Causes of hospitalisation among people living with HIV worldwide, 2014–23: a systematic review and meta-analysis

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Summary

Background Despite improved access to antiretroviral therapy (ART), HIV-related morbidity and mortality remain high. A previous review (2007–14) found that AIDS-related illnesses were the leading causes of hospitalisations. We aimed to summarise the causes of hospitalisations among people living with HIV from 2014 to 2023.

Methods For this meta-analysis we searched eight databases (Ovid Medline ALL, Ovid Embase Classic and Ovid Embase, Ovid Global Health, EBSCOhost CINAHL Complete, EBSCOhost Africa-Wide Information, Clarivate Analytics Web of Science Core Content, Clarivate Analytics Web of Science SciELO, and Global Index Medicus) on April 26, 2023. We included studies of any design that reported on the cause of admission to hospital for at least 20 people after Jan 1, 2014. We extracted summary-level data about CD4 cell counts, ART use, cause of admission, and incidence of death, and assessed risk of bias with the use of a modified Newcastle-Ottowa Scale. We constructed random effects models to estimate prevalence of various diseases as a cause of hospital admission.

Findings From the 19 629 records identified, we obtained data from 110 studies representing 100 628 hospital admissions. The weighted median CD4 count was 111 cells per µL (range of medians 25–713); 60% of admissions (95% CI 54–66) were people receiving ART. The most common cause of admission was AIDS-related illnesses (42% of admissions, 95% CI 35–49), including tuberculosis (19%, 15–23). The second most common cause was bacterial infection (26%, 20–33). AIDS-related illnesses were more common in WHO regions of South and Central America (62%, 53–71), Africa (49%, 39–60), Western Pacific (68%, 57–77), and South-East Asia (40%, 31–50) than in Europe (30%, 23–37) and North America (13%, 6–25). Wasting and parasitic infections were more common in children (malnutrition 31%, 11–63; parasitic infection 13%, 4–37) than in adults. In-hospital mortality was 17% (13–20), with substantial regional variation.

Interpretation Our results indicate providing high-quality care to hospitalised people with HIV-related conditions (AIDS-related illness and severe bacterial infections) should be prioritised.

Funding The Bill & Melinda Gates Foundation.

Lancet HIV 2025; 12: e355–66

Published Online March 26, 2025 https://doi.org/10.1016/S2352-3018(24)00347-3

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Introduction

Increased access to antiretroviral therapy (ART) in the past decade has led to a substantial decline in HIV transmission, morbidity, and death.[1] However, advanced HIV disease and serious illness due to complications of HIV remain a persistent problem.[2,3] To approach the global goals of achieving zero HIV-related deaths,[3] it is imperative to understand the causes of hospitalisation for people living with HIV to support the development of targeted interventions to prevent serious illness and mortality among people living with HIV.

A previous systematic review spanning 2007–14[4] found that AIDS-related infections and bacterial infections were the major causes of hospital admission and in-hospital mortality worldwide, but with considerable regional variation. Since 2014, access to effective ART has improved substantially, particularly since the 2015 WHO recommendations to offer ART to people living with HIV at any CD4 cell count.[5] In 2015, an estimated 47% of people living with HIV had started ART, compared with 76% in 2023.[6] This increased ART coverage might have affected causes of hospital admission among people with HIV. The cohort of people living with HIV has also aged in this time and there might be an increasing dual burden of illness from HIV-related opportunistic infections and non-communicable diseases.[7,8]

We therefore conducted an updated systematic literature review and meta-analysis to identify the causes of hospital admission and risk of in-hospital mortality among adults and children living with HIV worldwide.

Methods

Search strategy and selection criteria

We conducted a systematic review and meta-analysis. We included studies that reported causes of hospital admission for at least 20 children or adults living with HIV (consistent with the previous review[4]) admitted after Jan 1, 2014. Studies that spanned periods before and after Jan 1, 2014, were included if it was possible to disaggregate between pre-2014 and post-2014, or more than half of the

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Research in context

Evidence before this study

People living with HIV admitted to hospital are at high risk of in-hospital death. A previous review spanning 2007–14 identified studies that reported causes of hospital admission among people living with HIV worldwide. That review, which focused on admissions to hospital since 2007 (the period when antiretroviral therapy [ART] started to be more available worldwide), found that 20% of people living with HIV admitted to hospital between 2007 and 2014 died. The major causes of admissions to hospitals were AIDS-related illness and bacterial infections. Since 2015, guidelines worldwide have recommended starting ART as soon as possible after HIV diagnosis and treatment coverage has increased from 47% in 2015, to 76% in 2023. In addition, the cohort of people living with HIV has aged. These factors might have changed the causes of hospital admission among people living with HIV. A more recent review of studies published from Jan 1, 2003, to Nov 30, 2021, summarised outcomes among people with HIV after discharge from hospital. This review found that 19% of people were readmitted within 12 months and 14% had died, which indicated continued high mortality in people living with HIV admitted to hospital.

Added value of this study

We show that from 2014 to 2023, AIDS-related illness remained the most common cause for hospital admissions (42%, 95% CI 35–49, of admissions), and bacterial infections remained the second most common cause (26%, 20–33). The most common AIDS-related illness was tuberculosis, which caused 19% (15–23) of admissions. There were some regional variations, with AIDS-related illnesses being less common in Europe and North America than in other regions. Although 60% (54–66) of admissions were among people reporting ART use, median CD4 cell counts remained low (weighted median 111 cells per μL, range of medians 25–713). In-hospital mortality was 17% (95% CI 13–21), with substantial regional variation.

