Hospital readmissions among adults living with and without HIV in the US: findings from the Nationwide Readmissions Database

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eClinicalMedicine 2024;73: 102690
Published Online xxx
https://doi.org/10.1016/j.eclinm.2024.102690

Summary

Background Thirty-day hospital readmission measures quality of care, but there are limited data among people with HIV (PWH) and people without HIV (PWoH) in the era of universal recommendation for antiretroviral therapy. We descriptively compared 30-day all-cause, unplanned readmission risk between PWH and PWoH.

Methods A retrospective cohort study was conducted using the 2019 Nationwide Readmissions Database (2019/01/01–2019/12/31), an all-payer database that represents all US hospitalizations. Index (initial) admissions and readmissions were determined using US Centers for Medicare & Medicaid Services definitions. Crude and age-adjusted risk ratios (aRR) comparing the 30-day all-cause, unplanned readmission risk between PWH to PWoH were estimated using random effect logistic regressions and predicted marginal estimates. Survey weights were applied to all analyses.

Findings We included 24,338,782 index admissions from 18,240,176 individuals. The median age was 52(IQR = 40–60) years for PWH and 61(IQR = 38–74) years for PWoH. The readmission risk was 20.9% for PWH and 12.2% for PWoH (age-adjusted-RR:1.88 [95%CI = 1.84–1.92]). Stratified by age and sex, young female (age 18–29 and 30–39 years) PWH had a higher readmission risk than young female PWoH (aRR = 3.50 [95%CI = 3.11–3.88] and aRR = 4.00 [95%CI = 3.67–4.32], respectively). While the readmission risk increased with age among PWoH, the readmission risk was persistently high across all age groups among PWH. The readmission risk exceeded 30% for PWH admitted for hypertensive heart disease, heart failure, and chronic kidney disease.

Interpretation PWH have a disproportionately higher risk of readmission than PWoH, which is concerning given the aging profile of PWH. More efforts are needed to address readmissions among PWH.

Funding US National Institutes of Health.

Keywords: People with HIV; People without HIV; Readmissions; Comorbidities; Nationwide

Introduction

Hospital readmission is a widely-followed quality of care indicator used by payers.[1] A 30-day window following initial hospital discharge is generally considered a clinically meaningful timeframe to reduce preventable readmissions. More than 20% of 30-day readmissions may be prevented with improved inpatient, ambulatory and home-based interventions, potentially saving billions of dollars annually.[2] Since the implementation of the Affordable Care Act in the US, which established the Hospital Readmissions Reduction Program in 2012, the US Centers for Medicare & Medicaid Services (CMS)

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Research in context

Evidence before this study

We used the term "HIV AND (readmi* OR rehospital*)" to search PubMed for studies on HIV and hospital readmissions that were published before May 16, 2024, without language restrictions. Thirty-day hospital readmission is a widely-followed metric of quality of care. Most relevant studies on readmission among people with HIV (PWH) were conducted in the early 2010s, when antiretroviral therapy (ART) was not widely used and immune compromise was common. Those studies were often conducted with small sample sizes, and the estimated readmission risk ranged from 3% to 53% in developing countries and 9%–27% in developed countries. Different definitions of readmission and varying study populations preclude direct comparisons across those studies. The identified factors associated with an increased risk of readmission among PWH included low CD4+ T cell counts, extended hospital stays, patient directed discharges, and insufficient post-discharge care. There has been limited information on the role of socio-demographic factors and comorbidities on readmission risk among PWH. A US regional study in 2011 found that PWH had 1.5 times higher odds for readmission than people without HIV (PWoH). However, it remains unclear which subgroups of PWH have high readmission burden and how their risk of readmission compares to PWoH, particularly in the era of universal recommendations for ART in the US.

Added value of this study

This is among the first US nationwide studies on readmission risk among PWH. The large population size of more than 140,000 hospitalizations among PWH allowed granular characterization of the epidemiology of readmissions among PWH in the US. Unlike most prior studies, we used the definition of readmission from the US Centers for Medicare & Medicaid Services, and excluded planned readmissions. Our study is also among the first to comparatively characterize the risk of readmission between PWH and PWoH in the era of universal recommendation for ART. The results suggest that, even with high ART use in the US, PWH still had an excessive burden of readmission, including when stratified by all sociodemographic and diagnostic groups. Notably, we found several subgroups that may need special attention. Young female PWH (age < 40 years) had especially higher readmission risk than young female PWoH. Chronic heart and kidney diseases were also associated with high readmission risk among PWH.

Implications of all the available evidence

Even with high ART use in the US, the risk of readmission among PWH remains disproportionally higher than PWoH. The disparity was especially large among young females, who are usually considered as a low-risk group among PWoH. PWH hospitalized due to common non-HIV comorbidities had particularly high readmission risk. These data collectively highlight the inequities that PWH continue to face. With the aging of PWH, the burden of chronic comorbidities among PWH may increase and special care are needed for PWH to reduce potentially preventable readmissions. Future studies are needed to evaluate the preventability for readmissions.

has imposed financial penalties for hospitals whose Medicare patients have higher than expected 30-day all-cause unplanned readmissions following discharge from an initial (index) hospitalization.[3] From 2010 to 2016, hospitalizations of only Medicare patients had a decrease in the 30-day all-cause readmission risk (planned or unplanned) from 18.3% to 17.1%, while those uninsured had an increasing risk from 10.4% to 11.8%.[4] After 2016, hospitalizations paid by all payer groups had consistently similar readmission risk in the US.[5]

In 2019, there were over 1 million people living with HIV (PWH) in the US.[6] Hospitalizations among PWH have continued to decline since the introduction of antiretroviral therapy (ART), but gender, racial, and ethnic disparities have persisted.[7] PWH have historically been more likely to be readmitted than people without HIV (PWoH).[8] A study in 2011 suggested that some readmissions among PWH were potentially preventable and both clinical and social efforts were needed.[9] Studies from the early 2010s on the overall 30-day all-cause readmission risk among PWH in the US generated estimates between 19.3% and 25.2%.[8] One study of six clinical HIV cohorts in North America found that the 30-day all-cause readmission risk for PWH decreased from 20.1% to 16.3% between 2005 and 2018.[10] The readmission risk for PWH in developing countries ranged from 3.4% to 52.9%, though the definitions of readmission and the study populations were different across studies.[11] Most previous readmissions studies were conducted in small samples among PWH, have not included PWoH as a comparator and used data collected prior to 2016—the first year widespread implementation of universal recommendation of ART in the US—when immune compromise was more common.[12] There are limited nationwide data characterizing the current readmission risk among PWH and how it compares to PWoH in a setting of relatively high ART coverage.

In this descriptive epidemiologic study, we characterize the contemporary risk of all-cause, unplanned, 30-day hospital readmission among adults living with and without HIV in the US. Understanding the descriptive epidemiology of readmissions among PWH and PWoH is needed to identify disparities in readmission risk and determine which populations require increased efforts

to reduce readmissions. Indeed, the COVID-19 pandemic disrupted care to such a degree that the CMS excluded the first half of 2020 data from evaluating hospital performance.[13] As the clinical care in the US has gradually shifted back to pre-pandemic circumstances, it is important to understand hospital readmissions under standard conditions. Thus, we used the 2019 Nationwide Readmissions Database (NRD) to characterize hospital readmissions without the interference of the pandemic and provide evidence needed to target readmission reduction programs.

