropriate treatment and support is imperative if we are to optimise both the wellbeing and HIV clinical outcomes in this patient population.

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Table 1 Title:

Table 1

Frequencies (N, %) of Specific Mental Health Conditions and Comorbidities in the PRIME sample

Table 1 Legend:

Notes. Base sample sizes varied between n = 760 for some clinical outcomes and n = 844, depending on the measure used. % shares are provided relative to these baseline scores. IQR = Inter-Quartile Range; MDD = major depressive disorder. [a] based on Kruskal-Wallis test, [b] based on ANOVA, all other values are based on χ^2 tests., [c] >1 missed dose in last 7 days

Table 2 Title:

Table 2

Selection Criteria for Number of Classes in Latent Class Analysis

Notes. BIC = Bayesian Information Criterion; ABIC = Akaike's Bayesian Information Criterion; LMR-LRT = Lo-Mendell-Rubin Likelihood Ratio Test

Figure 1 Title:

Figure 1

5 Class Model Solution Based on Latent Class Analysis

Figure 1 Legend:

Notes. Radar chart illustrating average probabilities for each of the five classes to endorse the eight mental health indicators. MDD = major depressive disorder.

Table 3 Title:

Table 3

Prediction of class membership by demographic variables, using Class 1 ("few mental health symptoms") as a reference class

Table 3 Legend:

Notes. The categorical ethnicity variable was binary - coded into three categories (Black African, Black Other and Other), contrasting them to the non - explicitly coded fourth category of "White".

Table 4 Title:

Table 4

Class-specific probabilities of negative HIV-related outcomes, and odds- ratios of achieving each outcome, compared to reference class 2 ("low mental health symptoms")

Table 4 Legend

Notes. Prob = outcome probability for each class. OR = odds ratio.