Implications of all the available evidence

Despite greater availability of ART, people living with HIV continue to be admitted to hospital with AIDS-related illness, including tuberculosis and bacterial infections. To reduce HIV-related morbidity and mortality, governments, funders, researchers, policy makers, activists, and communities affected by HIV should focus attention on advanced HIV disease, and on diagnosis and treatment of opportunistic infections.

time period included was after Jan 1, 2014. We included studies that recruited all emergency hospital admissions, all admissions to hospital medical wards, or all hospital admissions among a group of people previously recruited into an outpatient cohort. We also included studies among people admitted to hospitals or wards specialised in infectious diseases or HIV, and studies in which participant inclusion required a CD4 cell count or ART criteria (eg, only people with CD4 counts <100 cells per μL). We included studies among people admitted to intensive care units (ICUs), when possible reporting these data separately to non-ICU cohorts because causes of admission might differ. We excluded studies in which all participants had the same syndrome or the same diagnosis (eg, studies of people living with HIV admitted to a trauma unit, or all people living with HIV admitted with hemiparesis). We also excluded studies in which the total denominator of admissions from other causes was not stated because we were unable to use these types of studies to understand the prevalence of any condition. No language, geographical, or age exclusions were applied.

See Online for appendix

With support from a specialist librarian (JF), we adapted the search strategy used in the 2014 review,[4] combining terms for hospital admission and HIV. Search terms used are shown in the appendix (pp 35–36). To increase geographical coverage, we searched eight databases (Ovid MEDLINE ALL, Ovid Embase Classic and Ovid Embase, Ovid Global Health, EBSCOhost CINAHL Complete, EBSCOhost Africa-Wide Information, Clarivate Analytics Web of Science Core Content, Clarivate Analytics Web of Science SciELO, and Global Index Medicus). We ran the search on April 26, 2023, and included articles published after Jan 1, 2014. After electronic database search and de-duplication, one author (RMB) manually removed irrelevant articles based on title and abstract review. The remaining articles were reviewed in a second title abstract review in duplicate by two of RMB, NS, and JE, with manuscripts allocated to pairs of reviewers at random. Finally, potentially relevant articles were reviewed at full text in duplicate (two of RMB, NS, and JE). Decisions about inclusion were made by consensus, including discussion among the three reviewers and other authors (NF, RHB, and PM).

The systematic review protocol is included in the appendix (pp 29–36). Institutional ethical approval was neither sought nor required as all data were from published studies.

Data analysis

We extracted summary-level data from reports into a spreadsheet, with an extraction tool piloted and amended after initial data extraction from ten papers. We extracted information including: location (country and WHO region); numbers of participants and number of admissions; year(s) of study data collection; setting (eg, medical wards *vs* intensive care units); gender distribution and cohort age group (adults, children, or both); cohort median CD4 cell count; current ART use; HIV viral load suppression and its per-study definition; diagnoses; and number of deaths and timing of

ascertainment of deaths. Diagnostic categories were based on a modified ICD-10 and were almost identical to the categories used in the 2014 systematic review,[4] with added categories for mpox and COVID-19. Details of definitions of each diagnostic group are presented in the appendix (pp 22). Our preferred definition of AIDS-related admission was based on the US Centers for Disease Control group C (CDC-C) criteria;[9] we accepted any other definition used by a study if it was not possible to otherwise extract data. We chose CDC-C criteria because this includes all types of tuberculosis (whereas the WHO staging system stage IV only includes extrapulmonary tuberculosis as a stage-defining condition) and papers often did not disaggregate between pulmonary and extrapulmonary tuberculosis. Causes of admission were divided into top-level causes and nested second-level causes categorisation (eg, bacterial infections was a top-level cause, and bacterial pneumonia a second-level cause nested within the top-level cause).

In cases in which one or more reports presented data from the same group of participants, we combined all available reports to extract data once for that cohort. We defined adults as people aged 18 years or older. Studies with a mixture of adults and children, or those in which age was not stated, were grouped with adult studies for the main analysis. Each initial extraction was done by one author (RMB, JE, NS, DSL, GB, LT, or AR). All authors extracting data were physicians with experience in caring for hospitalised people living with HIV. When possible, we extracted only one main diagnosis per admission. However, when a paper reported multiple diagnoses for a single patient, without any information about which was the main cause for admission, we included all diagnoses.

We developed a risk of bias tool with the use of a modified Newcastle-Ottawa Scale.[10] We identified sources of bias related to representativeness of the cohort—specifically when a restricted subset of all people admitted to hospital was included (eg, only people admitted to an infectious disease ward) or when a study included participants recruited before Jan 1, 2014. Bias related to ascertainment of outcomes was included when reporting of diagnoses was very limited, or when only one diagnosis had been assessed by laboratory criteria alone, rather than by laboratory and clinical criteria (eg, prevalence of cryptococcal antigenaemia). Additionally, we recorded instances when only an abstract was available. Papers were rated as having lower risk of bias if none of these concerns were present, and higher risk of bias if any of these factors were present.

We presented data descriptively (ie, number of studies, participants, proportion taking ART, and median CD4 cell count). To estimate causes of admission, proportion taking ART, viral load suppression, and death, we used a multilevel regression model with logit-transformed proportions and random effects with the use of meta (version 6.0) package in R (version 4.4).[11] We chose random effects because we considered the underlying types of admission causes would vary between study. We present data as proportions, with the use of Knapp–Hartung adjustment to calculate 95% CIs.[12] Knapp–Hartung adjustments are recommended when heterogeneity among effect sizes is anticipated and usually give more conservative (larger) CIs compared with a Wald interval.[13]

Most studies either did not distinguish between individuals and hospital admissions or presented demographics and diagnostic data per admission (rather than per person). Occasionally studies reported only demographic or diagnosis data per person rather than per admission when the same person had multiple admissions; we extracted the available data rather than discarding these studies. Therefore, we present results for admissions, acknowledging that on occasion data might have been presented per person and not per admission.

