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BRIEF REPORT

Gender Disparities in Statin Prescriptions in People With HIV With Low/Moderate to High Cardiovascular Risk

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The REPRIEVE trial suggests that primary cardiovascular disease (CVD) prevention could be considered among people with HIV at low CVD risk. We found cisgender women with low/moderate and high CVD risk are less likely to receive statins than cisgender men. Efforts are needed to guarantee equal access to statin-based CVD prevention.

Keywords. Cardiovascular prevention; gender disparities; people with HIV; prescription; statin.

With the availability of potent antiretroviral therapy, life expectancy in people with HIV in high-income countries is now in the range of the general population [1]. However, people with HIV experience higher rates of comorbidities, including cardiovascular diseases (CVD), even when accounting for traditional risk factors [2, 3]. The recent REPRIEVE clinical trial demonstrated that among people with HIV with a low to moderate CVD risk, statin use reduced the risk of major cardiovascular events by 35% [4]. Consequently, the latest interim European AIDS Clinical Society (EACS) guidelines recommend high-intensity statin therapy for individuals with a 10-year CVD risk above 10%, moderate-intensity statin therapy for those with a risk between 5% and 10%, and individualized consideration for those with a risk below 5%.

Previous work has shown that statins are often underprescribed in people with HIV [5, 6]. Demographic and socioeconomic factors also influence statins prescription patterns, including ethnic and gender disparities in people with HIV [7, 8]. Exploratory analyses of the REPRIEVE trial have shown that the risk of CVD might be underestimated in Black people and cisgender women with HIV [9], underlining the importance of considering these factors in clinical care.

Here, we aimed to explore whether gender and ethnicity influence statin prescriptions for CVD prevention in people with HIV in Switzerland, a high-income country with a high standard of care and more equitable access compared to countries such as the United States—where health insurance significantly impacts medication prescriptions.

METHODS

The Swiss HIV Cohort Study (SHCS) is a prospective multicenter cohort study enrolling people with HIV in Switzerland [10]. The SHCS is approved by the local ethical committees of the participating centers and written informed consent is obtained from all participants. Participants are followed-up biannually with clinical and behavioral data collection.

We computed the CVD risk at each follow-up visit using SCORE2 for participants between ages 40 and 70 years, and SCORE2-OP for participants aged >70 years of age [11, 12], as recommended by the most recent EACS guidelines [13]. We classified the CVD risk in 3 categories: low/moderate, high, or very high—as previously described (see Supplementary Section 1). The risk was calculated only if data on age, systolic blood pressure, and non–high-density lipoprotein (non-HDL) cholesterol values were available.

We included in the analysis participants who were not receiving a statin and whose first CVD risk score in a given category (low/moderate, high, or very high) occurred after 2015, when the systematic collection of comedications started in the SHCS. Of note, some participants could be classified into different risk categories over time (eg, initially receiving a low/moderate risk assessment, followed by a first high risk

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assessment a few years later). Participants who had experienced a previous cardiovascular event (see Supplementary Section 2) before the inclusion date were excluded from the analysis.

For each CVD risk category separately (low/moderate, high, very high), we employed a multivariable Cox regression to assess the impact of sociodemographic and HIV-related factors on the time between first available risk assessment until statin prescription or administrative censoring (date of the last follow-up visit until 31 October 2023). These factors include gender (cisgender women, cisgender men, transgender women—results on transgender women are not reported in the main result section because of insufficient data but are included in the Supplementary Materials), ethnicity as reported in the SHCS (White, Black, Hispano-American, Asian), age (per 10 years), intravenous drug use (yes/no), education level (mandatory school or less vs apprenticeship or any degree), body mass index (<18.5, between 18.5 and 25, between 25 and 30, and >30 kg/m^2), living alone (yes/no), current smoker (yes/no; imputed from the most recent value available if missing), physical activity (more vs less than twice per month), previous exposure to protease inhibitors, diabetes, non-HDL value (total cholesterol minus HDL), and family history of CVD. We report the corresponding adjusted hazard ratios (aHR) with 95% confidence intervals (CI).

