EDITORIAL COMMENT

Sleep and mood disturbances in people with HIV remain largely understudied

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Sleep disorders such as insomnia and sleep apnea, are more common in people with HIV (PWH) compared to the general population and have a long-term impact on not only mental but also on cardiac, respiratory, and metabolic health [1–5]. Potential contributing factors to the increased prevalence of sleep disorders in PWH include psychosocial factors such as anxiety, depression, alcohol and substance abuse, persistent inflammation, immune dysfunction and specific antiretroviral therapy such as efavirenz and integrase inhibitors [1–5]. Thus, the risk factors for sleep apnea in PWH may be different than the risk factors for sleep apnea in the general population. Given the complexity in the assessment of sleep disorders in PWH, data on the associations of risk factors with presence of sleep disorders in PWH remain limited and often controversial among studies [1–5].

In this issue of AIDS, Mazzitelli *et al.* [6] present results of a large single center cross-sectional study of risk factors for sleep disorders in 721 PWH on stable antiretroviral therapy (ART) in an Italian setting. The authors reported a very high prevalence (77%) of sleep disorders such as sleep apnea, insomnia, reduced sleep quality and daily sleepiness in this population. Over 60% of participants reported low sleep quality and over 30% of patients suffered from insomnia or obstructive sleep apnea. Anxiety and depression were detected in 28% and 16% of study participants. In this population with well controlled chronic HIV infection on contemporary ART, the authors found associations between sleep disorders and the same determinants (cardiovascular risk factors and mood disorders) observed in the general population but not with HIV-related parameters and specific antiretroviral regimens.

The association of sleep disturbances with risk factors in HIV has previously been studied [1–5]. Similar to what has previously been reported in PWH [1–5], Mazzitelli *et al.* [6] reported an overall high prevalence of self-reported poor-quality sleep and risk factors associated with sleep disorders in PWH such as age, BMI, hypertension, recreational drug use, depression and higher cardiovascular risk [1–5].

However, compared to prior studies, the study by Mazziteli *et al.* [6] has important differences. First, there was a substantial difference in the demographic and clinical characteristics of the study population compared to prior studies. This study included a European population in a modern setting. Second, compared to previous studies, this study is more representative of the cohorts of PWH in western countries. Specifically, >96% of the study participants were on modern ART regimens and with undetectable plasma viremia while most of the previous studies included PWH with heterogeneous plasma suppression, adherence, and immune reconstitution status [1–5]. Third, the study by Mazzitelli *et al.* [6] is the largest dataset that concomitantly assessed several factors that may be associated with sleep disorders in PWH (including cardiovascular risk factors). Fourth, unlike prior studies that used one or two disorders scales, four sleep disorders scales were concomitantly assessed to evaluate sleep disorders scales. Fifth, unlike other studies that utilized only the Framingham cardiovascular risk score, two independent scores were utilized to assess cardiovascular

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risk [Framingham risk score and the DAD (i.e. Data Collection on Adverse Effects of Anti-HIV Drugs Cohort) score]. This approach may allow a more comprehensive assessment of the cardiovascular risk in PWH with sleep disorders. Finally, the study by Mazzitelli *et al.* [6] also included a subgroup analysis of participants without anxiety and depression and consistently showed that HIV-related parameters were not associated with sleep disorders.

Overall, the study by Mazzitelli *et al.* [6] showed that factors associated with sleep disorders in PWH on contemporary ART, optimal viral control and immune reconstitution resemble most likely those observed in the general population. The main contributors to sleep disorders in PWH remain mood disorders, and the iatrogenic effects of drugs other than antiretrovirals. However, this study did not include a control uninfected group and was not designed to properly address causation between antiretrovirals and sleep disorders. To date, not a single study has focused on the associations between biomarkers of bacterial translocation, immune activation and inflammation with sleep disorders in PWH. Emerging evidence has suggested that abnormal immunological function may contribute to poor quality of sleep [7]. Thus, an unmet need in the field is the evaluation of the microbiome [8] and biomarkers of bacterial translocation and immune dysfunction in PWH in association with independent sleep disorders scales and cardiovascular risk factors. Assessment of both sleep and mood disorders in PWH may improve the overall assessment of these patients in the clinic but is often neglected in clinical practice.

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Conflicts of interest

There are no conflicts of interest.

References

1. Wu J, Wu H, Lu C, Guo L, Li P. **Self-reported sleep disturbances in HIV-infected people: a meta-analysis of prevalence and moderators.** *Sleep Med* 2015; **16**:901–907.
2. Ning C, Lin H, Chen X, Qiao X, Xu X, Xu X, *et al*. **Cross-sectional comparison of various sleep disturbances among sex- and age-matched HIV-infected versus HIV-uninfected individuals in China.** *Sleep Med* 2020; **65**:18–25.
3. Huang X, Li H, Meyers K, Xia W, Meng Z, Li C, *et al*. **Burden of sleep disturbances and associated risk factors: a cross-sectional survey among HIV-infected persons on antiretroviral therapy across China.** *Sci Rep* 2017; **7**:3657.
4. Allavena C, Guimard T, Billaud E, De la Tullaye S, Reliquet V, Pineau S, *et al*. **Prevalence and risk factors of sleep disturbance in a large HIV-infected adult population.** *AIDS Behav* 2016; **20**:339–344.
5. Chen YC, Lin CY, Li CY, Zhang Y, Ko WC, Ko NY. **Obstructive sleep apnea among HIV-infected men in the highly active antiretroviral therapy era: a nation-wide longitudinal cohort study in Taiwan, 2000–2011.** *Sleep Med* 2020; **65**: 89–95.
6. Mazzitelli M, Trunfio M, Milinkovic A, Castelli E, Sasset L, Leoni D, *et al*. **Sleep disturbances and their correlation with cardiovascular risk, obesity, and mood disorders in people living with HIV.** *AIDS* 2023; **37**:925–934.
7. Besedovsky L, Lange T, Haack M. **The sleep-immune crosstalk in health and disease.** *Physiol Rev* 2019; **99**:1325–1380.
8. Li Y, Hao Y, Fan F, Zhang B. **The role of microbiome in insomnia, circadian disturbance and depression.** *Front Psychiatry* 2018; **9**:669.