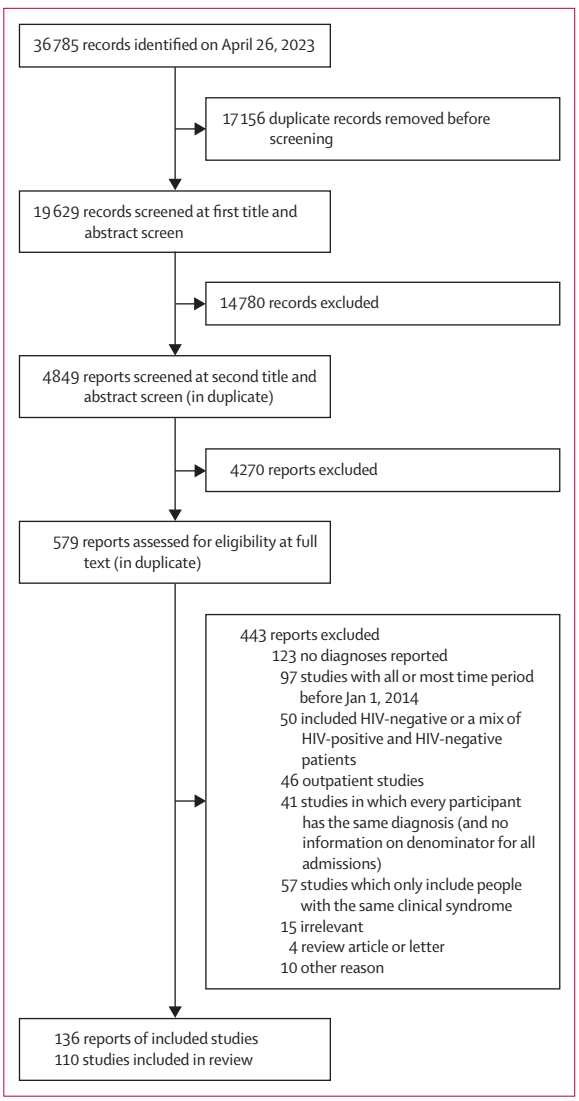

Figure 1: **Study selection**

	Number of studies	Number of people	Number of hospital admissions	Number of admissions with ≥1 diagnosis
Overall	110	91 114	100 628	54 728
World region				
Africa	35	39 620	39 734	13 704
USA	5	3924	8841	5742
America–Central and South	13	4394	4576	3131
Eastern Mediterranean	1	131	131	78
Europe	31	8505	10 813	6965
South-East Asia	8	2318	3195	1860
Western Pacific	9	32 222	33 338	23 248
Setting				
ICU*	14	3586	3609	3310
Infectious disease or HIV unit	30	18 228	18 938	7113
Medical wards	33	55 329	55 607	31 045
Outpatient cohort*	14	5997	12 483	9098
Paediatric wards	5	650	650	650
Whole hospital	14	7324	9341	3512
Age group				
Adults	94	87 033	96 403	51 529
Children	8	1064	1122	878
Both adults and children or unclear	8	3017	3103	2321
Risk of bias				
Lower risk of bias	18	9345	14 436	10 010
Higher risk of bias	92	81 769	86 192	44 718

ICU=intensive care unit. *Note that one ICU study and two outpatient cohort studies[14–16] were among children, giving a total of eight studies among children although only five on paediatric wards.

Table 1: **Summary of included studies**

We present data overall and for the main analysis divided into all studies among children, all studies among adults in ICUs, and studies among adults not in ICUs by WHO region. For WHO region of the Americas we split groups into the USA and Canada and rest of the Americas because causes of admissions and outcomes were likely to differ substantially between these countries due to major demographic and socioeconomic differences.[4] We presented data split by other groupings (eg, by setting and risk of bias) in the appendix (pp 19–21).

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Our database search yielded 19 629 unique records (figure 1). We included data from 110 studies, based on 136 separate reports of these 110 studies, comprising 91 114 participants and 100 628 admissions (table 1). All six WHO regions were represented, with most studies from Africa (35 studies, including eight in children and one in adults in ICUs), followed by Europe (31 studies, including three among adults in ICUs).

Overall, there were 37 595 men and boys (68·7% of participants in studies in which gender was reported), 17 119 women and girls, and four people (in two studies) with another gender identity; 34 studies did not report gender. There were data from 87 033 adults (94 studies), 1064 children (eight studies), and 3017 participants from eight studies with a mix of adults and children or studies in which age was not stated. All studies of children were from Africa. Median CD4 cell count was reported in 43 studies and ranged from 25 cells per µL to 713 cells per µL with a weighted median of 111 cells per µL. Overall, 60·0% (95% CI 53·6–66·1) of admissions were among people currently receiving ART (ART use reported in 47 studies), and 42·0% (35·0–49·0) of people had HIV viral load suppression (reported in 26 studies, of which 12 were in Europe).

