Clinical characteristics of women with HIV in the RESPOND cohort: a descriptive analysis and a comparison to men

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ABSTRACT

Clinical characteristics of women with HIV in the RESPOND cohort: a descriptive analysis and a comparison to men

BACKGROUND
Women with HIV are globally underrepresented in clinical research. Existing studies often focus on reproductive outcomes, seldom focus on older women and are often underpowered to assess sex/gender differences. We describe CD4, HIV viral load (VL), clinical characteristics, comorbidity burden and use of antiretroviral therapy (ART) among women with HIV in RESPOND and further compare to the men in RESPOND.

METHODS

RESPOND is a prospective, multi-cohort collaboration including over 34,000 people with HIV from across Europe and Australia. Demographic and clinical characteristics, including CD4/VL, comorbidity burden, and ART are presented at baseline, defined as the latter of 01-Jan-2012 or enrolment into the local cohort, stratified by age and sex/gender. We further stratify men by reported mode of HIV-acquisition, men-who-have-sex with men (MSM) and non-MSM.

RESULTS
Women account for 26.0% (n=9019) of the cohort, with a median age of 42.2 years [IQR:34.7-49.1]. The majority (59.3%) of women were of White ethnicity/race, followed by 30.3% Black. Most women (75.8%) acquired HIV heterosexually and 15.9% via injecting drug use. Nearly half (44.8%) were on boosted PI, 31.4% on NNRTI, and 7.8% on INSTI. Baseline year was 2012 for 73.2% of women and 4.2% had a baseline year >2019. Median CD4 was 523(IQR:350-722) cells/μl and 73.6% of women had a VL<200 copies/mL. Among the ART naïve, women were more likely than MSM to have CD4<200 cells/μL but less likely than non-MSM (P<0.001), and less likely to have VL≥100,000 copies/mL compared to both MSM and non-MSM (P<0.001). Women were also more likely to be free of comorbidity compared to both MSM and non-MSM (P<0.0001)

CONCLUSION

RESPOND women are diverse in age, ethnicity/race, CD4/VL and comorbidity burden, with important differences relative to men. This work highlights the importance of stratification by sex/gender for future research that may help improve screening and management guidelines specifically for women with HIV.

Background

Women remain under-represented in HIV-related clinical trials[1 2] and in HIV research in general[3 4] despite women with HIV now outnumbering men with HIV globally.[5-7] In many high-income countries, the HIV epidemic is largely driven by men who have sex with men (MSM), and cohort studies are often underpowered to assess differences between men and women. There are important sex/gender differences in treatment access[8] and pharmacokinetics[9] including biological factors, as well as social, cultural, and economic factors driving these inequalities.[10 11]

Racial/ethnic disparities in VL and CD4 counts have been described in the literature,[12-15] with non-White ethnicity/race often suggested to have poorer outcomes. In the assessment of racial/ethnic and sex/gender disparity, Beer et al[15] highlighted the importance of adjusting for the social determinants of health, and the benefit of examining sex/gender stratified by racial/ethnic groups. In this study, Black and Hispanic women had comparable levels of viral suppression to White women. In addition, this study showed that differences in ART adherence, demographics, poverty, education, and insurance accounted for the observed disparities even in Black women compared to White men. Whilst these examples are from a US setting and may not be generalisable to other developed countries, socio-economic disadvantage has been shown to be an important determinant of HIV health outcome even in settings with universal health care.[16] Mental health may also be an important confounder. Another study[17] showed that while low income and stigma predicted higher depression scores among both men and women, women experienced a significantly higher burden of depressive symptoms compared to men. Furthermore, among women over 40 years of age, depression scores increased, while a decrease was observed among men of the same age.

