Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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More evidence for worse COVID-19 outcomes in people with HIV

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The global effect of COVID-19 is enormous, and the havoc wrought is ongoing. Measuring the effect of COVID-19 on mortality is challenging, and analyses based on adjusted excess deaths suggest that mortality might be underestimated by the reported COVID-19 deaths.[1] Regardless, there have been millions of COVID-19 related deaths globally and it might be years before we fully understand the scale of COVID-19 related morbidity and mortality. From the start of the pandemic, the question of who is most at risk of severe COVID-19 outcomes, and therefore who should be prioritised for vaccination and other risk reduction measures, has been important. Relatively early in the pandemic, the OpenSAFELY analysis of approximately 11 000 COVID-19 related deaths in more than 17 million UK adults, identified several factors associated with an increased risk of death, including being male, older age, Black and South Asian ethnicity, socioeconomic deprivation, and several comorbidities (eg, diabetes, severe asthma, haematological cancers, and immunosuppression post-transplant).[2]

What about people living with HIV? Initial reports and case series did not show a higher risk of mortality but larger analyses, and crucially, analyses that were adjusted for age, showed a higher risk of COVID-19 death in people with HIV.[3] The relative impact of HIV differs across these studies, which is probably driven by variation between cohorts in health care and prevalence of other risk factors for worse COVID outcomes. However, how much any excess risk is driven by HIV per se as opposed to the fact that people with HIV are disproportionately affected by other negative health determinants is uncertain, although there is some evidence that HIV-specific factors could impact risk of worse COVID-19 mortality.[4,5]

In *The Lancet HIV* two Articles by Daniel K Nomah and colleagues[6] and Xueying Yang and colleagues[7] provide additional information on COVID-19 outcomes among people with HIV. Nomah and colleagues describe 749 COVID-19 cases in a Spanish cohort of 13 142 people with HIV,[6] although the absence of data on people without HIV means conclusions about the relative mortality risk of HIV cannot be drawn. Yang and colleagues describe the effect of HIV on adverse COVID-19 outcomes from an analysis of the National COVID Cohort Collaborative (N3C) data in the USA.[7] Of the 1 436 622 adult COVID-19 cases, 13 170 were in people living with HIV and of the 26 130 COVID-19 related deaths, 445 were in people living with HIV. HIV was associated with a 20% higher risk of hospitalisation, and a 29% higher risk of COVID-19 mortality after adjustment for different covariates.

Both Articles show an association between worse COVID-19 outcomes and established risk factors including older age and comorbidities, with the Spanish

cohort also showing worse outcomes in people not born in Spain, and the USA study in people of Black or African American or Hispanic or Latinx ethnicity. Both studies explored the effect of HIV markers on COVID-19 outcomes: Nomah and colleagues show worse outcomes in people with viraemia and CD4 counts of less than 200 cells per µL, although the CD4 association was lost in those with viral suppression, and Yang and colleagues found that CD4 counts less than 200 cells per µL were associated with a higher risk of mortality and viral suppression with a lower risk of hospitalisation, but unfortunately, viral load and CD4 data was available for just under 12% of the cohort.

This Spanish cohort also showed a higher risk of having a positive SARS-CoV-2 test (nucleic acid amplification test, antigen detection, or antibody testing) among migrants, men who have sex with men (MSM), and people with four or more comorbidities. Nomah and colleagues hypothesise that people not born in Spain are more likely to be exposed to SARS-CoV-2 through occupation or housing and that the higher risk in MSM is compatible with other cohorts describing risky sexual behaviours outside their homes among MSM in the UK, Brazil, and Portugal. This hypothesis is quite a leap considering the absence of adjustment for testing rates, and absence of data on reported sexual contacts or sexually transmitted infections.

The USA analysis suggests that the lower risk of mild or moderate COVID-19 in people with HIV could be explained either by the alleged protective effect of tenofovir or differences in health-seeking behaviour driven by factors such as stigma or lack of medical coverage. While both might be true, this study is unable to prove either. The tenofovir question is one that generates more speculation than evidence, and while a very small, randomised trial showed faster viral clearance in health-care workers with mild or moderate COVID-19,[8] a lack of convincing evidence for in vitro activity of tenofovir against SARS-CoV-2 means any benefit of tenofovir might not be the result of a direct antiviral effect.

Since COVID-19 emerged as serious threat to health globally, providing accurate advice to people with HIV, and their health-care providers, has been challenging. The studies from Nomah and colleagues and Yang and colleagues, add to the accumulating evidence for worse outcomes for people with HIV and support early guidance that people with HIV, particularly those with immune suppression, should be prioritised for COVID-19 risk reduction, including vaccination.[9] These studies also shine more light on the stark and harsh reality of the health inequities that have been magnified by COVID-19. Although the current inequalities in global COVID-19 vaccine coverage are a gross injustice, it will take more than a vaccine to address the socioeconomic disparities, structural racism, and political inaction that render the most vulnerable in society at greatest risk of harm.

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