By the end of their study follow-up period, 16·6% (95% CI 13·0–20·0) of participants had died (death outcomes reported in 66 studies). When restricted to 59 studies that reported in-hospital deaths (appendix pp 12–17), 16·2% (12·8–20·3) of people died during hospital admission (appendix pp 12–17). Overall, deaths were most common in people admitted to ICU (46%, 37–56), and were higher in the South-East Asia region (22%, 15–30) and the Africa region (19%, 16–23) than in other regions (table 2, appendix p 4).

We synthesised data concerning 61 704 diagnoses among 54 728 admissions. The most common cause of hospital admission worldwide, in all age groups, was AIDS-related illnesses, accounting for 42% (95% CI 35–49) of all admissions (figure 2, figure 3). AIDS-related illnesses included: tuberculosis (19%, 15–23, of admissions overall), *Pneumocystis jirovecii* pneumonia (7%, 5–10), and cryptococcal disease (5%, 4–7). Bacterial infections were the second most common cause of admissions overall (26%, 20–33). In general, the proportion of admissions related to non-communicable diseases was low. The most common non-infectious causes of admission overall were digestive (non-infectious), haematological, malnutrition, and cardiovascular, which each represented 6% of admissions (figure 3).

Considering region-specific diagnostic estimates, AIDS-related illnesses were the commonest cause of admission in both adults and children in all WHO regions except South-East Asia and North America, where bacterial infections were the most common cause of admission and AIDS-related illnesses were second. Bacterial infections were in the top three most common causes in all categories (table 3, appendix p 8). Most regional cause estimates were based on a small number of studies and have wide uncertainty. Malnutrition was a common cause of admission in children (31%, 95% CI 11–63), and all six studies were in Africa. The only non-communicable disease with an estimated prevalence of more than 10% in

	Overall	Children (Africa region studies only)	Adults in Africa*	Adults in the USA*	Adults in South and Central America*	Adults in Eastern Mediterranean*	Adults in Europe*	Adults in South-East Asia*	Western Pacific*	Adults in ICU (all regions)
Total number of studies	110	8	25	5	13	1	28	8	9	13
Sex										
Number of studies reporting	76	5	21	3	8	0	15	5	7	12
Proportion of men	37 595 (68·7%) of 54 714	234 (51·3%) of 456	4956 (44·5%) of 11 146	1504 (68·5%) of 2197	1887 (75·4%) of 2503	NR	3191 (73·3%) of 4356	539 (64·3%) of 838	23 098 (77·4%) of 29 845	2186 (64·8%) of 3373
CD4 cell count										
Number of studies reporting	43	2	13	1	7	0	9	4	2	5
Overall median CD4 count (cells per µL; min-max)†	111 (25–713)	512 (512–713)	173 (32–260)	156 (156–156)	136 (25–219)	NR	258 (76–510)	111 (97–282)	108 (38–108)	137 (44–324)
Current ART use										
Number of studies reporting	47	2	20	0	7	0	6	1	3	8
Crude proportion on ART	13 239 (55·9%) of 23 672	20 (25·3%) of 79	7113 (64·8%) of 10 976	NR	1292 (58·8%) of 2198	NR	1772 (60·4%) of 2934	153 (41·4%) of 370	1997 (47%) of 4250	892 (31·1%) of 2865
Meta-analysis proportion on ART (%, 95% CI)	60% (54–66)	25% (1–90)	66% (58–73)	NR	62% (47–74)	NR	70% (43–88)	41% (36–46)	39% (11–77)	55% (35–72)
Viral load suppression										
Number of studies reporting	26	0	3	1	5	0	12	0	2	3
Crude proportion viral load suppressed	4362 (40·5%) of 10 765	NR	747 (47%) of 1590	416 (32·5%) of 1279	603 (41·6%) of 1450	NR	1522 (52·6%) of 2896	NR	866 (28·4%) of 3046	208 (41·3%) of 504
Meta-analysis of viral load suppressed (%, 95% CI)	42% (35–49)	NR	45% (30–60)	33% (30–35)	34% (18–55)	NR	49% (38–61)	NR	26% 6–68)	40% (23–59)
In-hospital death‡										
Number of studies reporting	66	6	20	1	9	0	14	3	2	11
Crude proportion died	11 974 (20·6%) of 58 219	79 (16·5%) of 480	8252 (23·6%) of 34 973	9 (9·7%) of 93	262 (10·8%) of 2433	NR	333 (10·6%) of 3128	121 (21·8%) of 556	1194 (9%) of 13 323	1724 (53·3%) of 3233
Meta-analysis proportion died (%, 95% CI)	17% (13–21)	10% (2–35)	19% (16–23)	10% (5–18)	12% (6–22)	NR	8% (6–11)	22% (15–30)	9% (6–13)	46% (37–56)

NR=not recorded. *Excluding studies in ICUs. †Median is overall median across all studies. The range includes the minimum (lowest median in any study) and maximum (highest median CD4 cell count in any study). ‡For most studies this was survival to discharge; a small number used mortality at 28, 56, or 90 days (appendix pp 13–18).

Table 2: **Summary of admissions overall and by category**

adults in any region for which data from more than one study were available was cardiovascular disease in Europe (11% of admissions, 95% CI 6–18, five studies) and North America (10%, 8–11, four studies).

When we restricted analysis to the 18 studies with lower risk of bias,[19,21,25,26,28,34,52,57,72–81] AIDS-related admissions represented a smaller proportion of total admissions (29%, 95% CI 15–47). Distribution of other causes of admission was broadly similar to estimates for the whole group (appendix p 5).

