

# Since introduction of highly active antiretroviral therapy, HIV death rate has decreased

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In industrialized countries, persons infected sexually with HIV now appear to experience mortality rates similar to those of the general population in the first 5 years following infection, though a higher risk of death remains as the duration of HIV infection lengthens, according to a study in the July 2 issue of *JAMA*.

A number of studies have reported the dramatic decreases in mortality among individuals infected with human immunodeficiency virus (HIV) since the widespread introduction of highly active antiretroviral therapy (HAART) in industrialized countries. "It is important to provide up-to-date and robust estimates of expected mortality as anti-HIV drugs and strategies continue to improve. Such estimates help policy makers and those planning health care to monitor the effectiveness of treatments at a population level and provide an indicator of the ongoing and likely future impact of HIV disease on health care needs," the authors write.

Krishnan Bhaskaran, M.Sc., of the Medical Research Council Clinical Trials Unit, London, and colleagues evaluated changes in the excess mortality of HIV-infected individuals compared with expected mortality in the general uninfected population, adjusting for duration of HIV infection. Mortality following HIV seroconversion (development of antibodies in blood serum as a result of infection) in a large multinational collaboration of HIV seroconverter cohorts (CASCADE) was compared with expected mortality, calculated by applying general

population death rates matched on demographic factors. A model was created, adjusted for duration of infection, to assess changes over calendar time in the excess mortality among HIV-infected individuals. Data pooled in September 2007 were analyzed in March 2008, covering years at risk 1981-2006.

Of 16,534 individuals with median (midpoint) duration of follow-up of 6.3 years, a total of 2,571 individuals had died as of December 2006, compared with an estimated 235 deaths that would have been expected in a matched general population cohort. The excess mortality rate per 1,000 person-years (the number of individuals in the study times the number of years of follow-up per person) was 40.8 pre-1996, decreasing in each subsequent calendar period to 6.1 in 2004-2006. By 2004-2006, there was no evidence of any excess mortality to 5 years from seroconversion among those infected sexually. However, in the longer term, some excess mortality was still evident, with the cumulative excess probability of death in the first 10 years from seroconversion estimated to be 4.8 percent in those 15 to 24 years old, and 4.3 percent in those 45 years or older at seroconversion.

"Considering the first years following the widespread introduction of HAART, we have estimated an 88 percent reduction in excess mortality in 2000-2001 compared with pre-1996, corresponding closely to the 87 percent reduction in the standardized mortality ratio in 1997-2001 compared with pre-1996, as reported by the Swiss HIV cohort. Our more recent data show that reductions have continued to 2004-2006, with excess mortality in this period 94 percent lower than pre-1996 levels. Corresponding to these reductions, the uptake of HAART increased, and though this leveled off after 2001, there followed an increasing use of nonnucleoside reverse transcriptase inhibitor-based HAART as the first-line treatment regimen and a substantial increase in the boosting of protease inhibitor-based regimens," the authors write.

Older age at seroconversion was associated with a higher risk of excess mortality (for age 45 years or older compared with age 15-24 years), as was a reported exposure category of injection drug use (compared with sex between males). Females appeared to be at lower risk than males.

"Our results show the progress in reducing mortality among HIV-infected individuals toward the levels experienced by the general uninfected population. However, there is continuing excess mortality, particularly evident in those infected for 10 years or more. Ongoing monitoring of excess mortality will be important as new treatment advances are implemented in an attempt to further reduce mortality rates among HIV-infected individuals," the researchers conclude.

Source: JAMA and Archives Journals

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