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Research Paper

Prospective association of social circumstance, socioeconomic, lifestyle and mental health factors with subsequent hospitalisation over 6–7 year follow up in people living with HIV

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ABSTRACT

Background: Predictors of hospitalisation in people with HIV (PLHIV) in the contemporary treatment era are not well understood.
Methods: This ASTRA sub-study used clinic data linkage and record review to determine occurrence of hospitalisations among 798 PLHIV from baseline questionnaire (February to December 2011) until 1 June 2018. Associations of baseline social circumstance, socioeconomic, lifestyle, mental health, demographic and clinical factors with repeated all-cause hospitalisation from longitudinal data were investigated using Prentice-Williams-Peterson models. Associations were also assessed in 461 individuals on antiretroviral therapy (ART) with viral load $\leq$50 copies/ml and CD4 count $\geq$500 cells/ μl.
Findings: Rate of hospitalisation was 5.8/100 person-years (95% CI: 5.1–6.5). Adjusted for age, demographic group and time with diagnosed HIV, the following social circumstance, socioeconomic, lifestyle and mental health factors predicted hospitalisation: no stable partner (adjusted hazard ratio (aHR)=1.59; 95% CI=1.16–2.20 vs living with partner); having children (aHR=1.50; 1.08–2.10); non-employment (aHR=1.56; 1.07–2.27 for unemployment; aHR=2.39; 1.70–3.37 for sick/disabled vs employed); rented housing (aHR=1.72; 1.26–2.37 vs homeowner); not enough money for basic needs (aHR=1.82; 1.19–2.78 vs enough); current smoking (aHR=1.39; 1.02–1.91 vs never); recent injection-drug use (aHR=2.11; 1.30–3.43); anxiety symptoms (aHRs=1.39; 1.01–1.91, 2.06; 1.43–2.95 for mild and moderate vs none/minimal); depressive symptoms (aHRs=1.67; 1.17–2.38, 1.91; 1.30–2.78 for moderate and severe vs none/minimal); treated/untreated depression (aHRs=1.65; 1.03–2.64 for treated depression only, 1.87; 1.39–2.52 for depressive symptoms only; 1.53; 1.05–2.24; for treated depression and depressive symptoms, versus neither). Associations were broadly similar in those with controlled HIV and high CD4.
Interpretation: Social circumstance, socioeconomic disadvantage, adverse lifestyle factors and poorer mental health are strong predictors of hospitalisation in PLHIV, highlighting the need for targeted interventions and care.
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1. Introduction

Monitoring the risk and predictors of hospitalisations among people living with HIV (PLHIV) is important, as hospitalisation is a key indicator of serious morbidity and a significant contributor to healthcare costs [1,2].

The success of combination antiretroviral therapy (cART, a combination usually including three or more antiretroviral drugs from at least two drug classes) resulted in dramatic reductions in mortality and incidence of AIDS-defining illnesses among PLHIV from the mid-1990s [3]. Over time, non-AIDS related causes began to account for an increasing proportion of hospitalisations among PLHIV [4,5].

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Research in context

Evidence before this study

We conducted a comprehensive literature search on the Ovid MEDLINE database on 21 January 2019 and updated our search on 29 October 2020 to identify articles investigating predictors of hospitalisation in people living with HIV (PLHIV) in high income countries that included at least some data from 2008 onwards. 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) AND (predictor OR risk factor OR associated OR association OR socio-economic OR demographic OR gender OR immunologic* OR virologic* OR antiretroviral OR sexual orientation OR mental health OR lifestyle). We additionally searched the webpages of observational HIV cohorts for relevant publications. Of all studies identified, most did not include data beyond 2010 and were conducted in the US; the majority focused on demographic, clinical and HV-related factors rather than social, economic, mental health and lifestyle factors. We found no studies on predictors of hospitalisation from the UK in the contemporary cART era (post 2010) and only two from Europe (Italy), neither of which included socioeconomic or mental health factors.

Added value of this study

Our study is the most comprehensive analysis of predictors of hospitalisations in PLHIV in Europe in the contemporary cART era. It demonstrates that non-HIV related factors including social and economic circumstance, lifestyle factors and mental health, in addition to demographic and HIV-related factors, are strong predictors of subsequent all cause hospitalisation. Importantly, we found the association of socioeconomic disadvantage and poor mental health with subsequent hospitalisation to be at least as strong as that for smoking and alcohol dependency, and similarly strong specifically among people with virologically controlled HIV and high CD4 count.

Implications of all the available evidence

Our findings emphasize the need for support targeted to those with psychosocial and economic needs and highlight the importance of holistic care for PLHIV. Given the high costs of hospitalisation, targeted interventions could be cost-effective.

Previous longitudinal and cross-sectional studies in high-income settings in the cART era have found that demographic factors [6] (including older age [4,7-13], female gender [4,9,14], black or minority ethnicity [13,15]) and clinical HIV markers (including low CD4 count [4,7,9,11,13], high viral load [7,9,11,13,16], Hepatitis C or B coinfection [4,9,17] and ART non-adherence [16]) predict hospitalisation among PLHIV. Other studies found evidence that poor mental health was predictive of hospitalisation [8,12,14,18]; findings were less consistent for social [11,14], socioeconomic [10,12,14,19] and lifestyle factors [8,10,12,14,15,18,20]. Most studies of hospitalisation among PLHIV were conducted in the US, a setting without universal access to healthcare, and few included data beyond 2010 [4,9,14,16-18,20]. There has been little research on the predictors of hospitalisation among PLHIV in the last decade - the era of contemporary cART - particularly on the role of non-HIV related factors including social and economic circumstance and mental health.

This study includes a cohort of PLHIV recruited from a large London centre in the Antiretrovirals, Sexual Transmission Risk and Attitudes (ASTRA) questionnaire study in 2011 who consented to clinical data linkage. We assess the prospective associations of questionnaire-assessed social circumstance, socioeconomic, mental health and lifestyle factors at baseline with the subsequent rate of hospitalisation between 2011 and 2018. We also investigate these associations specifically among individuals with virologically controlled HIV and high CD4 count. To our knowledge, this is the first UK study to comprehensively assess predictors of hospitalisation among PLHIV in the current cART era.

2. Methods

The ASTRA study recruited people living with diagnosed HIV from eight HIV outpatient clinics in England from February 2011 to December 2012 [21]. All participants self-completed a confidential questionnaire that included sections on demographic, social circumstance, socioeconomic, mental health and lifestyle factors as well as clinical and HIV-related factors and sexual behaviour. The most recent viral load and CD4 count at baseline for each participant was documented from clinic records. Participants were additionally asked whether they consented to linkage of questionnaire data with routine clinic data. Ethical approval for the ASTRA study was obtained via the North West London research ethics committee (reference 10/H0720/70).

A total of 1336 patients at the Royal Free Hospital were invited to participate in ASTRA, 899 completed questionnaires (67%); of those 809 (90% of respondents) consented to linkage and 798 had sufficient follow-up information to be included in the present study. The study collected information on all hospitalisations occurring among the 798 individuals that were documented in their Royal Free Hospital medical records, covering the period from their date of questionnaire completion (February to December 2011; baseline) until 1 June 2018. Information on admissions to the Royal Free Hospital was obtained from electronic records of admissions and discharges routinely recorded in the hospital database. Information on admissions to hospitals other than the Royal Free was obtained through a comprehensive and detailed review of electronic and paper patient case notes, carried out for all 798 participants. The information collected included dates of admission and discharge, the admitting hospital, whether the admission was classified as an emergency and the causes of hospitalisation. The causes were classified by an HIV clinician using ICD-10 codes; up to five causes could be documented for every admission. Hospitalisations were defined as overnight stays at the hospital; day cases were not included.

Individuals were followed from the date of questionnaire completion (baseline) until June 2018, or their death or last clinic interaction if this occurred before June 2018. If an individual had a date of death recorded more than one year after their last clinic visit, this last visit was defined as the end of follow-up to reduce the risk of bias.

The main exposure variables of interest were:

Social circumstance factors: stable partner (living with partner; not living with partner; no stable partner); having children (yes; no); disclosure of HIV status to at least one person who is not a healthcare worker (yes; no); social support (1 (high) to 5 (low) based on modified version of Duke–UNC Functional Social Support Questionnaire) [22].

Socioeconomic factors: employment (employed; unemployed; sick/disabled; retired; other); housing (homeowner; renting (council, housing association or private); temporary/unstable/other); highest level of education (university or above; below university; none); financial hardship ("Do you have enough money to cover your basic needs?" Always; mostly; sometimes; no).

Lifestyle factors: smoking (never; ex; current); recreational drug use in past 3 months (injection drug use; non-injection use of

chemsex-associated drugs (methamphetamine; GHB/GBL; mephedrone); other non-injection drug use; no drug use); current alcohol consumption(first two questions of AUDIT-C score 0; 1–2; 3–4; 5–6; 7–8)[38]; evidence of alcohol dependency (CAGE 4-item questionnaire score 0; 1; 2; 3; 4) [23].

Mental health factors: depressive symptoms on PHQ-9 (none/minimal (total score 0–4); mild (5–9); moderate (10–14); severe (15–27)) [24]; depressive symptoms/current treatment ('medicine or other therapy') for depression (PHQ-9 <10 no treatment; PHQ-9 <10 on treatment; PHQ-9 ≥ 10 no treatment; PHQ-9 ≥ 10 on treatment); anxiety symptoms on GAD-7 (none/minimal (total score 0–4); mild (5–9); moderate (10–14); severe (15–21)) [25].

Additional factors of interest were demographic, HIV-related, and clinical factors: age (≤35; 36–50; 51–60; >60 years), 'demographic group' (men who have sex with men (MSM); Black African heterosexual men; heterosexual men of other ethnicity; Black African women; women of other ethnicity, using Public Health England classification of the key demographic groups of PLHIV) [26], baseline CD4 count (in cells/μl; >800; 500–800; 350–499; 200–349; ≤199); nadir CD4 count (in cells/μl; >349; 200–349; 50–199; <50); baseline viral load (≤50 copies/ml; >50 copies/ml); years since HIV diagnosis (<5; 5-<10; 10-<20; ≥20); ART status (on ART; stopped ART; never taken ART); ART non-adherence defined as having missed ≥2 days of ART at a time in the past 3 months (never/don't know; once; 2–3 times; >3 times); previous Hepatitis C diagnosis. Baseline values were used for all variables. CD4 count and VL were obtained from clinical records; other factors were obtained from the questionnaire.

