All-cause hospitalisation among people living with HIV according to gender, mode of HIV acquisition, ethnicity, and geographical origin in Europe and North America: findings from the ART-CC cohort collaboration

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Summary

Background Understanding demographic disparities in hospitalisation is crucial for the identification of vulnerable populations, interventions, and resource planning.

Methods Data were from the Antiretroviral Therapy Cohort Collaboration (ART-CC) on people living with HIV in Europe and North America, followed up between January, 2007 and December, 2020. We investigated differences in all-cause hospitalisation according to gender and mode of HIV acquisition, ethnicity, and combined geographical origin and ethnicity, in people living with HIV on modern combination antiretroviral therapy (cART). Analyses were performed separately for European and North American cohorts. Hospitalisation rates were assessed using negative binomial multilevel regression, adjusted for age, time since cART intitiaion, and calendar year.

Findings Among 23 594 people living with HIV in Europe and 9612 in North America, hospitalisation rates per 100 person-years were 16·2 (95% CI 16·0–16·4) and 13·1 (12·8–13·5). Compared with gay, bisexual, and other men who have sex with men, rates were higher for heterosexual men and women, and much higher for men and women who acquired HIV through injection drug use (adjusted incidence rate ratios ranged from 1·2 to 2·5 in Europe and from 1·2 to 3·3 in North America). In both regions, individuals with geographical origin other than the region of study generally had lower hospitalisation rates compared with those with geographical origin of the study country. In North America, Indigenous people and Black or African American individuals had higher rates than White individuals (adjusted incidence rate ratios 1·9 and 1·2), whereas Asian and Hispanic people living with HIV had somewhat lower rates. In Europe there was a lower rate in Asian individuals compared with White individuals.

Interpretation Substantial disparities exist in all-cause hospitalisation between demographic groups of people living with HIV in the current cART era in high-income settings, highlighting the need for targeted support.

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Introduction

In the era of combination antiretroviral therapy (cART), morbidity among people living with HIV is increasingly dominated by non-AIDS conditions.[1–4] Hospitalisation in people living with HIV is an important marker of serious morbidity capturing both non-AIDS and AIDS-related events, a marker of poorer health-care access,[5] and a significant contributor to health-care costs in high-income countries.[6] Assessing rates of hospitalisation as a marker of health outcomes can help to identify potential disparities in morbidity across subgroups of people living with HIV. Hospitalisation as an endpoint can also capture differences in access to care, as hospital admission could potentially result from delays in seeking or receiving timely primary care.

Several studies investigated the association of demographic factors with hospitalisation in people living with HIV and identified gender-based and race-based disparities.[7–12] However, most were conducted in the USA and findings are not easily generalisable to Europe due to differences in the demographic composition of the population of people living with HIV, structural drivers of the HIV epidemic, and health-care systems. Furthermore, no previous study has investigated the extent of demographic disparities in hospitalisation among people living with HIV in both Europe and North America. Such results give insight into which groups should be prioritised by policies and interventions.

We aimed to investigate the association of gender, mode of HIV acquisition, ethnicity, and geographical origin with the rate of all-cause hospitalisation, within Europe and separately within North America among people living with HIV on modern cART. We chose to

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Research in context

Evidence before this study

We conducted a comprehensive literature search on Ovid MEDLINE on Oct 6, 2021, to identify articles investigating disparities in hospitalisation between demographic groups of people living with HIV defined by gender, mode of HIV acquisition, ethnicity, and geographical origin in high-income countries. We used the following search terms to identify relevant studies (including MeSH terms): ("hospitalisation" OR "hospitalization" OR "patient admission" OR "inpatient" OR "inpatients" OR "hospital discharge") AND ("HIV" OR "HIV-1" OR "HIV-2" OR "human immunodeficiency virus" OR "HIV infection" OR "Acquired Immunodeficiency Syndrome"). We also searched the webpages of observational HIV cohorts that provided information on publications for relevant material. Original research studies of any type were included (excluding systematic reviews). We applied the following inclusion criteria: set in high-income countries; published from 2008 onwards; inclusion of some data from 2008 onwards; more than 100 individuals in the study population; and investigating at least one of the following factors: gender or sex; mode of HIV acquisition; ethnicity or race; or geographical origin or migration background. Of all the studies identified, most were conducted in North America (mainly the USA). We did not apply any language restirctions; however, our search only found articles in English. None of the studies considered more than one high-income region and only two studies considered migration background, however without considering geographical origin.

Added value of this study

Our study is one of the largest on hospitalisation in people living with HIV in high-income countries and the first to contrast multiple regions (the European and, separately, the North American region) by using consistent definitions of demographic variables. To our knowledge, this is also the first study to investigate differences according to a combined ethnicity and geographical origin variable to assess and disentangle the effects of both migration status and minority ethnicity. Our findings suggest that substantial demographic disparities in hospitalisation exist in both Europe and North America in the current era of combination antiretroviral therapy. Similarities between the regions include increased rates in women, heterosexual men, and in particular men and women who acquired HIV through injection drug use compared with gay, bisexual, and other men who have sex with men. We also found evidence of a potential healthy migrant effect in both regions, with migrants (those whose geographic origin was different from their study region) tending to have lower rates compared with non-migrants (those of European or North-American origin, respectively). Although there was no evidence of a higher hospitalisation rate in individuals with an ethnicity other than White (compared with White) in Europe, in North America Indigenous people had much higher rates and African American or other Black individuals somewhat higher rates than White North Americans.

Implications of all the available evidence

Our findings highlight the importance of the sociodemographic context in shaping health outcomes in people living with HIV. Women, individuals who acquired HIV through injection drug use, and Indigenous people and those with Black or African American ethnicity in North America could benefit from targeted care, support, and interventions to reduce their excess risk of hospitalisation. Intervention approaches aiming to attenuate these observed inequalities in hospitalisation rates, in particular between racial and ethnic groups, could be most successful when using expert knowledge of country-specific or region-specific contexts.

focus specifically on those people living with HIV who started on modern antiretroviral therapy (ART) regimens to exclude the possibility of toxicities from earlier ART regimens affecting the risk of hospitalisation and make the results relevant to people living with HIV on ART in the present day.