We identified only two eligible studies[34,35] that reported on numbers of patients admitted with COVID-19—one study in Germany reported that COVID-19 caused 15 (7%) of 193 admissions from March, 2020, to April, 2022,[34] and one study in Mexico reported 39 (17%) of 218 admissions due to COVID-19 during 2020.[35] We did not identify any studies that met our inclusion criteria and included people with a diagnosis of mpox. Many studies were conducted in infectious disease units or medical wards, so we were unable to estimate the prevalence of admissions due to trauma or surgical admissions from these studies. However, 15 studies included an estimate of trauma admissions[15,17,27,28,35,45,50,53,57,61,66,68,80–84] giving an estimate of 3·3%

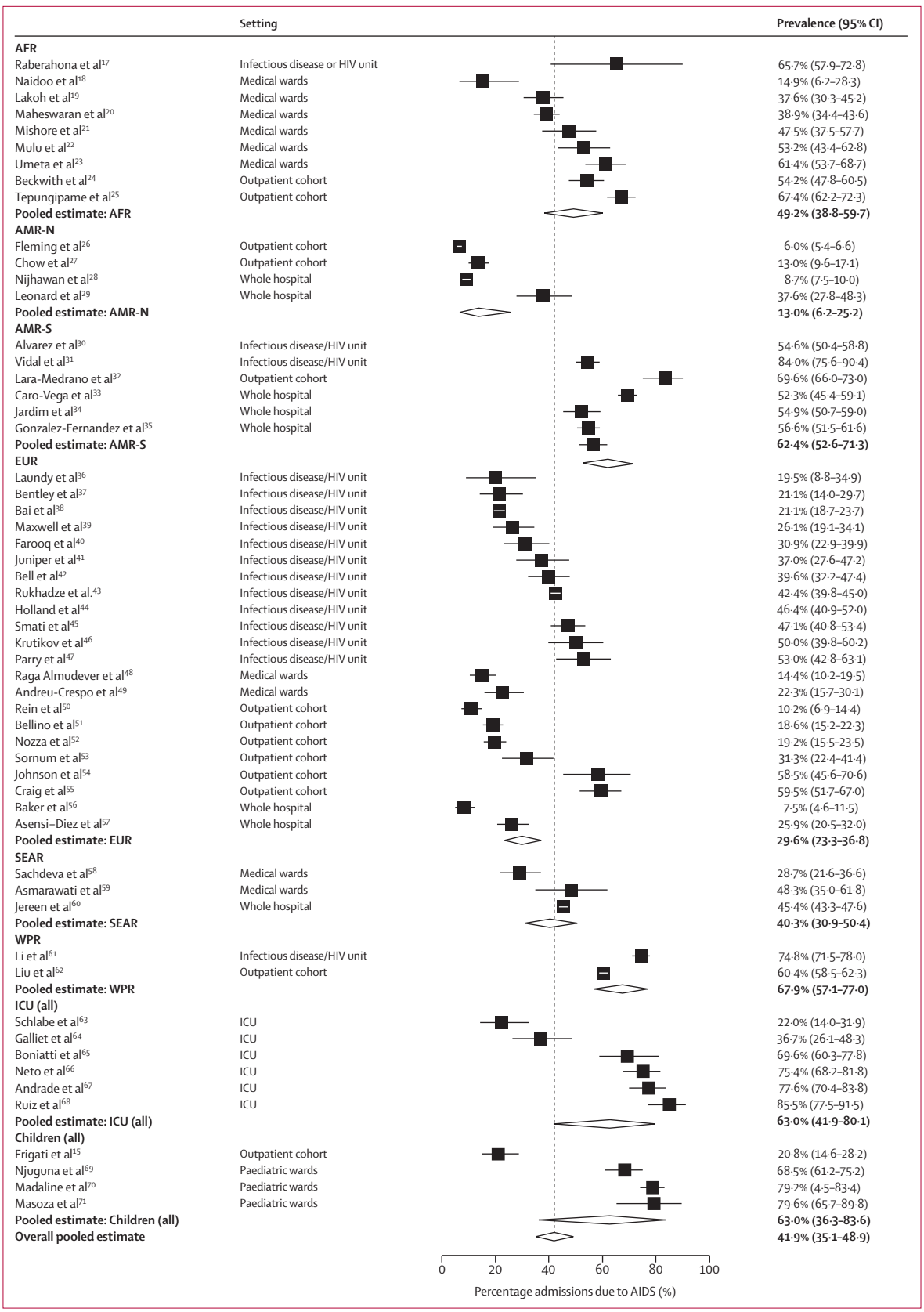

Figure 2: **Forest plot of prevalence of AIDS-related illnesses as a cause of hospital admission**
Dotted line is point estimate for pooled proportion of AIDS-related illness. Diamonds represent subgroup estimates and the bottom diamond the overall pooled estimate. AFR=Africa region. AMR-N=USA and Canada. AMR-S=American countries other than USA and Canada. EUR=Europe region. ICU=intensive care unit. SEAR=South-East Asia region. WPR=Western Pacific region.

