

All-cause hospitalization according to demographic group in people living with HIV in the current antiretroviral therapy era

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Objective: We investigated differences in all-cause hospitalization between key demographic groups among people with HIV in the UK in the current antiretroviral therapy (ART) era.

Design/Methods: We used data from the Royal Free HIV Cohort study between 2007 and 2018. Individuals were classified into five groups: MSM, Black African men who have sex with women (MSW), MSW of other ethnicity, Black African women and women of other ethnicity. We studied hospitalizations during the first year after HIV diagnosis (Analysis-A) separately from those more than one year after diagnosis (Analysis-B). In Analysis-A, time to first hospitalization was assessed using Cox regression adjusted for age and diagnosis date. In Analysis-B, subsequent hospitalization rate was assessed using Poisson regression, accounting for repeated hospitalization within individuals, adjusted for age, calendar year, time since diagnosis.

Results: The hospitalization rate was 30.7/100 person-years in the first year after diagnosis and 2.7/100 person-years subsequently; 52% and 13% hospitalizations, respectively, were AIDS-related. Compared with MSM, MSW and women were at much higher risk of hospitalization during the first year [aHR (95% confidence interval, 95% CI): 2.7 (1.7–4.3), 3.0 (2.0–4.4), 2.0 (1.3–2.9), 3.0 (2.0–4.5) for Black African MSW; other ethnicity MSW; Black African women; other ethnicity women respectively, Analysis-A] and remained at increased risk subsequently [corresponding aIRR (95% CI): 1.7 (1.2–2.4), 2.1 (1.5–2.8), 1.5 (1.1–1.9), 1.7 (1.2–2.3), Analysis-B].

Conclusion: In this setting with universal healthcare, substantial variation exists in hospitalization risk across demographic groups, both in early and subsequent periods after HIV diagnosis, highlighting the need for targeted interventions.

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Introduction

In the recent antiretroviral therapy (ART) era, non-AIDS comorbidities and age-related factors increasingly contribute to morbidity in people living with HIV (PLHIV) [1–3].

Hospitalization is an important outcome that captures AIDS and non-AIDS morbidity, as well as being a significant component of healthcare costs. However, there is little research on current rates and predictors of hospitalization among PLHIV in high-income countries. Previous studies suggest that there are disparities in hospitalization risk according to gender [4–8] and ethnicity [6,9,10], but findings are not consistent across studies or settings [11–17], which may reflect variations in the sociodemographic profile of the HIV epidemic. The majority of the literature comes from the USA, a setting without universal access to HIV care and treatment. Furthermore, only two studies included data beyond 2010 [7,8]. In addition, when examining demographic variation in hospitalization, most previous studies did not differentiate between MSM and other men, and none considered sex and ethnicity concurrently. Therefore, differences in hospitalization risk across key affected demographic groups were not directly identified.

This study investigated all-cause hospitalization in PLHIV in the Royal Free HIV Cohort study (RFHCS), London, from the period 2007 to 2018, assessing variation between key demographic groups defined by sex, sexual orientation and ethnicity. The results could help to inform interventions targeting high-risk groups to reduce hospitalizations and associated costs in PLHIV.

Materials and methods

Study participants and design

The RFHCS is an observational cohort study of HIV-positive individuals attending the Royal Free Hospital, London, UK, for outpatient HIV care. HIV-diagnosed patients were included in the present study if they had at least one outpatient clinic visit, defined as either a CD4⁺ cell count or viral load measurement, between 1 January 2007 and 31 January 2018. Ethical approval for the RFHCS was obtained from the London South East Research Ethics Committee (REC reference 19/LO/0091).

Hospital admission

Information on hospitalizations is collected routinely through annual clinical record reviews and includes

hospitalizations that occurred at the Royal Free Hospital. Internal validation of a subset of study participants has shown that this represents around 80% of all hospitalizations that occurred in individuals (data not shown). Hospitalizations were defined as overnight hospital stays. The information collected was admission and discharge dates and cause for each hospitalization categorized as AIDS and/or non-AIDS related.

We studied hospitalizations that occurred during the first year after HIV diagnosis (Analysis A) separately from those that occurred more than 1 year after diagnosis (Analysis B), as admission risk is particularly high around the time of diagnosis [18] (textbox). Individuals could be included in both Analysis A and Analysis B with different baselines. Analysis A considered only an individual's first hospitalization during the first year after diagnosis, whereas Analysis B considered all hospitalizations occurring more than 1 year after diagnosis, with multiple hospitalizations from individuals included. Individuals in Analysis A were followed from their date of diagnosis until the first of: date of hospitalization; death; 1 year post diagnosis; last clinic visit up to 31 January 2018. Individuals in Analysis B were followed from their first clinic attendance after 1 January 2007 that was more than 1 year after diagnosis, until the last of: date of death; last clinic visit or last hospitalization up to 31 January 2018. If an individual had a date of death recorded more than 1 year after their last clinic visit or last hospitalization, this last visit was defined as the end of follow-up instead of their date of death.

Individuals were excluded from Analysis A if they did not have a clinic visit within 3 months of diagnosis to exclude those that tested for HIV at the Royal Free, but chose to attend a different clinic for their care ($n=6$). We also excluded people who acquired HIV through injection drug use ($n=20$ in Analysis A; $n=137$ in Analysis B). This group had a particularly high hospitalization rate (72.7 per 100 person-years in Analysis A; 9.1 per 100 person-years in Analysis B) and represented a small proportion of the clinic population (<5% and were almost exclusively male).