Methods

Study design and participants

We combined data from European and North American cohorts participating in Antiretroviral Therapy Cohort Collaboration (ART-CC) with sufficient hospitalisation data.[13] To determine cohort inclusion, inform the analysis, and harmonise hospitalisation data, a survey was conducted among representatives from each ART-CC cohort management group with hospitalisation data available (appendix p 2). Conditions for cohorts' inclusion were: the ability to distinguish between overnight admissions and day admissions, as the analysis included overnight admissions only; the availability of hospitalisation data from 2007 onwards; and data on hospitalisation reported complete by cohort, also evidenced by broadly comparable rates of hospitalisation across cohorts in the same region. Three cohorts did not meet these criteria and were excluded. Of the nine cohorts included (ie, the Austrian HIV Cohort Study, the AIDS Therapy Evaluation in the Netherlands study, the Swiss HIV Cohort Study, and the VACH cohort in Spain for the European analysis and the Southern Alberta Cohort, the HIV Atlanta Veterans Affairs Cohort Study, the Kaiser Permanente Northern California cohort, the University of Washington HIV Cohort, and the Vanderbilt Comprehensive Care Clinic HIV Cohort for the North American analysis), seven collected hospitalisation data through clinical records; one through case reports provided by the patients' HIV physician; and one through linkage to a comprehensive government database on hospitalisations (appendix p 2). Four of nine cohorts

See Online for appendix

collected data on all hospitalisations that occurred at all hospitals, one was restricted to all hospitals within a specific hospital system; two collected all hospitalisations documented in the HIV clinical records; and two only included hospitalisations occurring at the hospital providing outpatient HIV care.

Participant inclusion criteria were identical across all selected cohorts: at least one outpatient clinic visit after Jan 1, 2007, defined as a recorded CD4 or HIV viral load measurement; gender recorded; first initiated ART after Jan 1, 2001 (to ensure individuals started on modern ART therapy; this excluded 16 342 [19%] of 86 010 individuals before applying the remaining inclusion criteria); and at least one day of follow-up. Baseline was defined as the time of the first clinic visit after both ART initiation and Jan 1, 2007. Individuals were followed up from their baseline visit until the date of death if the patient died or until the date of the last visit or drop out date. Cohort closure or administrative end of follow-up dates varied from 2015 to 2020. In total, 2732 (8%) of 33 206 individuals had follow-up of less than 1 year; this was broadly similar across demographic groups. Individual cohorts contributing to the collaboration were approved by ethics committees or institutional review boards and informed consent from patients was obtained for data to be used for research purposes. The ART-CC study was approved by the National Health Service Health Research Authority South West—Cornwall and Plymouth Research Ethics Committee, UK (REC reference 12/SW/0253).

Outcomes and variables of interest

The outcome of interest was the number of overnight all-cause hospitalisations over the follow-up period, with repeated hospitalisations from individuals included. Day cases were excluded as they include minor procedures and planned admissions that might not represent serious morbidity. The demographic predictors of interest were: combined gender and mode of HIV acquisition, ethnicity, and combined geographical origin and ethnicity. These factors were based on self-reporting by the patient at their first HIV clinic visit. On the basis of available variables and completeness of data (appendix p 3), we defined the variables shown in the appendix (p 4).

Statistical analysis

All analyses were conducted separately for North America and Europe. We calculated crude rates of hospitalisation by region and the demographic groups as the number of hospitalisations divided by the total person-time at risk, including repeated hospitalisations for the same individual. We further performed univariable and multivariable negative binomial regression. This was chosen because the extra dispersion parameter improved the fit of the null model compared with Poisson multilevel regression ($p<0·0001$, likelihood ratio test for both European and North American data). We split each participant's observation time into 1-year periods and counted all of their hospitalisations in this period. As there was non-independence due to repeated observations (calendar years) from individuals, we included a random intercept for each participant to capture between-participant variation. We examined the association of the three demographic predictors with hospitalisation, additionally adjusting in multivariable models for the following categorical variables: cohort as a fixed effect, and calendar year, age, and time since first cART initiation (all time-updated). Ethnicity and the combined ethnicity and geographical origin variable were not included in the same model. We restricted adjustment to the previously mentioned factors, as they were presumed to be associated with both the independent variables of interest (the demographic variables) and the outcome (hospitalisation) but not on the causal pathway from exposure to outcome (not a mediator). We did not adjust for CD4 count or viral load, as these are mediators of the relationship between demographic group and hospitalisation, but explored this in our additional analyses. We obtained adjusted incidence and incidence rate ratios with 95% CIs from the multivariable models. Statistical analyses were performed using Stata (version 16.1).

We conducted two sensitivity analyses: repeating the analysis without adjustment for time since first starting cART due to potential multicollinearity with age and calendar year and investigating the associations separately for different time periods (2007–11, 2012–15, and 2016–20). We also performed an additional analysis restricting the analysis to individuals with well controlled HIV at baseline (ie, a CD4 count ≥500 cells per μL and HIV RNA ≤50 copies per mL) to investigate the potential role of HIV disease stage at hospitalisation.

Role of the funding source

Funding for this project was awarded after peer review of a research proposal. After this, the funders played no further role in the analysis, presentation, or interpretation of study results.

Results

23 594 individuals from four cohorts were included in the European analysis and 9612 individuals from five cohorts were included in the North American analysis (appendix p 5). In Europe more than half of individuals had a baseline date between 2007 and 2009, whereas more North American participants had a baseline date from 2010 onwards (table 1). The North American population had a somewhat higher median age at baseline, a lower proportion of women, and a higher proportion who acquired HIV through sex between men. At baseline, the European population had a lower median CD4 count and CD4 nadir, a lower proportion with viral suppression, and a shorter median time since HIV diagnosis and since the start of ART. Information on ethnicity was unknown or unrecorded for 45·6% of people in the European population and 3·8% in the