The identification and management of comorbidities is increasingly important, given the long life expectancy among a now ageing population of people with HIV[18]. Yet studies on women with HIV often focus on reproductive outcomes while research among older and post-menopausal women remains lacking.[6] Women in the general population have been reported to have more comorbidities than men, and this risk is greater in women with HIV compared to men with HIV.[19] Women with HIV may also experience age-related comorbidities earlier than women without HIV.[20] However, the age at which the risk for these comorbidities starts to increase and the optimal timing for screening and other preventive interventions for these comorbidities is still poorly understood.[7]

Significant gaps remain in terms of data-driven evidence for women with HIV (and women in general) despite several calls to action in over more than two decades and as recently as 2024 for the inclusion of more women in clinical research.[3 6 21] These papers identify several approaches to narrow the evidence gap to help improve the health and well-being of women, including well-controlled and adequately powered studies,[3] and systematic approaches to sex/gender stratified data collection and analysis.[21] Better understanding of social, structural and environment factors are also critical to improving the health of women with HIV.[6] The aim of this study therefore was to present key demographic and clinical characteristics, including the use of ART, CD4/VL, and comorbidity burden among women with HIV, stratified by age group within the large and geographically heterogeneous RESPOND cohort. Leveraging the large sample size of RESPOND, we further compare women by ethnicity/race and region, and to the men in RESPOND stratified by reported mode of HIV-acquisition (MSM and non-MSM).

Methods

The International Cohort Consortium of Infectious Disease (RESPOND) is a prospective, multi-cohort collaboration with over 34,000 people with HIV from across Europe and Australia, as described in detail previously.[22] Characteristics of all participants enrolled in RESPOND up to November 2021 were presented at baseline: the latter of 01-Jan-2012 and enrolment into the local cohort. Transgender individuals (n=54 transgender men and n=1 transgender women) were excluded from analysis. ART at baseline was classified into 5 groups; the first three groups included at least two nucleos(t)ide analogue reverse transcriptase Inhibitors (NRTIs) as treatment backbone with either an integrase strand transfer inhibitor (INSTI), ritonavir or cobicistat boosted protease inhibitor (PI/b) or a non-nucleoside reverse transcriptase inhibitor (NNRTI)-arm. The fourth group were two drug regimens (2DR) including dolutegravir + lamivudine (DTG+3TC), raltegravir + boosted darunavir (RAL+DRV/b), DTG +DRV/b, DTG + rilpivirine (RPV), 3TC+DRV/b, RAL + etravirine (ETV), RAL +nevirapine (NVP), RPV +DRV/b and 3TC+ ATV/b following an earlier RESPOND study[23]. The fifth and 'Other' group included multi-class regimens, dual regimens not specified above and those without a double NRTI backbone. For all measurements, the closest measurements to baseline were presented within a window period of 12-months prior and 3-months post baseline.

Prevalence of prior AIDS, co-infections (HBV: hepatitis B positive surface antigen test and/or a prior positive HBV DNA test, and HCV: hepatitis C positive antibody test and/or received positive RNA and/or genotype tests or received HCV therapy) and clinical characteristics such as body mass index (BMI) were summarised at baseline. We also considered the following comorbidities: diabetes (documented diagnosis of diabetes and/or use of antidiabetic drugs and/or 2 consecutive blood glucose measures ≥11.1 mmol/L or HbA1c ≥6.5%), hypertension (systolic blood pressure measurements ≥140 and/or diastolic blood pressure ≥90 mmHg; or initiation of antihypertensives), dyslipidaemia (total cholesterol ≥240 mg/dL or HDL cholesterol <40 mg/dL or triglyceride ≥200 mg/dL or LDL cholesterol ≥160 mg/dL or use of lipid lowering medication), cardiovascular disease (CVD: myocardial infarction, stroke or invasive cardiovascular procedure), chronic kidney disease (CKD: estimated glomerular filtration rate <60 measured >3 months apart), non-AIDS defining malignancy (NADM), end-stage renal disease (ESDR: dialyses >3 months or renal transplantation) and end stage liver disease (ESLD: bleeding varices, hepatic encephalopathy grade III-IV, hepatorenal syndrome). Clinical characteristics were defined using definitions as described in previous RESPOND studies[24] via the RESPOND manual of operations for clinical events.[25] Comorbidity burden was determined by counting the presence of any one of the following conditions hypertension, diabetes mellitus, dyslipidaemia, CVD, NADM, ESLD, CKD and/or ESRD. Cohorts that were considered to have good quality reporting for >4 out of the 7 comorbidities were included in the index, otherwise all participants were recorded as unknown in comorbidity burden.

