



LETTERS TO THE EDITOR

RE: "ESTIMATION OF RISK OF CANCERS BEFORE OCCURRENCE OF ACQUIRED IMMUNODEFICIENCY SYNDROME IN PERSONS INFECTED WITH HUMAN IMMUNODEFICIENCY VIRUS"

Studies linking acquired immunodeficiency syndrome (AIDS) and cancer registries can examine whether the risk for particular cancers increases over time with respect to AIDS onset. Such a finding suggests that increasing immunosuppression related to human immunodeficiency virus (HIV) plays a causal role. In these studies, estimating cancer risk among persons with asymptomatic HIV infection during the period before AIDS onset is challenging. AIDS registries identify only those persons who have actually developed AIDS. Because some HIV-infected persons with cancer do not survive their cancer diagnosis to develop AIDS, linkage with AIDS registries will underascertain cancers for the pre-AIDS period. This problem will be serious for cancers with a high mortality rate.

We were thus surprised by the results reported by Li et al. (1), who compared registry-based methods for estimating cancer risk in Australians with asymptomatic HIV infection. These authors found that standardized incidence ratios for cancers arising during the 5-year pre-AIDS period, estimated retrospectively from a linkage of AIDS and cancer registries, were similar to those calculated prospectively from a linkage of HIV and cancer registries. They concluded that survival adjustment of the retrospectively derived standardized incidence ratios was not needed.

In the United States, we previously conducted a match of 11 AIDS and cancer registries (2). Our study included more than 300,000 persons with AIDS and thus was much larger than the Australian study (1), which included 8,118 AIDS cases. In deriving standardized incidence ratios for pre-AIDS periods in our study, we used cancer survival rates to adjust downward the expected counts of cancers because many HIV-infected persons with cancer die before developing AIDS (2).

Lung cancer is a good example. By using expected rates adjusted for survival, we previously reported a significant trend in standardized incidence ratios across time relative to AIDS onset (2), with standardized incidence ratios increasing from 1.23 (in the period -60 to -25 months relative to AIDS, based on 31 cases) to 2.59 (-24 to -7 months, 80 cases) to 2.63 (4 to 27 months, 239 cases). This trend was difficult to interpret, and, because there are few other data to support a link between immunosuppression and lung cancer, it may not have arisen from progressive HIV-related immunosuppression (2). Nonetheless, this trend would have been much more exaggerated if we had not adjusted the pre-AIDS standardized incidence ratios for survival. For instance, we roughly calculate that the unadjusted standardized incidence ratio for the period -60 to -25 months (midpoint, -42 months) relative to AIDS would have been $1.23 \times 0.14 = 0.17$ because the 42-month survival rate for lung cancer patients is only 14 percent (3). We argue that this is a gross underestimate, since it is improbable that HIV-infected

persons have a lower risk than the general population given their high prevalence of smoking (4).

We are uncertain why Li et al. (1) found that survival adjustment of pre-AIDS standardized incidence ratios was unnecessary. For many cancers in their study (e.g., lip and anal cancers, Hodgkin's disease), mortality is relatively low, while there were few data for individual cancers with high mortality. For example, the study included only two lung cancers. The small numbers for high-mortality cancers make it difficult to examine the impact of survival adjustment where it is most relevant. Finally, Li et al. suggest that cancer treatment accelerates HIV progression, which might counterbalance losses from cancer-related deaths. While we agree that treatment could have this effect, we know of no data to indicate that the effect would be of the same magnitude as cancer-related mortality.

In summary, survival adjustment of expected rates during the pre-AIDS period is necessary to avoid underestimating the pre-AIDS risk of cancer and drawing false conclusions about the effects of HIV-associated immunosuppression, especially for high-mortality cancers.

REFERENCES

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TWO AUTHORS REPLY

There has been a great deal of methodological debate about studies linking acquired immunodeficiency syndrome (AIDS) and cancer, especially about whether the pre-AIDS period can be used in calculating rates. We were in a unique