	Europe (n=23 594)	North America (n=9612)
Gender*		
Men	17 980 (76·2%)	8294 (86·3%)
Women	5614 (23·8%)	1318 (13·7%)
Age, years	41·6 (34·1–48·4)	44·6 (35·8–51·7)
≤30	4036 (17·1%)	1418 (14·8%)
31–40	7233 (30·7%)	2233 (23·2%)
41–50	8068 (34·2%)	3310 (34·4%)
51–60	3090 (13·1%)	1977 (20·6%)
61–70	896 (3·8%)	584 (6·1%)
71–80	229 (1·0%)	81 (0·8%)
>80	42 (0·2%)	9 (0·1%)
Baseline clinic visit date		
2007–09	14 016 (59·4%)	2334 (24·3%)
2010–12	3646 (15·5%)	4073 (42·4%)
2013–15	3363 (14·3%)	2369 (24·6%)
2016–19	2569 (10·9%)	836 (8·7%)
Mode of HIV acquisition		
Sex between men	9593 (40·7%)	6019 (62·6%)
Heterosexual	7960 (33·7%)	2006 (20·9%)
Injection drug use	3896 (16·5%)	947 (9·9%)
Other or unknown	2145 (9·1%)	640 (6·7%)
Ethnicity		
White	10 973 (46·5%)	5006 (52·1%)
Black†	1367 (5·8%)	2224 (23·1%)
Hispanic	198 (0·8%)	1313 (13·7%)
Asian	262 (1·1%)	487 (5·1%)
Indigenous	3 (<0·1%)	119 (1·2%)
Mixed	12 (0·1%)	0
Other	28 (0·1%)	99 (1·0%)
Unknown or unrecorded	10 751 (45·6%)	364 (3·8%)
Geographical origin		
Europe or North America	14 196 (60·2%)	2726 (28·4%)
Sub-Saharan Africa	1413 (6·0%)	274 (2·9%)
Latin America	817 (3·5%)	169 (1·8%)
Middle East and north Africa	222 (0·9%)	8 (0·1%)
Asia	345 (1·5%)	83 (0·9%)
Other western‡	92 (0·4%)	45 (0·5%)
Other	54 (0·2%)	9 (0·1%)
Unknown or unrecorded	6455 (27·4%)	6298 (65·5%)
CD4 count, in cells per μL	408 (251–594)	531 (334–737)
>800	6293 (26·7%)	2028 (21·1%)
500–800	5055 (21·4%)	3251 (33·8%)
350–499	4495 (19·1%)	1794 (18·7%)
200–349	4341 (18·4%)	1443 (15·0%)
50–199	2612 (11·1%)	806 (8·4%)
<50	760 (3·2%)	278 (2·9%)
Missing	38 (0·2%)	12 (0·1%)

(Table 1 continues in next column)

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	Europe (n=23 594)	North America (n=9612)
CD4 count nadir, in cells per μL	230 (112–378)	480 (242–709)
Viral suppression, ≤50 copies per mL	12 048 (51·1%)	6926 (72·1%)
Years since HIV diagnosis	4·8 (1·6–10·6)	8·3 (3·7–14·8)
≤5	10 705 (45·3%)	2230 (23·2%)
>5 to 10	4505 (19·1%)	1723 (17·9%)
>10 to 20	3796 (16·1%)	1826 (19·0%)
>20	4588 (19·4%)	3833 (39·9%)
Years since first antiretroviral therapy initiation	1·2 (0–3·7)	2·4 (0·3–5·3)
0§	6812 (28·9%)	1051 (10·9%)
>0 to ≤1	4509 (19·1%)	2256 (23·5%)
>1 to 5	8892 (37·7%)	3701 (38·5%)
>5 to 10	3105 (13·1%)	2089 (21·7%)
>10	276 (1·2%)	515 (5·4%)
Previous AIDS diagnosis	5535 (23·5%)	920 (9·6%)
Median follow-up time, years	7·6 (3·3–11·2)	4·3 (1·8–5·2)
Number of deaths	1809 (7·7%)	476 (5·0%)
Hospitalisation rate, per 100 person-years (95% CI)		
Total over follow-up	16·2 (16·0–16·4)	13·1 (12·8–13·5)
2007–11	18·8 (18·5–19·2)	18·1 (17·3–19·0)
2012–15	15·7 (15·4–16·0)	11·4 (11·0–11·9)
2016–20	13·5 (13·1–13·8)	12·3 (11·6–13·0)
Median age at hospitalisation,¶ years	46 (38–53)	48 (39–56)
Death rate, per 100 person-years (95% CI)	1·08 (1·03–1·13)	1·19 (1·08–1·30)
Median number of hospitalisations (IQR; range; in those hospitalised)	2 (1–3; 1–53)	1 (1–3; 1–36)
Number of people hospitalised		
With 0 hospitalisations	12 790 (54·2%)	7523 (78·3%)
With 1 hospitalisation	5255 (22·3%)	1075 (11·1%)
With 2–3 hospitalisations	3473 (14·7%)	652 (6·8%)
With 4–5 hospitalisations	1074 (4·6%)	183 (1·9%)
With >5 hospitalisations	1002 (4·2%)	179 (1·9%)

Data are n (%) or median (IQR) unless otherwise stated. *Self-described. †Covering Black ethnicity for Europe and African American or Black for North America. ‡Other western countries includes the USA, Canada, Australia, and New Zealand for the European analysis and any European country, Australia, and New Zealand for the North American analysis. §Date of starting antiretroviral therapy is the same as date of study entry. ¶Includes repeated hospitalisations for the same individual.

Table 1: **Sociodemographic and clinical characteristics at baseline and outcomes during follow-up**

North American population. Information on geographical origin was unknown for 27·4% in the European population and 65·5% in the North American population.

Median follow up was 7·6 years (IQR 3·3–11·2) in Europe and 4·3 years (1·8–5·2) in North America (table 1). There were 27 221 hospitalisations in Europe and 5260 in North America. Crude hospitalisation rates across the entire follow-up (per 100 person-years) were 16·2 (95% CI 16·0–16·4) in Europe (ranging from 11·5 [11·2–11·8] to 20·1 [19·3–20·8] across cohorts) and 13·1 (12·8–13·5) in North America (ranging from 8·7 [8·3–9·1] to 20·8 [19·9–21·8]). In both regions, the rate of hospitalisation decreased over time.

Median age at hospitalisation (including age at each repeated admission for the same individual) in Europe ranged from 40 years (IQR 32–49) in women with other or unknown modes of HIV acquisition to 48 years (40–57) in heterosexual men (appendix p 8), and from 37 years (31–44) in those with sub-Saharan African origin to 48 years (41–56) in those with unknown origin and White ethnicity and 48 years (42–54) in those with non-European western origin. In North America, median age at hospitalisation ranged from 40 years (IQR 32–51) in heterosexual women to 52 years (42–61) in men with other or unknown modes of HIV acquisition, and from 31 years (30–45) in those with North American origin and ethnicity other than White to 54 years (47–61) in those with other or unknown origin and White ethnicity.

The figure shows the crude hospitalisation rates according to the demographic predictors. The crude rates according to demographic group are also shown in the appendix (p 9). In both Europe and North America, gay, bisexual, and other men who have sex with men (GBMSM) had the lowest hospitalisation rates, with the highest rates in those who acquired HIV through injection drug use. Women had higher hospitalisation rates than men within all HIV acquisition groups except when comparing heterosexual men and women in Europe. Compared with the White ethnicity group, in Europe those who are Indigenous people or have mixed, or other ethnicities had higher rates and all other ethnicity groups had lower rates. In North America, hospitalisation rates were higher for Black or African American and Indigenous individuals than White individuals, and lower in those with Hispanic, Asian, or unrecorded ethnicities.

