

HIV-infection and comorbidities: a complex mix

In *The Lancet HIV*, Line Rasmussen and colleagues¹ report time trends in the risk of a range of severe age-related morbidities in HIV-positive and HIV-negative individuals in Denmark. The investigators noted increased risk of these morbidities in HIV-positive people compared with that in HIV-negative matched controls. However, this increased risk did not substantially increase with age; therefore, suggesting no greater increased risk effect of ageing in HIV-positive people than in HIV-negative populations. Similar findings have been reported in others studies. Data from the Veterans Aging Cohort Study Virtual Cohort (VACS)² showed an increased risk of myocardial infarction, end-stage renal disease, and non-AIDs defining cancers in HIV-positive veterans; however, these events occurred at similar ages as in HIV-negative veterans. In the D:A:D study, the increasing risk of cardiovascular disease, coronary heart disease, and myocardial infarction with increasing age was similar to that predicted from conventional cardiovascular risk equations such as the Framingham equation.³ Similarly, the results of the AGEHIV Cohort Study of some of these comorbidities in both HIV-positive and HIV-negative people showed an increased prevalence in HIV-positive individuals, with little evidence of a differing effect with age.⁴

For most of the comorbidities, Rasmussen and colleagues did not note substantial increases with increasing duration of HIV infection or duration on antiretroviral therapy.

The causes of these long-term clinical outcomes in HIV-positive individuals are a complex mix of HIV infection, antiretroviral treatment, co-infections such as hepatitis B and hepatitis C virus, and lifestyle factors such as cigarette smoking⁵ and use of alcohol and other drugs,⁶⁻⁸ which are much more prevalent in people with HIV than in those without. As in most other studies, Rasmussen and colleagues were unable to tell whether the HIV virus, its treatment, co-infections, or social-behavioural factors contributed to the increased risk of the age-related morbidities in HIV-positive individuals. Many studies of the comparison of HIV-positive and HIV-negative populations without data for co-infection and lifestyle factors have this limitation. Data from well matched HIV-positive and HIV-negative prospective cohort studies with detailed information about HIV,

treatment, co-infection, and social behavioural or lifestyle factors are needed to find out which of the factors increase the risk of age-related morbidities; however, such studies would need large numbers of participants with long follow-up.

One particularly interesting finding from Rasmussen and colleagues' analyses is a consistent pattern of declining relative risk of these age-related comorbidities with increasing age. The most likely explanation of this effect is a survivor bias, whereby HIV-positive patients most at risk of these events do not survive to older age. These patients are likely to be individuals who do not respond well to antiretroviral treatment, have detectable viral load, and have low CD4-positive cell counts, which are associated with an increased risk of all causes of death.⁹ Therefore, the most important factor for ensuring good health of HIV-positive individuals is early antiretroviral treatment, leading to long-term undetectable viral load.

The changes in the morbidity profile of ageing HIV-positive individuals have important implications for their management and treatment. For many people, HIV infection has now become a long-term manageable chronic illness, with the new challenge being the prevention and management of chronic illnesses that occur at increased rates. Understanding the contribution of HIV infection, antiretroviral treatment, and lifestyle factors to the development of these comorbidities in HIV-positive individuals could have a substantial effect on the design of the best screening and prevention strategies. In the absence of large prospective studies, the key steps to ensure healthy ageing in HIV-positive individuals are first treat patients early to achieve and maintain undetectable HIV viral load, and second reduce the prevalence of many of the traditional risk factors for the ageing-related morbidities, particularly smoking, which is probably the largest modifiable risk factor in HIV-positive patients.^{10,11}

*Kathy Petoumenos, Matthew Law

Kirby Institute, UNSW Australia, Sydney, NSW 2052, Australia (KP, ML)
kpetoumenos@kirby.unsw.edu.au

KP and ML have received unrestricted research funding from ViiV Healthcare, Bristol-Myers Squibb, Gilead Sciences, Janssen Cilag, Merck Sharp and Dohme, and Boehringer Ingelheim.



Science Photo Library

Published Online
May 28, 2015
[http://dx.doi.org/10.1016/S2352-3018\(15\)00082-X](http://dx.doi.org/10.1016/S2352-3018(15)00082-X)
See [Articles](#) page e288

- 1 Rasmussen LD, May MT, Kronborg G, et al. Time trends for risk of severe age-related diseases in individuals with and without HIV infection in Denmark: a nationwide population-based cohort study. *Lancet HIV* 2015; published online May 28. [http://dx.doi.org/10.1016/S2352-3018\(15\)00077-6](http://dx.doi.org/10.1016/S2352-3018(15)00077-6).
- 2 Althoff KN, McGinnis KA, Wyatt CM, et al. Comparison of risk and age at diagnosis of myocardial infarction, end-stage renal disease, and non-AIDS-defining cancer in HIV-infected versus uninfected adults. *Clin Infect Dis* 2015; **60**: 627–38.
- 3 Petoumenos K, Reiss P, Ryom L, et al. Increased risk of cardiovascular disease (CVD) with age in HIV-positive men: a comparison of the D:A:D CVD risk equation and general population CVD risk equations. *HIV Med* 2014; **15**: 595–603.
- 4 Schouten J, Wit FW, Stolte IG, et al. Comorbidity and ageing in HIV-infection: the AGEHIV Cohort Study. XIX International AIDS Conference; Washington, DC, USA; July 22–27, 2012. THAB0205.
- 5 Friis-Moller N, Weber R, Reiss P, et al. Cardiovascular disease risk factors in HIV patients—association with antiretroviral therapy. results from the DAD study. *AIDS* 2003; **17**: 1179–93.
- 6 Grierson J, Power J, Pitts M, et al. HIV futures 6: making positive lives count. Monograph series number 74. Melbourne, VIC: La Trobe University, Australian Research Centre in Sex, Health and Society, 2009.
- 7 Prestage G, Jin F, Kippax S, Zablotska I, Imrie J, Grulich A. Use of illicit drugs and erectile dysfunction medications and subsequent HIV infection among gay men in Sydney, Australia. *J Sex Med* 2009; **6**: 2311–20.
- 8 Lange RA, Hillis LD. Cardiovascular complications of cocaine use. *N Engl J Med* 2001; **345**: 351–58.
- 9 Smith C, Sabin CA, Lundgren JD, et al. Factors associated with specific causes of death amongst HIV-positive individuals in the D:A:D Study. *AIDS* 2010; **24**: 1537–48.
- 10 Petoumenos K, Worm S, Reiss P, et al. Rates of cardiovascular disease following smoking cessation in patients with HIV infection: results from the D:A:D study(*). *HIV Med* 2011; **12**: 412–21.
- 11 Althoff KN, Gange SJ, Jacobson L, Jing Y. Smoking outweighs HIV-related risk factors for non-AIDS-defining cancers. Conference on Retroviruses and Opportunistic Infections; Seattle, WA, USA; Feb 23–26, 2015.