Methods

Data source

We analyzed data from the 2019 NRD (January 1, 2019 to December 31, 2019), an all-payer, nationwide database sponsored by the Agency for Healthcare Research and Quality and developed for the Healthcare Cost and Utilization Project (HCUP).[14] The NRD is the largest publicly available readmission database in the US, which was constructed from the State Inpatient Databases with verified patient linkage IDs to track patients across hospitals within a state. However, the NRD does not track patients across states or calendar years. Each record in the NRD represents a single hospitalization. In-hospital transfers or same-day readmissions were collapsed into one single combined record in NRD. Each record includes up to 40 International Classification of Diseases 10th Revision Clinical Modification (ICD-10-CM) diagnosis codes and up to 25 ICD-10 Procedure Coding System (ICD-10-PCS) procedure codes.

The NRD was developed with a stratified, single-stage cluster sampling survey design. All discharges from all community hospitals (i.e., all hospitals but not federal hospitals, long-term acute care or rehabilitation facilities) in participating states, were included in the sample. Post-stratification weights to generate national estimates of the US general population were calculated by HCUP using hospital-level (census region, urban/rural location, teaching status, bed size, type of ownership) and patient-level (age, sex) characteristics.

The 2019 NRD included approximately 18 million discharges (unweighted) for patients with or without repeat hospitalizations from 30 US participating states (Supplemental Fig. S1). States with different Ending HIV Epidemic (EHE) priority levels had similar probability of inclusion in the 2019 NRD, which included 4 (7 total, 57%) Ending HIV Epidemic (EHE) priority states, 12 (20 total, 60%) states with EHE priority counties and 14 (24 total, 58%) non EHE priority states. However, state identifiers were not available in the database. Weighted, the NRD provides estimates for all US community hospitalizations (~35 million).

The NRD is a de-identified, publicly-available database. The study was deemed exempt from review by the Johns Hopkins Institutional Review Board and was conducted in accordance with the HCUP data use agreement.

Study population

The unit of observation was a hospitalization (i.e., a row in the database) as provided by HCUP. The unit of analysis was an eligible index admission as defined by the hospital-wide readmission measures from the CMS.[15] Briefly, we included all remaining hospital admissions as index admissions after implementing the following exclusion criteria: age < 18 years; hospitalizations for primary psychiatric diagnoses, rehabilitation, or medical treatment of cancer; and discharges ending in death, patient-directed discharges or hospitalizations with a discharge date in December (i.e., without the 30-day post discharge follow up window). A single patient could contribute one or multiple index admissions to the analysis.

Primary outcome

The primary outcome was the risk of 30-day, all-cause, unplanned readmission; Readmission risk was the proportion of all eligible index admissions that resulted in readmission. The observation period ranged from the discharge date of the index admission to 30-days post-discharge.

We focused on unplanned readmissions to be consistent with CMS protocol (i.e., planned readmissions were considered not have the outcome).[15] Certain procedures (i.e., bone marrow and organ transplant surgery) and primary diagnoses (i.e., chemotherapy, radiotherapy, rehabilitation care, fitting of prostheses, and adjustment of devices) were always considered planned. We also treated hospitalizations as planned if they had a potentially planned ICD-10-PCS procedure code and a primary ICD-10-CM diagnosis code of a non-acute condition (Supplemental Fig. S2).

If a patient had multiple readmissions within a single 30-day observation period, we only considered the first unplanned hospitalization during the 30-day period as a readmission. If the first hospitalization after the index admission was planned, any subsequent unplanned hospitalizations were not considered a readmission for that index admission, since the subsequent records could be related to the planned hospitalization.

A planned or unplanned readmission could also serve as an index admission if it met all the inclusion criteria for an index admission. Hereafter, the terms "readmissions" or "readmitted" refer to 30-day all-cause unplanned readmissions.

Assessment of variables

The independent variable of interest was patient HIV status. PWH were identified using Clinical Classifications Software Refined v2022.1(CCSR) for ICD-10-CM

code developed by HCUP.[16] We used the CCSR code INF006 (equivalent to ICD-10-CM codes B20, B9735, O98711, O98712, O98713, O98719, O9872, O9873, Z21) to define PWH. If any hospitalizations for a given patient indicated HIV infection, no matter if it was an incident or chronic infection, we assumed this person had HIV for all hospitalizations. The remaining hospitalizations excluding PWH were considered PWoH.

We defined the primary reason for index admissions using the first ranked ICD-10-CM code. However, similar to a previous validation study, if the top-ranked ICD-10-CM code was HIV or chronic hepatitis C virus infection (ICD-10-CM code B182), then we assigned the next highest-ranked other diagnosis as the primary reason for the index admission.[17] Consistent with multiple prior studies, we then used the CCSR to group the primary reason for index admission into clinically meaningful non-mutually exclusive categories.[8,10,17] We also created a separate category of AIDS-defining illnesses according to the U.S. Centers for Disease Control and Prevention and the final list of ICD-10-CM codes to define this category was confirmed by three clinicians (Supplemental Table S1).[18] We additionally created a separate category of non-AIDS-defining infections (i.e., infectious or parasitic diseases that were not AIDS-defining illnesses) and the ICD-10-CM codes are available upon request. Lastly, we excluded the code for AIDS-defining illness and non-AIDS-defining infections from all the other CCSR groups to allow these two categories to be mutually exclusive of the other categories.

Other variables of interest in the NRD included patient characteristics (age, sex, zip code-level median household income, clinical severity of illness, and primary payer) and hospital characteristics (bed size, teaching status, and rural or urban designation) (refer to patient and hospital characteristics hereafter). The All Patient Refined Diagnosis Related Groups (APRDRG) severity provided by HCUP were used to classify clinical severity of illness.[19] We used primary diagnosis of CCSR category Pregnancy, Childbirth and the Puerperium to define pregnancy status. Of note, data on race, ethnicity, or US state were not available in the NRD.

Statistical analysis

We comparatively described the distribution of 30-day all-cause unplanned readmission risk among adult PWoH and PWH in 2019 using a descriptive epidemiologic framework[20]; the purpose of the comparison by HIV status was not intended for causal inferences.

We assessed the association of HIV status with readmission risk using weighted three-level (hospital, patient, index admission level) random effect logistic regressions. Risk ratios (RR) were further estimated from average marginal estimates that were calculated using the *margins* command with Delta-method standard errors in Stata/MP, version 15 (Statacorp, College Station, TX). We estimated the association of HIV status with readmission risk overall and within strata of all the previously-mentioned patient and hospital characteristics (e.g., age, sex, zip code-level median household income, etc). We additionally estimated readmission risk within the strata of primary reason for index admission using the modified CCSR categories. We further evaluated the readmission risk by more specific CCSR subcategories that caused top two highest number of readmissions among PWH. For all analyses, we estimated age-adjusted risk ratios (aRR) treating age as a nuisance variable (i.e., a strong clinically-relevant determinant of readmission that we expected to differ substantially by HIV status).[20]

As a secondary analysis, a weighted multivariate random effect logistic regression including HIV status and all patient and hospital characteristics was conducted to assess if the association of HIV status with readmission was independent of all patient and hospital characteristics.