There were 65 individuals who were diagnosed with HIV while hospitalized, and we included these hospitalizations as outcomes in analysis A. In these cases, the date of admission was set to the date of HIV diagnosis, also defined as the start of follow-up. Hospitalizations related to pregnancy and childbirth ($n=1$ in Analysis A; $n=21$ in Analysis B) were excluded to restrict the analyses to hospitalizations related to illness and injuries. This also allowed for a more meaningful comparison of rates between women and men.

	Analysis A: First year post diagnosis	Analysis B: >1 year post diagnosis
Inclusion criteria	Newly diagnosed with HIV at Royal Free between 1 January 2007–31 January 2018	Attended the Royal Free between 1 January 2007–31 January 2018 and diagnosed with HIV for > 1 year
Exclusion criteria	HIV infected via injection drug use No clinic visits within 3 months of diagnosis	HIV infected via injection drug use
Baseline	Date of HIV diagnosis	First clinic visit after 1 January 2007 that is >1 year post HIV diagnosis
End of follow-up	First of: Hospitalization One year post diagnosis Last clinic visit up to 31 January 2018 Death	Last of: Last clinic visit up to 31 January 2018 Last hospitalization up to 31 January 2018 Death
Outcome	First hospitalization (any cause)	Hospitalizations (any cause; multiple events per patient allowed)

Demographic group

The main exposure of interest was demographic group, combining sex, sexual orientation and ethnicity. Individuals were classified into five mutually exclusive categories: MSM; Black African men who have sex with women (MSW); MSW of other ethnicity; Black African women; women of other ethnicity. This categorization is used by Public Health England (PHE) to define the main affected demographic groups of PLHIV in the UK [19]. Sex was self-defined using a binary classification, sexual orientation was derived using the proxy of reported mode of HIV acquisition and ethnicity was self-reported. In our categorization, ‘other ethnicity’ includes white; Black Caribbean and other Black that is not Black African ethnicity; mixed; Indian sub-continent; other Asian Chinese; other/unknown.

Statistical methods

In Analysis A, we assessed the unadjusted and adjusted association between demographic group and time to first hospitalization during the first year after diagnosis using Cox proportional hazards regression. The multivariable analysis was adjusted for age at HIV diagnosis and year of HIV diagnosis. In a secondary analysis, we additionally adjusted for the CD4⁺ cell count at diagnosis to assess the extent to which level of immunosuppression at diagnosis may account for any observed differences in hospitalization between demographic groups.

In Analysis B, we used Poisson regression with Generalised Estimating Equations (GEE) to assess unadjusted and adjusted associations between demographic group and rate of hospitalization from 1 year after diagnosis. Follow-up time was divided into one-month intervals. We assumed a first order autoregressive working correlation structure in our GEE model to account for the repeated hospitalizations from individuals. We adjusted for time updated current age, current calendar year and current time since diagnosis in the multivariable model. Similar to analysis A, in a secondary analysis, we additionally adjusted for CD4⁺ cell count at diagnosis to investigate whether level of immunosuppression at diagnosis accounted for long-term differences in hospitalization between key demographic groups. We also

alternatively adjusted for CD4⁺ cell count at baseline both because CD4⁺ cell count at diagnosis was missing for a large proportion of individuals (28–35% across demographic groups), and also to investigate its impact on the differences between groups.

We used SAS (version 9.4) for all statistical analyses and the ggplot2 package in R (RStudio version 1.2.1335) to create the figures.

Sensitivity analyses

We assessed the composite endpoint of hospitalization or death in both Analysis A and Analysis B.

We used zero-inflated Poisson and zero-inflated negative binomial models as alternative approaches to model the count of hospitalizations in Analysis B. All sensitivity analyses were consistent with results of the main analysis (data not shown).

Results

Analysis A: first year after HIV diagnosis

In Analysis A, 951 study participants were newly diagnosed with HIV during the study period (Table 1). A total of 434 (46%) individuals were MSM, 81 (9%) were Black African MSW, 146 (15%) were MSW of other ethnicity, 176 (19%) were Black African women and 114 (12%) women of other ethnicity. MSW had a higher median age at diagnosis compared to MSM and women. Black African MSW were more likely to be diagnosed earlier in the period than the other groups. Just over half of MSM were born in the UK, compared with less than 5% of Black African individuals, just under half of ‘other ethnicity MSW’, and about one-third of ‘other ethnicity women’. Women and MSW had a much lower median CD4⁺ cell count at diagnosis, compared with MSM. Women had a lower median viral load at baseline compared to MSM and MSW. The majority of MSM, MSW and women started ART within 3 months of diagnosis.

Table 1. Baseline characteristics of study participants in Analysis A and Analysis B.