3. Statistical analysis

We calculated rates of hospitalisation overall and by exposure categories as the number of hospitalisations divided by person-time at risk, including repeated hospitalisation from the same individual. We assessed the univariable and multivariable associations between each baseline factor and subsequent time to hospitalisation using Prentice-Williams-Peterson gap time models (PWP-GT) to calculate hazard ratios (HR) of repeated all-cause hospitalisation. PWP models are an extension of Cox regression models that allow for the analysis of multiple events by stratification, based on the prior number of events [27]. For every subsequent event, the population at risk includes only those with a previous event. Modelling the gap-time (the time between discharge from one hospitalisation to admission for the next, or censoring) ensures that the time during which the individual is still in hospital and therefore cannot be at risk does not contribute to the time to the next event/censoring. We used robust sandwich covariance matrix estimators to account for within-subject correlation for repeated hospitalisation. For these models, the data were truncated after the 4th hospitalisation to avoid unstable estimates due to small risk sets in later strata. In the multivariable analysis, each factor was considered separately, adjusted for the following core factors: demographic group, age group and time since HIV diagnosis, as defined above and shown in Table 1. These core factors were chosen as potential confounders not judged to be on the causal pathway between the exposures of interest and hospitalisation.

We also assessed associations among the subset of individuals who were on ART, with viral load ≤50 cells/ml and CD4 count ≥500 cells/μl at baseline and performed tests for interaction to investigate whether associations differed in this subset.

We conducted complete case analyses as the number of missing values for each variable was low (see Table 1).

We used SAS (version 9.4) for all statistical analyses and the ggplot2 package in R (R version 3.6.3) to create figures.

4. Role of the funding source

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

Table 1
Characteristics at baseline (questionnaire completion) of all people living with HIV (PLHIV) and those with controlled HIV and high CD4 count.

	All PLHIV	PLHIV with controlled HIV and high CD4 count[a]
N	798 (100%)	461 (100%)
Age (years)		
Median (IQR)	46 (40–51)	46 (40–52)
<=35	94 (12%)	47 (10%)
36–50	471 (59%)	277 (61%)
51–65	214 (27%)	113 (25%)
>65	19 (2.4%)	24 (5.2%)
Demographic group		
MSM	592 (74%)	349 (76%)
Black African heterosexual men	29 (3.6%)	15 (3.3%)
Other ethnicity heterosexual men	47 (5.9%)	20 (4.3%)
Black African women	65 (8.2%)	40 (8.7%)
Other ethnicity women	65 (8.2%)	37 (8.0%)
CD4 count in cells//μl		
Median (IQR)	621 (441–820)	731 (610–923)
>800	215 (27%)	188 (41%)
500–800	328 (41%)	273 (59%)
350–499	157 (20%)	–
200–349	67 (8.4%)	–
<=199	31 (3.9%)	–
CD4 count nadir in cells/μl		
Median (IQR)	189 (78–277)	200 (100–278)
>349	112 (14%)	56 (12%)
200–349	267 (33%)	176 (38%)
50–199	275 (34%)	164 (36%)
<50	144 (18%)	65 (14%)
Viral load ≤50 copies/ml	653 (82%)	461 (100%)
Years since HIV diagnosis		
Median (IQR)	11 (6–17)	12 (7–18)
<5	163 (20%)	57 (12%)

(*continued*)

Table 1 (*Continued*)

	All PLHIV	PLHIV with controlled HIV and high CD4 count[a]
5 – 10	201 (25%)	132 (29%)
10 - 20	325 (41%)	209 (45%)
≥20	109 (14%)	63 (14%)
ART status		
On ART	719 (92%)	461 (100%)
Stopped ART	14 (1.8%)	–
Never ART	50 (6.4%)	–
	Missing=15	
Time since started ART for those on ART		
Median in years (IQR)	8 (4–14)	8 (5–14)
<6 months	39 (5.5%)	7 (1.6%)
6 mth - 2 years	71 (10%)	37 (8.2%)
2 - 10 years	306 (43%)	215 (48%)
10 - 15 years	184 (26%)	123 (27%)
>=15 years	115 (16%)	68 (15%)
	Missing=83	Missing=11
ART non-adherence for those on ART – missed >= 2 days ART at a time in the past 3 months		
No / don't know	580 (81%)	384 (83%)
Yes, once	51 (7.1%)	35 (7.6%)
Yes, 2–3 times	55 (7.7%)	32 (7.0%)
Yes, >3 times	31 (4.3%)	9 (2.0%)
	Missing=81	Missing=1
Prior AIDS diagnosis (clinical record)	271 (34%)	163 (35%)
Disclosed HIV status	754 (95%)	436 (95%)
	Missing=5	Missing=3
Ever had Hep C	133 (17%)	67 (15%)
Employment		
Employed	473 (60%)	279 (62%)
Unemployed	125 (16%)	76 (17%)
Sick / disabled	102 (13%)	55 (12%)
Retired	53 (6.8%)	29 (6.4%)
Other	31 (4.0%)	14 (3.1%)
	Missing=14	Missing=8
Housing status		
Homeowner	310 (39%)	195 (43%)
Renting	406 (52%)	234 (51%)
Temporary / unstable / other	72 (9.1%)	28 (6.1%)
	Missing=10	Missing=4
Highest level of education		
University or above	394 (50%)	238 (52%)
Below university	318 (40%)	187 (41%)
No qualifications	74 (9.4%)	29 (6.4%)
	Missing=12	Missing=7
Financial hardship: Money for basic needs?		
Always	391 (50%)	231 (51%)
Mostly	208 (26%)	117 (26%)
Sometimes	112 (14%)	62 (14%)
No	76 (10%)	45 (9.9%)
	Missing=11	Missing=6
Current stable partner		
Yes, and living with partner	329 (41%)	199 (43%)
Yes, but not living with partner	120 (15%)	74 (16%)
No	345 (43%)	185 (40%)
	Missing=4	Missing=3
Has Children	185 (23%)	94 (21%)
	Missing=3	Missing=3
Social support score		
1 (highest)	255 (32%)	150 (33%)
2	265 (33%)	155 (34%)
3	135 (17%)	85 (19%)
4	88 (11%)	45 (10%)
5 (low)	49 (6.2%)	21 (4.6%)
	Missing=6	Missing=5
Smoking status		
Never	281 (36%)	156 (34%)
Ex-smoker	255 (32%)	147 (32%)
Current smoker	254 (32%)	156 (34%)
	Missing=8	Missing=2
Recreational drug use in past 3 months		
No	434 (54%)	246 (53%)
Non-IDU, other	254 (32%)	152 (33%)
Non-IDU chemsex drugs	87 (11%)	51 (11%)
IDU	23 (2.9%)	12 (2.6%)
Alcohol dependency (CAGE score)		
0 (no)	528 (67%)	311 (68%)

(*continued*)

Table 1 (*Continued*)

	All PLHIV	PLHIV with controlled HIV and high CD4 count[a]
1	119 (15%)	72 (16%)
2	82 (10%)	41 (8.9%)
3	50 (6.3%)	27 (5.9%)
4 (strong dependency)	14 (1.8%)	9 (2.0%)
	Missing=5	Missing=1
Alcohol consumption (modified AUDIT score)		
0 (none)	141 (18%)	81 (18%)
1–2 (low)	200 (26%)	121 (27%)
3–4	227 (29%)	135 (30%)
5–6	178 (23%)	96 (21%)
7–8 (high)	33 (4.2%)	17 (3.8%)
	Missing=19	Missing=11
Symptoms of anxiety (GAD-7 score)		
0–4 (no anxiety)	459 (58%)	261 (57%)
5–9	177 (22%)	108 (23%)
10–14	82 (10%)	41 (8.9%)
15–21 (severe anxiety)	80 (10%)	51 (11%)
Depressive symptoms (PHQ-9 score)		
0–4 (none/minimal)	427 (54%)	253 (55%)
5–9 (mild)	163 (20%)	95 (21%)
10–14 (moderate)	105 (13%)	55 (12%)
>=15 (severe)	103 (13%)	58 (13%)
PHQ-9 depression and receiving treatment for depression		
PHQ-9 <10, no treatment	526 (66%)	304 (66%)
PHQ-9 <10, on treatment	64 (8.0%)	44 (9.5%)
PHQ-9 ≥ 10, no treatment	115 (14%)	62 (13%)
PHQ-9 ≥ 10, on treatment	93 (12%)	51 (11%)

MSM=men who have sex with men; ART=antiretroviral therapy.
[a] on antiretroviral therapy with viral load ≤50 copies/ml and CD$ count ≥500 cells/μl.

5. Results

Of 798 included individuals, 592 (74%), 76 (9.5%) and 130 (16%) were MSM, heterosexual men and women respectively; median age (IQR) was 46 (40–51) years (Table 1). Median follow-up time was 6 years; there were 274 hospitalisations and 17 deaths over 4710 person-years of observation, with 153 people (19%) being hospitalised at least once. In total, 202 (74%) hospitalisations were emergencies (Table 2). The overall rate of hospitalisation was 5.8/100 person-years (95% CI: 5.1–6.5). The rate of re-admission among those previously hospitalised was 64.2/100 person-years (52.7–75.7). The median time between discharge and re-admission in those with repeated hospitalisation was 237 days (IQR 54–583). Seventeen (18%) readmissions were within 30 days of discharge.

The most common ICD-10 classified causes of hospitalisation were diseases of the circulatory (46; 16.8%), digestive (36; 13.1%) and respiratory systems (32; 11.7%), infectious and parasitic diseases (30; 11.0%), injury, poisoning and other consequences of external causes (29; 10.6%), genitourinary diseases (27; 9.9%) and neoplasms (25; 9.1%).

Rates of hospitalisation according to the exposures of interest are shown in Fig. 1, unadjusted and adjusted hazard ratio are given in Table 3.