All previously mentioned analyses were also conducted further stratified by sex. As women hospitalized due to pregnancy had low readmission risk and lower proportion of women with HIV were pregnant, we additionally conducted sensitivity analyses excluding hospitalizations due to pregnancy, delivery or puerperium (i.e., pregnant females).

Seven percent of the patients either visited multiple hospitals or experienced a one-year increase in age within NRD 2019, leading to inconsistent weights within individuals and a lack of hierarchical structure between hospitals and patients. As methods for crossed random effect regressions that accommodate the survey design are not validated, we handled the data from these 7% of patients as distinct individuals whenever the survey weight changed. This involved creating a new study ID by combining the original study ID with the hospital ID and the weights assigned to these patients.

To increase comparability with previously published studies, we conducted a sensitivity analysis restricting the analysis to each patient's first index admission (i.e., without repeated measures).

Unless specified, all analyses accounted for the complex survey design and survey weights to generate nationwide estimates. Variances were estimated using Taylor series linearization. The prevalence of missingness was under 2% for all variables and available-case methods (i.e., including all observations with available data on the variables of interest in each statistical test) were used to handle missing values. Data analyses were performed in Stata and R version 4.2 (R-Core Team, Vienna, Austria).

Role of funding

The funding sources were not involved in the study design, data analysis, interpretation of findings, or the decision to submit this manuscript for publication.

Results

Study population

The NRD included 18,132,856 unweighted observations, representing 35,399,480 weighted hospitalizations in the US (all the numbers hereafter are weighted) (Fig. 1A–B). After applying exclusion criteria, the study included 24,338,782 index admissions occurring among 18,240,176 patients. PWH comprised 89,820 (0.5%) of the patients and 144,672 (0.6%) of the index admissions.

Characteristics of first recorded (baseline) index admissions

At first recorded index admissions, the median age was 52 (IQR = 40–60) years for PWH and 61 (IQR = 38–74) years for PWoH (Table 1). The age distribution between PWH and PWoH were substantially different (Supplemental Fig. S3). The majority of PWH included were male (68.2%), while the majority of PWoH were female (60.6%) (Table 1). PWH were more likely to reside

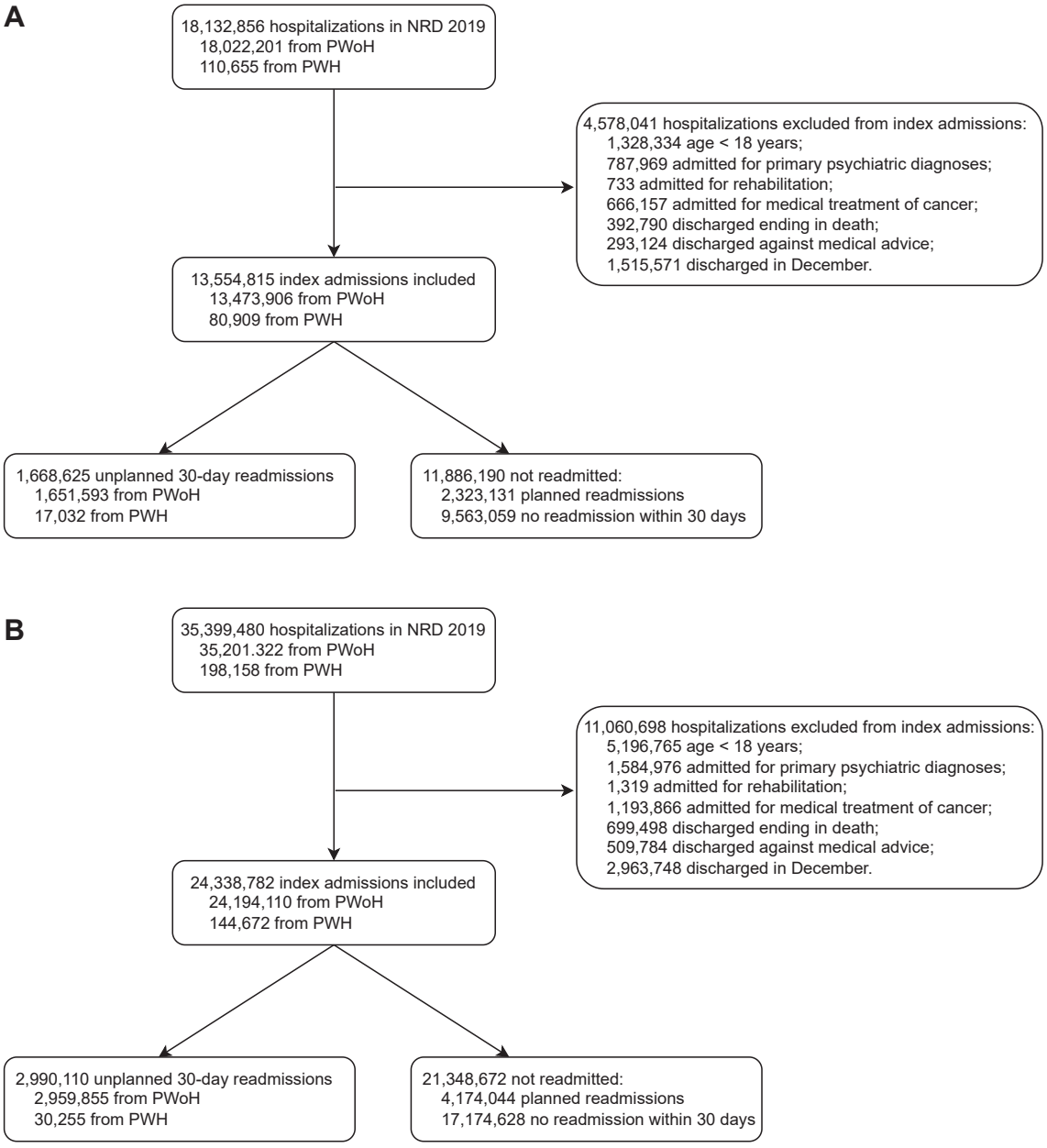

Fig. 1: Flowchart of the index admissions and readmissions with (A) unweighted sample sizes and (B) weighted population sizes. Note: One person may contribute to one or more index hospitalizations in the study population. Among the index admissions excluded, the subcategories may overlap so the excluded numbers exceed the total.