For both regions, individuals who were migrants compared with non-migrants (those whose geographical origin was the same as their study region) had lower rates.

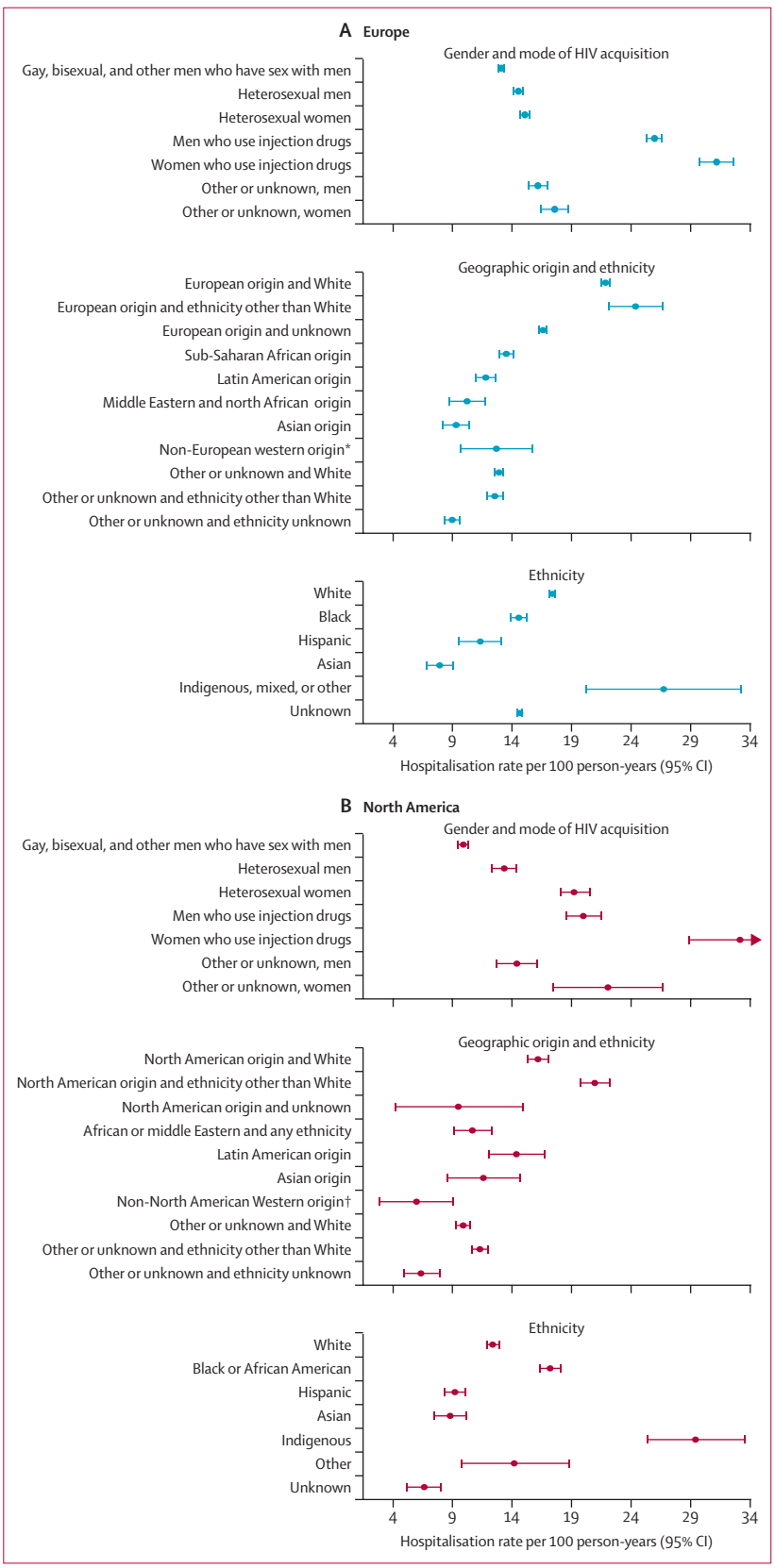

Figure: **Crude rates of hospitalisation and 95% CIs according to gender and mode of HIV acquisition, combined geographic origin and ethnicity, and ethnicity only in Europe and North America**

*Includes the USA, Canada, Australia, and New Zealand. †Includes Europe, Australia, and New Zealand.

Table 2 shows the covariate-adjusted incidence rates, unadjusted rate ratios, and adjusted rate ratios from the negative binomial regression, for Europe and North America. For gender and mode of HIV acquisition the pattern of associations were the same in the two regions: for example, individuals with a history of injection drug use had the highest rates in both regions, and GBMSM the lowest. However, the incidence rate ratios suggest that the variation in rates across groups was greater for the North American than European cohorts.

With regard to ethnicity, for both regions hospitalisation rates were lower for the Hispanic and Asian ethnicity groups compared with White ethnicity group but only for Asian individuals in the European data did the association

