The Journal of Infectious Diseases

EDITORIAL COMMENTARY

Noncommunicable Diseases in People Living With HIV: Time for Integrated Care

Marc van der Valk[1,3] and Peter Reiss[1,2,3,4,5]

[1]Division of Infectious Diseases, Department of Internal Medicine, and [2]Department of Global Health, Academic Medical Center, [3]Amsterdam Infection and Immunity Institute, [4]Stichting HIV Monitoring, and [5]Amsterdam Institute for Global Health and Development, Amsterdam, the Netherlands

Keywords. HIV; non-aids related comorbidities; aging; cohort study.

Access to effective antiretroviral therapy (ART) for many, albeit far from all, people living with human immunodeficiency virus (HIV) has significantly decreased global AIDS-related morbidity and mortality, allowing an increasing proportion of adults in many regions of the world who are living with HIV and receiving ART to survive into old age. In 2013, the Joint United Nations Programme on HIV/AIDS reported that 10% of the adult HIV-infected population in low- and middle-income countries and 30% in high-income countries, or 3.6 million people living with HIV globally, were aged >50 years [1]. These patients are experiencing an increasing burden of aging-related noncommunicable diseases (NCDs) [2]. HIV healthcare providers, including infectious diseases clinicians, therefore need to increasingly transition from a focus on sustaining HIV suppression and immune restoration to a focus on managing and preventing NCDs.

A similar trend is confirmed by Gallant et al [3], in this issue of *The Journal of Infectious Diseases*, for a large number of US patients living with HIV who received healthcare coverage from commercial, Medicaid, and Medicare payers during 2003–2013, based on their analysis of data from administrative claims databases. These 3 payers jointly provide healthcare coverage for >46 million people living in the United States, and the data reported may, therefore, be reasonably representative for the entire country.

Hypertension, dyslipidemia, and endocrine disease were the most common comorbidities observed and were approximately twice as prevalent in Medicare payer–covered patients as compared to those covered by commercial and Medicaid payers, which is most likely a reflection of differences in mean age (71.5 years, compared with 42.2 and 41.6 years, respectively). When comparing prevalence between 2003 and 2013, significant increases were observed for most but not all comorbidities across payers. Unfortunately, the authors do not provide separate demographic and clinical characteristics of the patient populations studied in each of these 2 years, which could potentially have shed further light on factors underlying these increases.

In addition, the authors present the results of a case-control analysis in which presumably HIV-negative controls were matched to a subset of the HIV-positive case patients receiving ART, by payer, calendar year of index case patient inclusion, 5-year age group, sex, and geographic region (defined by first zip code digit). Ethnicity and socioeconomic status may have important impacts on the genetic, behavioral, and lifestyle-related risks of developing several of these comorbidities. However, the authors were not able to match patients by ethnicity, owing to limitations within the available databases, and first zip code digit is likely an inadequate variable on which to match for socioeconomic status. Furthermore, no details are provided concerning potential changes in the proportions of HIV-positive patients with suppressed viremia, differences in $CD4^+$ T-cell counts, or changes in the use of specific ART regimens, each of which may also impact the risk of developing several of the comorbidities that were documented. Thus, without being able to account for such factors, any differences in comorbidity prevalence between cases and controls over calendar time, as presented in Figures 2 and 3 [3], should be interpreted with caution and do not allow robust conclusions with respect to distinguishing the contributions of HIV, ART, and traditional risk factors for NCDs.

Across payer databases, particularly high rates of hypertension and hyperlipidemia were observed, which, in 2013, affected 25%–65% and 21.5%–47.5% of HIV-positive individuals, respectively. Both are important cardiovascular risk factors that significantly contribute to the increased risk of cardiovascular comorbidities among HIV-positive individuals receiving ART, as reported by ourselves and others [4, 5]. In a recent analysis of data from our AGEhIV Cohort Study, which prospectively compares comorbidities and their risk factors between aging HIV-positive patients (largely with suppressed viremia due to ART) and HIV-negative controls

Received 20 September 2017; editorial decision 20 September 2017; accepted 27 September 2017.

Correspondence: M. van der Valk (m.vandervalk@amc.uva.nl).

The Journal of Infectious Diseases® 2017;XX00:1–3

DOI: 10.1093/infdis/jix525

who are highly comparable with respect to demographic, behavioral, and lifestyle characteristics, we found that, even in a large academic HIV clinic, management of these cardiovascular risk factors was as poor as for the controls. Twenty percent of the HIV-positive study participants were classified as having a high risk for cardiovascular disease, and 10% were eligible for secondary prevention activities. Of those at high risk for cardiovascular disease or eligible for secondary prevention, 57% and 42%, respectively, had systolic blood pressures above guideline-recommended thresholds, and 81% and 57%, respectively, had cholesterol levels above guideline-recommended thresholds [6]. The study by Gallant et al reinforces the urgent need for HIV healthcare providers in the United States to reorganize long-term care for people living with HIV in such a manner that the prevention and management of highly prevalent comorbidities become fully integrated.