	Overall N = 18,240,176	PWoH N = 18,150,357	PWH N = 89,820
Age, years, n (%)			
18–29	2,441,919 (13.4)	2,434,600 (13.4)	7319 (8.1)
30–39	2,480,058 (13.6)	2,465,417 (13.6)	14,641 (16.3)
40–49	1,521,729 (8.3)	1,504,998 (8.3)	16,731 (18.6)
50–59	2,385,466 (13.1)	2,357,927 (13.0)	27,539 (30.7)
60–69	3,268,304 (17.9)	3,250,585 (17.9)	17,718 (19.7)
70–79	3,213,222 (17.6)	3,208,334 (17.7)	4888 (5.4)
≥80	2,929,479 (16.1)	2,928,496 (16.1)	982 (1.1)
Sex, n (%)			
Male	7,212,537 (39.5)	7,151,266 (39.4)	61,271 (68.2)
Female	11,027,639 (60.5)	10,999,091 (60.6)	28,548 (31.8)
Non-pregnant	7,736,538 (42.4)	7,710,885 (42.5)	25,653 (28.6)
Pregnant	3,291,102 (18.0)	3,288,207 (18.1)	2895 (3.2)
Zip code median household income, n (%)			
$1–$47999	5,255,065 (29.1)	5,212,198 (29.0)	42,867 (48.4)
$48000–$60999	4,801,506 (26.6)	4,780,384 (26.6)	21,121 (23.8)
$61000–$81999	4,497,728 (24.9)	4,481,705 (25.0)	16,023 (18.1)
≥$82000	3,477,586 (19.3)	3,468,999 (19.3)	8586 (9.7)
Primary payer, n (%)			
Medicare	8,350,350 (45.8)	8,317,827 (45.9)	32,523 (36.3)
Medicaid	3,145,489 (17.3)	3,116,950 (17.2)	28,540 (31.8)
Private insurance	5,414,414 (29.7)	5,397,016 (29.8)	17,397 (19.4)
Self-pay	670,757 (3.7)	663,424 (3.7)	7333 (8.2)
No charge	79,883 (0.4)	78,896 (0.4)	987 (1.1)
Other	556,916 (3.1)	554,075 (3.1)	2841 (3.2)
APRDRG Severity of Illness, n (%)			
Minor loss of function	6,211,346 (34.1)	6,198,259 (34.2)	13,087 (14.6)
Moderate loss of function	7,362,494 (40.4)	7,323,787 (40.4)	38,707 (43.1)
Major loss of function	3,497,687 (19.2)	3,470,431 (19.1)	27,256 (30.3)
Extreme loss of function	1,167,629 (6.4)	1,156,861 (6.4)	10,767 (12.0)
Bed size of hospital, n (%)			
Small	3,503,205 (19.2)	3,489,918 (19.2)	13,287 (14.8)
Medium	5,030,040 (27.6)	5,006,612 (27.6)	23,428 (26.1)
Large	9,706,931 (53.2)	9,653,827 (53.2)	53,105 (59.1)
Teaching status of hospitals, n (%)			
Metropolitan non-teaching	3,381,179 (18.5)	3,368,559 (18.6)	12,620 (14.1)
Metropolitan teaching	13,174,150 (72.2)	13,100,348 (72.2)	73,802 (82.2)
Non-metropolitan hospital	1,684,847 (9.2)	1681,450 (9.3)	3398 (3.8)
Hospital urban-rural designation, n (%)			
Large metropolitan areas ≥1 million residents	9,816,269 (53.8)	9,754,730 (53.7)	61,539 (68.5)
Small metropolitan areas ≥1 million residents	6,739,060 (36.9)	6,714,177 (37.0)	24,883 (27.7)
Micropolitan areas	1,255,388 (6.9)	1,252,621 (6.9)	2767 (3.1)
Non-urban	429,459 (2.4)	428,829 (2.4)	631 (0.7)

PWH: people with HIV; PWoH: people without HIV; APRDRG: all patient refined diagnosis related groups. Note: data were presented in n (column %) and all numbers were weighted estimates. Values in subcategories may not add to overall due to rounding. Pregnancy state was identified using primary diagnosis of Clinical Classifications Software Refined (CCSR) category of Pregnancy, Childbirth and the Puerperium. The All Patient Refined Diagnosis Related Groups (APRDRG) severity provided by HCUP were used to classify clinical severity of illness as defined by 3M. https://hcup-us.ahrq.gov/db/nation/nis/APR-DRGsV20MethodologyOverviewandBibliography.pdf. Different states may have different definition in hospital bed size. A detailed definition is provided by HCUP. https://hcup-us.ahrq.gov/db/vars/hosp_bedsize/nrdnote.jsp. Other primary payer includes Worker's Compensation, CHAMPUS, CHAMPVA, Title V, and other government programs. A person only contributed to one index admission in this table.

Table 1: **Characteristics of the first recorded index admission of the study population.**

in lower-income zip code areas, be covered by Medicaid, and be admitted to metropolitan teaching hospitals. The median length of stay was 3 [IQR = 2–6] days among PWH and 3 [IQR = 2–5] days among PWoH; PWH (49.3%) were more likely to be hospitalized ≥4 days than PWoH (37.7%). The median number of diagnoses

(excluding HIV diagnoses) was 13 [IQR = 9–18] diagnoses among PWH and 11 [IQR = 6–18] diagnoses among PWoH. Lower proportion of PWH were pregnant female than PWoH (3.2% vs. 18.1%). Non-pregnant female PWH, compared to either non-pregnant female PWoH or male PWH, were more likely to reside in lowest-income areas and less likely to be covered by private insurance (Supplemental Table S2).

Readmission risk by patient and hospital characteristics for all index admissions

Overall, 30,255 (20.9%) hospitalizations from PWH and 2,959,855 (12.2%) from PWoH resulted in readmission within 30 days post discharge (RR = 1.70 [95% CI = 1.66–1.73]) (Fig. 2). After adjusting for age, PWH had a greater risk of readmission than PWoH (age-adjusted RR [aRR] = 1.88 [95%CI = 1.84–1.92]). In the multivariate model that included all patient and hospital-level characteristics, HIV status was still independently associated with readmission (fully-adjusted RR = 1.33 [95%CI = 1.30–1.36]) (Supplemental Table S3). This independent association between HIV status and readmission risk was observed among males and females in sex-stratified multivariate models. Other factors that were independently associated with readmission risk in the entire study population (both PWoH and PWH) included higher severity of illness, male sex, and residing in lower income area.

The readmission risk was significantly higher among PWH than PWoH for all subgroups examined, particularly those 18–29 (aRR = 3.21 [95%CI = 2.98–3.43]) and 30–39 years (aRR = 2.93 [95%CI = 2.80–3.07]), females (aRR = 2.18 [95%CI = 2.12–2.25]), and with lowest level of severity of illness (aRR = 2.23 [95%CI = 2.11–2.34]) (Fig. 2). With increasing age, the risk of readmission increased from 5.9% for PWoH aged 18–29 years to 14.7% for PWoH aged ≥ 80 years. However, among PWH, all age groups had similar high readmission risk. Stratified by sex, PWH still had elevated risk of readmission than PWoH for all subgroups (Supplemental Tables S4 and S5). Notably, stratified by both age and sex, the disparity in readmission risk between PWH and PWoH was especially large among young females (<40 years), and the findings persisted even after excluding females admitted due to pregnancy (Fig. 3). In the sensitivity analysis that excluded pregnant females, the overall findings qualitatively remained similar, though the effect sizes generally became smaller (Supplemental Fig. S4).