	Adjusted rate per 100 person-years*	Univariable model†		Multivariable model‡	
		Incidence rate ratio (95% CI)	p value	Adjusted incidence rate ratio (95% CI)	p value
European cohorts					
Gender and mode of HIV acquisition	..	..	<0·0001	..	<0·0001
Gay, bisexual, and other men who have sex with men	12·4 (11·8–12·9)	1 (ref)	..	1 (ref)	..
Heterosexual men	14·3 (13·5–15·2)	1·22 (1·13–1·31)	..	1·16 (1·08–1·24)	..
Heterosexual women	15·7 (14·8–16·6)	1·27 (1·18–1·35)	..	1·27 (1·18–1·36)	..
Men who inject drugs	25·9 (24·2–27·5)	2·09 (1·94–2·25)	..	2·09 (1·94–2·25)	..
Women who inject drugs	31·4 (27·8–34·9)	2·54 (2·25–2·88)	..	2·54 (2·25–2·86)	..
Other or unknown, men	16·1 (14·6–17·7)	1·21 (1·08–1·34)	..	1·31 (1·18–1·45)	..
Other or unknown, women	19·3 (16·7–21·9)	1·47 (1·28–1·70)	..	1·56 (1·36–1·80)	..
Ethnicity	..	..	<0·0001	..	0·0003
White	16·1 (15·4–16·7)	1 (ref)	..	1 (ref)	..
Black§	16·1 (14·4–17·8)	0·98 (0·88–1·09)	..	1·00 (0·90–1·11)	..
Hispanic	12·9 (9·3–16·6)	0·72 (0·54–0·95)	..	0·80 (0·61–1·07)	..
Asian	9·6 (7·3–12·0)	0·55 (0·43–0·70)	..	0·60 (0·47–0·76)	..
Indigenous, mixed, or other	20·6 (9·0–32·2)	1·18 (0·66–2·08)	..	1·28 (0·73–2·26)	..
Unknown or unrecorded	16·9 (16·1–17·8)	1·06 (0·99–1·13)	..	1·05 (0·99–1·13)	..
Geographic origin and ethnicity	..	..	<0·0001	..	<0·0001
European origin and White	22·6 (21·2–24·1)	1 (ref)	..	1 (ref)	..
European origin and ethnicity other than White	23·5 (18·7–28·3)	1·04 (0·84–1·27)	..	1·04 (0·85–1·27)	..
European origin and unknown ethnicity	22·4 (21·0–23·9)	0·98 (0·91–1·05)	..	0·99 (0·93–1·06)	..
Sub-Saharan African origin and any ethnicity	24·5 (21·5–27·5)	1·09 (0·97–1·24)	..	1·08 (0·96–1·23)	..
Latin American origin and any ethnicity	21·5 (18·2–24·8)	0·88 (0·75–1·03)	..	0·95 (0·81–1·11)	..
Middle Eastern and north African origin and any ethnicity	18·4 (13·5–23·4)	0·77 (0·58–1·01)	..	0·81 (0·62–1·07)	..
Asian origin and any ethnicity	14·8 (11·5–18·2)	0·63 (0·50–0·79)	..	0·66 (0·52–0·82)	..
Non-European western origin¶ and any ethnicity	21·8 (12·1–31·5)	0·83 (0·53–1·31)	..	0·96 (0·62–1·51)	..
Other or unknown origin and White	8·0 (7·3–8·6)	0·36 (0·32–0·41)	..	0·35 (0·31–0·40)	..
Other or unknown origin and ethnicity other than White	7·9 (7·3–8·6)	0·35 (0·29–0·41)	..	0·35 (0·30–0·41)	..
Other or unknown origin and unknown ethnicity	9·1 (7·9–10·3)	0·41 (0·36–0·47)	..	0·40 (0·35–0·46)	..
Age, years	..	..	<0·0001	..	<0·0001
<30	15·9 (14·9–17·0)	1 (ref)	..	1 (ref)	..
31–40	15·0 (14·3–15·6)	0·85 (0·79–0·91)	..	0·94 (0·88–1·01)	..
41–50	15·5 (14·9–16·1)	0·81 (0·75–0·86)	..	0·97 (0·91–1·04)	..
51–60	16·4 (15·6–17·1)	0·73 (0·68–0·79)	..	1·03 (0·95–1·11)	..
61–70	23·3 (21·5–25·1)	0·99 (0·90–1·09)	..	1·47 (1·33–1·62)	..
71–80	31·9 (28·8–36·0)	1·27 (1·10–1·47)	..	2·00 (1·73–2·31)	..
>80	29·5 (20·9–38·1)	1·11 (0·83–1·51)	..	1·85 (1·38–2·50)	..
Time since first initiation of combination antiretroviral therapy, years	..	..	<0·0001	..	<0·0001
≤1	25·3 (24·0–27)	1 (ref)	..	1 (ref)	..
>1 to 5	15·2 (14·6–15·8)	0·60 (0·57–0·63)	..	0·60 (0·57–0·63)	..
>5 to 10	15·0 (14·4–15·5)	0·57 (0·54–0·60)	..	0·59 (0·56–0·63)	..
>10	16·0 (15·2–16·8)	0·50 (0·47–0·53)	..	0·63 (0·59–0·68)	..

(Table 2 continues on next page)

remain after adjustment. In both regions, rates were higher for the Indigenous people and other ethnicity groups compared with the White ethnicity groups. However, the CI for the Indigenous people, mixed, or other ethnicity group in the European data was wide. In contrast, individuals of Black ethnicity had a comparable hospitalisation rate to those of White ethnicity in Europe, whereas in North America, rates were higher for individuals who were of Black or African American ethnicity compared with White individuals.

When considering the combined geographical origin and ethnicity variable in the European cohorts, individuals of European, non-European western (ie, the USA, Canada, Australia, and New Zealand), sub-Saharan African, and Latin American origin had similar hospitalisation rates, with lower rates for individuals of Middle Eastern and north African and Asian origin, and considerably lower rates for those with unknown geographical origin. In the North American cohort, CIs were wide for some geographical origin regions due to high levels of missing data. Nonetheless, those of non-North-American origin generally had lower hospitalisation rates than those of North American origin.