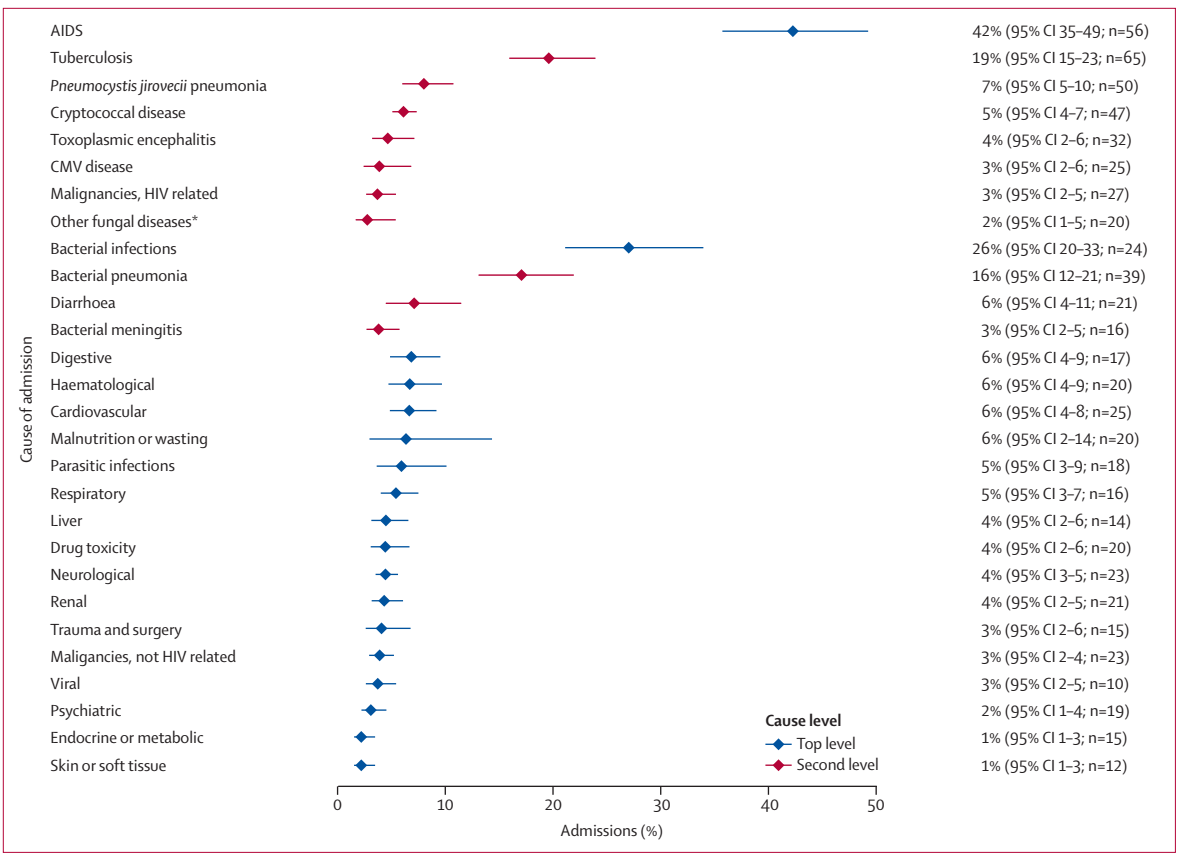

Figure 3: **Meta-analysis of causes of hospitalisation**
Right-hand column provides estimates of percentage of admissions due to each cause. CMV=cytomegalovirus. *Other fungal diseases include histoplasmosis, isosporiasis, talaromycosis, and other fungal diseases unspecified as a second-level cause, and exclude oral and oesophageal candidiasis and cryptococcal disease.

(95% CI 1·7–6·0%) of hospital admissions due to trauma or surgical causes (appendix p 9).

Discussion

Globally between 2014 and 2023, AIDS-related illnesses were the most common cause of admission to hospital for people living with HIV, with tuberculosis being the most common AIDS-related illness. This finding was consistent across age groups, almost all WHO regions, and restricting the analyses to studies with a lower risk of bias. In addition, bacterial infections accounted for a quarter of admissions, and these would also be considered indicators for advanced HIV disease.[84] These results suggest that despite increased access to HIV testing and ART treatment, complications of HIV remain common and advanced HIV disease remains a persistent clinical and public health problem.[83] The consequences of hospital admission remain severe, with an estimated 17% dying during or shortly after hospitalisation.

Compared with the earlier systematic review[4] covering the period from 2007 to 2014, AIDS-related illnesses remained common (46% of all admissions in 2007–14 *vs* 42% of all admissions in this review). The proportion of people reporting taking ART at admission was slightly higher (56% *vs* 43%). Pooled estimates of in-hospital deaths were similar.

We did not determine the incidence of hospital admission per person-year for people living with HIV. The overall incidence of hospital admissions is likely declining, even as the proportion of admissions caused by AIDS-related illnesses remains high. One study[85] from the USA showed the incidence of opportunistic illness-related hospitalisations reduced from 2660 admissions per 100 000 people-with-HIV-years in 2012, to 1784 in 2018. In Malawi, hospital admissions of people who tested positive for HIV decreased by 34% between 2012 and 2017.[86] Although the population-level incidence of people living with HIV becoming seriously unwell might be declining, potentially leading to fewer admissions overall, this review highlights that among individuals who are seriously unwell, HIV-related causes (ie, both AIDS-defining and severe bacterial infections) are the biggest cause of hospital admissions.