Among PWH, females (vs. males), those with lower income zip code areas (vs. higher income zip codes), paid by Medicaid (vs. private insurance), higher level of severity (vs. low severity level), and treated in hospitals in large cities (vs. rural hospitals) had higher readmission risk (Supplemental Table S6). Similar patterns were found among PWoH, except by sex. Among PWH, non-pregnant females were more likely to be readmitted compared to males (aRR = 1.09 [95%CI = 1.06–1.13]), but among PWoH, non-pregnant females had significantly lower readmission risk than males (aRR = 0.92 [95% CI = 0.91–0.92]).

Causes of all index admissions and readmissions

The top causes of index admissions were non-AIDS defining infection (19.3% PWoH and 30.5% PWH) and circulatory diseases (20.2% PWoH and 15.5% PWH) (Supplemental Table S7). Among PWH, 4678 (3.2%) index admissions were caused by AIDS defining illnesses. The percentages of index admission/readmission pairs which had primary reasons for admission within the same diagnostic category were 41.7% for PWoH and 37.4% for PWH, respectively. The most frequent overall primary diagnostic categories for readmissions were non-AIDS defining infection (23.1% PWoH and 26.8% PWH) and circulatory disease (21.9% PWoH and 17.1% PWH).

Readmission risk by primary reason of all index admissions

Overall, the readmission risk for PWoH was 12.2% and 20.9% for PWH. The top three primary diagnosis categories of index admissions that had the highest readmission risk for PWoH were blood diseases (23.5%), AIDS defining illnesses (22.2%), and respiratory diseases (19.3%), while for PWH were blood (30.2%), genitourinary diseases (27.2%), and respiratory diseases (26.1%) (Fig. 4). AIDS-defining illness also resulted in high readmission risk (25.1%) among PWH. Compared to PWoH, PWH still had higher readmissions risk for all index admission primary diagnostic groups (including both infectious and non-infectious causes). Readmission risk was particularly high (risk > 30%, number of readmissions > 1000) among PWH admitted due to fluid and electrolyte disorders (primarily hyperkalemia and fluid overload), hypertension complications (primarily hypertensive heart disease), heart failure, and chronic kidney diseases (Supplemental Fig. S5). Stratified by sex, the magnitude of the elevated readmission risk between PWH and PWoH was larger among females than males for most diagnoses (Supplemental Tables S8 and S9). The readmission risk for female PWH and male PWH hospitalized due to AIDS defining illness was 22.7% and 26.2%, respectively.

Sensitivity analysis

In the main analysis, PWH had a median number of 2 readmissions (IQR = 1–4) and PWoH had a median number of 1 readmission (IQR = 1–3). In the sensitivity analysis that included only the first recorded index admission, the readmission risk was lower for both PWoH (5.9%) and PWH (10.6%) as compared to the main analysis. However, the risk ratios for readmission by HIV status were similar to the main analysis (Supplemental Figs. S6 and S7).

Characteristics	PWoH Readmission, n(%)	PWH Readmission, n(%)	RR (95%CI)	aRR (95%CI)
Overall	2959855 (12.2)	30255 (20.9)	1.70 (1.66, 1.73)	1.88 (1.84, 1.92)
Age				
18-29	162544 (5.9)	2054 (19.3)	3.19 (2.97, 3.42)	3.21 (2.98, 3.43)
30-39	211063 (7.4)	4960 (21.7)	2.99 (2.85, 3.13)	2.93 (2.80, 3.07)
40-49	241739 (12.1)	5869 (21.5)	1.81 (1.73, 1.88)	1.80 (1.73, 1.87)
50-59	451096 (13.8)	9202 (20.6)	1.53 (1.48, 1.57)	1.53 (1.48, 1.58)
60-69	630218 (13.8)	6086 (20.7)	1.50 (1.45, 1.56)	1.50 (1.45, 1.56)
70-79	643441 (14.2)	1666 (20.4)	1.42 (1.33, 1.51)	1.43 (1.34, 1.52)
≥80	619753 (14.7)	418 (24.3)	1.63 (1.47, 1.80)	1.62 (1.45, 1.80)
Sex				
Male	1426020 (14.2)	19937 (20.5)	1.43 (1.40, 1.46)	1.52 (1.49, 1.56)
Female	1533835 (10.8)	10318 (21.7)	1.97 (1.91, 2.03)	2.18 (2.12, 2.25)
Non-pregnant	1422823 (13.3)	10083 (22.8)	1.69 (1.64, 1.74)	1.79 (1.73, 1.84)
Pregnant	111012 (3.2)	235 (7.0)	2.12 (1.75, 2.50)	2.12 (1.75, 2.48)
Median Zip code household income				
$1-$47999	974949 (13.6)	15830 (22.3)	1.63 (1.59, 1.68)	1.76 (1.72, 1.81)
$48000-$60999	780589 (12.2)	6850 (20.4)	1.66 (1.60, 1.72)	1.84 (1.78, 1.90)
$61000-$81999	677217 (11.5)	4758 (19.2)	1.66 (1.60, 1.72)	1.86 (1.79, 1.92)
≥$82000	492227 (11.0)	2427 (18.4)	1.68 (1.58, 1.77)	1.92 (1.82, 2.02)
Primary payer				
Medicare	1858554 (15.3)	12711 (22.4)	1.43 (1.40, 1.47)	1.32 (1.29, 1.35)
Medicaid	483943 (11.9)	11397 (23.5)	2.03 (1.96, 2.09)	1.67 (1.63, 1.72)
Private insurance	458494 (7.2)	3382 (14.3)	1.98 (1.89, 2.08)	1.88 (1.80, 1.96)
Self-pay	79951 (9.8)	1735 (17.1)	1.78 (1.67, 1.89)	1.79 (1.68, 1.90)
No charge	12131 (11.9)	312 (21.8)	1.84 (1.52, 2.16)	1.84 (1.53, 2.14)
Other	63960 (9.3)	645 (16.1)	1.79 (1.61, 1.97)	1.87 (1.68, 2.05)
APRDRG Severity of Illness				
Minor loss of function	375413 (5.3)	1921 (11.2)	2.14 (2.02, 2.26)	2.23 (2.11, 2.34)
Moderate loss of function	1129327 (11.6)	10175 (17.5)	1.50 (1.46, 1.54)	1.63 (1.59, 1.68)
Major loss of function	1062128 (19.3)	13237 (26.4)	1.35 (1.32, 1.38)	1.40 (1.37, 1.43)
Extreme loss of function	392836 (21.1)	4922 (25.7)	1.21 (1.17, 1.25)	1.21 (1.17, 1.25)
Bed size of hospital				
Small	539878 (11.7)	4058 (19.8)	1.68 (1.60, 1.77)	1.90 (1.81, 1.99)
Medium	809032 (12.2)	8060 (21.4)	1.74 (1.68, 1.80)	1.93 (1.87, 2.00)
Large	1610945 (12.4)	18137 (21.0)	1.68 (1.63, 1.73)	1.84 (1.79, 1.89)
Teaching status of hospital				
Metropolitan non-teaching	546382 (12.2)	4476 (22.0)	1.80 (1.72, 1.88)	2.03 (1.94, 2.12)
Metropolitan teaching	2152685 (12.3)	24701 (20.8)	1.68 (1.64, 1.72)	1.84 (1.80, 1.88)
Non-metropolitan hospital	260788 (11.8)	1077 (20.2)	1.71 (1.56, 1.87)	1.97 (1.80, 2.13)
Hospital urban-rural designation				
Large metropolitan areas >= 1 million residents	1633319 (12.5)	21315 (21.3)	1.71 (1.66, 1.76)	1.88 (1.82, 1.93)
Small metropolitan areas >= 1 million residents	1065748 (12.0)	7863 (20.0)	1.63 (1.57, 1.68)	1.81 (1.75, 1.87)
Micropolitan areas	194290 (11.8)	891 (20.5)	1.73 (1.56, 1.90)	1.97 (1.79, 2.15)
Non-urban	66498 (11.7)	187 (18.8)	1.65 (1.28, 2.02)	1.91 (1.51, 2.32)