	Adjusted rate per 100 person-years*	Univariable model†		Multivariable model‡	
		Incidence rate ratio (95% CI)	p value	Adjusted incidence rate ratio (95% CI)	p value
(Continued from previous page)					
Calendar year	..	..	<0·0001	..	<0·0001
2007–08	19·1 (18·2–20·1)	1 (ref)	..	1 (ref)	..
2009–10	19·1 (18·2–20·0)	0·96 (0·91–1·01)	..	1·00 (0·95–1·05)	..
2011–12	18·0 (17·2–18·8)	0·89 (0·85–0·94)	..	0·94 (0·89–0·99)	..
2013–14	17·0 (16·3–17·7)	0·84 (0·80–0·89)	..	0·89 (0·84–0·94)	..
2015–16	15·7 (15·0–16·4)	0·78 (0·74–0·82)	..	0·82 (0·77–0·87)	..
2017–20	10·0 (9·5–10·5)	0·49 (0·47–0·52)	..	0·52 (0·49–0·56)	..
North American cohort					
Gender and mode of HV acquisition	..	..	<0·0001	..	<0·0001
Gay, bisexual, and other men who have sex with men	10·1 (9·1–11·1)	1 (ref)	..	1 (ref)	..
Heterosexual men	12·6 (10·3–14·9)	1·36 (1·12–1·64)	..	1·24 (1·02–1·52)	..
Heterosexual women	18·7 (15·6–21·9)	1·94 (1·63–2·32)	..	1·85 (1·54–2·21)	..
Men who inject drugs	22·0 (17·9–26·2)	2·28 (1·88–2·77)	..	2·17 (1·79–2·64)	..
Women who inject drugs	33·5 (20·9–46·0)	3·73 (2·55–5·46)	..	3·31 (2·26–4·83)	..
Other or unknown, men	14·6 (10·8–18·4)	1·47 (1·13–1·92)	..	1·44 (1·10–1·88)	..
Other or unknown, women	24·4 (12·4–36·4)	2·37 (1·44–3·88	..	2·41 (1·47–3·95)	..
Ethnicity	..	..	<0·0001	..	0·0003
White	13·1 (11·7–14·5)	1 (ref)	..	1 (ref)	..
Black§	15·1 (13·1–17·0)	1·23 (1·07–1·41)	..	1·15 (0·99–1·33)	..
Hispanic	11·1 (8·9–13·2)	0·76 (0·63–0·92)	..	0·84 (0·69–1·02)	..
Asian	11·5 (8·1–14·8)	0·74 (0·55–1·00)	..	0·87 (0·65–1·17)	..
Indigenous	25·4 (14·9–35·9)	2·29 (1·50–3·49)	..	1·93 (1·27–2·94)	..
Other	18·3 (6·3–30·2)	1·21 (0·63–2·35)	..	1·39 (0·72–2·67)	..
Unknown	8·4 (5·3–11·4)	0·60 (0·41–0·87)	..	0·64 (0·44–0·93)	..
Geographic origin and ethnicity	..	..	0·004	..	0·005
North American origin and White	15·0 (12·5–17·4)	1 (ref)	..	1 (ref)	..
North American origin and ethnicity other than White	17·2 (14·1–20·2)	1·23 (1·01–1·50)	..	1·15 (0·94–1·40)	..
North American origin and unknown ethnicity	10·7 (0·6–20·7)	0·56 (0·21–1·48)	..	0·71 (0·28–1·84)	..
African or Middle Eastern origin and any ethnicity	9·6 (6·4–12·9)	0·71 (0·50–0·99)	..	0·64 (0·46–0·91)	..
Latin American origin and any ethnicity	16·1 (9·9–22·3)	1·06 (0·72–1·57)	..	1·08 (0·73–1·59)	..
Asian origin and any ethnicity	12·2 (5·5–18·8)	0·77 (0·45–1·34)	..	0·81 (0·47–1·41)	..
Non-North American western origin‖ and any ethnicity	6·2 (5·0–11·9)	0·39 (0·15–0·98)	..	0·41 (0·17–1·04)	..
Other or unknown origin and White	12·0 (9·9–14·1)	0·90 (0·70–1·17)	..	0·80 (0·62–1·04)	..
Other or unknown origin and ethnicity other than White	12·5 (10·3–14·7)	0·92 (0·71–1·19)	..	0·83 (0·64–1·08)	..
Other or unknown origin and unknown ethnicity	8·0 (4·6–11·4)	0·59 (0·37–0·94)	..	0·54 (0·34–0·86)	..

(Table 2 continues on next page)

	Adjusted rate per 100 person-years*	Univariable model†		Multivariable model‡	
		Incidence rate ratio (95% CI)	p value	Adjusted incidence rate ratio (95% CI)	p value
(Continued from previous page)					
Age, years	..	..	<0·0001	..	<0·0001
<30	11·5 (9·5–13·6)	1 (ref)	..	1 (ref)	..
31–40	11·3 (9·9–12·8)	0·95 (0·80–1·14)	..	0·98 (0·82–1·18)	..
41–50	12·0 (10·6–13·2)	1·00 (0·83–1·20)	..	1·03 (0·85–1·25)	..
51–60	15·7 (13·8–17·7)	1·31 (1·08–1·59)	..	1·36 (1·11–1·67)	..
61–70	22·5 (18·3–26·7)	1·87 (1·48–2·36)	..	1·95 (1·52–2·50)	..
71–80	36·8 (23·1–50·6)	3·16 (2·12–4·71)	..	3·19 (2·12–4·80)	..
>80	56·1 (0·9–111·3)	4·60 (1·70–12·47)	..	4·85 (1·79–13·16)	..
Time since first initiation of combination antiretroviral therapy, years	..	..	<0·0001	..	<0·0001
≤1	18·0 (15·3–20·7)	1 (ref)	..	1 (ref)	..
>1 to 5	11·6 (10·4–12·9)	0·66 (0·57–0·76)	..	0·64 (0·55–0·73)	..
>5 to 10	14·0 (12·5–15·4)	0·79 (0·69–0·92)	..	0·72 (0·62–0·83)	..
>10	15·2 (13·0–17·4)	0·85 (0·72–1·00)	..	0·71 (0·59–0·84)	..
Calendar year	..	..	0·022	..	0·0001
2007–08	16·5 (14·0–19·0)	1 (ref)	..	1 (ref)	..
2009–10	15·1 (13·0–17·3)	0·95 (0·82–1·11)	..	0·92 (0·79–1·07)	..
2011–12	14·6 (12·9–16·3)	0·98 (0·85–1·13)	..	0·88 (0·76–1·03)	..
2013–14	13·1 (11·7–14·5)	0·89 (0·77–1·03)	..	0·79 (0·68–0·93)	..
2015–16	13·0 (11·6–14·5)	0·95 (0·82–1·10)	..	0·79 (0·67–0·93)	..
2017–20	9·5 (7·8–11·2)	0·73 (0·60–0·89)	..	0·58 (0·46–0·72)	..

*Incidence (95% CI). Obtained from the multivariable models. †Adjusted for fixed cohort effect. ‡The model is mutually adjusted except for ethnicity in the European analysis and mutually adjusted except for the combined geographic origin and ethnicity variable in the North American data. Estimates for ethnicity are adjusted for all variables except for combined geographic origin and ethnicity. Estimates for the combined geographic origin and ethnicity variable are adjusted for all variables except for ethnicity. Covariates age, time since first started combination antiretroviral therapy, and calendar year were time-updated. §Covering Black ethnicity for Europe and African American or Black for North America. ¶Includes the USA, Canada, New Zealand, and Australia. ||Includes Europe, Australia, and New Zealand (appendix p 4).

Table 2: **Adjusted and unadjusted incidence rates and adjusted rates of hospitalisation for associations of sociodemographic factors in European and North American cohorts**

Age over 50 years and ART initiation within 1 year previously, and earlier calendar year were also positively associated with hospitalisation in both regions.

The results of the sensitivity analyses were overall consistent with the main results. After excluding adjustment for time since first started cART, associations were similar to the main analysis in both regions (appendix pp 10–11). The analysis that considered associations separately by calendar period was limited by small numbers (appendix pp 12–13). Most associations were broadly similar across time without evidence of linear trends, except for an attenuation across time in the differences between gender and mode of HIV acquisition groups in Europe.