RESULTS

A total of 12 253 SHCS participants had at least one follow-up visit after 2015. Of those, 2300 (18.8%) were included in the low/moderate CVD risk score analysis (1557 cisgender men; 721 cisgender women; median age, 43 years); 2226 (18.1%) in the high CVD risk score analysis (1846 cisgender men; 365 cisgender women; median age, 46 years); and 698 (5.70%) in the very high CVD risk score analysis (646 cisgender men; 52 cisgender women; median age, 60 years) (Supplementary Sections 3, 4.1, 5.1, and 6.1).

Statins were not commonly prescribed in the low/moderate and high-risk categories, with respectively 7.9% and 13.7% of SHCS participants receiving a statin prescription at some point following the risk assessment. Statin prescriptions were higher in people at very high CVD risks versus those at low/moderate and high risk, with 29.4% of them receiving a statins prescription at some point after the risk assessment.

We found no significant differences in statin prescription between people of White and Black ethnicity across all CVD risk categories, with aHR ranging from 1.01 (95% CI, .65-1.56) in the high-risk category to 1.34 (95% CI, .67-2.69) in the very high-risk category (Figure 1 and Supplementary Sections 4.2, 5.2, and 6.2). In the low/moderate risk category, Asian people were more likely to receive a statin than White people (aHR 2.22; 95% CI, 1.19-4.16).

Importantly, among people with a low/moderate and high CVD risk, cisgender women were less likely to be prescribed a statin compared to cisgender men, with aHR of 0.47 (0.31-0.72) and 0.53 (0.37-0.75), respectively (Figure 1 and Supplementary Sections 4.2, 5.2, and 6.2). However, in the very high CVD risk category, there were no significant gender-related prescription differences, with an aHR of 0.76 (0.36-1.60).

DISCUSSION

In the SHCS, the proportion of people with HIV receiving statins (8%-30%) was low compared to international figures, but similar

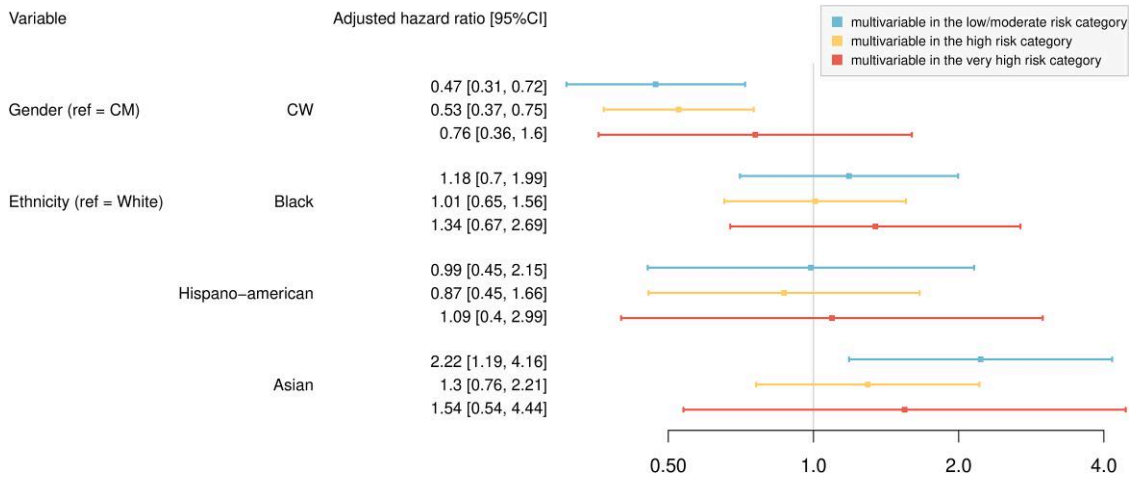

Figure 1. Adjusted hazard ratios and 95% confidence intervals (CI) for statins prescriptions by gender (cisgender women vs cisgender men) and ethnicity (people of Black, Hispano-American, and Asian ethnicity vs White ethnicity) in each CVD risk category: low/moderate (blue), high (yellow), and very high (red)). CVD risk was calculated using the SCORE2 or SCORE2-OP. Adjusted for age (per 10 y), intravenous drug use (yes/no), education level (mandatory school or less vs apprenticeship or any degree), body mass index (less than 18.5, between 18.5 and 25, between 25 and 30, and more than 30 kg/m^2), living alone (yes/no), current smoker (yes/no; imputed from the most recent value available if missing), physical activity (more vs less than twice a month), previous exposure to protease inhibitors, diabetes, non-HDL value (total cholesterol minus HDL), and family history of CVD. CM, cisgender men, CW, cisgender women.