5.1. Social circumstance

Rates of hospitalisation were higher among individuals with children, those without, or not living with, a stable partner, and those who had not disclosed their HIV status (Fig. 1). Hospitalisation rates increased with lower levels of social support. In the PWP unadjusted analysis (Table 3), having children and having no stable partner were significant predictors of hospitalisation, with evidence of a trend for lower social support. There was no association with disclosure. Patterns of association were similar after adjustment.

5.2. Socioeconomic factors

Individuals with lower socioeconomic status, including non-employment, rented or unstable housing and financial hardship, as well as those without educational qualifications, had higher rates of hospitalisation. In the PWP unadjusted analysis, non-employment, rented housing and greater financial hardship strongly predicted hospitalisation, whereas education did not. Associations were similar after adjustment, except that the elevated risk associated with being retired was attenuated due to adjustment for age.

Table 2
Hospitalisations and mortality during follow-up: All study participants during follow-up of all study participants and those with controlled HIV and high CD4 count.

	All PLHIV (*N* = 798)	PLHIV with controlled HIV and high CD4 count (*N* = 461)[a]
Median follow-up time in years (IQR)	6.4 (6.0–6.6)	6.4 (6.1–6.7)
Number of deaths during follow-up	17 (2.1%)	9 (1.95%)
Hospitalisations during follow-up	274 (100%)	100 (100%)
Emergency hospitalisations	202 (74%)	60 (60%)
Number of hospitalisations during follow-up		
0 hospitalisations	645 (81%)	385 (84%)
1 hospitalisation	97 (12%)	59 (13%)
2 hospitalisations	31 (3.9%)	12 (2.6%)
3 hospitalisations	6 (0.8%)	3 (0.7%)
4 hospitalisations	8 (1.0%)	2 (0.4%)
5 hospitalisations	7 (0.9%)	0 (0%)
>5 hospitalisations	4 (0.5%)	0 (0%)

PLHIV=people living with HIV; IQR=interquartile range.
[a] on antiretroviral therapy with viral load ≤50 copies/ml and CD$ count ≥500 cells/μl

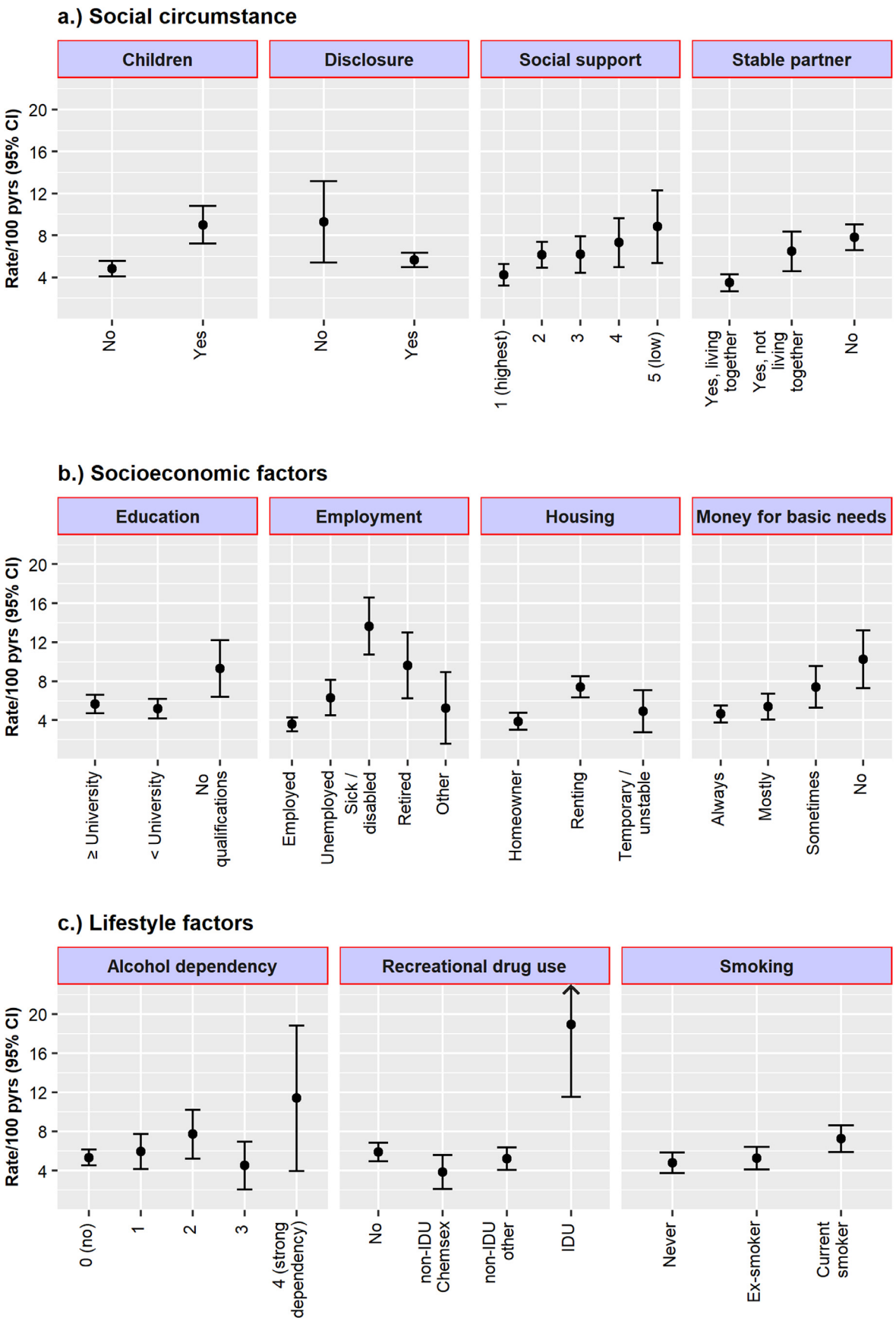

Fig. 1. Crude rates of hospitalisation and 95% confidence intervals (CI) according to a.) social circumstance, b.) socioeconomic, c.) lifestyle and d.) mental health factors. Pyrs=person-years.

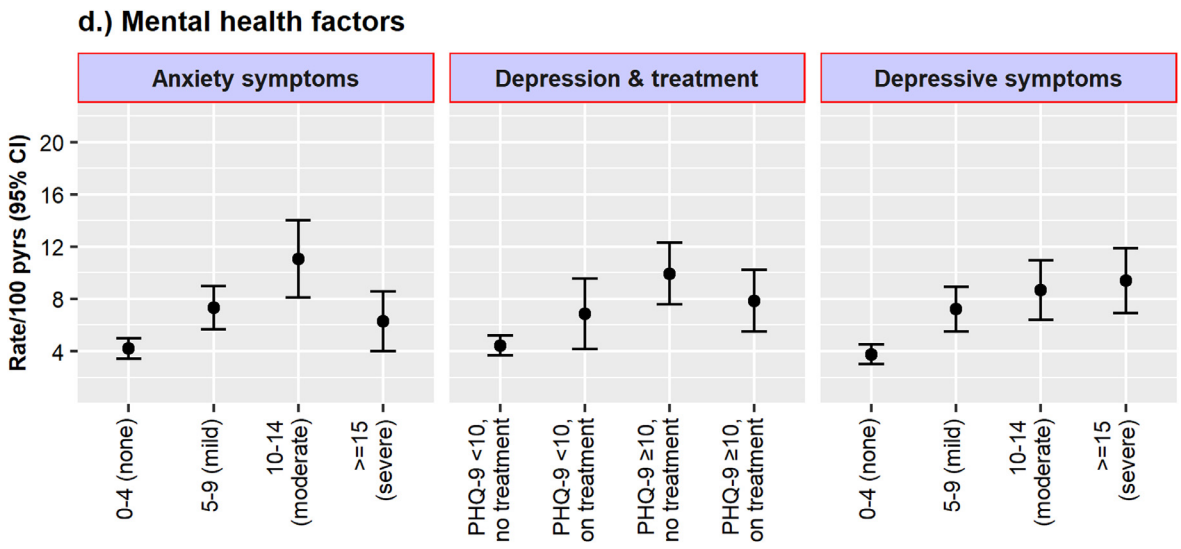

Fig. 1 Continued.

Table 3
Unadjusted and adjusted hazard ratios of hospitalisation according to social circumstance, socioeconomic, lifestyle and mental health factors.

	Unadjusted HR (95% CI)	p-value; test for trend	Demographic adjusted HR (95% CI)*	p-value; test for trend
Social circumstance factors				
Current stable partner		0.04		0.02
Yes, and living with partner	1.0		1.0	
Yes, but not living with partner	1.39 (0.92, 2.11)		1.43 (0.94, 2.17)	
No	1.55 (1.10, 2.18)		1.59 (1.16, 2.20)	
Has children		0.004		0.02
No	1.0		1.0	
Yes	1.51 (1.14, 1.99)		1.50 (1.08, 2.10)	
Social support score		0.35;		0.41;
1 (highest)	1.0	0.09 (t)**	1.0	0.11 (t)**
2	1.20 (0.87, 1.66)		1.19 (0.86, 1.66)	
3	1.04 (0.70, 1.56)		1.03 (0.68, 1.55)	
4	1.36 (0.93, 1.99)		1.36 (0.92, 2.01)	
5 (low)	1.56 (0.96, 2.53)		1.51 (0.92, 2.46)	
Disclosure of HIV status		0.19		0.28
Yes	1.0		1.0	
No	1.27 (0.89, 1.80)		1.22 (0.85, 1.76)	
Socioeconomic factors				
Employment		<0.0001		<0.0001
Employed	1.0		1.0	
Unemployed	1.65 (1.15, 2.36)		1.56 (1.07, 2.27)	
Sick / disabled	2.48 (1.78, 3.47)		2.39 (1.70, 3.37)	
Retired	1.98 (1.32, 2.98)		1.33 (0.79, 2.22)	
Other	1.38 (0.73, 2.61)		1.43 (0.71, 2.85)	
Housing status		0.02		0.003
Homeowner	1.0		1.0	
Renting	1.60 (1.16, 2.20)		1.72 (1.26, 2.37)	
Temporary / unstable / other	1.35 (0.83, 2.19)		1.46 (0.88, 2.43)	
Highest level of education		0.11;		0.35;
University or above	1.0	0.30 (t)**	1.0	0.48 (t)**
Below university	0.95 (0.73, 1.24)		0.95 (0.73, 1.24)	
No qualifications	1.41 (0.97, 2.06)		1.28 (0.85, 1.91)	
Financial hardship: Money for		0.04;		0.04;
basic needs?	1.0	0.005 (t)**	1.0	0.005
Always	1.17 (0.85, 1.61)		1.20 (0.86, 1.67)	(t)**
Mostly	1.41 (1.01, 1.97)		1.36 (0.98, 1.90)	
Sometimes	1.74 (1.15, 2.63)		1.82 (1.19, 2.78)	
No				
Lifestyle factors				
Smoking status		0.13		0.11
Never	1.0		1.0	
Ex-smoker	1.08 (0.77, 1.51)		1.10 (0.79, 1.54)	
Current smoker	1.35 (1.00, 1.82)		1.39 (1.02, 1.91)	
Recreational drug use in past 3 months				
No	1.0	0.01	1.0	0.009