Risk probabilities were calculated using the D:A:D (Data-collection on Adverse Effects of Anti-HIV Drugs) risk models for CVD[26] and for CKD.[27] The reduced CVD D:A:D model was used as recommended for participants highly exposed to ART. Participants were excluded from the CVD model if they had a prior CVD at baseline. Eligible participants for the CKD model were participants with baseline eGFR>60, at least 3-months follow-up data, ≥3 eGFR measurements and no prior CKD at baseline. An ART component was included in the CKD risk model so that individuals with any prior exposure to boosted protease inhibitor excluding lopinavir/ritonavir (LPV/r) and those on tenofovir (TDF) had an equivalent of 2-point increased risk, and those with prior exposure to atazanavir or LPV/r had a 1-point increased risk.

Age group was categorised as 18-29, 30-39, 40-44, 45-49,50-54, and ≥55-years; with five-year age-groupings chosen after 40-years to align with potential age of onset of menopause, as data on

menopause were not available. Data were stratified by sex/gender and age-group. Men without MSM as mode of HIV-acquisition are referred to as non-MSM throughout.

Sex/gender and ethnicity/race were used interchangeably given individual participating cohorts collect a combination of these variables. Sex/gender difference in categorical variables were assessed using chi-square test of association and 95% confidence intervals [95%CI] were presented for unadjusted analysis. Continuous variables were presented as medians with interquartile range (IQR), P-values (where appropriate) were calculated from the Wilcoxon-Mann-Whitney test.

Adjusted Logistic regression was used to assess sex/gender-differences in CD4/VL, comorbidity burden (without comorbidity prevalent at baseline), ART and history of clinical characteristics at baseline. Models for CD4/VL were restricted to the ART naïve, those participants with first ART commencing ≥baseline date and with VL≥200 copies/mL. This definition of ART naïve was chosen, as more women had VL<200 copies/mL among those with first ART initiation after baseline. Models for CD4/VL adjusted *a priori* for sex/gender, age, ethnicity/race, smoking, RESPOND region and baseline year. Odds ratio (OR) and adjusted odds ratio (aOR) with 95% confidence intervals and Wald P-values were presented for the adjusted sex/gender estimates. Baseline year was categorised: 2012, >2012 & ≤2014, >2014 & ≤2016, >2016 & ≤2018, and >2018. Models to compare sex/gender-differences in clinical characteristics, ART (multinomial logit) and comorbidity burden were adjusted for sex/gender, age, ethnicity/race, RESPOND region, baseline year and duration of ART (years). We did not adjust for injecting drug use (IDU) per se, given men were identified via mode of HIV-acquisition and the identification of IDU as mode of HIV-acquisition does not represent current use, nor history of IDU. Imputation for missing data was not done, however models were fit with a separate category for missing data; and were re-run excluding missing. All statistical analyses were performed using Stata version 17.0 and/or SAS Enterprise Guide Version 8.0

Results

Demographics:

Of the 34,695 participants enrolled in RESPOND up to November 2021, 9,019 (26.0%) were women, with a median age at baseline of 42-years [IQR: 35-49]. The majority (44.4%) of women were from western European cohorts (Table 1), and were of White (59.3%), Black (30.3%) and Asian (4.6%) ethnicity/race. Due to small numbers among women, Hispanic/Latino people are grouped with 'Other' ethnicity/race for presentation. Of the women ≥50 years, 69.3%, 21.8% and 2.7% were of White, Black and Asian ethnicity/race respectively, compared to 56.5%, 32.6%, 5.1 % in women < 50 years. Over 75% of women acquired HIV heterosexually and 15.9% through IDU. Baseline year for the majority (73.2%) of women was 2012, and 84.0% were ART experienced at baseline. At baseline, most women were receiving either a combination of 2 NRTI plus boosted PI (PI/b) (44.8%) or NNRTI (31.4%) and 7.8% were receiving an INSTI. Across the age groups, slightly more women <40 years of age of were receiving PI/b (46.3%) and INSTI (8.9%), compared to 40.4% and 8.2% in women over 50 years, and fewer (26.0%) younger women (<40 years) were receiving NNRTI compared to 36.4% of women over 50. While among the 16% of ART naïve women, 34.6% initiated ART with a regimen containing 2 NRTI plus INSTI, 30.6% PI/b, and 26.1% an NNRTI (Table2b). Nearly half (46.0%) of women ≥50 initiated with an INSTI compared to 31.3% of women aged <40 years. (Table S2). Median CD4 at baseline was 523 (IQR:350-722) cells/μl, with 51.3% of all women with a baseline CD4 count above 500 cells/μl and 73.6% with a VL < 200 copies/mL (Table 3a). Fewer younger women (<40 years) had CD4 >500 cells/μl compared to women ≥40 years (46.0% vs 55.1%), and fewer had VL < 200 copies (57.6% vs 77.3%) (Table S3). Among the ART naïve, median CD4 was 371 (IQR:194-555) cells/μl (Table 3b). CD4 and VL stratified by region and ethnicity/race among the ART naïve (Table S4) show similar estimates between

