No increase in risk of death for patients with well-controlled HIV, reports AIDS journal

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For HIV-infected patients whose disease is well-controlled by modern treatment, the risk of death is not significantly higher than in the general population, according to a study published in *AIDS*, official journal of the International AIDS Society.

The study suggests that patients with undetectable viral loads and near-normal levels of immune cells on state-of-the art antiretroviral therapy (ART) can expect to have about the same risk of death as people without HIV. The article is available on the *AIDS* journal homepage and in the March 13 print edition.

What's the Risk of Death with Well-Controlled HIV?

Dr Alison Rodger of University College London and colleagues assessed mortality rates in a group of patients with "optimally treated" HIV, drawn from two major trials of treatment for HIV infection: the ESPRIT and SMART trials. The analysis included nearly 3,300 patients who were not injecting drug users and who received continuous ART. On treatment, all had achieved undetectable HIV levels and had relatively high levels of CD4+ cells, a key population of immune cells—at least 350 cells/mm3. (A CD4+ cell count of 500 to 1,000 cells/mm3 is considered normal.)

The patients' average age was 43 years; 80 percent were men. Rates and causes of death in these patients with well-controlled HIV were compared with those in the general population.

During a median follow-up of about three years, 62 of the patients died. The most common causes of death were cardiovascular disease or sudden death, responsible for 31 percent of deaths; and non-HIV-related cancers, 19 percent. Only two deaths (three percent) were considered AIDS-related.

Patients with below-normal CD4+ cell counts (350 to 499 cells/mm3) were at elevated risk of death. Based on the standardized mortality ratio, the risk of death in this group was 77 percent higher than in the general population.

With Normal CD4+ Cell Counts, No Increase in Mortality

However, in HIV-infected patients with a CD4+ cell count of 500 cells/mm3 or higher, the risk of death was not significantly higher than in the general population. For this group, the risk of death was essentially normal regardless of how low the CD4+ cell count dipped during treatment, as long as it returned to normal.

Over the years, effective ART regimens for HIV infection have become simpler, less toxic, and more effective. "Due to the success of ART, it is relevant to ask if death rates in optimally treated HIV are higher than the general population," the researchers write.

Previous studies have suggested that, with successful treatment, mortality risk approaches that of people without HIV. However, these studies have had important limitations, including a lack of complete information on patient outcomes. The use of comprehensive follow-up data from the ESPRIT and SMART trials overcomes this limitation.

The new study provides the best evidence yet that, with effective ART that achieving good disease control, the mortality rate for people with HIV is essentially the same as in the general population. Dr Rodger and colleagues conclude, "Our data support the importance of early diagnosis and treatment to improve clinical outcomes and it is likely that much of the excess mortality associated with HIV would be preventable with timely diagnosis of HIV and initiation of ART."

Further studies will be needed to clarify the implications for HIV treatment, including the best

time to start ART based on CD4+ cell counts. The researchers also note that other causes of illness or death emerge as the current generation of treated HIV-infected people continues to age.

"Rodger and colleagues add to the considerable body of evidence on which early treatment initiation guidelines are based," commented Veronica Miller, PhD, Director of the Forum for Collaborative HIV Research. "Together with studies indicating equal benefit across risk groups, including injecting drug users, as long as individuals are maintained in care, this study further validates universal testing with immediate linkage and retention in care policies."

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