

HIV appears to moderately increase the risk of death even in people with high CD4 count

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New research published Online First by *The Lancet* suggests that HIV may increase the risk of death in people who have not taken antiretroviral treatment (ART) and have CD4 count greater than 350 cells per μL , but any such increase appears relatively modest. Because ART might reduce the risk of death in such patients, these findings support the need for continuing studies of the risks and benefits of starting ART at CD4 counts greater than 350 cells per μL . The Article is written by Rebecca Lodwick and Professor Andrew Phillips, HIV Epidemiology and Biostatistics Group, University College London Medical School, UK, and colleagues.

The study included data from 23 European and North American cohorts. Standardised mortality ratios (SMRs) were calculated, adjusted by age, sex, and year, and stratified by risk group. Data were included for patients aged 20–74 years who had at least one CD4 count greater than 350 cells per μL while ART naive. Mortality for four risk groups was investigated—men who have sex with men, heterosexual people, injecting drug users, and those at other or unknown risk.

Data were analysed for 40 830 patients contributing 80 682 person-years of follow-up. Of 419 deaths, 401 were used in the SMR analysis: 100 men who have sex with men (SMR 1.30—or a 30% increased risk compared with the general population); 68 heterosexual people (SMR 2.94, close to three times increased risk); 203 injecting drug users (SMR 9.37, more than nine times increased risk); and 30 in the other or unknown risk category (4.57). Compared with CD4 counts of 350 cells

per μL , death rate was 23% lower in patients with counts of 500 cells per μL and 34% lower for counts of 700 cells per μL or greater.

The authors say: "The increase in risk was substantial in injecting drug users and the heterosexual group but was small in men who have sex with men. This finding suggests that much of the raised risk in the former two risk groups probably results from confounding by socioeconomic and lifestyle factors rather than being an effect of HIV infection itself. The magnitude of the raised risk in the MSM group is more likely to reflect the effect of HIV itself. "

The authors say this is consistent with findings from other studies that show an increased risk of death in the siblings of people with HIV infection compared with the siblings of a control population without HIV infection, i.e, it is probably the social or other circumstances that the person finds themselves in that increases the risk of death, rather than the HIV infection itself.

The authors conclude: "These data suggest that HIV may increase the risk of death in people who have not taken ART and have CD4 count greater than 350 cells per μL , but any such increase appears relatively modest. Because ART might reduce the risk of death in such patients, these findings support the need for continuing studies of the risks and benefits of starting ART at CD4 counts greater than 350 [cells](#) per μL ."

In a linked Comment, Dr Ingrid Bassett, Massachusetts General Hospital, Boston, MA, USA, and Dr Paul Sax, Brigham and Women's Hospital, Harvard Medical School, Boston, USA, ask if similar results would be recorded in poorer settings, and say that the effect of untreated HIV infection on mortality with higher CD4 counts would probably be even higher due to higher levels of infectious diseases in such settings.

They conclude: "Lodwick and colleagues' study is one of the largest

observational studies to analyse increased mortality in less-advanced HIV infection. Whether starting antiretrovirals at higher [CD4](#) cell counts than are recommended in US and European guidelines reduces this risk remains unknown; at least one trial comparing immediate versus deferred antiretrovirals in these patients is in progress. With the results of this study probably years away, clinicians must aggressively screen, prevent, and treat risk factors for chronic diseases that seem to account for the residual excess mortality in early HIV-infection. Factors include tobacco use, intravenous drug use, hyperlipidaemia, hypertension, diabetes, obesity, and viral hepatitis. Even for those with relative immune competence, [HIV](#) infection remains a foe with many faces."

Provided by Lancet

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