The strengths of this review are the comprehensive search strategy including regional databases, coverage of studies from all age groups and WHO regions, and the large number of patients included. The major limitation is the quality of underlying data, in particular diagnostics

	Children (all studies from the Africa region)	Adults in Africa*	Adults in the USA*	Adults in America (areas other than the USA)*	Adults in Eastern Mediterranean*	Adults in Europe*	Adults in South-East Asia*	Adults in Western Pacific*	Adults in ICU (all regions)
AIDS (95% CI)	63% (36–84); n=4	49% (39–60); n=9	13% (6–25); n=4	62% (53–71); n=6	NR	30% (23–37); n=22	40% (31–50); n=3	68% (57–77); n=2	63% (42–80); n=6
Tuberculosis (95% CI)	10% (5–19); n=6	26% (21–32); n=23	NR	25% (15–38); n=4	29% (22–37); n=1	6% (2–12); n=8	42% (33–52); n=5	23% (16–33); n=6	13% (7–24); n=12
Pneumocystis jirovecci pneumonia (95% CI)	1% (0–92); n=2	4% (3–5); n=11	1% (1–1); n=2	7% (4–13); n=4	15% (9–22); n=1	5% (3–8); n=11	8% (3–24); n=4	30% (18–45); n=3	16% (10–25); n=12
Cryptococcal disease (95% CI)	NR	6% (5–8); n=15	2% (1–4); n=1	8% (5–13); n=8	NR	1% (0–4); n=5	7% (5–9); n=4	6% (3–9); n=7	5% (3–8); n=7
Other fungal diseases† (95% CI)	NR	0% (0–1); n=2	NR	6% (3–12); n=5	NR	0% (0–100); n=3	9% (6–12); n=1	6% (2–14); n=5	2% (1–5); n=4
Bacterial infections (95% CI)	11% (7–18); n=1	24% (14–38); n=7	20% (16–25); n=1	13% (9–19); n=3	NR	26% (19–35); n=5	42% (29–56); n=4	NR	44% (28–62); n=3
Bacterial pneumonia (95% CI)	30% (15–50); n=6	12% (8–18); n=12	3% (3–4%); n=2	NR	10% (6–16); n=1	16% (9–25); n=6	12% (8–18); n=1	17% (4–51); n=2	25% (15–38); n=9
Digestive (95% CI)	5% (2–10); n=1	5% (4–7); n=4	7% (6–8); n=3	NR	NR	7% (3–15); n=6	0% (0–100); n=1	NR	10% (7–15); n=2
Haematological (95% CI)	6% (1–38); n=2	9% (5–15); n=7	3% (2–4); n=1	NR	NR	3% (1–5); n=4	17% (12–24); n=1	6% (3–9); n=3	7% (1–28); n=2
Cardiovascular (95% CI)	1% (0–5); n=1	6% (4–10); n=8	10% (8–11); n=4	1% (0–2); n=1	NR	11% (6–18); n=5	0% (0–100); n=1	3% (2–3); n=1	6% (4–9); n=4
Malnutrition or wasting (95% CI)	31% (11–63); n=6	8% (1–49); n=3	2% (1–2); n=2	3% (1–7); n=2	NR	3% (0–17); n=4	0% (0–100); n=1	NR	1% (0–4); n=2
Parasitic infections (95% CI)	13% (4–37); n=4	6% (3–12); n=6	NR	17% (12–23); n=1	NR	1% (1–2); n=1	1% (0–52); n=2	NR	3% (1–7); n=4
Respiratory (95% CI)	1% (0–5); n=1	3% (2–6); n=4	5% (4–6); n=3	NR	NR	8% (5–11); n=6	0% (0–100); n=1	NR	8% (4–15); n=1
Malignancies, not HIV related	1% (0–5); n=1	1% (1–2); n=6	3% (2–5); n=3	2% (1–4); n=1	NR	7% (5–9); n=9	0% (0–100); n=1	3% (3–4); n=1	1% (0–7); n=1
Drug toxicity (95% CI)	NR	3% (2–5); n=6	NR	2% (0–13); n=2	NR	4% (2–8); n=9	0% (0–100); n=1	20% (17–23); n=1	8% (4–15); n=1
Neurological (95% CI)	1% (0–3); n=1	4% (2–6); n=8	2% (2–3); n=1	2% (1–4); n=1	NR	3% (2–5); n=6	5% (2–13); n=3	8% (7–8); n=1	4% (1–12); n=2
Trauma and surgery (95% CI)	5% (1–18); n=2	2% (1–5); n=1	3% (1–7); n=2	2% (1–4); n=1	NR	5% (3–7); n=4	NR	1% (1–2); n=1	4% (1–24); n=4

Data are prevalence (%, 95% CI; number of studies). NR=not reported. ICU=intensive care unit. *Excluding individuals in ICU. †Other fungal diseases include histoplasmosis, isosporiasis, talaromycosis, and other fungal diseases unspecified as a second-level cause; excludes oral and oesophageal candidiasis and cryptococcal disease.

Table 3: **Causes of admissions by region**

and definitions for each cause of admission. Most studies did not describe definitions (eg, for bacterial infection), diagnostic methods (eg, what laboratory tests were used on whom), or rationale or type of schema (eg, ICD-10) used to delineate diagnoses. A key strength of our study is that all data extractors were experienced physicians who used standardised rules to guide the approach to extractions to ensure consistency and accuracy. Nevertheless, we experienced challenges in matching information reported in papers to a harmonised diagnostic schema in our extraction tool. Other limitations include those intrinsic to systematic reviews without individual-patient level data; we are unable to disaggregate to subcohort level, for example to report diagnoses by individual CD4 cell count. Since hospitalisation and its synonyms are non-specific search terms, our search returned more than 19 000 records, even after optimisation by a specialist librarian. Only one author reviewed the bulk of excluded papers, which might have led to us missing some papers.

