Clinical features of, and risk factors for, severe or fatal COVID-19 among people living with HIV admitted to hospital: analysis of data from the WHO Global Clinical Platform of COVID-19

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Summary

Background WHO has established a Global Clinical Platform for the clinical characterisation of COVID-19 among hospitalised individuals. We assessed whether people living with HIV hospitalised with COVID-19 had increased odds of severe presentation and of in-hospital mortality compared with individuals who were HIV-negative and associated risk factors.

Methods Between Jan 1, 2020, and July 1, 2021, anonymised individual-level data from 338 566 patients in 38 countries were reported to WHO. Using the Platform pooled dataset, we performed descriptive statistics and regression analyses to compare outcomes in the two populations and identify risk factors.

Findings Of 197 479 patients reporting HIV status, 16 955 (8·6%) were people living with HIV. 16 955 people living with HIV were from Africa; 10 603 (62·9%) were female and 6271 (37·1%) were male; the mean age was 45·5 years (SD 13·7); 6339 (38·3%) were admitted to hospital with severe illness; and 3913 (24·3%) died in hospital. Of the 10 166 people living with HIV with known antiretroviral therapy (ART) status, 9302 (91·5%) were on ART. Compared with individuals without HIV, people living with HIV had 15% increased odds of severe presentation with COVID-19 (aOR 1·15, 95% CI 1·10–1·20) and were 38% more likely to die in hospital (aHR 1·38, 1·34–1·41). Among people living with HIV, male sex, age 45–75 years, and having chronic cardiac disease or hypertension increased the odds of severe COVID-19; male sex, age older than 18 years, having diabetes, hypertension, malignancy, tuberculosis, or chronic kidney disease increased the risk of in-hospital mortality. The use of ART or viral load suppression were associated with a reduced risk of poor outcomes; however, HIV infection remained a risk factor for severity and mortality regardless of ART and viral load suppression status.

Interpretation In this sample of hospitalised people contributing data to the WHO Global Clinical Platform for COVID-19, HIV was an independent risk factor for both severe COVID-19 at admission and in-hospital mortality. These findings have informed WHO immunisation policy that prioritises vaccination for people living with HIV. As the results mostly reflect the data contribution from Africa, this analysis will be updated as more data from other regions become available.

Introduction

As of April 28, 2022, more than 509 million COVID-19 cases and 6·2 million deaths were reported globally. Low-income and middle-income countries (LMICs), notably Brazil, India, and South Africa, have reported high numbers of COVID-19 cases. At the same time, 37·7 million people are living with HIV worldwide and 1·5 million became newly infected with HIV in 2020, the majority (67%) of whom are in sub-Saharan Africa. Characterising populations at increased risk of severe or fatal COVID-19 is critical for appropriate prioritisation of interventions, particularly in areas where resources are limited, the health-care system is stretched, there is a high prevalence of communicable diseases such as HIV and tuberculosis affecting the burden and severity of COVID-19, and where vaccine coverage is unacceptably low. As of December, 2021, fewer than 7% of people in Africa had received at least one dose of a COVID-19 vaccine, but this proportion is progressively increasing (23% as of 28 April 2022).

People living with HIV have underlying immune dysregulation, putting them at risk for opportunistic
All these factors might—in analyses have now reported an increased risk of mortality factor for severe COVID-19. However, three meta-analyses from high-income countries with small numbers of early single-centre cohort studies and meta-analyses the other showed no overall increased risk for intensive risk for severe disease requiring hospitalisation, and one found that people living with HIV has shown conflicting findings across observational studies and geographical regions, and estimating the extent to which this risk is modified by other factors has been limited by small sample sizes or geographic restraints. Studies from the UK and South Africa found that people living with HIV have an increased mortality risk for COVID-19, but similar conclusions were not drawn from studies from Belgium or Spain. Although early single-centre cohort studies and meta-analyses of data from high-income settings with small numbers of cases did not find HIV to be a risk factor for severe COVID-19, larger population cohorts and meta-analyses of larger datasets found that people living with HIV had a moderately increased risk of mortality. Broader geographical representation is required to expand understanding on how HIV infection impacts clinical outcomes secondary to hospitalisation with COVID-19.

