

Comment on: Gooden TE, Gardner M, Wang J, Chandan JS, Beane A, Haniffa R, Taylor S, Greenfield S, Manaseki-Holland S, Thomas GN, Nirantharakumar K. The risk of mental illness in people living with HIV in the UK: a propensity-score matched cohort study *Lancet HIV*

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Increased risk of mental illness in people with HIV

People with HIV who are diagnosed promptly and treated can now anticipate a life expectancy similar to that of people without HIV.¹ However, despite this remarkable narrowing of the gap in mortality risk, a stark disparity in mental health, evident in the early days of the epidemic,² appears to persist. Studies across a range of countries and settings, using a variety of measurement tools, have consistently found a high burden of depressive symptoms among people with HIV,³ with some reporting a two-fold higher prevalence compared to general population or HIV-negative control groups.⁴

The relationship between HIV and mental health is likely to operate in both directions, with poor mental health being a risk factor for acquisition of HIV, as well as a potential consequence of it. A key question, therefore, is whether HIV increases risk of development of new mental illness. The retrospective cohort analysis conducted by Gooden and colleagues⁵ in *the Lancet HIV* is one of few studies to address this question, and the first in the UK. Using data from a primary care database from 2000-2020, the investigators compared incidence of a first diagnosis of mental illnesses (depression, anxiety or severe mental illness) between over 7000 people with HIV and a matched number of people without HIV.⁵ Careful matching of baseline characteristics of HIV-positive and HIV-negative groups, achieved using propensity scores, ensured close similarity with respect to key variables (including age, year, sex, ethnicity, Townsend deprivation quintile), reducing confounding. Compared to the HIV-negative group, people with a diagnosis of HIV had a higher rate of subsequent first diagnosis of mental illness (adjusted hazard ratio 1.6, 95% CI: 1.4, 1.9). Corresponding adjusted hazard ratios for specific first diagnoses were 1.9 (1.7, 2.2) for depression; 1.4 (1.2, 1.7) for anxiety; 2.2 (1.4, 3.4) for severe mental illness. The elevated risk of mental illness was present for people

whose index date (date of HIV diagnosis or cohort entry) was in 2000-2009 and those with index date in 2010-2019.

By excluding from analysis those with a previous recorded diagnosis of mental illness at baseline, the investigators were able to capture 'incident' (first) diagnoses, adding to evidence of temporality (the HIV diagnosis came before the mental illness diagnosis) and therefore causality. The limitation, however, is that even though a diagnosis of mental illness is new, the symptoms that led to it may not be. An outcome based on recorded diagnoses will underestimate occurrence of mental health disorders, and the likelihood of getting a formal diagnosis may differ between those with and without HIV. We might expect the direction of bias to be greater diagnosis among the HIV-positive group, because of increased contacts with health services, with new opportunities for medical recognition of pre-existing psychological symptoms. The authors also note the possibility of the converse - experiences of stigma may reduce engagement with primary care and resulting opportunities for diagnosis of mental illness.

Notably, in subgroup analyses, the excess risk associated with HIV was present only among men. This raises the possibility of residual confounding by sexual orientation, a factor not well recorded in primary care, which the investigators could not control for. The HIV-positive group most likely included a higher proportion of gay and bisexual men, whose risk of mental health problems may be elevated due to minority stress, stigmatisation and discrimination. However, sexual orientation does not seem to explain differences in prevalence of poor mental health between people with and without HIV.⁴ Additionally, the investigators' sensitivity analyses suggested limited impact of any unobserved confounding.

Despite some limitations of the data, the findings of increased risk of mental illnesses among people with HIV, from this large well-conducted primary care-based study in a setting of universal access to healthcare, add significantly to a small number of previous longitudinal studies only one of which had a matched comparison group.⁵ The results emphasise the need to prioritise the detection, management and prevention of mental health conditions among people with HIV, including greater awareness of the risk, regular screening for depression, prompt treatment with evidence-based interventions, and appreciation of the socioeconomic context with links to appropriate support. Crucially, we need to better understand the reasons for this disparity in risk of mental illness, in this era of excellent HIV prognosis. A key pathway may relate to adverse social consequences of living with HIV: stigma, discrimination, and lack of social support, factors strongly linked to depression.⁶

Other contributors may include co-morbidities, recreational drug use, specific antiretrovirals, or a biological mechanism related to chronic immune activation. We also need more information on whether people with HIV have a greater risk of mental illness than people with other chronic health conditions.⁷ Gaining insight into causal pathways should help us develop more effective, tailored intervention and prevention strategies.

In addition to the profound impact of psychological distress on quality of life, increasing evidence suggests that mental health is a critical determinant of other health outcomes among people with HIV. Studies have found depression is associated with non-adherence to treatment,⁸ viral non-suppression,⁹ risk of hospital admission¹⁰ and mortality.⁹ For some endpoints, the predictive power of a depression measure appears as strong as that seen for commonly measured clinical factors. Yet unfortunately, measures of mental health have been missing from many of our secondary care-based HIV databases that have been the mainstay of research into HIV prognosis. This study by Gooden and colleagues further underlines the need for collection of these data, together with closely linked socioeconomic factors, as part of routine HIV care.

COI: FCL declares no conflict of interest

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