(*continued*)

Table 3 (*Continued*)

	Unadjusted HR (95% CI)	p-value; test for trend	Demographic adjusted HR (95% CI)*	p-value; test for trend
Non-IDU chemsex drugs	0.75 (0.46, 1.22)		0.98 (0.57, 1.67)	
Non-IDU other	0.93 (0.70, 1.24)		0.96 (0.70, 1.31)	
IDU	1.80 (1.18, 2.73)		2.11 (1.30, 3.43)	
Alcohol dependency (CAGE score)		0.32;		0.36;
	1.0	0.32 (t)**	1.0	0.25 (t)**
0 (no)	0.90 (0.61, 1.34)		0.95 (0.64, 1.42)	
1	1.30 (0.92, 1.83)		1.34 (0.95, 1.90)	
2	0.93 (0.46, 1.87)		0.97 (0.47, 1.99)	
3	1.92 (0.81, 4.58)		1.62 (0.78, 3.34)	
4 (strong dependency)				
Alcohol consumption (modified AUDIT score)		0.03;		0.04;
0 (none)	1.0	0.89 (t)**	1.0	0.81 (t)**
1–2 (low)	0.62 (0.44, 0.89)		0.59 (0.41, 0.86)	
3–4	0.77 (0.56, 1.05)		0.80 (0.56, 1.13)	
5–6	0.77 (0.51, 1.18)		0.84 (0.54, 1.31)	
7–8 (high)	1.24 (0.71, 2.14)		1.06 (0.63, 1.80)	
Mental health factors				
Anxiety symptoms (GAD-7 score)		0.002;		0.002;
0–4 (no anxiety)	1.0	0.002 (t)**	1.0	0.002 (t)**
5–9 (mild)	1.40 (1.02, 1.92)		1.39 (1.01, 1.91)	
10–14 (moderate)	1.98 (1.41, 2.79)		2.06 (1.43, 2.95)	
>=15 (severe anxiety)	1.30 (0.87, 1.94)		1.31 (0.87, 1.98)	
Depressive symptoms(PHQ-9 score)		0.007;		0.005;
0–4 (none/minimal)	1.0	0.0003 (t)**	1.0	0.0002 (t)**
5–9 (mild)	1.34 (0.92, 1.94)		1.34 (0.93, 1.95)	
10–14 (moderate)	1.63 (1.15, 2.31)		1.67 (1.17, 2.38)	
>=15 (severe)	1.81 (1.26, 2.60)		1.91 (1.30, 2.78)	
PHQ-9 depression and receiving treatment for depression		0.003		0.0004
PHQ-9 <10, no treatment	1.0		1.0	
PHQ-9 <10, on treatment	1.50 (0.97, 2.37)		1.65 (1.03, 2.64)	
PHQ-9 ≥ 10, no treatment	1.74 (1.29, 2.34)		1.87 (1.39, 2.52)	
PHQ-9 ≥ 10, on treatment	1.49 (1.03, 2.16)		1.53 (1.05, 2.24)	
Demographic and clinical factors				
Demographic group		0.008		0.007
MSM	1.0		1.0	
Black African heterosexual men	1.17 (0.71, 1.93)		1.19 (0.72, 1.96)	
Other heterosexual men	1.85 (1.27, 2.68)		1.93 (1.32, 2.82)	
Black African women	0.84 (0.56, 1.25)		0.90 (0.59, 1.37)	
Other women	1.43 (0.95, 2.14)		1.49 (0.97, 2.30)	
Age (years)		0.01;		0.005;
<=35	1.0	0.02 (t)**	1.0	0.05 (t)**
36–50	1.00 (0.66, 1.52)		0.85 (0.55, 1.31)	
51–60	1.11 (0.70, 1.76)		0.92 (0.57, 1.50)	
>60	1.76 (1.10, 2.82)		1.60 (0.97, 2.66)	
CD4 count (cells/μl)		<0.0001;		<0.0001;
>800	1.0	<0.0001 (t)**	1.0	<0.0001 (t)**
500–800	0.97 (0.70, 1.36)		0.99 (0.71, 1.37)	
350–499	1.54 (1.07, 2.20)		1.56 (1.09, 2.22)	
200–349	1.58 (1.04, 2.38)		1.45 (0.89, 2.34)	
<=199	2.49 (1.70, 3.65)		2.53 (1.72, 3.74)	
CD4 count nadir (cells/μl)		0.01		0.13
>349	1.0	0.003 (t)**	1.0	0.027 (t)**
200–349	1.13 (0.69, 1.83)		1.05 (0.64, 1.81)	
50–199	1.33 (0.83, 2.13)		1.19 (0.74, 1.93)	
<50	1.80 (1.13, 2.87)		1.55 (0.94, 2.57)	
HIV viral load		<0.0001		<0.0001
≤50 copies/ml	1.0		1.0	
>50 copies/ml	1.73 (1.33, 2.26)		1.86 (1.41, 2.45)	
Years since HIV diagnosis		0.059;		0.085;
<5	1.0	0.087 (t)**	1.0	0.04 (t)**
5-<10	0.83 (0.55, 1.25)		0.87 (0.58, 1.31)	
10-<20	1.02 (0.73, 1.42)		1.14 (0.82, 1.59)	
>=20 years	1.41 (0.97, 2.04)		1.47 (0.99, 2.16)	
ART status		0.36		0.39
On ART	1.0		1.0	
Stopped ART	1.54 (0.74, 3.21)		1.60 (0.78, 3.29)	
Never ART	0.81 (0.48, 1.38)		0.90 (0.49, 1.64)	
ART non-adherence – missed >= 2 days ART at a time in past 3 months		0.0004;		0.0006;
No / don't know	1.0	0.0004	1.0	0.0004 (t)**
Yes, once	1.70 (1.09, 2.65)	(t)**	1.86 (1.16, 2.99)	
Yes, 2–3 times	1.70 (1.15, 2.50)		1.71 (1.16, 2.52)	
Yes, >3 times	2.16 (1.47, 3.18)		2.00 (1.33, 3.01)	
Not on ART	1.50 (1.01, 2.23)		1.62 (1.05, 2.49)	
Ever had Hepatitis C		0.14		0.19

(*continued*)

Table 3 (*Continued*)

	Unadjusted HR (95% CI)	p-value; test for trend	Demographic adjusted HR (95% CI)*	p-value; test for trend
No /missing	1.0		1.0	
Yes	1.23 (0.94, 1.62)		1.22 (0.91, 1.63)	

MSM= men who have sex with men; IDU=injection drug use; ART=antiretroviral therapy; *adjusted for demographic group, age, years since HIV diagnosis; **t*=test for trend. After truncating the data after the 4th hospitalisation, a total sum of 251 hospitalisations were used in the regression model.

Table 4
Unadjusted and adjusted hazard ratios of hospitalisation according to social circumstance, socioeconomic, lifestyle and mental health factors in individuals with controlled HIV (CD4 >=500; virally suppressed; on ART) at baseline.

	Unadjusted HR (95% CI)	p-value; test for trend	Demographic adjusted HR (95% CI)*	p-value; test for trend
Social circumstance				
Current stable partner		0.30		0.31
Yes, and living with partner	1.0		1.0	
Yes, but not living with partner	1.50 (0.85, 2.64)		1.49 (0.88, 2.55)	
No	1.38 (0.85, 2.24)		1.28 (0.80, 2.04)	
Has children		0.18		0.23
No	1.0		1.0	
Yes	1.37 (0.87, 2.16)		1.50 (0.78, 2.90)	
Social support score		0.31;		0.076;
1 (highest)	1.0	0.95 (t)**	1.0	0.61 (t)**
2	0.93 (0.58, 1.49)		0.82 (0.50, 1.34)	
3	0.70 (0.39, 1.25)		0.55 (0.30, 1.00)	
4	1.53 (0.78, 2.99)		1.35 (0.68, 2.68)	
5 (low)	0.55 (0.09, 3.62)		0.43 (0.09, 2.02)	
Disclosure of HIV status		0.46		0.50
Yes	1.0		1.0	
No	0.69 (0.26, 1.83)		0.71 (0.26, 1.91)	
Socioeconomic factors				
Employment		0.003		0.02
Employed	1.0		1.0	
Unemployed	1.43 (0.80, 2.57)		1.33 (0.75, 2.37)	
Sick / disabled	2.02 (1.17, 3.49)		1.68 (0.97, 2.91)	
Retired	2.49 (1.35, 4.57)		1.75 (0.80, 3.82)	
Other	3.09 (1.42, 6.71)		3.14 (1.49, 6.60)	
Housing status		0.22		0.063
Homeowner	1.0		1.0	
Renting	1.47 (0.95, 2.26)		1.69 (1.09, 2.60)	
Temporary / unstable / other	1.29 (0.48, 3.45)		1.63 (0.62, 4.29)	
Highest level of education		0.88;		0.74;
University or above	1.0	0.68	1.0	0.91
Below university	1.11 (0.73, 1.69)		1.08 (0.71, 1.64)	
No qualifications	1.03 (0.47, 2.27)		0.79 (0.35, 1.75)	
Financial hardship: Money for basic needs?		0.13;		0.05;
Always	1.0	0.02 (t)**	1.0	0.007 (t)**
Mostly	1.37 (0.86, 2.17)		1.53 (0.95, 2.46)	
Sometimes	1.57 (0.88, 2.82)		1.55 (0.85, 2.82)	
No	1.96 (1.01, 3.78)		2.34 (1.23, 4.49)	
Lifestyle factors				
Smoking status		0.68		0.68
Never	1.0		1.0	
Ex-smoker	0.97 (0.59, 1.59)		1.04 (0.64, 1.69)	
Current smoker	1.18 (0.72, 1.96)		1.24 (0.74, 2.06)	
Recreational drug use in past 3 months		0.23		0.19
No	1.0		1.0	
Non-IDU chemsex drugs	0.98 (0.56, 1.71)		1.40 (0.73, 2.69)	
Non-IDU other	1.22 (0.77, 1.93)		1.27 (0.78, 2.06)	
IDU	2.00 (0.98, 4.08)		2.47 (1.09, 5.64)	
Alcohol dependency (CAGE score)		0.02;		0.04;
0 (no)	1.0	0.51 (t)**	1.0	0.36 (t)**
1	0.55 (0.30, 1.03)		0.66 (0.35, 1.25)	
2	1.78 (1.08, 2.93)		1.90 (1.13, 3.21)	
3	0.72 (0.23, 2.25)		0.77 (0.24, 2.52)	
4 (strong dependency)	1.53 (0.46, 5.10)		1.41 (0.50, 3.93)	
Alcohol consumption (modified AUDIT score)		0.04;		0.25;
0 (low)	1.0	0.99 (t)**	1.0	0.84 (t)**
1–2	1.01 (0.55, 1.83)		0.89 (0.49, 1.64)	
3–4	0.81 (0.44, 1.50)		0.81 (0.43, 1.51)	
5–6	0.72 (0.36, 1.46)		0.75 (0.36, 1.54)	
7–8 (high)	2.15 (1.04, 4.48)		1.84 (0.80, 4.23)	
Mental health factors				
Anxiety symptoms (GAD-7 score)		0.02;		0.02;