Evidence in context

Evidence before this study
PubMed was searched for studies published between Feb 1, 2020, and July 31, 2021, in English, using the search strings “HIV (and) COVID-19, people living with HIV (and) COVID-19, HIV (and) COVID-19 (and) severity, and HIV (and) COVID-19 (and) mortality (or) death”. Evidence regarding the risk of adverse COVID-19 outcomes in people living with HIV has shown conflicting findings across observational studies and geographical regions, and estimating the extent to which this risk is modified by other factors has been limited by small sample sizes or geographic restraints. Studies from the UK and South Africa found that people living with HIV have an increased mortality risk for COVID-19, but similar conclusions were not drawn from studies from Belgium or Spain. Although early single-centre cohort studies and meta-analyses of data from high-income settings with small numbers of cases did not find HIV to be a risk factor for severe COVID-19, larger population cohorts and meta-analyses of larger datasets found that people living with HIV had a moderately increased risk of mortality. Broader geographical representation is required to expand understanding on how HIV infection impacts clinical outcomes secondary to hospitalisation with COVID-19.

Added value of this study
To our knowledge, this is the largest analysis to date exploring the association between HIV infection and clinical outcomes in people hospitalised with COVID-19 using individual patient-level data. The strength of the WHO Clinical Platform lies in the wide representation of contributing countries (38 countries, with 22 from low-income and middle-income countries), and in the collection of individual-level data of 16,955 people living with HIV and 180,524 people who were HIV-negative using standardised definitions and tools.

Implications of all the available evidence
Underlying conditions were more frequently observed in people living with HIV, stressing the need for this population to stay as healthy as possible, regularly take their antiretroviral therapy medications, and prevent and manage underlying conditions that can increase the risk of adverse outcomes. The increased risk of poor outcomes in people living with HIV hospitalised for COVID-19 should be considered when prioritising SARS-CoV-2 vaccination among vulnerable groups. These findings have informed the WHO Strategic Advisory Group of Experts on Immunization roadmap for prioritising the use of COVID-19 vaccines in the context of limited supply, which now includes HIV infection among the chronic conditions to consider in vaccine prioritisation. Countries should consider including people living with HIV as a priority group for COVID-19 vaccination according to their epidemiological context. Data contribution to the WHO Platform is ongoing, to further explore the reasons for adverse outcomes beyond the variables assessed in this dataset, including the potential influence of CD4 cell counts.

Infections, autoimmune diseases, and cancer. Overall, people living with HIV are more prone to disordered T-lymphocyte and B-lymphocyte, and cytokine–interferon responses, and polyclonal (yet ineffective) antibody production, and are more commonly affected by non-communicable diseases, including diabetes and cardiovascular diseases. All these factors might—in principle—put them at higher risk for severe or fatal disease when co-infected with SARS-CoV-2. However, before this study, the evidence to support this hypothesis was sparse and inconsistent, with most analyses based on small and geographically limited samples. A study that analysed data from sites across the UK found that people living with HIV had an increased risk of mortality, whereas studies from Belgium and Spain did not. Data from within regions have also been conflicting. In two studies from New York state (USA), one found that people living with HIV are at increased risk for severe disease requiring hospitalisation, and the other showed no overall increased risk for intensive care unit (ICU) admission, intubation, or mortality. Early single-centre cohort studies and meta-analyses from high-income countries with small numbers of people living with HIV did not find HIV to be a risk factor for severe COVID-19. However, three meta-analyses have now reported an increased risk of mortality among people living with HIV.Additionally, recent studies found an increased risk of severe outcomes among people living with HIV, particularly in those with detectable viremia and increased odds of death in people living with HIV, with older age and male sex being risk factors. Recent data from South Africa also found that HIV infection was an independent risk factor for in-hospital mortality.

