

Liver disease and healthy life-expectancy with HIV

As HIV infection shifts to become a chronic condition, studies addressing the quantity and quality of the life gained by people living with HIV (PLHIV) are essential. Healthy life expectancy is an health indicator that quantifies and qualifies life expectancy and provides the expected number of years of life lived in good health adjusted by the different morbidity patterns of a population. With this method, a population-based cohort study by Robert Hogg and colleagues¹ in *The Lancet HIV* shows that healthy life expectancy among PLHIV has room for improvement.

The researchers analysed data from 9310 adults HIV-infected and 501313 HIV-uninfected adults from British Columbia, Canada, and reported that healthy life expectance in PLHIV who had ever used antiretroviral therapy (ART) was 27 years shorter in men and 36 years shorter in women than in their uninfected counterparts. Directly adjusted mortality rates were also substantially higher for PLHIV than for HIV negative individuals: 36.5 deaths per 1000 person-years for HIV-infected women versus 5.8 deaths per 1000 person-years for HIV-uninfected women. As for comorbidities, liver diseases were seven times more prevalent among HIV-infected men and renal diseases were five times more prevalent; among women, the relative risk of age-adjusted prevalence was about ten-fold higher in those with HIV for both diseases. Interestingly, the proportion of time lived in a healthy state was similar for the two populations. Together, these results expose the toll of comorbidities on the life expectancy of PLHIV.

HIV-related and non-HIV-related factors contribute to the higher mortality and lower life expectancy for PLHIV than for the general population. Immune status at start of ART is a decisive HIV-related factor, whereas non-HIV related factors include sociodemographics (sex, socioeconomic status) and behaviours (smoking, alcohol use, and illicit drug use) as well as comorbidities.² A study from the USA showed that HIV-infected individuals who start ART with CD4 counts greater than 350 cells per μL are more likely to die at older ages and of non-AIDS causes than those who start with greater immunological impairment.³ Moreover, if predictors of mortality (CD4 cell count, hepatitis B infection, hepatitis C infection, smoking, depression, unemployment, and hypertension) were adjusted for in the analysis then the

hazards of death for the two populations converged.³ Similarly, studies from Brazil⁴ and Thailand⁵ show that life expectancy for PLHIV increased with increasing CD4 cell count at the start of ART. Furthermore, the Thai study⁵ found that life expectancy for HIV-infected individuals with CD4 cell counts greater than 350 cells per μL reached that of the general population.⁵ In a meta-analysis, life expectancy differed with country's income,⁶ while in a high-income country (Swiss HIV Cohort Study) life expectancy differed by education level.⁷ Hence, life expectancy for HIV-infected individuals can, and probably will, reach that of uninfected populations when we address HIV disease progression with early ART as well as social inequalities and behaviours that increase the risk of mortality of HIV-infected individuals.

As for the role of comorbidities in HIV-specific mortality, findings from Hogg and colleagues¹ could result from the effect of HIV on the natural history of hepatitis C.⁸ Compared with patients who are monoinfected with hepatitis C, patients who are coinfecting with HIV and hepatitis C have accelerated progression to cirrhosis.⁹ In the Cohorts of Spanish Network on HIV/AIDS, excess mortality from hepatitis C infection in HIV-infected individuals compared with the general population as measured by standardised mortality ratio (per 100 person-years) were shown for all-cause mortality (11.5 [95% CI 9.9–13.4] vs 2.4 [1.9–3.1]) and liver-related mortality (22.4 [14.6–34.3] vs 1.8 [0.6–5.7]).¹⁰ Fortunately, options are currently available to address hepatitis C. New therapeutic regimens (direct-acting antiviral drugs) that target specific hepatitis C genome regions offering increased efficacy (sustained virological response $\geq 90\%$) in short duration and simplified oral dosing are available.¹¹ As such, high-coverage of well established prevention strategies coupled with direct-acting antiviral drugs treatment could greatly contribute to decreasing hepatitis C incidence and prevalence.¹² Additionally, early ART might reduce rates of liver fibrosis progression in PLHIV regardless of hepatitis B or hepatitis C coinfection.¹³ Ultimately, reduced hepatitis C coinfection and progression to end-stage liver disease might lead to an improvement in healthy life expectancy of PLHIV.

In sum, the high prevalence of liver disease in PLHIV compared with in HIV-uninfected individuals as well

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as its effect on healthy life expectancy warrants careful monitoring. In this regard, three strengths of the study by Hogg and colleagues¹ (the use of a health indicator that accounts for morbidity and mortality, the population-based nature of the cohorts with health information derived from multiple data sources, and the exploration of the ordering of the diseases on the study's results in sensitivity analyses) set important benchmarks for future studies.

Hugo Perazzo, *Paula M Luz

Instituto Nacional de Infectologia Evandro Chagas, Fundação Oswaldo Cruz, Rio de Janeiro 21040-360, Brazil
 paula.luz@ini.fiocruz.br

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