(*continued*)

Table 4 (*Continued*)

	Unadjusted HR (95% CI)	p-value; test for trend	Demographic adjusted HR (95% CI)*	p-value; test for trend
0–4 (no anxiety)	1.0	0.006	1.0	0.01 (t)**
5–9 (mild)	1.67 (1.03, 2.71)	(t)**	1.59 (0.98, 2.58)	
10–14 (moderate)	2.35 (1.34, 4.13)		2.48 (1.38, 4.47)	
>=15 (severe anxiety)	1.47 (0.83, 2.61)		1.47 (0.78, 2.79)	
Depressive symptoms (PHQ-9 score)		0.02;		0.03;
0–4 (none/minimal)	1.0	0.004 (t)**	1.0	0.009 (t)**
5–9 (mild)	1.01 (0.54, 1.89)		0.97 (0.53, 1.79)	
10–14 (moderate)	1.84 (1.12, 3.03)		1.82 (1.09, 3.01)	
>=15 (severe)	1.96 (1.12, 3.42)		1.91 (1.03, 3.51)	
PHQ-9 depression and receiving treatment for depression		0.009		0.02
PHQ-9 <10, no treatment	1.0		1.0	
PHQ-9 <10, on treatment	1.55 (0.83, 2.92)		1.48 (0.76, 2.89)	
PHQ-9 ≥ 10, no treatment	2.21 (1.37, 3.57)		2.04 (1.25, 3.33)	
PHQ-9 ≥ 10, on treatment	1.80 (0.99, 3.28)		1.96 (1.05, 3.67)	
Demographic and clinical factors				
Demographic group		0.17		0.066
MSM	1.0		1.0	
Black African heterosexual men	0.64 (0.20, 2.12)		0.76 (0.23, 2.49)	
Other heterosexual men	2.27 (1.10, 4.67)		2.78 (1.34, 5.74)	
Black African women	1.08 (0.58, 2.00)		1.18 (0.63, 2.19)	
Other women	0.70 (0.28, 1.75)		0.71 (0.28, 1.78)	
Age (years)		0.02;		0.026;
<=35	1.0	0.03 (t)**	1.0	0.16 (t)**
36–50	0.96 (0.51, 1.79)		0.66 (0.33, 1.33)	
51–60	1.15 (0.57, 2.31)		0.75 (0.34, 1.68)	
>60	2.24 (1.12, 4.48)		1.55 (0.65, 3.68)	
CD4 count nadir (cells/μl)		0.39		0.46
>349	1.0	0.15 (t)**	1.0	0.27 (t)**
200–349	1.73 (0.62, 4.86)		1.68 (0.65, 4.33)	
50–199	2.21 (0.79, 6.16)		2.03 (0.80, 5.11)	
<50	1.81 (0.61, 5.41)		1.66 (0.60, 4.60)	
Years since HIV diagnosis		0.05;		0.03;
<5	1.0	0.02 (t)**	1.0	0.01 (t)**
5-<10	0.96 (0.41, 2.24)		0.90 (0.39, 2.07)	
10-<20	1.55 (0.72, 3.34)		1.62 (0.73, 3.61)	
>=20 years	2.21 (0.94, 5.15)		2.29 (0.93, 5.67)	
ART non-adherence – missed >= 2 days ART at a time in past 3 months		0.36;		0.38;
No / don't know	1.0	0.092	1.0	0.10 (t)**
Yes, once	1.12 (0.57, 2.20)	(t)**	1.14 (0.57, 2.29)	
Yes, 2–3 times	1.71 (0.94, 3.12)		1.70 (0.92, 3.12)	
Yes, >3 times	1.35 (0.42, 4.33)		1.36 (0.40, 4.60)	
Ever had Hepatitis C		0.44		0.33
No /missing	1.0		1.0	
Yes	1.24 (0.72, 2.12)		1.31 (0.76, 2.26)	

MSM= men who have sex with men; IDU=injection drug use; ART=antiretroviral therapy; *adjusted for demographic group, age, years since HIV diagnosis; **t=test for trend. After truncating the data after the 4th hospitalisation, a total sum of 97 hospitalisations were used in the regression model.

5.3. Lifestyle factors

Recreational injection drug use was strongly associated with higher hospitalisation rates and an increased hazard in the unadjusted PWP analysis, but non-injection drug use (including non-injection chemsex drug use) was not. After adjustment, the association for injection drug use was stronger, due to the fact that all but one injection drug user in the cohort were MSM, who had a lower rate of hospitalisation than the other demographic groups. There was a J-shaped association between level of alcohol consumption and hospitalisation, with the highest hazard in the group with highest consumption. Alcohol dependency was not significantly associated with hospitalisation. There was a trend for an increased hazard for current smokers compared to non-smokers.

5.4. Mental health factors

Depressive symptoms and anxiety symptoms were strongly associated with higher hospitalisation rates and an increased hazard in unadjusted and adjusted PWP analyses. For the variable incorporating depressive symptoms and current treatment for depression, the hazard was higher in all three groups with evidence of current depression compared to those without.

5.5. Demographic and clinical factors

Higher rates of hospitalisation were associated with being a heterosexual man or woman of ethnicity other than Black African, age greater than sixty, lower CD4 count, CD4 nadir <50, viral non-suppression, greater ART non-adherence, time since HIV diagnosis greater than 20 years.

5.6. Associations with hospitalisations among people with controlled HIV and high CD4 count

There were 461 participants on ART with VL<50c/mL and CD4 count >500 at baseline. One hundred hospitalisations occurred in 76 (16%) people over 2746 person-years of observation. Sixty (60%) were emergencies, a lower proportion compared to the overall study population. The rate of hospitalisation was 3.6/100 person-years (95% CI: 2.9–4.4) and the rate of re-admission was 47.3/100 person-years (28.0–66.7). For comparison, in individuals without controlled HIV and high CD4 count, the rate of hospitalisation was 8.9/100 person-years (7.5–10.2). In those with controlled HIV and high CD4 count the pattern of associations was broadly similar to that in the whole cohort. In particular, in the adjusted analysis, socioeconomic disadvantage, injection drug use, alcohol dependency and poor

mental health were predictive of hospitalisation; but the associations of social support and 'no partner' with hospitalisation appeared weaker (Table 4). None of the tests for interaction comparing associations between those with and without virological control and high CD4 count were significant ($p>0.05$ for all factors in Table 4).

6. Discussion

To our knowledge, this analysis, using linkage between questionnaire responses, routine clinic data and a detailed review of hospital records, is the most comprehensive analysis of predictors of hospitalisations in PLHIV in Europe in the contemporary cART era. Socioeconomic disadvantage, social circumstances, evidence of mental health disorders and adverse lifestyle factors were all predictive of subsequent hospitalisation, in addition to demographic and clinical factors.

Our findings emphasize the need for differentiated care and targeted interventions to support socially disadvantaged groups, and to help detect, treat and prevent mental health problems and modify adverse lifestyle factors, to improve health outcomes in PLHIV. It is important to note that the association of factors such as financial hardship and poor mental health with subsequent hospitalisation was as strong as that for smoking and alcohol dependency, and similar among people with controlled HIV and high CD4 count. As universal treatment with antivirals is now standard practice for all PLHIV in the UK (regardless of CD4 count) these wider social and economic determinants of health should receive increasing focus as key predictors of morbidity in PLHIV.

There is little research on the impact of social support, relationship and family status on the risk of hospitalisation in PLHIV. Two US studies did not find an association between marital status and hospitalisation [11,14], whereas we found that not having a stable partner and having children were associated with higher hazard of hospitalisation in all PLHIV, with evidence for an effect of lower social support. The effect of having children was not attenuated after adjusting for demographic group, and was similar in those with and without a current partner (test for interaction=0.60). Those with children and no partner were at the highest risk of hospitalisation. Furthermore, there was an interaction between demographic group and having children (p = 0.0492). In four of the five demographic subgroups, those with children had a higher hospitalisation rate than those without (crude rate ratios from 1.7 to 4.5), but among Black African women, those with children had a lower rate (rate ratio=0.42).