An increasing comorbidity burden, including an increasing risk of cardiovascular disease, among those aging with HIV can also be expected to have an increasing impact in terms of healthcare cost. In a recently reported study from Quebec, Canada, costs among HIV-positive patients were 3 times those among HIV-negative patients, even when the price of ART was excluded from calculations [7]. Renal comorbidity was associated with the highest costs, followed by bone and cardiovascular diseases. The majority (65%) of included patients were aged 20–49 years, and only a small proportion (6.1%) were aged ≥65 years. A recently presented similar case-control study from France showed that annual healthcare costs for people living with HIV, excluding the cost of ART, was 4 times that for matched controls (€9952 vs €2593) [8]. In a multivariate analysis exploring predictors of incremental cost, the impact of chronic cardiovascular disease was considerable. Also in this study, the majority of included patients (83.5%) were ≤60 years of age.

A model based on data from the ATHENA HIV observational cohort in the Netherlands predicts that, between 2015 and 2030, the annual cardiovascular disease incidence and cost will increase by 55% and 36%, respectively. Traditional prevention interventions (ie, intensified monitoring and treatment of hypertension and dyslipidemia and activities to encourage smoking cessation) would, according to the model, avert the largest number of annual cardiovascular disease cases, as well as reduce cumulative cardiovascular disease–related costs the most, and much more so than avoiding particular antivirals [9].

As appropriately disclosed in the article by Gallant ea [3], Gilead Sciences, one of the leading pharmaceutical companies in the field of HIV treatment, supported this study and employs one of the coauthors. The studies from Canada and France that looked at healthcare cost in relation to incremental comorbidity were also supported by Gilead Sciences [7, 8]. Such studies, importantly, contribute to raising awareness about the importance of comorbidities in terms of optimizing long-term care for aging patients living with HIV, as well as healthcare utilization and costs. One could question, however, whether pharmaceutical companies, in the era of value-based drug pricing, should be the only ones supporting such analyses. We would rather urge policy makers, insurance companies, and research agencies to structurally support and undertake this type of research in close collaboration with all relevant stakeholders, including pharmaceutical companies, in the field. This will contribute to an improved and cost-effective integration of prevention and management of chronic noncommunicable comorbidities in our HIV care systems and, thereby, increase the long-term quality of life and resilient aging of our patients.

Note

Potential conflicts of interest. M. v. d. V. reports receiving the following support outside the submitted work: personal fees from Abbvie, Johnson and Johnson, and BMS; grants and personal fees from Gilead; grants, personal fees, and nonfinancial support from MSD; and personal fees from ViiV. P. R. reports receiving the following support outside the submitted work: grants from ViiV Healthcare, Gilead Sciences, Merck, and Janssen Pharmaceutica and other support from ViiV Healthcare, Gilead Sciences, and Janssen Pharmaceutica. Both authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

1. Joint United Nations Programme on HIV/AIDS (UNAIDS). HIV and aging, a special supplement to the UNAIDS report on the global AIDS epidemic 2013. Geneva: UNAIDS, 2017. http://www.unaids.org/sites/default/files/media_asset/20131101_JC2563_hiv-and-aging_en_0.pdf. Accessed 17 October 2017.
2. Losina E, Hyle EP, Borre ED, et al. Projecting 10-yr, 20-yr and lifetime risks of cardiovascular disease in persons living with HIV in the US. Clin Infect Dis 2017 65:1266-71.
3. Gallant J, Hsue PY, Shreay S, Meyer N. Comorbidities among US patients with prevalent HIV infection—a trend analysis. J Infect Dis **2017**. In this issue.
4. Freiberg MS, Chang CC, Kuller LH, et al. HIV infection and the risk of acute myocardial infarction. JAMA Intern Med **2013**; 173:614–22.
5. Schouten J, Wit FW, Stolte IG, et al.; AGEhIV Cohort Study Group. Cross-sectional comparison of the prevalence of age-associated comorbidities and their risk factors between HIV-infected and uninfected individuals: the AGEhIV cohort study. Clin Infect Dis **2014**; 59:1787–97.
6. van Zoest RA, van der Valk M, Wit FW, et al.; AGEhIV Cohort Study Group. Suboptimal primary and

secondary cardiovascular disease prevention in HIV-positive individuals on antiretroviral therapy. Eur J Prev Cardiol **2017**; 24:1297–307.
7. Tossonian HL, Lorgeoux R, Baribeau V, Lachaine J, Prevalence of comorbidities and impact of HIV and comorbidities on health care resource utilization [abstract 3865]. Presented at: 9th IAS Conference on HIV Science, Paris, France, 23–26 July 2017.
8. Pourcher VB, Bouee S, Gourmelin J. Comorbidities in people living with HIV (PLWHIV) compared to general population: an epidemiological analysis using a claims database in France [abstract 2094]. Presented at: 9th IAS Conference on HIV Science, Paris, France, 23–26 July 2017.
9. Smit M, van Zoest RA, Nichols B, et al. Cardiovascular disease prevention policy in HIV: recommendations from a modelling study, Clin Infect Dis 2017. https://doi.org/10.1093/cid/cix858.