	MSM	Black African MSW	Other ethnicity MSW	Black African women	Other ethnicity women
Analysis A: first year after HIV diagnosis					
N (total = 951)	434	81	146	176	114
2007–2009	181 (42%)	42 (52%)	45 (31%)	80 (45%)	42 (37%)
2010–2012	124 (29%)	25 (31%)	39 (27%)	47 (27%)	42 (37%)
2013–2018	129 (30%)	14 (17%)	62 (42%)	49 (28%)	30 (26%)
Age in years					
Median (IQR)	38 (31–46)	43 (35–49)	43 (34–51)	39 (33–45)	37 (29–46)
≤35	176 (41%)	19 (23%)	40 (27%)	56 (32%)	49 (43%)
36–50	181 (42%)	46 (57%)	63 (43%)	99 (56%)	44 (37%)
51–65	67 (15%)	13 (16%)	38 (26%)	20 (11%)	18 (16%)
>65	10 (2%)	3 (4%)	5 (3%)	1 (0.6%)	3 (3%)
Born in the UK (missing = 173)	206 (56%)	3 (4%)	48 (48%)	6 (4%)	27 (30%)
CD4 ⁺ cell count in cells/μl					
Median (IQR)	435 (252–625)	215 (39–361)	244 (53–545)	238 (105–368)	264 (94–445)
>800	43 (10%)	1 (1%)	5 (4%)	4 (2%)	6 (6%)
500–800	123 (29%)	8 (11%)	36 (26%)	18 (11%)	16 (15%)
350–499	87 (21%)	11 (14%)	15 (11%)	27 (16%)	23 (21%)
200–349	86 (21%)	20 (26%)	19 (14%)	46 (27%)	24 (22%)
50–199	47 (11%)	16 (21%)	32 (23%)	53 (32%)	22 (20%)
<50	32 (8%)	20 (26%)	33 (24%)	20 (12%)	18 (17%)
Median viral load (IQR) in log copies/ml	4.79 (4.15–5.38)	4.74 (3.95–5.53)	4.91 (3.93–5.55)	4.54 (3.48–5.20)	4.57 (3.63–5.50)
On ART within 3 months after diagnosis	268 (62%)	67 (83%)	113 (77%)	142 (81%)	84 (74%)
Analysis B: >1 year after HIV diagnosis					
N (total = 4207)	2,361	331	423	667	425
Baseline date					
2007–2009	1653 (70%)	223 (67%)	220 (52%)	434 (65%)	261 (61%)
2010–2012	331 (14%)	59 (18%)	84 (20%)	108 (16%)	76 (18%)
2013–2018	377 (16%)	49 (15%)	119 (28%)	125 (19%)	88 (21%)
Age in years					
Median (IQR)	41 (35–47)	44 (38–49)	44 (36–51)	39 (34–45)	39 (33–46)
≤35	560 (24%)	47 (14%)	93 (22%)	190 (28%)	140 (33%)
36–50	1413 (60%)	212 (64%)	211 (50%)	404 (61%)	226 (53%)
51–65	353 (15%)	62 (19%)	97 (23%)	66 (10%)	52 (12%)
>65	35 (1%)	10 (3%)	22 (5%)	7 (1%)	7 (2%)
Born in the UK (missing = 1538)	825 (58%)	8 (3%)	117 (44%)	15 (3%)	79 (30%)
CD4 ⁺ cell count at baseline in cells/μl					
Median (IQR)	536 (389–734)	381 (230–533)	435 (292–676)	426 (275–587)	464 (287–646)
>800	436 (19%)	20 (6%)	57 (14%)	48 (7%)	53 (13%)
500–800	865 (37%)	79 (24%)	101 (25%)	202 (31%)	127 (31%)
350–499	554 (24%)	78 (24%)	105 (26%)	165 (26%)	99 (24%)
200–349	337 (15%)	82 (25%)	87 (21%)	139 (21%)	79 (19%)
50–199	109 (5%)	46 (14%)	52 (13%)	68 (11%)	42 (10%)
<50	21 (1%)	18 (6%)	6 (1%)	25 (4%)	11 (3%)
CD4 ⁺ cell count at diagnosis in cells/μl					
Median (IQR)	410 (240–601)	171 (63–326)	260 (54–487)	228 (90–385)	270 (97–490)
>800	151 (6%)	4 (1%)	14 (3%)	13 (2%)	17 (4%)
500–800	437 (19%)	22 (7%)	59 (14%)	58 (9%)	50 (12%)
350–499	334 (14%)	27 (8%)	43 (10%)	75 (11%)	41 (10%)
200–349	323 (14%)	52 (16%)	55 (13%)	120 (18%)	57 (13%)
50–199	189 (8%)	80 (24%)	61 (14%)	135 (20%)	67 (16%)
<50	122 (5%)	47 (14%)	69 (16%)	82 (12%)	43 (10%)
missing	805 (34%)	99 (30%)	122 (29%)	184 (28%)	150 (35%)
Median CD4 ⁺ cell count nadir (IQR), in cells/μl	250 (130–415)	140 (42–279)	194 (56–371)	187 (68–331)	199 (77–360)
Viral suppression (≤50 copies/ml)	1569 (66%)	229 (69%)	275 (65%)	423 (63%)	288 (68%)
Years since diagnosis					
Median	5.9	4.5	3.9	4.1	4.8
>1–5 years	1069 (45%)	180 (54%)	240 (57%)	380 (57%)	216 (51%)
>5–10 years	513 (22%)	91 (27%)	92 (22%)	177 (27%)	114 (27%)
10–20 years	652 (28%)	59 (18%)	69 (16%)	106 (16%)	84 (20%)
> 20 years	127 (5%)	1 (0.3%)	22 (5%)	4 (0.6%)	11 (3%)
Ever taken ART	1837 (78%)	289 (87%)	334 (79%)	569 (85%)	342 (80%)
Currently on ART	1732 (73%)	276 (83%)	320 (76%)	513 (77%)	307 (72%)
Years since first started ART					
Median (IQR) ^a	4.9 (1.3–9.7)	3.6 (1.2–7.6)	3.1 (1.0–7.7)	3.1 (1.0–6.7)	3.5 (1.1–7.8)
0–1 year	276 (15%)	45 (16%)	67 (20%)	120 (21%)	67 (20%)

Table 1 (continued)