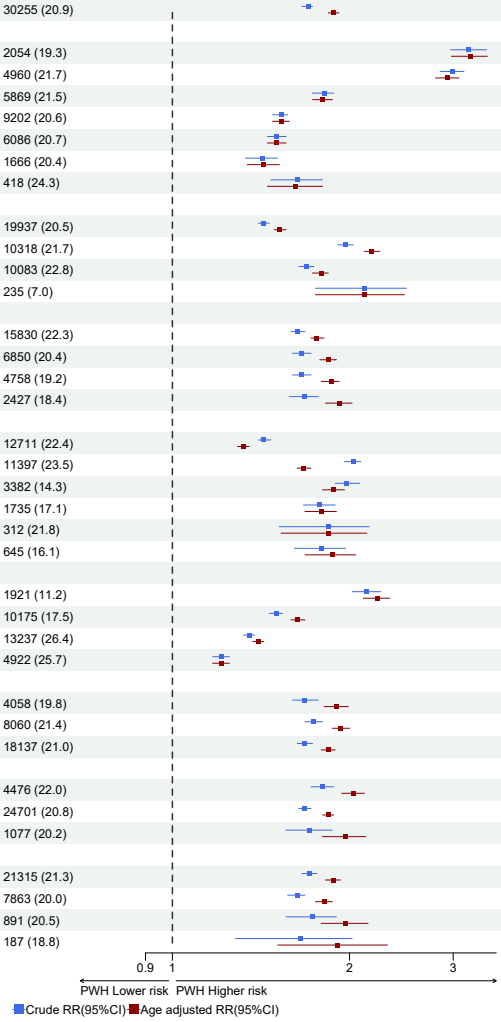

Fig. 2: Comparison of the 30-day all-cause unplanned readmission risk between people with and without HIV overall and stratified by index admission characteristics. Abbreviations: PWH: people with HIV; PWoH: people without HIV; RR: risk ratio; aRR: age adjusted risk ratio; APRDRG: all patient refined diagnosis related groups. Note: number of readmissions and readmission risk (%) among index admissions were presented and all numbers were weighted estimates. RR and aRR were estimated using predicted marginal estimates (margins command in Stata) after random effect logistic regressions, and PWoH was the reference group. Pregnancy state was identified using primary diagnosis of Clinical Classifications Software Refined (CCSR) category of Pregnancy, Childbirth and the Puerperium. Other primary payer includes Worker's Compensation, CHAMPUS, CHAMPVA, Title V, and other government programs. The All Patient Refined Diagnosis Related Groups (APRDRG) severity provided by HCUP were used to classify clinical severity of illness as defined by 3M. https://hcup-us.ahrq.gov/db/nation/nis/APR-DRGsV20MethodologyOverviewandBibliography.pdf. Different states may have different definitions of hospital bed size. A detailed definition is provided by HCUP. https://hcup-us.ahrq.gov/db/vars/hosp_bedsize/nrdnote.jsp. A person may contribute to one or more index admissions.

Discussion

In the US, PWH had significantly higher readmission risk than PWoH overall and for all sociodemographic, clinical, and diagnostic subgroups examined. Notably, young PWH had especially higher readmission risk than young PWoH and the excess readmission risk for PWH was greater among females than males. PWH admitted due to acute exacerbations or overall worsening of chronic heart and kidney diseases had a particularly high risk of readmission. Our study suggests that in a developed country with generally high ART use, PWH still have excessive readmissions compared to PWoH, and non-HIV-related chronic conditions and infections need special attention in hospital care.