The higher risk among PLHIV with children may be explained by competing responsibilities, increased stress or greater financial or time pressures, which take a parent's emphasis away from maintaining their own health. On the other hand, those living with a partner were at lower risk of hospitalisation, which is consistent with lower rates observed among those with high levels of social support. The mechanisms by which social support could protect against hospitalisation are complex, and may include protecting against depression, having greater emotional or financial resources to cope with difficulties, reducing stigma, increasing healthcare-seeking behaviour and maintaining engagement in health and wellbeing. There was no clear evidence for an effect of non-disclosure on hospitalisation; this is consistent with previous analyses of the whole ASTRA study population that found no difference according to overall non-disclosure in prevalence of depression, ART non-adherence and virological non-suppression [28]. Our results highlight the importance of social circumstance in determining health outcomes. Patients caring for children and those with limited support networks may benefit from additional services and interventions, e.g. family and childcare support, peer support, counselling, or specific health interventions.

Our findings show that markers of current socioeconomic disadvantage (non-employment, less secure housing situation and financial hardship) were strong predictors of hospitalisation among PLHIV, whereas level of education was not significantly associated. Two US studies from 2012 and 2014 found that being employed was associated with a reduced hospitalisation rate [14,19], while two other studies found no association with monthly income, [10,12] and results relating to education were inconsistent in PLHIV [10,12,14,19]. A US study found an association between unstable housing or homelessness and increased rate of hospitalisation in PLHIV [29]. To our knowledge, there are no recent European studies investigating the association of socioeconomic factors with hospitalisation.

Previous results from ASTRA showed the marked associations of socioeconomic factors with non-adherence to antiretrovirals and viral non-suppression [30]. The present results demonstrate similarly strong associations with a wider measure of morbidity.

The mechanisms by which lack of financial resources and other socioeconomic disadvantages lead to increased hospitalisation are likely to be complex and may include competing pressures and responsibilities other than personal health, delaying seeking health care, as well as the strong link with depression [31] and higher prevalence of adverse lifestyle factors. There may also be differential vulnerability and susceptibility to mediators such as depression, i.e. the effect of depression on health outcomes may be stronger in groups with socioeconomic disadvantage, implying the presence of interaction [32]. It was beyond the scope of our study to investigate the specific causal pathways behind the associations of socioeconomic factors with hospitalisation. To examine the possibility of the associations being driven by injection drug use as a contributor to inequalities, we repeated the unadjusted analysis for socioeconomic factors after excluding individuals who injected drugs at baseline. We found that the associations were similar to the main analysis and, therefore, that injection drug use does not appear to drive the associations (Appendix). Our results among PLHIV parallel those in the general population, emphasising the importance of socioeconomic disadvantage as a critical determinant of health outcomes and the need for interventions to mitigate this effect.

There was a strong association of recent injection drug use with hospitalisation. US studies found that use of illicit drugs such as opiates, crack, cocaine and heroin are associated with hospitalisation in PLHIV [10,12,13,18,20]. Although we did not ask about specific injection drugs in our study, we did ask about drug type for drug use in general. A number of drugs were much more commonly reported in injection drug users compared to non-injection drug users, these included chemsex drugs (methamphetamine, GHB/GBL, mephedrone) as well as opiates, crack, cocaine and anabolic steroids. Injection drug users were a small proportion of all drug users, but at much higher risk of hospitalisation. There has been concern about the perceived increase in injection of chemsex drugs ('slamming') in the UK; further research on the health effects is needed. There were weak, non-significant, associations of hospitalisation with smoking, which was found to be associated in other studies [15,18]. We found a J-shaped association with alcohol consumption, with higher rates of hospitalisation in non-drinkers, and more so in heavy drinkers, compared to low or intermediate drinking levels. This appears consistent with literature on alcohol as a risk factor for mortality [33]. Most other studies in PLHIV have examined binary alcohol classifications; three found an association between hazardous alcohol consumption and hospitalisation [8,15,20], while four did not [10,12,14,18].

Smoking and high levels of alcohol consumption or dependency would be expected to impact on hospitalisations due to known associations with a range of common chronic diseases, including cancer, respiratory and heart diseases. We would also expect an association of alcohol abuse and chronic Hepatitis C with risk of liver related complications in the longer term that may increase hospitalisation risk. The associations for injection drug use and alcohol were of a greater magnitude in those with controlled HIV and high CD4 count, suggesting lifestyle factors may become even stronger predictors of

morbidity as timely diagnosis and early ART reduces health problems related to uncontrolled HIV.

In our analysis, depression (including symptoms and currently treated depression) and anxiety symptoms were strong predictors of hospitalisation in PLHIV, at least as much so in those with controlled HIV. Our findings are consistent with previous studies from the US that investigated the impact of depression [8,12,18] and anxiety [8,14] and other mental health problems [16] on hospitalisation in PLHIV. Depression may be a key mediator through which social and socioeconomic factors impact on hospital admissions, for example through the effect of poor mental health on physical health and health seeking behaviours, lower adherence to ART and other treatments, co-existing physical illness, and in part through admissions directly due to mental health. PLHIV with treated depression but without symptoms according to PHQ-9 also had a higher hazard of hospitalisation than people without evidence of depression, perhaps because treated depression may indicate more severe mental health problems. Co-morbidities among those with depression, and perhaps the treatment itself, may also have adverse effects on health and wellbeing. The findings highlight the need for regular routine assessment of mental health among PLHIV and for adequate mental health support and treatment.

As reported in a previous study at this London centre [6], we found that women and heterosexual men of ethnicity other than Black African were at higher risk of hospitalisation compared to MSM. We also found an increased hazard of hospitalisation in individuals over the age of 60, with little variation in risk across the younger age groups. Other studies had similar findings, most of which were reporting an increased risk in the oldest age groups only [7-9,17], reflecting trends in the general population. Of several studies that did not find an association most considered age as a continuous rather than categorical variable and therefore potentially missed an elevated risk in the oldest age groups [10-12,14].

Our results confirm the importance of HIV surrogate markers such as low CD4 count and viral non-suppression, and self-reported ART non-adherence, in predicting hospitalisation. There was also evidence for an effect of longer time since HIV diagnosis (particularly $>$20 years), which may reflect an adverse effect on health of longer time with uncontrolled HIV as well as the impact of being diagnosed in the period before effective ART. We previously reported strong associations between longer time since HIV diagnosis and higher prevalence of physical symptom distress, mental health problems and functional problems, independently of age [34]. Other studies reported some evidence of the opposite association: a negative relationship between time since HIV diagnosis and hospitalisation, [7,11] although a high risk among newly diagnosed individuals may contribute to this [6]. Hepatitis C co-infection has previously been found to predict hospitalisation [9,17].

In our study, hospitalisations occurring outside of the Royal Free Hospital may have been missed if not reported to the HIV physician by the patient, general practitioner or other hospital, or if this information was not documented. Thus, we may have underestimated the true rate of hospitalisation, although this may be expected to impact less on associations. We studied baseline predictors of hospitalisations over a 6- 7-year follow-up period. This may underestimate associations for factors likely to change over time such as HIV-related clinical factors, adverse lifestyle factors and mental health symptoms. The rate of hospitalisation of 5.8/100 person-years in our study population was lower than in some other recent studies in other high income settings [13,35-37]. Our study population had a high median CD4 count (621 cells/μl) and included a low proportion of individuals with recent diagnosis (3.6% of individuals were within their first year after diagnosis at baseline) for whom hospitalisation rates are particularly high [6]. Our data are from a high-income setting, and so are not generalizable to resource-limited settings.

In summary, in addition to clinical and demographic factors, social circumstance, socioeconomic, lifestyle and mental health factors are important predictors of hospitalisation in PLHIV in the UK in the modern ART era and will likely remain key determinants of health in the future. This highlights the importance of holistic care for PLHIV and targeted support for those with psychosocial and economic needs. A more detailed understanding of causal mechanisms and of the direct and indirect effects of these factors on hospitalisation is needed to inform possible interventions. Given the high costs of hospitalisation such interventions could be cost-effective.

Author contributions

SMR, FCL and CJS conceived the idea for the analysis, with input from all authors. SMR drafted the analysis plan and conducted all analyses, with input from FCL and CJS. FCL, AJR, ANP, MAJ, LS, AM, ASp, SC originally conceived and designed the ASTRA study; AJR, JM, MAJ were responsible for data collection at the Royal Free Hospital. FCL, CS, SM, FB, MAJ, AJR, ANP designed the hospitalisation sub-study; CC, ASt were responsible for data collection. SMR drafted the first draft of the manuscript, and all authors provided substantive input into this and subsequent drafts.

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Data sharing statement

Anonymised data are available upon request to the senior author (contact: f.lampe@ucl.ac.uk).

Declaration of Competing Interest

CS reports grants from ViiV Healthcare and personal fees from Gilead Sciences outside the submitted work; SR reports a PhD stipend from the Royal Free Charity but no conflicts of interest exist. All other authors have no conflicts of interest to declare related to the submitted work.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.eclinm.2020.100665.

Appendix

Appendix 1. Distribution of hospitalisations according to exposure/stratification variables. PLHIV=people living with HIV