	MSM	Black African MSW	Other ethnicity MSW	Black African women	Other ethnicity women
>1–5 years	650 (35%)	135 (47%)	140 (42%)	247 (43%)	137 (40%)
>5–10 years	506 (28%)	71 (25%)	71 (21%)	151 (27%)	98 (29%)
10–20 years	392 (21%)	38 (13%)	53 (16%)	51 (9%)	39 (11%)
>20 years	13 (1%)	0 (0%)	3 (0.9%)	0 (0%)	1 (0.3%)
Prior AIDS diagnosis	506 (21%)	119 (36%)	127 (30%)	221 (33%)	101 (24%)
Prior non-AIDS diagnoses					
Myocardial infarction	21 (0.9%)	2 (0.6%)	3 (0.7%)	1 (0.1%)	1 (0.2%)
Stroke	12 (0.5%)	13 (3.9%)	7 (1.7%)	8 (1.2%)	5 (1.2%)
Diabetes	56 (2.4%)	30 (9.1%)	32 (7.6%)	27 (4.0%)	12 (2.8%)
Coronary revascularization	20 (0.8%)	2 (0.6%)	3 (0.7%)	1 (0.1%)	1 (0.2%)
Renal failure/dialysis	13 (0.6%)	15 (4.5%)	11 (2.6%)	15 (2.2%)	6 (1.4%)
Liver cirrhosis	21 (0.9%)	4 (1.2%)	9 (2.1%)	3 (0.4%)	4 (0.9%)
Osteoporosis	12 (0.5%)	1 (0.3%)	6 (1.4%)	8 (1.2%)	5 (1.2%)
Cancer	29 (1.2%)	8 (2.4%)	6 (1.4%)	5 (0.7%)	6 (1.4%)
Any of the above	151 (6.4%)	61 (18.4%)	65 (15.4%)	55 (8.2%)	33 (7.8%)

ART, antiretroviral therapy, IQR, interquartile range; MSW, men who have sex with women; MSM, men who have sex with men.

There were nine deaths (<1%) during the first year after HIV diagnosis and 213 (22% of individuals) hospitalizations (Table 2). Overall, 52% of hospitalizations had at least one AIDS-related cause. MSW had a higher proportion of AIDS-related admissions than women and MSM. The overall rate of hospitalization in the first year after diagnosis was 30.7 per 100 person-years. The rate varied from 15.5/100 person-years in MSM to 52.8/100 person-years in other ethnicity MSW (Fig. 1a). The Kaplan–Meier estimate of hospitalization risk by one year from diagnosis was 23.0% (20.2–25.7%). This percentage was highest in other ethnicity MSW (36.2%; 28.3–44.1%), followed by Black African MSW (34.8%; 24.1–45.4%), other ethnicity women (34.2%; 25.3–43.0%),

Black African women (23.9%; 17.5–30.3%), and MSM (13.0%; 9.8–16.2%).

In unadjusted Cox regression analysis (Table 3), compared with MSM, the hazard of hospitalization was around three times higher in Black African MSW, other ethnicity MSW and women, and about twofold higher in Black African women. After adjustment for age and date of diagnosis, the associations were marginally attenuated in the MSW groups only. Table 3 also summarizes adjusted associations of age, date of diagnosis and CD4⁺ cell count with hospitalization. Older age at diagnosis was associated with hospitalization. There was a weaker U-shaped association between

Table 2. Outcomes of individuals in Analysis A and Analysis B.

	MSM	Black African MSW	Other ethnicity MSW	Black African women	Other ethnicity women
Analysis A: first year after HIV diagnosis					
Number of deaths during follow-up	2 (0.46%)	3 (0.9%)	2 (0.5%)	0 (0%)	2 (0.5%)
Hospitalizations during follow-up ^a	55 (13%)	27 (33%)	52 (36%)	41 (23%)	38 (33%)
% with at least one AIDS-related cause	28 (51%)	16 (59%)	29 (56%)	21 (51%)	16 (42%)
% with at least one non-AIDS-related cause	33 (57%)	12 (44%)	28 (54%)	23 (56%)	24 (63%)
Analysis B: >1 year after HIV diagnosis					
Follow-up time in years, median (IQR)	8.2 (3.2–10.6)	7.7 (3.7–10.5)	5.5 (2.2–10.2)	7.7 (2.4–10.6)	7.0 (2.8–10.5)
Number of deaths during follow-up (%)	85 (3.6%)	15 (4.5%)	17 (4.0%)	19 (2.8%)	13 (3.1%)
Hospitalizations during follow-up ^a	359	80	109	130	94
% with at least one AIDS-related cause	29 (8%)	10 (13%)	29 (27%)	21 (16%)	10 (11%)
% with at least one non-AIDS-related cause	327 (91%)	63 (79%)	87 (80%)	122 (94%)	92 (98%)
Number of persons hospitalized before baseline (%)	439 (19%)	99 (30%)	115 (27%)	201 (30%)	118 (28%)
Number of persons hospitalized during FU (%)	253 (11%)	51 (15%)	69 (16%)	95 (14%)	65 (15%)
0 hospitalizations	2108 (89%)	280 (85%)	354 (84%)	572 (86%)	360 (85%)
1 hospitalization	186 (8%)	35 (11%)	45 (11%)	72 (11%)	46 (11%)
2–3 hospitalizations	61 (3%)	15 (4.5%)	21 (5%)	19 (3%)	16 (4%)
4–5 hospitalizations	4 (0.2%)	0 (0%)	3 (0.7%)	4 (0.6%)	3 (0.7%)
>5 hospitalizations	2 (0.1%)	1 (0.3%)	0 (0%)	0 (0%)	0 (0%)

FU, follow-up; MSM, men who have sex with men; MSW, men who have sex with women.

