Research letters

Mortality in the Swiss HIV Cohort Study (SHCS) and the Swiss general population

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Because of high death rates in the past, patients with HIV-1 cannot obtain life insurance. We measured mortality rates in the Swiss HIV Cohort Study (SHCS) from 1997 to 2001 and compared them with those of the Swiss reference population. In patients who were successfully treated with highly active anti-retroviral therapy (HAART), and who were not also infected with the hepatitis C virus, excess death rates were below five per thousand per year. Patients with successfully treated cancer have much the same excess death rates but are not excluded from life insurance policies.

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Mortality in patients with HIV-1 is still perceived to be much higher than that of the general population. High rates of mortality preclude life insurance in major European countries, and in the USA. The inability to obtain life insurance hampers business opportunities and gives rise to social limitations.

Highly active anti-retroviral therapy (HAART) has reduced mortality in patients with HIV-1. Moreover, the deaths that still occur are not distributed uniformly among the HIV-1-infected population, but cluster in subgroups, such as those with treatment failure, and those coinfected with hepatitis C.[1] In patients without these risk factors, excess mortality is expected to be low.

The Swiss HIV Cohort Study (SHCS) is an ongoing study of HIV-positive patients from seven large hospitals in Switzerland, with follow-up visits every 6 months.[2] Any consenting HIV-positive adult above 18 years of age can be included. Clinical events, such as opportunistic diseases and deaths, are recorded. Available laboratory results include HIV-1 viral load, CD4 counts, and, since 1997, hepatitis C serology.

6547 patients in the SHCS attended a follow-up visit at the study centre after Jan 1, 1997. 4681 (71%) of these patients were Swiss, of whom 3963 (85%) had hepatitis C serology available. We used the data for these 3963 patients to determine mortality. Prognostic factors assessed were presence or absence of antibody to the hepatitis C virus, and success of treatment, defined as attaining, at least once, a CD4 count of greater than 250 cells/μL after Jan 1, 1997, after more than 6 months on HAART. Analysis of mortality started with the date of the CD4 count indicating success in the successfully treated patients, and with the first cohort visit after Jan 1, 1997, in all others. Patients were followed up until Dec 31, 2001, or until death, whatever occurred first. We also checked the official death registries of the Swiss Federal Office of Statistics. These registries contained all deaths occurring in Switzerland, and all deaths of Swiss citizens occurring elsewhere, between Jan 1, 1997, and Dec 31, 2001.

The excess death rate of SHCS patients, in extra deaths per 1000 per year, was calculated on the basis of the most recent age-specific and sex-specific Swiss population mortality. We calculated CIs for the excess death rate,[3] on the basis of the assumption that for the unknown mortality q' the following equation is valid:

$$\frac{q-q'}{\sqrt{\frac{q'\cdot(1-q')}{B}}} \approx N(0,1)$$

where q is the measured mortality and B denotes follow-up years. Statistical analysis was done with Stata Statistical Software (version 7.0).

The table shows the mortality data for the 3963 patients in the SHCS in whom information on hepatitis C serology was available, with a total of 12 911 patient-years of follow-up (median 3·69 years, IQR 1·93–2·72). Of the 3963 patients in our sample, there were 341 recorded deaths (345 after correction, see below), yielding an excess death rate of 23·9 per 1000 patient-years (95% CI 21·3–26·8). However, with simple laboratory investigations effected 6 months or later than the start of HAART, subgroups can be identified which have much lower, or much higher excess death rates than the total population (table).

We were concerned that some of the patients who had dropped out of the SHCS might be dead, and that we might therefore underestimate mortality. In the SHCS, patients are

	Hepatitis-C negative			Hepatitis-C positive		
	Patients (follow-up years)	Deaths	EDR (95% CI)	Patients (follow-up years)	Deaths	EDR (95% CI)
All	2318 (7598)	134	14·0 (11·3–17·2	1645 (5313)	211	38·1 (33·2–43·7)
Successfully treated patients						
CD4 >250 (cells/μL)	1567 (4498)	35	4·2 (2·0–7·2)	944 (2521)	59	21·7 (16·5–28·4)
CD4 >250 (cells/μL), and viral load <400 (copies/mL)	1281 (3594)	25	3·4 (1·1–6·7)	726 (1894)	42	20·5 (14·8–28·1)
CD4 >250 (cells/μL), and viral load >400 (copies/mL)	274 (861)	10	8·0 (2·7–17·6)	215 (618)	17	25·9 (15·6–42·0)
CD4 >250 (cells/μL), and viral load <400 (copies/mL), but CD4 nadir <250 cells/μL before HAART	545 (1564)	11	3·1 (0·0–8·6)	425 (1118)	28	23·3 (15·6–34·2)
Patients with unsuccessful treatment						
CD4 count never >250 cells/μL	257 (620)	76	117·4 (93·9–145·6)	309 (777)	89	112·7 (92·2–137·0)

Excess death rates (EDR) per 1000 patient-years in Swiss patients of the SHCS, 1997–2001

recorded as drop-outs if they withdraw consent, move out of Switzerland, or miss appointments during more than 12 months. There were 127 drop-outs among the 1567 hepatitis C negative, successfully treated patients. Using the death registry of the Swiss Federal Office of Statistics, as well as population records at the last recorded place of residence, we determined that on Dec 31, 2001, 123 of the drop-outs were alive, whereas four had died and were included in the table.

In patients successfully treated for HIV-1, hepatitis C status contributed strongly to excess death rates. Hepatitis C status is closely linked to intravenous drug use. There were too few hepatitis C negative drug users (and hepatitis C positive non-drug users) in our sample to tease apart the respective effects of liver disease and intravenous drug use. As opposed to eliciting a history of drug use, the measure of hepatitis C antibody offers the advantage of objectivity and reliability.

Excess death rates in successfully treated hepatitis C negative Swiss patients were below five per thousand patient-years (table). Friis-Moller and colleagues[4] showed that HAART is associated with a risk of myocardial infarction that amounts to about one death per 1000 patient-years of follow-up. This risk might partly account for the excess death rate recorded in successfully treated patients.

It did not seem to matter that patients were immunosuppressed before starting HAART (table). As expected, in the category of patients who reached a CD4 count of greater than 250 cells/μL on HAART, attainment of a low viral load seems to further decrease mortality (table). Follow-up is still short. However, of 2511 patients meeting our definition of success—ie, a CD4 count of greater than 250 cells/μL at least 6 months after starting treatment, 2171 (87%) still had a CD4 count above 250 cells/μL at last follow-up. For these patients, mortality is likely to remain low during the next few years.

Successful treatment of HIV in hepatitis C positive patients results also in a significant reduction of excess death rates, but the rates remain much higher than those of hepatitis C negative individuals. The table probably underestimates the difference between the low-risk, and the high-risk categories, because the vital status of low-risk drop-outs was checked, by contrast with the vital status of high-risk drop-outs.

In conclusion, successfully treated HIV-positive and hepatitis C negative patients have a short term mortality as low as, or lower than that of, patients with cancer who have been successfully treated (excess death rate in the range of five to 20 per 1000 patient-years[5])—a group that is able to obtain life insurance. This study provides preliminary actuarial evidence that life coverage could be considered under specific conditions.

Contributors

B Hirschel, with help from M Egger and M Rickenbach, wrote the study protocol, supervised the analysis, and wrote the report. C Jaggy, C Schwarz, and J von Overbeck did the analysis. B Ledergerber and M Rickenbach extracted the data for the Swiss HIV Cohort Study and prepared them for analysis. All other authors collaborated in establishing the final study protocol and contributed to the report.

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