	All PLHIV (*N* = 798)		PLHIV with controlled HIV and high CD4 count (*N* = 461)	
	Total number of events (*N* = 274); person-years (total=4710)	Events used in models after truncation after 4th event (*N* = 251); gap time (total=4683)	Total number of events (*N* = 100); person-years (total=2746)	Events used in models after truncation after 4th event (*N* = 97); gap time (total=2746)
Social circumstance				
Current stable partner				
Yes, and living with partner	67; 1931	64; 1929	31; 1184	31; 1183
Yes, but not living with partner	46; 712	42; 707	23; 444	21; 444
No	160; 2049	144; 2028	46; 1104	45; 1.106
Has children				
No	174; 3613	160; 3599	73; 2179	70; 2179
Yes	98; 1087	89; 1074	25; 558	25; 557
Social support score				
1 (highest)	64; 1515	64; 1505	32; 904	32; 900
2	97; 1574	84; 1563	33; 926	31; 925
3	49; 793	42; 793	15; 496	14; 501
4	37; 507	34; 503	16; 268	16; 267
5 (low)	25; 283	24; 280	2; 122	2; 122
Disclosure of HIV status				
Yes	251; 4442	229; 4416	97; 2592	94; 2592
No	22; 237	21; 235	3; 135	3; 135
Socioeconomic factors				
Employment				
Employed	101; 2820	92; 2821	46; 1691	43; 1695
Unemployed	46; 729	44; 725	16; 454	16; 453
Sick / disabled	83; 609	72; 588	20; 329	20; 325
Retired	31; 323	30; 319	12; 172	12; 172
Other	8; 152	8; 152	5; 57	5; 56
Housing status				
Homeowner	73; 1878	63; 1878	35; 1182	32; 1186
Renting	176; 2373	162; 2352	58; 1378	58; 1374
Temporary / unstable / other	20; 407	20; 400	6; 168	6; 167
Highest level of education				
University or above	131; 2317	120; 2304	49; 1412	48; 1415
Below university	99; 1908	93; 1898	45; 1136	43; 1133
No qualifications	39; 419	33; 415	5; 160	5; 160
Financial hardship: Money for basic needs?				
Always	110; 2364	97; 2352	42; 1414	39; 1415
Mostly	65; 1206	63; 1200	25; 687	25; 687
Sometimes	47; 633	46; 631	16; 358	16; 358
No	46; 448	39; 441	15; 257	15; 256
Lifestyle factors				
Smoking status				
Never	81; 1695	76; 1688	34; 960	37; 911
Ex-smoker	78; 1484	70; 1468	28; 866	28; 863
Current smoker	108; 1485	99; 1481	38; 907	32; 960
Recreational drug use in past 3 months				
No	151; 2565	141; 2544	47; 1465	45; 1465
Non-IDU chemsex drugs	19; 495	18; 491	9; 289	9; 286
Non-IDU other	79; 1518	76; 1521	40; 926	39; 929
IDU	25; 132	16; 126	4; 67	4; 66
Alcohol dependency (CAGE score)				
0 (no)	166; 3112	157; 3097	67; 1844	65; 1842
1	43; 722	35; 723	11; 441	10; 446
2	37; 479	34; 473	16; 240	16; 237
3	13; 288	13; 288	4; 167	4; 167
4 (strong dependency)	9; 79	7; 71	2; 47	2; 47
Alcohol consumption (modified AUDIT score)				
0 (none)	65; 808	59; 797	17; 465	17; 464
1–2 (low)	43; 1190	43; 1189	28; 728	28; 727
3–4	81; 1363	75; 1351	25; 819	25; 818
5–6	57; 1055	50; 1055	20; 577	17; 582
7–8 (high)	17; 186	14; 183	8; 100	8; 97
Mental health				
Anxiety symptoms (GAD-7 score)				
0–4 (no anxiety)	115; 2722	107; 2708	43; 1559	40; 1561
5–9 (mild)	76; 1039	69; 1033	30; 652	30; 651
10–14 (moderate)	54; 488	49; 484	16; 240	16; 239
>=15 (severe anxiety)	29; 461	26; 457	11; 295	11; 295
Depressive symptoms (PHQ-9 score)				
0–4 (none/minimal)	95; 2533	91; 2525	40; 1514	40; 1511
5–9 (mild)	68; 945	58; 936	20; 564	17; 568

(*continued*)

(*Continued*)

	All PLHIV (*N* = 798)		PLHIV with controlled HIV and high CD4 count (*N* = 461)	
	Total number of events (*N* = 274); person-years (total=4710)	Events used in models after truncation after 4th event (*N* = 251); gap time (total=4683)	Total number of events (*N* = 100); person-years (total=2746)	Events used in models after truncation after 4th event (*N* = 97); gap time (total=2746)
10−14 (moderate)	56; 646	51; 641	20; 342	20; 342
>=15 (severe)	55; 586	51; 581	20; 326	20; 326
PHQ-9 depression and receiving treatment for depression				
PHQ-9 <10, no treatment	138; 3114	125; 3099	49; 1808	46; 1809
PHQ-9 <10, on treatment	25; 364	24; 362	11; 270	11; 270
PHQ-9 ≥ 10, no treatment	68; 685	64; 680	25; 370	25; 370
PHQ-9 ≥ 10, on treatment	43; 547	38; 542	15; 298	15; 298
Demographic and clinical factors				
Demographic group				
MSM	175; 3495	161; 3481	74; 2073	71; 2074
Black African heterosexual men	14; 175	13; 171	2; 92	2; 92
Other heterosexual men	38; 287	35; 285	11; 125	11; 124
Black African women	14; 367	14; 366	8; 228	8; 228
Other women	33; 387	28; 380	5; 228	5; 228
Age				
<=35	27; 529	25; 526	8; 267	8; 267
36−50	143; 2798	131; 2780	51; 1673	51; 1669
51−60	71; 1094	63; 1090	29; 661	26; 665
>60	33; 289	32; 287	12; 145	12; 145
CD4 count (cells/μl)			–	–
>800	56; 1285	54; 1282		
500−800	79; 1942	76; 1944		
350−499	74; 917	66; 904		
200−349	41; 399	33; 397		
<=199	24; 166	22; 156		
CD4 count nadir (cells/μl)				
>349	22; 627	22; 626	5; 295	5; 295
200−349	71; 1597	68; 1591	34; 1070	34; 1066
50−199	103; 1615	88; 1608	45; 986	44; 991
<50	78; 872	73; 858	16; 396	14; 395
HIV viral suppression (≤50 copies/ml)			–	-
Yes	189; 3866	172; 3849		
No	85; 845	79; 833		
Years since HIV diagnosis				
<5	49; 930	48; 922	7; 321	7; 321
5-<10	53; 1182	45; 1174	17; 781	17; 781
10-<20	118; 1954	106; 1943	55; 1276	52; 1277
>=20 years	54; 645	52; 643	21; 368	21; 367
ART status			–	–
On ART	237; 4255	217; 4233		
Stopped ART	7; 66	6; 66		
Never ART	12; 293	12; 292		
ART non-adherence −missed >= 2 days ART at a time in past 3 months				
No / don't know	150; 3463	145; 3452	79; 2297	76; 2298
Yes, once	31; 286	22; 280	7; 199	7; 198
Yes, 2−3 times	28; 319	26; 318	12; 193	12; 193
Yes, >3 times	28; 175	24; 170	2; 52	2; 52
Not on ART/missing	37; 467	34; 462	0; 6.0	0; 6.0
Ever had Hepatitis C				
No /missing	212; 3940	198; 3920	83; 2351	80; 2352
Yes	62; 770	53; 763	17; 395	17; 394

Appendix 2. Details of scales used in ASTRA questionnaire to assess social support; alcohol dependency/consumption; depressive and anxiety symptoms

Modified Duke-UNC Functional Social Support Questionnaire

"Here is a list of some things that other people do for us that may be helpful or supportive. Please read each statement carefully and place a tick in the column that is closest to your situation. Give only one answer for each row."

Five statements (I have people who care what happens to me; I get love and affection; I get chances to talk to someone I trust about my personal problems; I get invitations to go out and do things with other people; I get help when I am sick in bed) to respond to on a scale from 1 to 5 (1=Much less than I would like; 2=Less than I would like; 3=Some, but would like more; 4=Almost as much as I would like; 5=As much as I would like); responses are summed to form the overall score from 5 to 25: 1= score 25 (Highest possible); 2 = 20–24; 3 = 15–19; 4 = 10–14; 5 = 5–9 (Low).

Alcohol dependency based on CAGE 4-item questionnaire

CAGE 4-item questionnaire: "Have you ever felt you should cut down on your drinking?"; "Have people annoyed you by criticising your drinking?"; "Have you ever felt bad or guilty about your drinking?"; "Have you ever had a drink first thing in the morning to steady your nerves or get rid of a hangover?"

Respondents reply "yes (1)" or "no (0)" to each question and numbers are summed to form the score from 0 to 4 (no evidence of dependency to strong evidence of dependency).

Alcohol consumption based on first two questions from WHO AUDIT-C score

Modified AUDIT-C score derived from first two variables of AUDIT-C questionnaire: "How often do you have a drink containing alcohol?"; "How many units do you drink on a typical day when you are drinking?". Categories are: 0 (non-drinker); 1–2 (1 or 2 drinks 2-4 times per month or less; 3 or 4 drinks monthly or less); 3–4 (1 or 2 drinks at least twice a week; 3 or 4 drinks 2-4 times per month or 2-3 times per week; 5 or 6 drinks 2-4 times per month or less; 7-9 drinks monthly or less); 5–6 (3 or 4 drinks 4 or more times a week; 5 or 6 drinks at least 2 to 3 times a week; 7-9 drinks 2-4 times per month or 2-3 times per week; 10+ drinks 2-4 times per month or less); 7–8 (7-9 drinks 4 or more times a week; 10+ drinks at least 2-3 times per week).

Symptoms of anxiety according to Generalised Anxiety Disorder Assessment (GAD-7 score)

'Over the past 2 weeks, how often have you been bothered by any of the following problems?'

1 Feeling nervous, anxious or on edge.
2 Not being able to stop or control worrying.
3 Worrying too much about different things.
4 Becoming easily annoyed or irritated.
5 Trouble relaxing.
6 Being so restless that it is hard to sit still.
7 Feeling afraid as if something awful might happen.

Response options: Not at all (coded as 0); Several days (coded as 1); More than half the days (coded as 2); Nearly every day (coded as 3).

Numbers are summed to form the score from 0 to 21 (none/minimal (total score 0–4); mild (5–9); moderate (10–14); severe (15–21).

Symptoms of depression according to the Patient Health Questionnaire 9-tem scale (PHQ-9 score)

Over the past 2 weeks, how often have you been bothered by any of the following problems?'

1 Little interest or pleasure in doing things.
2 Feeling down, depressed or hopeless.
3 Trouble falling or staying asleep, or sleeping too much.
4 Feeling tired or having little energy.
5 Poor appetite or overeating.
6 Feeling bad about yourself – or that you are a failure or have let yourself or your family down.
7 Trouble concentrating on things, such as reading the newspaper or watching television.
8 Moving or speaking so slowly that other people could have noticed/being so restless that it is hard to sit still.
9 Thoughts that you would be better off dead or of hurting yourself in some way.

Response options: Not at all (coded as 0); Several days (coded as 1); More than half the days (coded as 2); Nearly every day (coded as 3).

Numbers are summed to form the score from 0 to 27 (none/minimal (total score 0–4); mild (5–9); moderate (10–14); severe (15–27).