^aUp to three causes could be recorded for a single hospitalization.

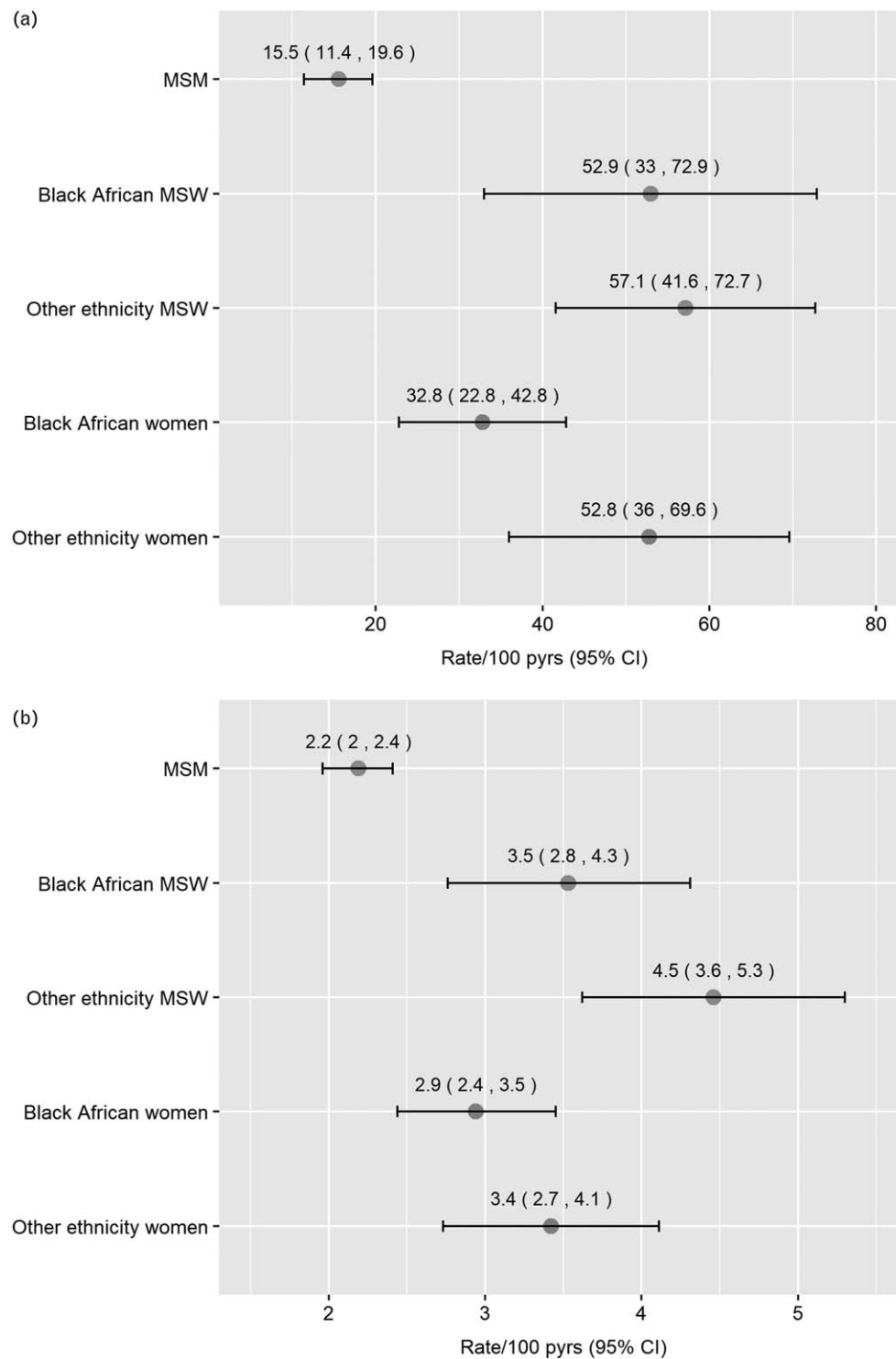


Fig. 1. Crude rates of hospitalization and 95% confidence intervals according to demographic group in Analysis A (first year after HIV diagnosis; a) and Analysis B (>1 year after HIV diagnosis; b). CI, confidence interval; MSW, men who have sex with women. Pyrs, person-years.

date of diagnosis and hospitalization, with some evidence of an increased hazard of hospitalization in individuals diagnosed between 2010 and 2012 compared with earlier and later years. Lower CD4⁺ cell count at diagnosis was strongly associated with higher

hazard of hospitalization; this was apparent for CD4⁺ cell count categories less than 200cells/ μ l.

In a model additionally adjusted for CD4⁺ cell count at diagnosis, hazard ratios (95% CI) were 1.4 (0.8–2.3); 2.0

Table 3. Associations of demographic group and covariates with hazard of hospitalization in Analysis A (first year after HIV diagnosis).