In addition to imprecision due to poorly documented diagnostics and definitions, access to diagnostics differs over time and between regions, which might lead to either over-reporting or under-reporting of conditions in different hospitals and regions based on constellations of symptoms. For example, toxoplasma encephalitis might be diagnosed differently in a hospital with MRI scanners and a neuroradiology multidisciplinary team compared with a hospital with no neuroimaging available. Therefore, determining whether apparent differences between regions (eg, as seen for *P jirovecci* pneumonia) represent real variation in pathology or are the result of small numbers of studies and differences in diagnostic approaches is difficult. Non-HIV malignancies were less common than we anticipated (3%). Although this result

could reflect a small number of cancer cases among people with HIV admitted to hospital, it might also be related to low availability of histopathology services to diagnose cancer. Similarly, although we assume the true prevalence is high, it is possible that tuberculosis is overdiagnosed or underdiagnosed in some settings where good diagnostics for tuberculosis or for tuberculosis mimics (eg, histoplasmosis) are unavailable. In most studies, non-infectious causes of admission were uncommon. This result might represent low availability of diagnostic tests, that treating clinicians did not adequately consider non-infectious causes, or a genuine low proportion of admissions. There were a large number of people included in the denominator of admissions who did not have a cause of admission extracted. This finding mostly reflects aggregation of reported data (eg, if a study reported only prevalence of AIDS-defining illness and other causes the other category could not be extracted); however, it might also indicate that often people are admitted to hospital and a diagnosis is never reached for their illness, perhaps in part due to limited capacity for investigations.

There were few data for children living with HIV (and no data for children outside of Africa) and few data for specific region and diagnosis combinations. This scarcity of data meant that there were sometimes more studies reporting on second-level causes than top-level causes, which occasionally led to unexpected results. For instance, we estimated that there were more children with bacterial pneumonia (30%, pooled from six studies [14,15,68-70,80,81]) than with all bacterial infections combined (11%, estimate from one study[15] only). Accordingly, the point estimates for each cause should be interpreted with caution, especially when small numbers of studies contributed. The estimate for viral load suppression comes from a relatively small number of studies, which were disproportionately in Europe. There was only one study from the Eastern Mediterranean region—an area which is experiencing a growing HIV epidemic[87] and where more epidemiological studies are needed. We also noted that very few studies reported participants with a non-binary gender identity, and we urge future studies to collect and report more detailed data about gender.

Overall, our research highlights that despite much improved access to ART and several countries achieving UN Programme on HIV/AIDS 95-95-95 targets, advanced HIV disease (ie, AIDS-related, and bacterial infections) remains the most common cause of hospital admissions among people living with HIV. Accessing HIV testing, initiating ART, and achieving virological suppression (as measured by 95-95-95 targets) are only the first steps in the pathway to lifelong high-quality HIV care.[88] Based on our review, ART use at admission to hospital was relatively high, and presumably the number of people who had ever used ART was higher (although not consistently reported across studies); however, AIDS-related illnesses remained very common. People living with HIV admitted to hospital are a heterogeneous group with complex care needs. In-hospital interventions including early diagnosis of advanced HIV disease, expedited opportunistic infection diagnosis and prevention, and ART adherence support and linkage to care are essential to reduce longer-term morbidity and mortality within this high-risk group.[89] Furthermore, for people who do have established illness related to HIV, better evidence to guide diagnosis and treatment in hospital of major opportunistic infections is urgently needed. Some recent trials on improving treatments for cryptococcal meningitis[90] and ongoing trials on HIV-associated disseminated tuberculosis are welcome, but there is scope for more research to address optimal treatment for bacterial infections and opportunistic diseases, and to optimise inpatient care more broadly.[91] We also recommend that more research is done to better define the causes of hospitalisation in this ART era. Although we identified 110 studies, few were among children and most studies included had methodological concerns. Even among studies at low risk of bias, there was little standardisation of how diagnoses were arrived at and grouped for reporting. High-quality studies of unselected people living with HIV admitted to hospital, with access to diagnostic tools and standardised definitions of cause of admission, should be prioritised.[92]

In conclusion, our findings emphasise that advanced HIV disease and AIDS-related illnesses remain a persistent global problem despite much improved access to ART. Advanced HIV disease and complications were more common causes of admission in some regions than others, suggesting that access (considered broadly) to diagnosis and ART is inequitable around the world. Although it is crucial to identify advanced HIV disease and provide support before people become unwell, improving quality of care among people admitted to hospital should also be a key priority for national governments and partner agencies as they work to achieving the UNAIDS goals of zero HIV-related deaths.

Contributors

NF conceived the study. RMB and NF designed the study. RMB and JF designed the search strategy. JF ran the search and de-duplication of results. RMB, JE, and NS reviewed articles for inclusion, including PM, NF, RHB, JNJ as needed. RMB, JE, NS, AR, LT, DSL, and GB extracted data from included papers. RMB conducted the statistical analysis, with assistance from PM. RMB wrote the first draft, and all authors contributed to revisions and approved the final manuscript. RMB and JE accessed and verified the data. All authors had full access to the data in the study and had final responsibility for the decision to submit for publication.

Declaration of interests

RMB, DSL, and JNJ all receive funding from UK National Institute of Health Research to their institution. RMB is funded by UK National Institute of Health Research (CL-2023–20–001). JNJ and DSL have also received funding from US Centers for Disease Control to their institution. DSL has received salary support from Janssen to his institution. RHB has received support from National Institutes of Health. JNJ has served on Data Safety Monitoring Boards for three trials related to hospitalised people living with HIV (Harvest, ARTIST, and ASTRO trials). PM is Data Safety Monitoring Board chair for a trial related to

hospitalised people living with HIV (IMPROVE trial). All other authors declare no competing interests.

Data sharing

Summary data extracted from primary papers and full search strategy for all databases are available at LSHTM Data Compass (https://doi.org/10·17037/DATA.00004347).

Acknowledgments

This study was funded by The Bill & Melinda Gates Foundation through a grant to WHO.

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