Appendix 3. Unadjusted hazard ratios (HRs) for socioeconomic factors in the complete study population after excluding individuals who injected drugs at baseline (n = 23) (HRs (95% CI):

Employment (vs. employed): unemployed: 1.71 (1.17, 2.50), sick/disabled: 2.66 (1.89, 3.75), retired: 2.15 (1.43, 3.25), other: 1.47 (0.78. 2.80);

Housing (vs. homeowner): renting: 1.79 (1.28, 2.51), temporary / unstable / other: 1.48 (0.89, 2.47);

Education (vs. university or above): below university: 0.96 (0.73, 1.26); no qualifications: 1.47 (1.01, 2.15);

Money for basic needs (vs. always): mostly: 1.25 (0.90, 1.73); sometimes: 1.46 (1.03, 2.07); never: 1.72 (1.12, 2.66)).

References

[1] Nosyk B, Lima V, Colley G, Yip B, Hogg RS, Montaner JS. Costs of health resource utilization among HIV-positive individuals in British Columbia, Canada: results from a population-level study. Pharmacoeconomics 2015;33(3):243–53.
[2] Leon-Reyes S, Schafer J, Fruh M, Schwenkglenks M, Reich O, Schmidlin K, et al. Cost estimates for HIV care and patient characteristics for health resource utilisation from linkage of claims data with the Swiss HIV Cohort Study. Clin Infect Dis 1 March 2019;Volume 68(Issue 5):827–33. doi: 10.1093/cid/ciy564.
[3] Palella Jr. FJ, Delaney KM, Moorman AC, Loveless MO, Fuhrer J, Satten GA, et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV outpatient study investigators. N Engl J Med 1998;338(13):853–60.
[4] Bellino S, Borghetti A, Lombardi F, Camoni L, Ciccullo A, Baldin G, et al. Trends of hospitalisations rates in a cohort of HIV-infected persons followed in an Italian hospital from 1998 to 2016. Epidemiol Infect 2019;147:e89.
[5] Ford N, Shubber Z, Meintjes G, Grinsztejn B, Eholie S, Mills EJ, et al. Causes of hospital admission among people living with HIV worldwide: a systematic review and meta-analysis. Lancet HIV 2015;2(10):e438–44.
[6] Rein S, Lampe F, Johnson M, Bhagani S, Miller R, Chaloner C, et al. All-cause hospitalisation according to demographic group in people living with HIV in the current ART era: recent findings from a cohort study in the UK [in press]. AIDS 2020.
[7] Luz PM, Bruyand M, Ribeiro S, Bonnet F, Moreira RI, Hessamfar M, et al. AIDS and non-AIDS severe morbidity associated with hospitalizations among HIV-infected patients in two regions with universal access to care and antiretroviral therapy, France and Brazil, 2000-2008: hospital-based cohort studies. BMC Infect Dis 2014;14:278.
[8] Choi BY, DiNitto DM, Marti CN, Choi NG. Impact of mental health and substance use disorders on emergency department visit outcomes for HIV patients. West J Emerg Med 2016;17(2):153–64.
[9] Crowell TA, Berry SA, Fleishman JA, LaRue RW, Korthuis PT, Nijhawan AE, et al. Impact of hepatitis coinfection on healthcare utilization among persons living with HIV. J Acquir Immune Defic Syndr 2015;68(4):425–31.
[10] Weiser SD, Hatcher A, Frongillo EA, Guzman D, Riley ED, Bangsberg DR, et al. Food insecurity is associated with greater acute care utilization among HIV-infected homeless and marginally housed individuals in San Francisco. J Gen Intern Med 2013;28(1):91–8.
[11] Emuren L, Welles S, Polansky M, Evans AA, Macalino G, Agan BK, et al. Lower health-related quality of life predicts all-cause hospitalization among HIV-infected individuals. Health Qual Life Outcomes 2018;16(1):107.
[12] Chartier M, Carrico AW, Weiser SD, Kushel MB, Riley ED. Specific psychiatric correlates of acute care utilization among unstably housed HIV-positive adults. AIDS Care 2012;24(12):1514–8.

[13] Davy-Mendez T, Napravnik S, Wohl DA, Durr AL, Zakharova O, Farel CE, et al. Hospitalization rates and outcomes among persons living with human immunodeficiency virus in the southeastern United States, 1996–2016. Clin Infect Dis 2020;71(7):1616–23.
[14] Mannes ZL, Hearn LE, Zhou Z, Janelle JW, Cook RL, Ennis N. The association between symptoms of generalized anxiety disorder and appointment adherence, overnight hospitalization, and emergency department/urgent care visits among adults living with HIV enrolled in care. J Behav Med 2018;01:01.
[15] Akgun KM, Gordon K, Pisani M, Fried T, McGinnis KA, Tate JP, et al. Risk factors for hospitalization and medical intensive care unit (MICU) admission among HIV-infected veterans. J Acquir Immune Defic Syndr 2013;62(1):52–9.
[16] Scott Sutton S, Magagnoli J, Hardin JW. Impact of pill burden on adherence, risk of hospitalization, and viral suppression in patients with HIV infection and AIDS receiving antiretroviral therapy. Pharmacotherapy 2016;36(4):385–401.
[17] Cammarota S, Citarella A, Manzoli L, Flacco ME, Parruti G. Impact of comorbidity on the risk and cost of hospitalization in HIV-infected patients: real-world data from Abruzzo region. [Erratum appears in Clinicoecon Outcomes Res. 2018 Nov 08;10:731; PMID: 30510435]. ClinicoEcon 2018;10:389–98.
[18] Hotton AL, Weber KM, Hershow RC, Anastos K, Bacchetti P, Golub ET, et al. Prevalence and predictors of hospitalizations among HIV-Infected and at-risk HIV-uninfected women. J Acquir Immune Defic Syndr 2017;75(2):e27–35.
[19] Soong TR, Jung JJ, Kelen GD, Rothman RE, Burah A, Shahan JB, et al. Is inadequate human immunodeficiency virus care associated with increased ED and hospital utilization? A prospective study in human immunodeficiency virus-positive ED patients. Am J Emerg Med 2012;30(8):1466–73.
[20] Tolson C, Richey LE, Zhao Y, Korte JE, Brady K, Haynes L, et al. Association of substance use with hospitalization and virologic suppression in a southern academic HIV clinic. Am J Med Sci 2018;355(6):553–8.
[21] Speakman A, Rodger A, Phillips AN, Gilson R, Johnson M, Fisher M, et al. The 'Antiretrovirals, sexual transmission risk and attitudes' (ASTRA) study. Design, methods and participant characteristics. PLoS One 2013;8(10):e77230.
[22] Broadhead WE, Gehlbach SH, de Gruy FV, Kaplan BH. The duke-UNC functional social support questionnaire. Measurement of social support in family medicine patients. Med Care 1988;26(7):709–23.
[23] Mayfield D, McLeod G, Hall P. The CAGE questionnaire: validation of a new alcoholism screening instrument. Am J Psychiatry 1974;131(10):1121–3.
[24] Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med 2001;16(9):606–13.
[25] Spitzer RL, Kroenke K, Williams JB, Lowe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med 2006;166(10):1092–7.
[26] Public Health England (PHE). Trends in new HIV diagnoses and in people receiving HIV-related care in the United Kingdom: data to the end of December 2018. London; 2019.
[27] Prentice RL, Williams BJ, Peterson AV. On the regression analysis of multivariate failure time data. Biometrika 1981;68(2):373–9.
[28] Daskalopoulou M, Lampe FC, Sherr L, Phillips AN, Johnson MA, Gilson R, et al. Non-disclosure of HIV status and associations with psychological factors, ART non-adherence, and viral load non-suppression among people living with HIV in the UK. AIDS Behav 2017;21(1):184–95.
[29] Clemenzi-Allen A, Neuhaus J, Geng E, Sachdev D, Buchbinder S, Havlir D, et al. Housing instability results in increased acute care utilization in an urban HIV clinic cohort. Open Forum Infect 2019;6(5) ofz148.
[30] Burch LS, Smith CJ, Anderson J, Sherr L, Rodger AJ, O'Connell R, et al. Socioeconomic status and treatment outcomes for individuals with HIV on antiretroviral treatment in the UK: cross-sectional and longitudinal analyses. Lancet Public Health 2016;1(1):e26–36.
[31] Lampe F, Speakman A, Phillips A, Sherr L, Gilson R, Johnson M, et al. Depression and virological status among UK HIV outpatients: results from a multicentre study. HIV Med 2012;13 4-.
[32] Diderichsen F, Hallqvist J, Whitehead M. Differential vulnerability and susceptibility: how to make use of recent development in our understanding of mediation and interaction to tackle health inequalities. Int J Epidemiol 2019;48(1):268–74.
[33] Stockwell T, Zhao J, Panwar S, Roemer A, Naimi T, Chikritzhs T. Do "Moderate" drinkers have reduced mortality risk? A systematic review and meta-analysis of alcohol consumption and all-cause mortality. J Stud Alcohol Drugs 2016;77(2):185–98.
[34] McGowan JA, Sherr L, Rodger AJ, Fisher M, Miners A, Anderson J, et al. Age, time living with diagnosed HIV infection, and self-rated health. HIV Med 2017;18(2):89–103.
[35] Seng R, Mutuon P, Riou J, Duvivier C, Weiss L, Lelievre JD, et al. Hospitalization of HIV positive patients: significant demand affecting all hospital sectors. Rev Epidemiol Sante Publique 2018;66(1):7–17.
[36] Lazar R, Kersanske L, Xia Q, Daskalakis D, Braunstein SL. Hospitalization rates among people with HIV/AIDS in New York city, 2013. Clin Infect Dis 2017;65(3):469–76.
[37] Davy-Mendez T, Napravnik S, Hogan BC, Althoff KN, Gebo KA, Moore RD, et al. Hospitalization rates and causes among persons with HIV in the US and Canada, 2005-2015. J Infect Dis 2020;21:21.
[38] Bush K, Kivlahan DR, McDonell MB, Fihn SD, Bradley KA, Ambulatory Care Quality Improvement Project (ACQUIP). The AUDIT Alcohol Consumption Questions (AUDIT-C): An Effective Brief Screening Test for Problem Drinking. Arch Intern Med 1998;158(16):1789–95. doi: 10.1001/archinte.158.16.1789.