	Events	PY	Rate/100PY	Unadjusted		Adjusted ^a	
				HR (95% CI)	P	HR (95% CI)	P
Demographic group							
MSM	55	354	15.5	1.0	<0.0001	1.0	<0.0001
Black African MSW	27	51	52.9	2.96 (1.87–4.70)		2.69 (1.69–4.28)	
Other ethnicity MSW	52	91	57.1	3.21 (2.20–4.69)		2.98 (2.03–4.37)	
Black African women	41	125	32.8	1.94 (1.29–2.90)		1.95 (1.30–2.93)	
Other ethnicity women	38	72	52.8	2.99 (1.98–4.53)		2.96 (1.95–4.48)	
Age at diagnosis (years)							
<35	49	260	18.8	1.0	<0.0001	1.0	<0.0001
36–50	101	318	31.8	1.68 (1.19–2.36)		1.61 (1.14–2.28)	
51–65	53	104	51.0	2.52 (1.71–3.71)		2.32 (1.57–3.45)	
>65	10	12	83.3	3.68 (1.86–7.26)		3.46 (1.74–6.89)	
Date of diagnosis							
2013–2018	79	286	27.6	1.0	0.0873	1.0	0.0698
2010–2012	75	190	39.5	1.37 (0.97–1.93)		1.47 (1.04–2.08)	
2007–2009	59	217	27.2	1.00 (0.71–1.40)		1.12 (0.79–1.58)	
CD4 ⁺ cell count at diagnosis (cells/ μ l)							
>800	5	52	9.6	1.0	<0.0001	1.0	<0.0001
500–800	11	171	6.4	0.64 (0.22–1.83)		0.58 (0.20–1.68)	
350–499	15	136	11.0	1.09 (0.39–2.99)		0.98 (0.35–2.71)	
200–349	25	158	15.8	1.55 (0.59–4.06)		1.31 (0.50–3.45)	
50–199	75	96	78.1	6.39 (2.58–15.80)		5.04 (2.01–12.67)	
<50	76	47	161.7	10.46 (4.23–25.89)		7.57 (3.01–19.04)	

CI, confidence interval; HR, hazard ratio; MSM, men who have sex with men; MSW, men who have sex with women; PY, person-years of observation.

^aAdjusted for demographic group, age at diagnosis and date of diagnosis.

(1.3–2.9); 1.3 (0.8–1.9); 2.1 (1.3–3.2); for Black African MSW, other ethnicity MSW, Black African women and other ethnicity women, respectively. This suggests that late diagnosis explains a significant part of the differences across key demographic groups in hospitalization in the first year, but it does not appear to fully explain the elevated risk for other ethnicity MSW and other ethnicity women in particular.

Analysis B: more than 1 year after HIV diagnosis

A total of 4207 individuals were included in Analysis B (Table 1). Most individuals entered follow-up in 2007–2009. MSM had a higher median baseline and nadir CD4⁺ cell count than women and MSW. Overall, about two-thirds of participants were virally suppressed and 75% were on ART at baseline, with the highest percentage observed for Black African MSW. Overall, 26% of participants had a prior AIDS diagnosis; this proportion was lowest in MSM and highest in Black African individuals. Black African and other ethnicity MSW were about twice as likely to have a prior non-AIDS diagnosis compared to MSM and women. CD4⁺ cell count at diagnosis was available for 2847 (68%) individuals.

Median follow-up was 7.6 years. There were 149 deaths (3.5%) during follow-up (Table 2). Overall, 533 of 4207 people (13%) were hospitalized at least once and 772 hospitalizations occurred overall. The large majority of hospitalizations in all groups were non-AIDS-related. Despite this, other ethnicity MSW had a considerably higher proportion of AIDS-related hospitalizations than other demographic groups. Of those individuals who

were hospitalized, 72% had one hospitalization, 25% had two or three hospitalizations, 2.6% were hospitalized four or five times and less than 1% more than five.

The overall crude rate of hospitalization for this period was 2.7 per 100 person-years, considerably lower than the overall rate of 30.7 during the first year after diagnosis. This rate was highest in other ethnicity MSW, followed by Black African MSW, other ethnicity women, Black African women and MSM (Fig. 1b).

Overall, the association of demographic group with hospitalization was weaker than that seen in the first year after diagnosis (Table 4). Compared with MSM, the unadjusted rate of hospitalization in each of the other groups was 1.4-to-twofold higher. This association was not attenuated after adjustment for current age, calendar year and years since diagnosis.

Being over 65 years of age and earlier calendar year were strongly associated with a higher rate of hospitalization in the period from 1 year post diagnosis. CD4⁺ cell count at diagnosis was also associated with hospitalization in this period; this was driven by the higher rate among those with missing CD4⁺ cell count.

In the secondary analysis, after additionally adjusting for CD4⁺ cell count at diagnosis, incidence rate ratios (IRRs) (95% CI) were 1.6 (1.1–2.3); 2.0 (1.5–2.7); 1.5 (1.1–1.9); 1.6 (1.2–2.2) for Black African MSW, other ethnicity MSW, Black African women and other ethnicity women, respectively. This suggests that the

Table 4. Associations of demographic group and covariates with incidence rate of hospitalization in Analysis B (>1 year after HIV diagnosis).

