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Excess mortality after HIV seroconversion has greatly decreased in the past 10 years

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Questions

What is the risk for death in HIV-infected persons compared with the general population?

Has this risk changed since the introduction of highly active antiretroviral therapy?

Methods

Design

Inception cohort followed for a median 6.3 years.

Setting

10 European countries, Australia, and Canada.

Patients

16 534 patients 15 years of age at HIV seroconversion (median age 29 y, 78% men) who had well-estimated dates of seroconversion (within 18 mo) and exposure to HIV through injection drug use (18% of patients), sex between men (57%), or heterosexual sex (24%).

Prognostic factors

Calendar period of follow-up (before 1996, 1996 to 1997, 1998 to 1999, 2000 to 2001, 2002 to 2003, and 2004 to 2006), sex, age at seroconversion, and HIV exposure category.

Outcomes

Mortality, excess mortality compared with the general uninfected population, and excess mortality in recent years compared with before 1996.

Main results

2571 HIV-infected persons died compared with 235 expected deaths in a matched general population cohort. Overall mortality was 23 per 1000 person-years (95% CI 22 to 24) and excess mortality over that of the general population was 21 per 1000 person-years (CI 20 to 22). Data by calendar period are shown in the Table. Risk for excess mortality was higher in men, persons who were older at seroconversion, and those with HIV exposure from injection

drug use. In persons with sexual HIV exposure, by 2004 to 2006 mortality in the first 5 years since seroconversion did not differ from that of the general population, although mortality remained increased in persons with a longer duration of infection.

Conclusions

Persons infected with HIV had higher mortality than did the general population, but mortality and excess mortality have greatly decreased in the past 10 years. By 2004 to 2006, HIV seroconversion from sexual exposure was not associated with increased mortality in the first 5 years.

Commentary

The study by the CASCADE Collaboration provides unique data to assess mortality in HIV-infected individuals in the Western world, where potent antiretroviral therapy has been available for > 12 years. The remarkable decline in excess mortality from “before 1996” to 1996 to 2006 is a testament to the clinical effectiveness of these drugs. This study confirms that HIV/AIDS is no longer an immediate death sentence: Individuals infected with HIV can expect mortality risks approaching those of noninfected individuals, at least in the first few years.

HIV therapy is lifelong, and although newer medications have fewer adverse effects, they still require long-term commitment by the patient. The results of Bhaskaran and colleagues should encourage adherence to treatment and a hopeful outlook in persons living with HIV. Duration of treatment will become even longer with the trend toward treating HIV at earlier stages (1). Unfortunately, in North America and Europe, HIV infection is usually detected relatively late in its natural history (2). Recommendations for early detection of HIV infection (3) will be important for earlier treatment of HIV.

The study by Bhaskaran and colleagues could not do more than minimally examine causes of death. Because HIV-infected individuals now survive longer, comorbid conditions not previously associated with HIV/AIDS are being seen with increasing frequency, including cardiovascular diseases and non-AIDS cancer (1). Much of the increasing risk for these diseases may be caused by aging, but some portion may be attributable to HIV and its treatment. How these diseases will affect future morbidity and mortality in persons living with HIV is not yet known.

Persons in whom injection drug use was the mode of HIV transmission have not had the same benefit from antiretroviral therapy as other risk groups. In this study, persons infected by injection drug use had a 4-fold greater risk for dying than those infected through sexual transmission. It is likely that both poor adherence to therapy and additional drug-related causes of death contributed to this difference. Nevertheless, the message is that injection drug use cannot be ignored when treating HIV infection.

Acknowledgments

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Table 1

Mortality after HIV seroconversion at median 6.3 years

Calendar year of follow-up	Mortality/1000 person-years	Excess mortality/1000 person-years*	Hazard ratio for excess mortality (95% CI) [†]
Before 1996	43	41	1 (reference)
1996 to 1997	33	31	0.54 (0.48 to 0.60)
1998 to 1999	14	12	0.17 (0.14 to 0.20)
2000 to 2001	12	9.5	0.12 (0.10 to 0.14)
2002 to 2003	11	8.5	0.10 (0.08 to 0.12)
2004 to 2006	8.6	6.1	0.06 (0.05 to 0.08)

* Compared with mortality in a matched general population cohort.

[†] Risk for excess mortality from HIV in recent years compared with before 1996, adjusted for age at seroconversion, sex, and HIV exposure category.