The final additional analysis included a subgroup of 6130 (26%) of 23 594 individuals in Europe and 4525 (47%) of 9612 individuals in North America who had well controlled HIV at baseline (appendix pp 14–16). Here, in both regions, the disparity in rates between heterosexual men, men and women who inject drugs, and men with other or unknown modes of HIV acquisition compared with GBMSM was somewhat smaller, suggesting that differences between these groups could be driven in part by HIV-related admissions. This effect was not observed for heterosexual women and women with other or unknown modes of HIV acquisition, which could be influenced by pregnancy-related and childbirth-related admissions. The associations of ethnicity and geographical origin with hospitalisation were broadly similar to that in the main analysis, with the following exceptions. In the European population, individuals with sub-Saharan African origin had higher hospitalisation rates than White Europeans, which was not the case in the entire study population. Furthermore, the lower rates in those with Asian origin compared with European origin observed in the main analysis disappeared. In the North American data, within the North American origin group, the higher rate in those with ethnicities other than White was less apparent. Particularly for the combined geographical origin and ethnicity variable, it should be noted that the results have wide CIs.

Discussion

To our knowledge, this study is one of the largest on hospitalisation in people living with HIV in high-income settings and the first to contrast multiple regions through consistent definitions of demographic variables. Although somewhat stronger in the North American region, disparities across gender and mode of HIV acquisition groups had a similar pattern in both regions, suggesting there could be commonality in disadvantaging factors. In both regions we found lower hospitalisation rates among migrants, although this was more pronounced in European cohorts. Ethnicity categories were necessarily coded differently in the different regions, but there were some notable findings in the North American cohorts, in particular the extent to which rates were elevated for Indigenous individuals compared with other groups, and to a lesser extent for Black or African American individuals. This finding might imply a role of context-specific factors, such as culture, prejudice, access to and experience of health-care systems, and socioeconomic disadvantage. Intervention approaches aiming to attenuate these observed inequalities in hospitalisation rate might be most successful when using expert knowledge of country-specific or region-specific contexts.

GBMSM had the lowest adjusted rates of hospital admissions, followed by heterosexual individuals, then the other or unknown groups, and finally the groups who inject drugs had the highest rates. Women had higher rates within each subgroup. Several North American (mainly US) studies[14–18] and one European study[7] showed higher rates in women compared with men as a whole, whereas other US studies[9,19,20] and most European studies[10,11,21] did not. Only one study differentiated between GBMSM and other men and found no difference between women and heterosexual men (contrary to our finding) and a lower rate in GBMSM (consistent with our findings).[9] When considering the subgroup with well controlled HIV at baseline, differences between GBMSM and other groups were somewhat weakened compared with the main analysis, except for women with heterosexual or other or unknown modes of HIV acquisition. Further, GBMSM were less likely to have a previous AIDS diagnosis than all other gender and mode of HIV acquisition groups (appendix pp 6–7), suggesting the disparities seen are in part due to HIV-related admissions, most likely linked in part to late diagnosis. This finding is consistent with findings from a previous study that disparities in hospitalisation between GBMSM and other men and women are particularly wide during the first year after HIV diagnosis, for which hospitalisation rates are particularly high and predominantly AIDS-related.[10]

When considering women, a lower median age at hospitalisation across all modes of HIV acquisition groups in both regions (appendix p 8) suggests that pregnancy-related admissions could account for some of the increased hospitalisation rates. Nonetheless, a large part of the variation in risk between GBMSM and heterosexual men and women is most likely driven by factors such as socioeconomic circumstances and poverty,[22–24] which is strongly associated with hospitalisation.[11] Structural barriers to care such as stigma,[25] low social support, and low engagement and retention in care are likely to play a role.[26] Such factors might act through a variety of mechanisms to effect hospital admissions, for example psychological and stress-related conditions; lifestyle factors; difficulties with treatment adherence to HIV and other medications;[27] delays in seeking health care; difficulties accessing health care; and quality of health care received. For individuals who inject drugs, admissions directly related to injection drug use most likely also contribute to a higher hospitalisation rate than other modes of HIV acquisition. Women and men who acquired HIV through heterosexual contact or through injection drug use should receive additional support to close gaps in long-term health outcomes. As our results suggest that similar disparities exist in both regions, a focused effort across countries and regions on prioritising these groups could be needed.

The association between ethnicity and hospitalisation must be considered in a region-specific context. In North America, compared with White individuals, we found higher rates of hospitalisation in Black or African American individuals and particularly in Indigenous people but not in Asian, Hispanic, and other and unknown ethnicities. Previous research in the USA has found increased hospitalisation rates in African American or other Black individuals compared with White people living with HIV[12,15,16,18,19,28,29] with effect sizes similar to those in our analysis. Furthermore, studies have found comparable or lower risks in Hispanic individuals[15,28] than White individuals and, similar to our study, a single study of Indigenous Native Hawaiians found a considerably higher risk compared with White people living with HIV.[30] Downstream effects of structural racism could include late HIV diagnosis, challenges to care engagement, and more frequent HIV care interruptions,[31] hindering long-term ART treatment success and increasing HIV-related hospitalisation risk. However, results were very similar when restricting to those with well controlled HIV at baseline and similar hospitalisation disparities have also been observed in the general US population.[32] Thus, these disparities by ethnicity might not fully be explained by HIV-related factors but also reflect disparities in chronic disease morbidity and health-care access more generally. It is well documented that the persisting effects of colonialisation and racism experienced by Indigenous Peoples in North America and other high-income countries are linked to inequities in social and structural determinants of health, socioeconomic inequalities, substance use, distrust of health and medical services,[33,34]

and fear and experience of stigma and discrimination. A 2019 systematic review focused on the experiences of Indigenous Peoples from North America, Australia, and New Zealand concluded that a disconnect remains between the clinical priorities in the HIV care framework and lived experiences.[35] In our study, the population of Indigenous Peoples in both the USA and Canada includes very diverse groups with different cultural traditions and experiences that might face very particular challenges. Qualitative research is needed to understand the barriers faced by Indigenous peoples in different settings and how they could best be addressed. Concrete interventions could include peer support, new approaches for health and prevention interventions, subsidising travel and other health-care-related expenses, and specific training for health professionals. Additionally, a commitment to addressing structural racism and discrimination as core barriers to long-term health and treatment success is needed.[36]

In the European analysis, rates of hospitalisation across ethnic groups were similar except for lower rates in Hispanic and Asian individuals, the former in univariable analysis only. Ethnic disparities in North America might be more apparent than in Europe, potentially because a higher proportion of individuals in Europe have access to universal health care. However, there is a scarcity of research on the health effects of racism and racial disparities in health in Europe compared with the USA. It is important to interpret the results for the single ethnicity variable in the European analysis with caution as some countries prohibit the collection of data on ethnicity, and we had low numbers of individuals in some ethnicity groups.