to the general Swiss population [14]. We found that cisgender women with HIV and at low/moderate or high CVD risk were approximately half as likely to receive statin therapy than cisgender men. At very high CVD risk, prescription patterns were similar across gender. Gender differences in statin prescriptions have been reported in the general population [15–17]. This could result from a combination of systemic factors, prescription differences in healthcare provider prescriptions, and patient acceptance and medication adherence. Previous studies have shown that statins discontinuation rates are higher in women versus men, and mostly because of a higher rate of adverse events experienced by women [18, 19]. Consequently, medical doctors might be more hesitant to prescribe a statin to female patients. Acceptance of statin medication is also lower among women compared to men [20], potentially because of concerns about muscle pain, a common side effect, or reluctance toward polypharmacy. Additionally, CVD risk perception has been shown to be lower in women, both from women themselves [21] and their care providers [22, 23], therefore affecting the choice of CVD prevention strategies. Statin prescriptions were also shown to depend on socioeconomic parameters [24, 25], potentially affecting gender-related patterns in statins prescription given that women in the SHCS have on average lower socioeconomic positions than men [26]. Cisgender women with HIV at low/moderate and high CVD risk are not only half as likely to receive statins, but their CVD risk might also be underestimated [9], suggesting that they receive suboptimal care for CVD.

Although disparities in statin prescriptions among different ethnicities have been previously reported [7, 16], we found no significant differences between White and Black people with HIV in the SHCS. Interestingly, we found that Asian people were more likely to be prescribed statins than White people in the low/moderate CVD risk category. Conflicting results have been reported when comparing people of White and Asian ethnicity [16, 27]. This could be explained by different country-specific healthcare systems, and variations in the communities included under the "Asian" ethnicity umbrella.

Our study has limitations because it only assessed the time between a first CVD risk assessment in a given category (low/moderate, high, very high) until statin prescription. To gain a fuller picture, it would be interesting to analyze longitudinal trajectories for each patient because CVD risk is assessed at each follow-up visit. This would allow us to also understand the role of lifestyle adjustments in CVD prevention (eg, smoking cessation, physical activity). Although our study identified gender differences in statin therapy, the current analysis does not elucidate the underlying reasons for these disparities. This study is observational by design, and it is therefore not possible to draw conclusions on the causality between these gender differences and statin prescription. Finally, given the recency of the new EACS guidelines, follow-up analyses will be needed to evaluate whether they have initiated changes in clinical practice.

In conclusion, our findings provide opportunities to address inequalities in CVD management across gender in people with HIV and ensure equal access to adequate treatments. Given the REPRIEVE results, the ideal strategy for prescribing statins in primary prevention needs to be defined in clinical care. Efforts are needed to ensure a good communication between clinicians and people with HIV to ensure that people at risk initiate therapy. Finally, further research is needed to understand the gender gap in statin prescription and to develop methods to address it.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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Data availability. The individual level datasets generated or analyzed during the current study do not fulfill the requirements for open data access: (1) The SHCS informed consent states that sharing data outside the SHCS network is only permitted for specific studies on HIV infection and its complications, and to researchers who have signed an agreement detailing the use of the data and biological samples; and 2) the data is too dense and comprehensive to preserve patient privacy in persons living with HIV.

According to the Swiss law, data cannot be shared if data subjects have not agreed or data are too sensitive to share. Investigators with a request for selected data should send a proposal to the respective SHCS address (www.shcs.ch/contact). The provision of data will be considered by the Scientific Board of the SHCS and the study team and is subject to Swiss legal and ethical regulations and is outlined in a material and data transfer agreement.

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