To inform public health interventions around the prevention and management of COVID-19, our study aimed to explain these conflicting results and generate more conclusive data on the association between HIV infection and severe or fatal COVID-19 among people admitted to hospitals globally, and particularly in sub-Saharan Africa.

In April, 2020, WHO launched the WHO Global Clinical Platform on COVID-19, which is a secure, web-based database of anonymised individual-level clinical data of hospitalised patients with suspected or confirmed COVID-19 from health facilities across the world. Using data from this platform, we assessed whether people living with HIV hospitalised with COVID-19 were at increased risk of severe or critical presentation on admission and of in-hospital mortality compared with hospitalised HIV-negative individuals with COVID-19, and investigated risk factors associated
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with severe or critical illness at hospital admission and in-hospital mortality among people living with HIV hospitalised for COVID-19.

Methods

Data sources

Ministries of Health, research networks, and health facilities were formally invited by WHO to contribute anonymised clinical data to the WHO Platform using a standardised Case Report Form (CRF)\(^2\) and data dictionary.

The WHO CRF contains a standardised set of variables to be collected on hospital admission, daily, and at the time of hospital discharge. Information includes demographics, pregnancy status, country, vital signs and other anthropometrics, underlying conditions, chronic medications, clinical features, laboratory testing, therapeutics, admission to an ICU, use of oxygen, use of mechanical ventilation, complications arising due to COVID-19, and clinical outcomes (discharge, death, transfer to another facility, or remaining hospitalised at the time of data entry).

Study design and population

All patients admitted to a health-care facility with laboratory-confirmed or clinically suspected COVID-19 were eligible for inclusion. Cases were defined as severe or critical, according to a modified definition from WHO Clinical Management Guidelines of COVID-19,\(^7\) if they met one or more of the following conditions at hospital admission: \(\text{SpO}_2\) of less than 90%; respiratory rate of more than 30 breaths per min in adults and children older than 5 years (≥40 breaths per min in children aged 1–5 years, ≥50 breaths per min in children aged 2 years to 11 months, ≥60 breaths per min in children aged <2 months); received extracorporeal membrane oxygenation; admitted to ICU; received an inotrope or vasopressor; or received oxygen therapy or either invasive or non-invasive ventilation. Cases not meeting any of the conditions above were categorised as mild or moderate.

Data collection was retrospective, prospective, or both. Many facilities in LMICs were trained by WHO on data entry. Additionally, research networks, health facilities, and authors of published articles (identified through a rapid review of PubMed) were invited to share their datasets and data dictionaries. When definitions were consistent with the WHO CRF, variables were transferred to the WHO Clinical Platform.

The analysis plan was submitted to the WHO Ethical Review Committee, which granted a waiver from ethical review clearance because this was anonymised clinical surveillance. Ethical clearance was obtained, where necessary, by relevant institutional or national bodies.

Statistical analysis

Descriptive and regression analyses were done to summarise demographic and clinical characteristics by HIV status and to evaluate their association with disease severity at hospital admission, and in-hospital mortality (primary outcomes). Records with missing data were excluded when determining distributions across outcome levels; \(\chi^2\) tests and student t-tests were used to assess the relationship between clinical characteristics and primary outcomes. Multivariable logistic regression models using generalised estimating equations were fitted to evaluate whether HIV infection was an independent risk factor for severe or critical illness and proportional hazards models were fitted to evaluate whether HIV infection was a risk factor for in-hospital mortality. The models were adjusted in variance estimation for potential correlation for clustering at the country level.

Age, sex, and HIV status were included in the models a priori. Other covariates were considered for inclusion in the model when they were: reported in more than 80% of the cases; not highly correlated with other variables using a correlation matrix threshold of more than 0.8; independently associated with both the outcomes and HIV status at a p value of less than 0.10. Included covariates were retained in the final model if they were found to be significant at p values of less than 0.05 (appendix 2 pp 7–10).