	Events	PY	Rate/100 PY	Unadjusted		Adjusted ^a	
				IRR (95% CI)	<i>P</i>	IRR (95% CI)	<i>P</i>
Demographic group							
MSM	359	16 410	2.19	1.0	<0.0001	1.0	<0.0001
Black African MSW	80	2265	3.53	1.62 (1.15–2.27)		1.68 (1.19–2.38)	
Other ethnicity MSW	109	2445	4.46	2.04 (1.52–2.74)		2.06 (1.53–2.78)	
Black African women	130	4418	2.94	1.35 (1.04–1.75)		1.46 (1.13–1.88)	
Other ethnicity women	94	2751	3.42	1.58 (1.16–2.15)		1.66 (1.23–2.25)	
Current age							
≤35	88	3181	2.77	1.0	0.0065	1.0	0.0026
36–50	404	16 162	2.50	0.90 (0.69–1.17)		0.93 (0.70–1.24)	
51–65	218	7892	2.76	0.98 (0.74–1.31)		1.11 (0.79–1.56)	
>65	62	1054	5.88	2.08 (1.41–3.06)		2.37 (1.56–3.60)	
Current calendar year							
2017–2018	23	2274	1.01	1.0	<0.0001	1.0	<0.0001
2015–2016	160	5925	2.70	2.79 (1.71–4.54)		2.90 (1.78–4.72)	
2013–2014	105	5695	1.84	1.90 (1.15–3.12)		2.07 (1.25–3.43)	
2011–2012	152	5355	2.84	2.91 (1.78–4.77)		3.33 (2.01–5.51)	
2009–2010	161	4911	3.28	3.39 (2.07–5.55)		4.02 (2.42–6.68)	
2007–2008	171	4106	4.16	4.32 (2.66–7.02)		5.26 (3.18, 8.71)	
Current years since diagnosis							
>1–5	150	4849	3.09	1.0	0.5265	1.0	0.2908
>5–10	199	7753	2.57	0.83 (0.64–1.08)		0.88 (0.67–1.15)	
>10–20	317	12 004	2.64	0.85 (0.66–1.08)		1.01 (0.77–1.32)	
>20	106	3684	2.88	0.92 (0.67–1.27)		1.24 (0.86–1.79)	
CD4⁺ cell count at diagnosis (cells/μl)							
>800	33	1290	2.56	1.0	<0.0001	1.0	<0.0001
500–800	70	4332	1.62	0.63 (0.37–1.08)		0.61 (0.35–1.05)	
350–499	88	3778	2.33	0.91 (0.54–1.54)		0.85 (0.51–1.44)	
200–349	90	4441	2.03	0.79 (0.48–1.32)		0.72 (0.43–1.20)	
50–199	96	3886	2.47	0.97 (0.58–1.63)		0.75 (0.44–1.27)	
<50	76	2527	3.01	1.18 (0.71–1.98)		0.92 (0.54–1.57)	
Missing	319	8035	3.97	1.57 (0.99–2.49)		1.47 (0.92–2.35)	

CI, confidence interval; IRR, incidence rate ratio; MSM, men who have sex with men; MSW, men who have sex with women; PY, person-years of observation.

^aAdjusted for demographic group, current age, current calendar year, current years since diagnosis.

elevated risk of hospitalization in the period from 1 year post diagnosis that was apparent for MSW and women groups compared with MSM could not be explained by differences in CD4⁺ cell count at diagnosis.

Alternatively adjusting for CD4⁺ cell count at baseline, alongside age, calendar year and time since diagnosis, further attenuated the association with demographic group but the rate remained elevated in other ethnicity MSW and women [IRRs (95% CI): 1.3 (0.9–1.8); 1.8 (1.3–2.4); 1.1 (0.8–1.5); 1.5 (1.1–2.1) for Black African MSW, other ethnicity MSW, Black African women and other ethnicity women, respectively].

Discussion

To our knowledge, this is the first study to investigate the association between demographic group and all-cause hospitalization in PLHIV in the recent ART era in the UK. Black African and other ethnicity MSW and women were at a higher risk of hospitalization than MSM during the first year after diagnosis and, to a lesser extent, in the subsequent stages of the infection. In these four

demographic groups, the rate of hospitalization was about 10/15-fold higher during the first year after diagnosis than the subsequent period, while in MSM it was about seven-fold higher, than the subsequent period.

Overall, our results provide evidence of substantial variation across key demographic groups in hospitalization risk among PLHIV in a setting with universal free access to healthcare. This highlights the need for differentiated care and targeted interventions to close gaps between key groups in terms of long-term health outcomes. There was a higher proportion of AIDS-related admissions during the first year after diagnosis that was particularly high in MSW. Hospitalizations more than 1 year after diagnosis were predominantly caused by non-AIDS conditions; however, MSW still had a higher proportion of AIDS-related admissions than other groups, corroborated by a lower median CD4⁺ cell count in this group.

There are several possible reasons for the observed differences between the groups. The higher rates of hospitalization in MSW and women compared with MSM and the increased number of AIDS-related admissions during the first year after HIV diagnosis in

these groups may be partially explained by a higher proportion of individuals that are diagnosed late. In the UK, late diagnosis is more common among heterosexual individuals than MSM, and among individuals with Black African ethnicity compared with white [20]. In our analysis, adjustment for CD4⁺ cell count at diagnosis explained an important part of the differences between the groups in hospitalization during the first year after diagnosis, showing that late diagnosis was a major factor in the variation in early admissions. CD4⁺ cell count at diagnosis did not explain the ongoing but smaller variation in hospitalization risk between demographic groups in the subsequent period. This suggests that factors additional to late diagnosis play a role in demographic variation in admissions.

Another reason for differences in hospitalization risk between sex and ethnicity groups could be differences in socioeconomic disadvantage and poverty; these factors may be linked to increased risk of several non-AIDS related conditions. In the UK, there is universal free access to healthcare (including HIV diagnosis, antiretroviral therapy, hospital consultations), which might be expected to reduce socioeconomic inequalities that could lead to differences in risk of hospitalization. Nevertheless, socioeconomic status was shown by previous studies in settings with universal healthcare to be an important factor in determining virological outcomes [21] and hospitalization risk [4]. Structural barriers to care such as stigma and lower engagement and retention in care in MSW and women [22] could also be a possible explanation, if health problems are less likely to be addressed before they necessitate hospital admission. Low engagement in care and health service utilization might be particularly relevant for the higher risk of hospitalization in MSW as there is evidence that HIV-positive heterosexual men may face particularly challenging barriers when seeking help and accessing services [23–25].