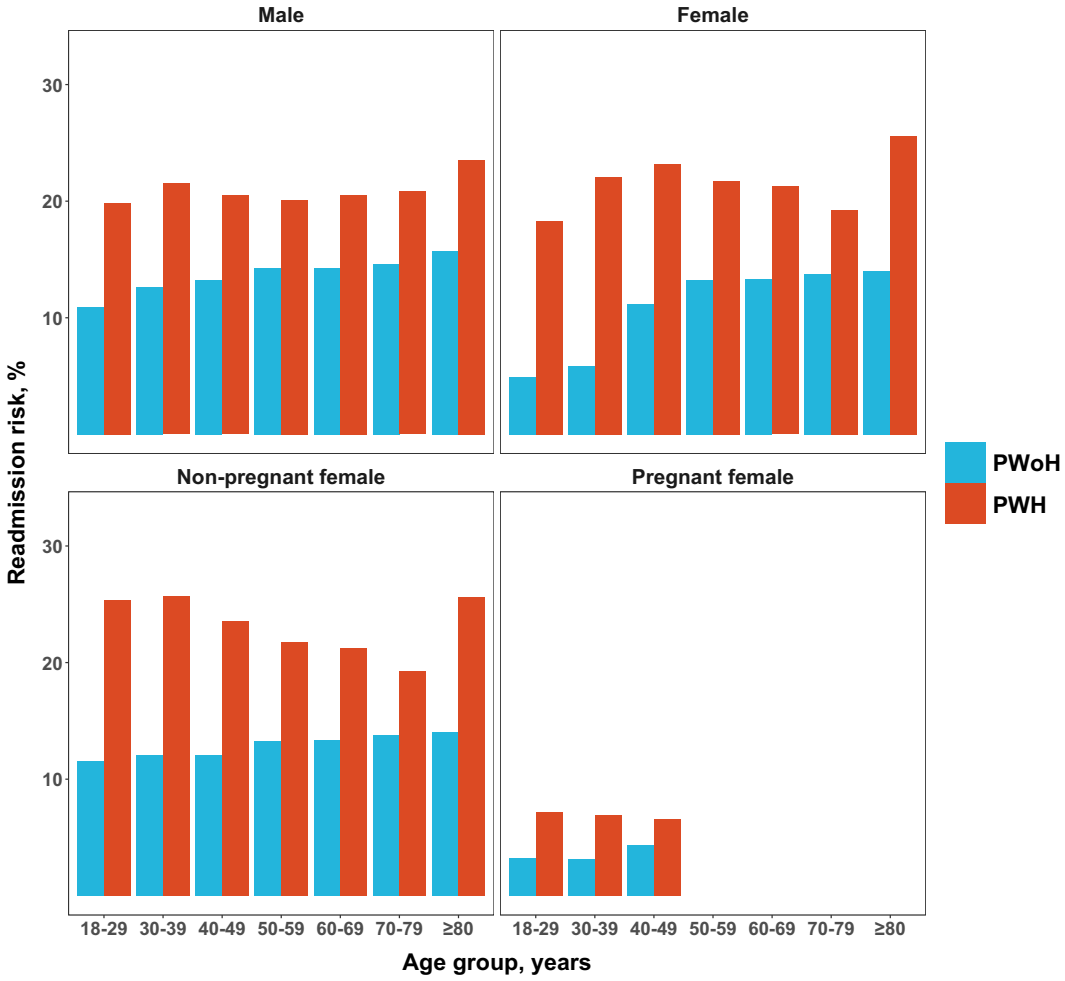

Fig. 3: Comparison of 30-day all-cause unplanned readmission risk between people with and without HIV stratified by age and sex. Abbreviations: PWoH: people without HIV; PWH: people with HIV. Note: All numbers were weighted estimates. Proportions were tabulated without accounting for repeated measures. Pregnancy state was identified using primary diagnosis of Clinical Classifications Software Refined (CCSR) category of Pregnancy, Childbirth and the Puerperium. A person may contribute to one or more index admissions.

With high ART use, HIV has become a chronic disease, and PWH have a life expectancy similar to PWoH.[21] Despite these advances in HIV care, PWH still have higher readmission risk than PWoH, even adjusting for sociodemographic and clinical factors or stratified by initial hospitalization diagnosis. This is likely due to complications of HIV including inflammation and comorbidities, as well as social factors that are more common among PWH including substance use and negative social and structural determinants of health (e.g., stigma). Additionally, our study indicates that PWH living in low income areas had higher readmission risk. Among a cohort population of PWH in care with 83% HIV viral suppression, the readmission risk was 16.3% in 2018.[10] However, 66% PWH had viral suppression in the US in 2019,[6] and the estimated nationwide readmission risk for PWH in our study was 20.9%. The differences in viral suppression and readmission risk highlight the importance of maintaining viral suppression to reduce readmission burden among PWH.

HCUP estimated that the readmission risk was 14.0% for the general population in 2019 without excluding planned readmissions.[5] Our estimates for unplanned readmission risk among PWoH was 12.2%, which is consistent. The readmission risk was only 5.9% for PWoH and 10.6% for PWH in our study if we only included the first index admission for each patient, which suggests that people who were readmitted were more likely to be repeatedly readmitted and they may need special attention. This also highlighted that policy makers and researchers should be cautious about the

Primary diagnosis of index admission	PWoH Readmission, n(%)	PWH Readmission, n(%)	RR (95%CI)	aRR (95%CI)
AIDS defining illness	11691 (22.2)	1176 (25.1)	1.11 (1.04, 1.19)	1.11 (1.03, 1.18)
Non-AIDS defining infection	697342 (14.9)	8364 (19.0)	1.27 (1.23, 1.30)	1.43 (1.39, 1.48)
Neoplasms	19299 (8.3)	204 (21.2)	2.51 (2.19, 2.83)	2.71 (2.37, 3.05)
Diseases of the Blood, Blood Forming Organs, and the Immune Mechanism	79202 (23.5)	881 (30.2)	1.33 (1.22, 1.43)	1.28 (1.18, 1.38)
Endocrine, Nutritional and Metabolic Diseases	184648 (13.8)	2218 (25.8)	1.89 (1.80, 1.98)	1.99 (1.90, 2.08)
Mental, Behavioral and Neurodevelopmental Disorders	106138 (16.9)	1396 (23.5)	1.41 (1.33, 1.50)	1.39 (1.31, 1.48)
Diseases of the Nervous System	111077 (13.8)	1182 (20.8)	1.53 (1.43, 1.63)	1.56 (1.46, 1.66)
Diseases of the Eye and Adnexa	1729 (8.9)	49 (19.1)	2.11 (1.43, 2.79)	2.17 (1.48, 2.86)
Diseases of the Ear and Mastoid Process	1209 (5.3)	*	*	*
Diseases of the Circulatory System	699477 (14.3)	5374 (23.9)	1.65 (1.60, 1.71)	1.77 (1.71, 1.83)
Diseases of the Respiratory System	234754 (19.3)	2495 (26.1)	1.36 (1.30, 1.42)	1.43 (1.37, 1.49)
Diseases of the Digestive System	349973 (15.2)	3003 (23.7)	1.59 (1.52, 1.65)	1.64 (1.58, 1.71)
Diseases of the Skin and Subcutaneous Tissue	15141 (12.0)	207 (19.7)	1.65 (1.42, 1.88)	1.72 (1.48, 1.95)
Diseases of the Musculoskeletal System and Connective Tissue	45268 (2.4)	443 (7.2)	2.97 (2.53, 3.41)	2.91 (2.48, 3.34)
Diseases of the Genitourinary System	308856 (19.1)	3123 (27.2)	1.43 (1.37, 1.48)	1.55 (1.49, 1.61)
Pregnancy, Childbirth, and the Puerperium	105295 (3.2)	218 (7.0)	2.08 (1.72, 2.44)	2.07 (1.71, 2.43)
Certain Conditions Originating in the Perinatal Period	*	*	*	*
Congenital Malformations, Deformations and Chromosomal Abnormalities	1266 (3.8)	15 (15.0)	3.84 (1.81, 5.86)	4.20 (1.98, 6.41)
Symptoms, Signs and Abnormal Clinical and Laboratory Findings	65604 (14.4)	801 (22.9)	1.60 (1.49, 1.71)	1.58 (1.47, 1.68)
Injury, Poisoning and Certain Other Consequences of External Causes	227730 (11.8)	1944 (18.9)	1.59 (1.51, 1.67)	1.70 (1.62, 1.79)
External Causes of Morbidity	18637 (13.4)	380 (19.7)	1.40 (1.25, 1.56)	†
Factors Influencing Health Status and Contact with Health Services	3940 (4.0)	129 (13.7)	3.28 (2.45, 4.11)	3.33 (2.48, 4.18)

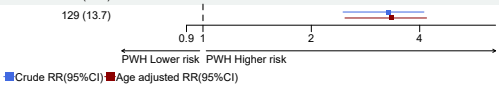

Fig. 4: Comparison of the 30-day all-cause unplanned readmission risk between people with and without HIV by primary reasons for index admission. Abbreviations: PWoH: people without HIV; PWH: people with HIV; RR: risk ratio; aRR: age adjusted risk ratio. Note: number of readmissions and readmission risk (%) among each index admission diagnostic subgroup were presented and all numbers were weighted estimates. RR and aRR were estimated using predicted marginal estimates (*margins* command in Stata) after random effect logistic regressions, and PWoH was the reference group. AIDS defining illness and non-AIDS defining infection were exclusive to other Clinical Classifications Software Refined (CCSR) categories. Since cancers were excluded from index admissions per CMS guidelines, the category of neoplasms only included benign neoplasms and symptoms. Factors influencing health status and contact with health services includes administrative, prophylactic, aftercare and other management encounters. *Tabulated data ≤10 were suppressed per HCUP guidelines. †Model failed to converge. A person may contribute to one or more index admissions.

specific definitions of index admission and readmissions when interpreting results from readmission studies.