women of Black and White ethnicity/race, the proportion with CD4 <200 cells/µl 25.8% (95% CI [21.3-30.4]) and 22.5% [19.6-25.3] and VL≥100,000 copies/mL: 25.6% [21.0-30.1] and 28.0% [24.9-31.1] respectively. Comparison by ethnicity/race and region among the ART naïve are limited by low numbers; n=44 ART naïve Asian women, and a younger population among eastern European cohorts (37.3% aged <30 years) compared to 24.9% among western European cohorts.

At baseline 28.4% of women ever smoked, and among women with recorded BMI, 56.1% of women were in normal weight range (Table 1). Overall, 62.0% of women reported one or more comorbidities, with more women of White and Asian ethnicity/race reporting one or comorbidity (66.5% [65.2, 67.8] and 68.4% [63.7, 73.1] respectively) compared to 53.8% [51.9, 55.8] reported among women of Black ethnicity/race (Table S6).

Characteristics compared to MSM and non-MSM:

Women were younger than both MSM (P<0.001) and non-MSM men (P<0.001) (Table 4). Approximately 25.0% of women were diagnosed with HIV after 2010, compared to 38.2% of MSM and 27.9% of non-MSM. More women were under-weight: BMI<18.5 (4.8%, 95% CI: [4.3-5.2]) compared to both MSM and non-MSM, with 2.1% [1.9-2.3] and 2.7% [2.2.3-3.0] respectively and women were more often obese: BMI>30 (8.2%) compared to men (3.8% and 6.5% respectively among MSM and non-MSM). Fewer women were current smokers 22.3% [21.4-23.1] compared to 26.6% [25.9-27.3] among MSM and 34.7% [33.8-35.7] among non-MSM, and fewer women were ART naïve at baseline 16.0% [15-3-16.8] compared to 26.3% [25.6-27.0] among MSM and 18.1% [17.3-18.9] among non-MSM (Table 4).

CD4 and VL:

CD4 count and VL at baseline also varied by sex/gender (P<0.001) (Table 3a). More women had CD4 <200 cells/µL compared to MSM (9.8%, 95%CI: [9.2-10.4] vs. 6.5% [6.2-6.9]) though fewer compared to non-MSM (13.1% [12.4-13.7]). Similarly, fewer women had CD4≥500 cells/µL compared to MSM (51.3% [50.2-52.3] vs. 57.3% [56.5-58.0]), and more compared to non-MSM (44.2% [43.2-45.2]). Mean, and median CD4-nadir was lower among women compared to MSM, but higher compared to non-MSM. A marginally higher proportion of women were virologically suppressed (VL<200 copies/mL) (69.0% [68.1-70.0]) at baseline compared to both MSM (66.1% [65.3-66.8]) and non-MSM (67.4% [66.4-68.3]). Among the ART-naïve (Table 3b), CD4-nadir cells/µL was also lower among women 360 [IQR:169-489] compared to MSM 426 [IQR:291-556] and higher compared to non-MSM 337[IQR:169-489]; a greater proportion of women had CD4 < 200 cells/µL (25.3% [23.0-27.5]) compared to MSM (15.8% [14.7-16.9]) but less than non-MSM (32.2% [30.0-34.4]), and fewer women had VL ≥100,000 copies/mL (27.5% [25.2-29.8]) compared to both MSM (33.0% [31.8-34.6]) and non-MSM (40.0% [37.6-42.3]).