Some of the differences in hospitalization between men and women might be explained by differences in the prevalence of behavioural factors such as smoking or alcohol consumption, which are risk factors for a number of health conditions. Biological differences, for example related to reproduction or the hormonal system, that predispose women or men to some conditions may also play a role. However, this is not likely to be a major reason for the differences observed in this population, which were particularly marked between MSM and MSW.

The demographics of the HIV-positive population and the key groups affected differ across high-income settings. In the UK, the population of PLHIV includes a high proportion of women and MSW that migrated from sub-Saharan Africa. There is evidence from both Europe and North America that MSM have more favourable ART outcomes (being more likely to achieve viral suppression

and have higher CD4⁺ cell counts, and less likely to experience nonadherence and viral rebound) compared with women and heterosexual men, and that people of white ethnicity have more favourable treatment outcomes than people of Black and other minority ethnicity [21,26–32]. Several US studies and one Canadian study also found evidence that HIV-positive women [4–7,9,33] and Black, Hispanic and other minority individuals [6–10,34,35] are at a higher risk of hospitalization than men and people of white ethnicity respectively. However, these findings were not consistent across all studies. Other US studies [11–15], one French study [16] and one that combined data from France and Brazil [17] did not find a statistically significant association between gender and hospitalization. Several other US studies did not find an association between ethnicity and hospitalization in PLHIV [11,14,15]. However, in our analysis, we found hospitalization risk to be higher in MSW than in women, and higher in ‘other ethnicity’ MSW and women than Black African MSW and women.

It should be noted that among those newly diagnosed in Analysis A, MSM were less likely to be on ART within 3 months after diagnosis and also had a higher median CD4⁺ cell count at diagnosis. The British HIV Association’s (BHIVA) guidelines recommended ART initiation for individuals with CD4⁺ cell counts of 350 cells/ μ l or less until they were revised in 2015 to recommend ART initiation regardless of CD4⁺ cell count [36]. Despite this later ART initiation, MSM still had a lower hospitalization rate than the other demographic groups likely in part due to the higher CD4⁺ cell count in this group.

Unlike previous studies, we used a classification that combined sex, sexual orientation and ethnicity, which enabled us to directly compare risk across key demographic groups. We found strong evidence that MSW have a considerably higher risk of hospitalization than MSM. Three US studies investigated differences in hospitalization between MSM and individuals who acquired HIV via heterosexual contact (both men and women) [6,7,13]; one found a significantly lower rate in MSM after adjustment for other factors (including age; sex; ethnicity; CD4⁺ cell count; viral load; hepatitis serostatus; ART use; insurance; calendar year) [7].

There are some limitations to this study. We used a binary categorization of sex, as it was recorded clinically. We used the PHE categorization of the main affected demographic groups, in which three key groups – MSM, Black African MSW and Black African women are defined, which make up the majority of individuals living with HIV. However, the remaining two ‘other ethnicity’ categories of MSW and women are heterogeneous groups; we did not have sufficient power to compare all the different ethnicity categories within these. When we separated these two ‘other ethnicity’ groups into

'white' and 'other nonwhite' ethnicity, we found hospitalization risk tended to be lower for the former group, albeit still elevated compared with MSM (Supplementary Figure 1, <http://links.lww.com/QAD/B899>). Another limitation is that we were only able to consider hospitalizations that occurred at the Royal Free hospital, which results in some underestimation of the true rates. In an internal validation of a subset of study participants using more complete hospitalization data that identified hospitalizations at other hospitals, we found that about 80% of all hospitalizations identified occurred at the Royal Free, and that MSM were somewhat more likely to be admitted to hospitals other than the Royal Free compared with 'non-MSM' individuals. If the estimated ascertainment bias found in that substudy applied equally to the 'non-MSM' groups in our whole study population, the incidence rate ratios comparing MSM and women to MSM would be 13% lower (in relative terms) than we estimated. Even after accounting for this potential bias, there would still be substantial differences in the rate of hospitalization between demographic groups in Analysis B. We do not think such biases would operate to the same extent in Analysis A as individuals were more likely to be hospitalized for AIDS-related causes during that period, for which they are more likely to be hospitalized at the Royal Free Hospital, where they also receive HIV outpatient care. In addition, differences between demographic groups were much larger in analysis A, and the effect of any differential bias is likely to be very small. We could only consider the cause of hospitalization in the broad categories of AIDS and non-AIDS related. Furthermore, results are based on a single clinic; however, we believe the groups defined to be broadly representative of those in the UK as a whole. We did not have data on socioeconomic factors, and so were unable to assess the extent to which these may account for the differences in hospitalization risk between demographic groups.

In summary, among PLHIV in the UK in the modern ART era, Black African and other ethnicity MSM and women have considerably higher rates of hospitalization than MSM. Although this variation is most marked during the first year after diagnosis, it persists in the subsequent period. Among those hospitalized, MSM are more likely to be admitted for AIDS-related causes than MSM and women, both in the early and subsequent periods after diagnosis. Further research is needed on reasons for these variations in clinical outcomes including investigations into causal relationships to establish whether targeted interventions are needed.

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All authors contributed to the study concept. S.R. analysed the data and wrote the draft manuscript. C.S. and FL supervised the data analysis and interpretation of the data. All authors contributed to subsequent drafts and approved the final article for submission.

Conflicts of interest

No conflicts of interest declared by authors. S.R. receives a Royal Free Charity scholarship to fund PhD research.

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