In both regions, we found lower hospitalisation rates among migrants (whose geographical origin was different to their study regions) than non-migrants. One study conducted in Canada and one in Italy examined hospitalisation according to migration status, without distinguishing between region of origin. Whereas the Canadian study found a lower risk for HIV-related and all-cause hospitalisation in migrants compared with non-migrants,[37] the Italian study found some evidence that non-Italian nationality was associated with an increased risk of all-cause and non-AIDS-related hospitalisation but not with AIDS-defining hospitalisation.[3] A previous ART-CC analysis found lower mortality in migrants from sub-Saharan Africa, Asia, or other western (ie, Europe [for the North American analysis], the USA and Canada [for the European analysis], Australia, and New Zealand) countries but not from Latin America or the Middle Eastern or north African regions.[38] There are two competing potential hypotheses. One hypothesis is the well known so-called healthy migrant effect that arises as migrants are often young, self-selected to be in good health,[39] and might have certain socioeconomic advantages compared with some non-migrant populations. Our associations were not attenuated after adjustment for age and the other covariates, but we could not account for comorbidities or socioeconomic factors, which might explain the lower hospitalisation rate. The competing hypothesis is that recent migrants (ie, those who have moved within the past year) might be less able or more reluctant to access health services, which could be reflected in a lower rate of contacts with care than non-migrants. Barriers to accessing these services could result from unfamiliarity with local health systems, a lack of insurance, language barriers, experiences of discrimination or distrust, and worries of losing employment when accessing medical services.[40] However, this second hypothesis is unlikely to fully explain the migrant effect on hospitalisation in our analysis, since a similar association was observed in a previous ART-CC analysis for mortality, for which this hypothesis cannot be applied.[38] Our findings suggest that migration status is associated with lower rates of hospitalisation and specific minority ethnicities are associated with higher rates of hospitalisation. This potential difference in association emphasises the importance of recording and accounting for both factors and appreciating the nuances in how these factors can be measured differently across studies and settings. Further research is needed to elucidate the potential contributions of factors including structural racism, anti-migrant policies, number of comorbidities, and potential barriers in accessing health services to differences in health outcomes among specific migrant, country of origin, and minority ethnic groups.

An important question is whether the demographic disparities in hospitalisations that we observed are due to differences in antiretroviral treatment outcomes such as viral non-suppression. Investigating this question would provide insight into whether efforts are best focused on improving HIV-related outcomes or on chronic disease comorbidity. Future research should formally address this question using causal inference methods such as causal mediation analysis. We indirectly addressed this question by performing an additional analysis restricted to those with well controlled HIV at baseline. Although the findings should not be overinterpreted because of wide CIs, our findings suggest that ongoing differences in CD4 and viral load are unlikely to fully explain demographic disparities. Interventions probably need to be more holistic and go beyond ART adherence support for long-term viral suppression.

Our study has several strengths. A multicohort approach across two high-income regions and the consistencies in definition of demographic variables allowed us to evaluate similarities and differences in associations. Evidence from Europe, in particular on hospitalisation rates across ethnicity and geographical origin groups, was previously lacking. Furthermore, to our knowledge, this study is the first to consider hospitalisation differences according to geographical origin and to consider a combined ethnicity and

geographical origin variable that differentiates migrant and non-migrant minority ethnic groups.

The true rate of hospitalisation might have been underestimated to some extent and to varying degrees across cohorts due to differences in data collection and the source of hospitalisation data. However, any potential underestimation would most likely be similar across ethnic and geographical groups and therefore might not have a strong effect on associations. Furthermore, we did not have information on planned (eg, for childbirth) and emergency admissions or on cause-specific hospitalisation, which would have helped us gain insight into drivers of morbidity across groups. Within our two regional groups, cohorts might differ in health-care systems, criteria for admission, and data collection, which could affect hospitalisation rates; we adjusted for cohorts to help account for this. In comparing Europe and North America, we chose to focus on relative associations that we expect to be less affected by these differences. Furthermore, the inclusion of five clinical sites with diverse access to health care to represent the North American region could somewhat limit the generalisability. There was also a lack of social and socioeconomic data, which is rarely collected in observational HIV databases, but should increasingly be incorporated into routine data collection to allow for investigations into the drivers of demographic differences. Overall, our findings only apply to ART-experienced people living with HIV who have been on modern ART regimens; however, since cART is now recommended for all, this represents a large proportion of the HIV-positive population.

In summary, our study provides evidence that substantial disparities exist in all-cause hospitalisation, a broad marker of morbidity and access to care, between demographic and ethnic groups of people living with HIV in the current cART era in Europe and North America, with some specific differences between the regions. This finding highlights the importance of the sociodemographic context in shaping health outcomes in people living with HIV.

Contributors

SMR, CJS, and FCL conceived the idea for the analysis, with input from all authors. SMR drafted the analysis plan and conducted all analyses, with input from CJS, FCL, SMI, AT, and JACS. SMR drafted the first version of the manuscript, and all authors provided substantive input into this and subsequent drafts and made the decision to submit for publication. SMR and SMI have directly accessed and verified the data.

Declaration of interests

SMR reports fellowship payments from the Royal Free Charity. FCL reports grants from the National Institute for Health and Care Research paid to their institution. JACS and SMI report grants from the National Institutes of Health paid to their institution. JACS also received grants from the UK National Institute for Health and Care Research paid to their institution. MvdV received grants and consulting fees from Gilead, ViiV, and MSD paid to their institution. GW reports grants from Gilead and Roche Diagnostics and honoraria from Gilead, ViiV, and MSD. MJG participated on advisory boards for Merck, Gilead, and ViiV. HMC and JC report separate grants from the National Institutes of Health paid to their institution. HMC received grants from ViiV and AHRQ paid to their institution. LW reports grants from ANRS MIE. All other authors declare no competing interests.

Data sharing

Data sharing agreements between the individual cohorts and ART-CC prevent us from sharing the study data with third parties. Investigators interested in accessing these data should contact the individual cohorts, details of which are given in the appendix (p 5).

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