Young female PWH had an especially greater risk of readmission than young female PWoH. This disparity was only partly explained by pregnancy. When we excluded hospitalizations due to pregnancy, the discrepancy of readmission risk between PWH and PWoH was still the largest among young females. In 2019, 57% of females and 35% of males with HIV in the US were African American, while African Americans only accounted for 15% of the general population.[6] Female PWH are more likely to be in marginalized groups, live in poverty, experience HIV-related stigma from health care providers and have comorbidities.[22,23] Young PWH in general are also less likely to have health insurance, adhere to ART, be retained in HIV care, and thus less likely to achieve and maintain HIV viral suppression.[24,25] Our findings that non-pregnant female PWH were more likely to reside in lowest-income areas and were less likely to be covered by private insurance are consistent with these prior studies. In addition, although the NRD does not provide reliable measurement of substance use (e.g., by patient survey), other studies in the US indicated that young female PWH have higher prevalence of injection drug use than young female PWoH.[26,27] All of these factors may be compounded and contribute to the elevated risk of readmission among young female PWH.

PWH admitted due to all infectious and non-infectious causes had higher readmission risk than their PWoH counterparts. Both PWH and PWoH admitted due to AIDS defining illness and genitourinary diseases had high readmission risk. PWoH who had AIDS defining illness were usually immunocompromised, and thus had similar high readmission risk to PWH. Uncontrolled HIV infection leads to both immune dysfunction and chronic inflammation that, in turn, predispose to infections (both AIDS defining and non-AIDS defining) and vascular events.[28] Low CD4, which marks risk for AIDS defining illness, has previously been shown to be strongly associated with all-cause readmission risk.[29] Among PWH in our study, the relatively low percentage (3.2%) of index admissions due to AIDS defining illness (lower than approximately 10–15% of admissions seen in studies from the early 2000s) suggests improved, though still incomplete, ART coverage, viral control, and immune reconstitution over the past two decades.[29] Continued work toward the goal of universal ART coverage remains an imperative. Notably, 30 days is generally too short for full immune recovery among persons with advanced HIV (e.g., CD4 < 200 cells/microliter) who appropriately initiate ART during an index admission. Thus, some 30-day readmissions among people with advanced HIV may be unavoidable even with optimal pre and post-discharge care, and the readmission risk for AIDS defining

illness is still high in our study.[29,30] These again highlight the importance of long-term ART and viral suppression among PWH.

More than 1 in 3 PWH hospitalized for hypertensive heart disease, heart failure, fluid disorders or chronic kidney diseases were readmitted, suggesting that providers should pay particular attention to PWH with chronic heart and kidney diseases, and post discharge blood pressures and fluid management may be important. Although HIV care models are heterogeneous, all models should ensure that there is both HIV care and subspecialty care access to best manage common conditions. Additional research is needed to evaluate prevention of readmissions among PWH.

There are several strengths of this study. First, using the NRD that represents all US hospitalizations, our study is among the first to characterize the nationwide readmission risk among PWH in the era of high ART use. The NRD 2019 included 30 states in the US, and the proportion of the inclusion of the EHE prioritized states was similar to non-prioritized states, which may increase the generalizability of our finding to hospitalized PWH in the US. Our study is among the few readmission studies that applied CMS methodology which intentionally excludes planned readmissions. Additionally, our study is among the few that included PWoH as a comparator to PWH, allowing a comprehensive evaluation of the readmission risk between PWH and PWoH, and also within PWH and PWoH, overall and by key factors.

There are several limitations. First, administrative health databases, including the NRD, were created for billing or budget purposes, and less for elaborating clinical information. As previously described, some factors of interest (e.g., ART use, CD4 count, substance use) were not available. Thus, we are unable to describe the risk of readmission by these unmeasured factors, estimate the causal effect of HIV on the risk of readmission (which requires controlling for these unmeasured factors), or conduct mediation analyses. Our findings are nevertheless highly relevant for policy makers and public health authorities who will often be limited to administrative databases when making decisions about policies and resource allocation. Second, the NRD could not track an individual across states. If a patient was admitted to hospitals in multiple states, each state provided a separate ID for the same individual. However, an analysis conducted by the HCUP demonstrated that excluding out-of-state readmissions had minimal impact on readmission risk estimates.[14] Third, due to limitations of available software procedures, we simplified the design by duplicating individuals in the dataset who transitioned to a different hospital or age during the study period. This affected only seven percent of patients and we expect the impact on RR estimates of ignoring the within-person correlation for these few events to be minimal. Indeed, the RR estimates were similar in the sensitivity analysis restricted to the first recorded index admission. Lastly, since out-of-hospital mortality was unknown, we did not account for the competing risk of mortality. However, a recent study evaluating six clinical HIV cohort in North America found that competing risk of mortality is unlikely to affect readmission estimates among PWH.[10] The lack of accounting for competing risk likely only has a minor impact on this descriptive analysis.

In summary, PWH had a higher risk of readmission compared to PWoH overall and for all subgroups examined. The disparity in readmission risk by HIV status was particularly large among groups who are usually considered at lower risk for health events in the general population: females and young adults. Furthermore, PWH admitted due to exacerbations of chronic comorbidities, especially chronic heart and kidney diseases, had a high risk of readmission. As PWH are living longer globally, the prevalence of these age-related, chronic comorbidities will increase, which may lead to even higher readmission burden among PWH in the future. To control the potential increasing burden, clinicians may need to address more comprehensive needs of PWH prior to discharge. Future studies are needed to evaluate the preventability and driving reasons for readmission, such as determining how much of the readmission is due to suboptimal care during the index admission, social determinants of health, or from persisting immune suppression due to uncontrolled HIV.

Contributors

XZ, EUP, SAB, KAG and AART conceptualized this study and wrote the original manuscript. XZ and EUP verified and analyzed the data. AGA, TD, and BH contributed to the methodology. All authors critically reviewed and revised the final manuscript, and interpreted the findings in a broader context. All authors had final responsibility for the decision to submit for publication.

Data sharing statement

The Nationwide Readmissions Database is a publicly available deidentified database that is available by purchase from the Healthcare Cost and Utilization Project (HCUP).

Declaration of interests

KNA declares support from US National Institute of Health, Coursera, Trio Health, and International Workshop on HIV and Hepatitis C Observational databases. Other authors declare no potential conflicts of interest.

Acknowledgements

This study was supported in part from the National Institute of Diabetes and Digestive and Kidney Diseases (R01DK131926 [AART]), the National Institute of Allergy and Infectious Diseases (T32AI102623 [EUP]), the National Institute on Drug Abuse (F31DA054849 [EUP]), and the Division of Intramural Research, National Institute of Allergy and Infectious Diseases (TCQ, ADR, OL). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. The conclusions reached by the authors do not represent the opinions or stances of the Agency for Healthcare Research and Quality (AHRQ).

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.eclinm.2024.102690.

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