Among the naïve, after adjustment for age, ethnicity/race, smoking, baseline year and RESPOND region, women were more likely to have CD4 < 200 cells/µL compared to MSM with an adjusted odds (aOR)1.62[1.36-1.93] and less likely to have CD4>500 cells/µL (aOR=0.72[0.62-0.84]). Compared to ART-naïve non-MSM, women were less likely to have CD4 counts below < 200 cells/µL (aOR=0.77[0.65-0.92]), and marginally more likely to have CD4>500 cells/µL (aOR=1.19 [1.00-1.41]). Women were also less likely to have VL≥ 100,000 copies/mL compared to both MSM (aOR=0.73[0.62-0.85]) and non-MSM (aOR=0.62[0.5-0.73]) (Table 3b).

Comorbidity:

Unadjusted comorbidity burden and unadjusted rates for specific comorbidities at baseline varied by sex/gender (Table S5). More women overall were without prevalent comorbidity compared to MSM (26.9% [95%CI: 26.0-27.8] vs. 20.8% [20.2-21.4]) and similar compared to non-MSM (26.2% [25.3-27.1]). Rates of CVD, hypertension, dyslipidaemia, diabetes, HBV and ESLD were similar or lower in women compared to MSM and/or non-MSM. While CKD at baseline was higher in women compared to both MSM and non-MSM. Women also had higher rate of ESRD compared to MSM, yet similar to non-MSM. More cancers were also reported among women compared to both MSM and non-MSM (Note: of these, 17.5% of cancers attributed to breast cancer, while lung cancers were reported in 8.7%, 7.3%, and 11.6% of all NADM cases in women, MSM and non-MSM respectively). The 5-year predicted risk for CVD and CKD was low overall, however, women had a lower median 5-year CVD risk compared to both MSM and non-MSM (P<0.001), while the CKD risk for women was similar to MSM but lower than the risk for non-MSM (p<0.001).

After adjustment for baseline year, smoking, ethnicity/race, RESPOND region and time on ART (years), women remained more likely than both MSM and non-MSM to be without prevalent comorbidity at baseline (aOR=1.55[1.43-1.67]. Women were more likely to have had an AIDS defining illness (aOR=1.12 [1.04-1.21]), HCV (aOR=4.51 [4.12-4.94]), NADM (aOR=1.59 [1.34-1.85]), CKD (aOR=2.38 [1.94-2.92]), and fracture (aOR=1.46 [1.23-1.72]); and less likely to have HBV (aOR=0.78 [0.73-0.84]), dyslipidaemia (aOR=0.71 [0.66,-0.76]), hypertension (aOR=0.62 [0.58-0.67]) and CVD (aOR=0.66 [0.57-0.78]) reported at baseline. While compared to non-MSM, women were more likely to have had CKD (aOR=2.14 [1.71-2.67]) and NADM (aOR=1.84 [1.53-2.21]) and less likely to have diabetes (aOR=0.56 [0.47-0.66]), hypertension (aOR=0.64 [0.59-0.70]) and CVD (aOR=0.61 [0.52, 0.72]) reported. Women were also less likely than non-MSM to have an AIDS defining illness, ESRD, ESLD, HBV and HCV coinfection, and fracture reported at baseline (Table S7, Figure 1).

ART at baseline

ART class also varied by sex/gender, P<0.001 (Table 2a). At baseline fewer women were on INSTI-based regimens: 7.6% [95%CI: 7.0-8.1] compared to 15.3% [14.7-15.8] among MSM and 8.8% [8.3-9.4] among non-MSM. More women were on PI/b-based regimens (44.8% [43.7-45.8]), compared with 32.3% [31.6-33.0] among MSM and 41.8% [40.8-42.8] of non-MSM. Fewer women were on NNRTI-based ART (31.4% [30.4-32.3]) relative to both MSM and non-MSM (35.0% [34.3-35.7] and 34.3% [33.4-35.3] respectively). Among those on INSTIs at baseline, more women were on raltegravir (RAL): 30.6% [27.1-34.1] compared to 12.5% [11.2-13.8] and 18.6% [16.0-21.2] among MSM and non-MSM.

Sex/gender differences in ART use at baseline was most notable for younger participants (Table S1) dominated by differences in PI/b and INSTIs between women and MSM aged <30-years. Among participants aged <30-years with known regimen, the proportion on INSTI based ART was 40.1% [95%CI: 37.8-42.5] among MSM and 15.8% [13.4-18.2] among women. Among those <30-years, 55.7% [52.5-59.0] of women and 25.9% [23.8-28.0] MSM were on PI/b ART.

Among the ART naïve, fewer women initiated an INSTI (34.6% [95%CI: 32.1-37.0] compared to MSM (45.6% [44.1-47.1], while similar compared to non-MSM 38.0% [35.7-40.3] (Table 2b). More women initiated a PI/b as part of their first ART regimen (30.6% [28.2-33.0] compared to MSM 21.1% [19.9-22.3], and similar compared to non-MSM 27.3% [25.2-29.4]. Sex/gender differences attenuated at age-groups ≥50-years for women compared to MSM, and among age-groups ≥45-years for women compared to non-MSM (Table S2). After adjustment for baseline year, smoking, ethnicity/race, RESPOND region and years on ART (Table S8), women were more likely to be on PI/b aOR=1.88[1.62-2.17]and NNRTI aOR=1.31[1.13-1.52] versus INSTI compared to MSM, while results were similar compared to non-MSM at baseline. Among the ART naïve, women were also more likely to initiate

PI/b aOR=1.70[1.39-2.08] vs. INSTI compared to ART naïve MSM, while results were comparable to ART naive non-MSM for all ART initiated after baseline.

Discussion

RESPOND women are diverse in age, treatment use and clinical history at baseline. Most women were <50-years of age at baseline, White and from western Europe. Compared with men, women were younger, more were of Black ethnicity/race, had higher BMI, and were more treatment experienced at baseline. Sex/gender differences were observed in CD4, VL, ART regimen at baseline, and in comorbidity risk and burden. These analyses highlight the importance of stratification by sex/gender, ethnicity/race and age to better understand the sex/gender difference observed in clinical cohorts from settings where the HIV epidemic is predominately MSM.

Studies have frequently reported higher CD4 and lower VL[28-30] for women relative to men among the treatment naïve. While we also found a lower likelihood of having high VL (≥100,000 copies/mL) among ART naïve women compared to all men (MSM and non-MSM), CD4 outcomes favoured women only when compared to non-MSM. Research has shown that male sex/gender, higher age, IDU and heterosexual mode of HIV-acquisition is linked to late diagnosis[31-33] and this is likely also reflected here, where CD4<200 cells/µL may be a surrogate for delayed diagnosis. Among non-MSM, 36.2% reported IDU as mode of HIV acquisition, and this group had the highest proportion with CD4<200 cells/µL, MSM the lowest. The CD4 differences observed in our study support the assertion that social determinants of health have a critical role in CD4 outcomes.

Differences in the use of ART will reflect local and international guidelines,[34] national strategy plans and procurement mechanisms. Sex/gender-differences were most notable in PI/b and INSTI use and/or initiation, particularly for women compared to MSM, and particularly among the youngest participants <40-years. While some of these unadjusted differences in ART would be attributed to variability in baseline year and HIV disease stage, after adjustment for key confounders including baseline year and age, women remained less likely, compared to MSM, to be on INSTI and less likely to initiate INSTI (more likely to initiate PI/b) among the ART naïve. Lower INSTI uptake may have been driven by earlier pregnancy concerns around some INSTIs, or fear of weight gain which has been linked to INSTI use, with a greater risk among women and non-whites[35-37] Studies from RESPOND and others[37 38] have also shown higher incidence of hypertension and diabetes with INSTI regimens compared to NNRTIs.

Many women in RESPOND had at least one comorbidity reported on or prior to baseline, and although the overall comorbidity rate was found to be lower in women compared to MSM and non-MSM, there were distinct differences by sex/gender in the prevalence for several comorbidities. We observe differences in CVD, hypertension (lower among women) and CKD (higher among women), whereas higher prevalence of NADM is most likely accounted for by breast cancer. While we were unable to adjust for important social determinants of health, these groupings allow a sex/gender comparison given vastly different socio-economic status between women, MSM and non-MSM in RESPOND. Sex/gender and HIV-associated CVD and CKD has a multifaceted pathogenesis. Some research has suggested that women with HIV have an elevated risk of CVD[39] compared to men with HIV, and that CMV co-infection may play a stronger role in CVD in women with HIV.[40 41] Earlier D:A:D studies found evidence of a strong association between impaired eGFR and CVD.[42] We observed lower overall CVD risk for women, lower prevalence of CVD and hypertension compared to MSM and non-MSM. Although we did not adjust for individual ARVs where cumulative exposure may be nephrotoxic,[43-45]

the higher observed CKD prevalence among women is consistent with a recent study from the USA[46] which reported higher risk for women after adjustment for APOL1 and substance use.

Cohort studies can lack generalisability and the adjustment for the underlying sex/gender differences in socio-economic factors that influence health and access to healthcare,[47] and this is a major limitation here also. Social determinants such as poverty, isolation, stigma, socio-cultural norms, lack of employment, education, immigration, caring responsibilities, and mental health may have a unique impact on access to care, and on the clinical outcomes for women, and it is not possible to adjust for, or to describe within RESPOND. While our primary aim was to describe the women in RESPOND, we also provide a comparison to men, as men dominate this cohort (74%) and many other HIV cohorts in developed countries. Although adjustments have been made for known confounders, we acknowledge that these models do not capture, in its entirety, the underlying cause of the observed sex/gender-differences. We do not have menopause data and we were also not able to adjust for contemporaneous IDU, or history of IDU, as IDU was only identified as mode of HIV-acquisition. A strength of this work, however, is the large and heterogeneous cohort, and the ability to describe women across different age strata, which has lacked prominence in the literature. Another strength is the comparison of women to MSM and non-MSM. Differences may be less biological, and more about disparities in the underlying social determinants of health; and the ability to compare women to MSM is not possible within the standard approach of simply adjusting for (sex/gender: male, female), and adjusting for mode of HIV-acquisition. Within this ageing cohort, retaining numbers of women in older age-groups and diverse ethnic/racial groups will be increasingly important in the assessment of age, ethnicity/race and sex/gender interactions.

We have shown that the RESPOND cohort provides data for a diverse population of women, with clear differences relative to men in terms of treatment, CD4, VL, ART and comorbidity. Our data suggest that women may be engaging in care later MSM, with the potential for poorer long-term outcomes. Improving the overall health of women with HIV requires more detailed understanding of the multidimensional consequences for women with HIV. Future research should collect, and present, data that includes both clinical factors in addition to social determinants of health.

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Conflict of Interest

FB has received lecture fees and a research grant from Gilead, all outside the submitted work.

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JG is an employee and stockholder of Gilead Sciences.

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Data sharing

The RESPOND Scientific Steering Committee (SSC) encourages the submission of concepts for research projects. Online research concepts should be submitted to the RESPOND secretariat (respond. rigshospitalet@regionh.dk); for guidelines on how to submit research concepts see the RESPOND governance and procedures. The secretariat will direct the proposal to the relevant Scientific Interest Group, where the proposal will initially be discussed for scientific relevance before being submitted to the SSC for review. Once submitted to the SSC, the research concept's scientific relevance, relevance to RESPOND's ongoing scientific agenda, design, statistical power, feasibility, and overlap with already approved projects will be assessed. Upon completion of the review, feedback will be provided to the proposer or proposers. In some circumstances, a revision of the concept might be requested. If the concept is approved for implementation, a writing group will be established consisting of the proposers (up to three people who were centrally involved in developing the concept), representatives from RESPOND cohorts, and representatives from the Statistical Department and Coordinating Center. All individuals involved in the process of reviewing these research concepts are bound by confidentiality. All data within RESPOND from individual cohorts are de-identified. The present RESPOND data structure and a list of all collected variables and their definition can be found online. For any inquiries regarding data sharing, please contact the RESPOND secretariat (respond.rigshospitalet@regionh.dk).

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