See Online for appendix 2

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(A) 38 countries contributing clinical data on people living with HIV hospitalised with COVID-19: Argentina, Belarus, Belgium, Brazil, Burkina Faso, Cameroon, Chile, China, Colombia, Democratic Republic of Congo, Dominican Republic, France, Germany, Ghana, Guinea, Hungary, India, Iran, Italy, Jordan, Mexico, Niger, Nigeria, Panama, Peru, Portugal, South Korea, Romania, Russia, Saudi Arabia, Singapore, South Africa, Spain, Switzerland, USA, UK, Zambia, Zimbabwe. (B) 25 countries contributing clinical data on people living with HIV hospitalised with COVID-19: Argentina, Panama, Peru, Portugal, South Korea, Romania, Russia, Saudi Arabia, Singapore, South Africa, Spain, Switzerland, Dominican Republic, France, Germany, Ghana, Guinea, Hungary, India, Iran, Italy, Jordan, Mexico, Niger, Nigeria, Panama, Peru, Portugal, South Korea, Romania, Russia, Saudi Arabia, Singapore, South Africa, Spain, Switzerland, USA, UK, Zambia, Zimbabwe.
Based on the above criteria, the following conditions were considered as potential covariates: asplenia, asthma, chronic cardiac disease, chronic kidney disease, chronic liver disease, chronic neurological disorder, chronic pulmonary disease, current smoking, diabetes, hypertension, malignant neoplasms, obesity, and tuberculosis. Tuberculosis was defined as current (active) or previous infection. We also considered a composite covariate based on number or burden of conditions (none, 1–2, ≥3 conditions) in a separate model.

In addition, using the same approach described above, we conducted a regression analysis to assess risk factors for disease severity at admission and in-hospital mortality among people living with HIV.

Lastly, we conducted exploratory subgroup analyses to assess the impact of geographical location, viral load, and antiretroviral therapy (ART) on mortality and severity. All analyses were conducted in SAS version 9.4, or R version 3.6.3.

**Role of the funding source**

There was no funding source for this study.

**Results**

This analysis reflects the findings from 197,479 cases (16,955 people living with HIV and 180,524 people who were HIV-negative) submitted to the WHO Global COVID-19 Clinical Platform between Jan 1, 2020, and July 1, 2021, from 38 countries (figure; appendix 2 p 2 shows countries submitting >30 patients). 184,805 (93.6%) of the 197,479 admitted cases and 16,398 (96.7%) of 16,955 people living with HIV were hospitalised with laboratory-confirmed COVID-19 (179,886 [98.3%] of 182,911 and 16,149 [99.2%] of 16,283 people living with HIV in the African region). 6,162 (97.2%) of 6,330 people living with HIV with severe presentation at hospital admission and 3,913 (98.4%) of 3,849 people living with HIV who died had laboratory-diagnosed COVID-19.

16,283 (96.0%) of 16,955 people living with HIV were from Africa, largely from South Africa (n=16,008). Other regions contributing data of people living with HIV were the Americas (n=395), European region (n=256), Western Pacific/South East Asia (n=20), and the Eastern Mediterranean Region (n=1). 10,166 (59.9%) of 16,955 people living with HIV reported ART information and 9,302 (91.5%) received treatment.

Compared with people who were HIV-negative, people living with HIV were more likely to be female and younger than 45 years; the mean age was 45.5 years (SD 13.7), and 12,531 (7.6%) were older than 65 years versus 47,237 (26.7%) of the people who were HIV-negative (p<0.0001; table 1). The presence of at least one underlying condition was more frequent among people living with HIV (60.8%) compared with people who were HIV-negative (46.0%). All conditions except hypertension, neurological disorders, obesity, and diabetes were more frequent in people living with HIV (table 1).

| Number of underlying conditions | Total (n=197,479) | People living with HIV (n=16,955) | HIV-negative (n=180,524) | p value |
|---------------------------------|------------------|---------------------------------|----------------------------|---------|
| None  | 102,621          | 60,19 (39.3%)               | 96,602 (54.0%)           | <0.0001 |
| ≥1    | 184,805          | 88,075 (47.7%)              | 78,928 (43.4%)           |         |
| ≥2    | 179,886          | 83,415 (44.4%)              | 76,471 (41.9%)           |         |
| ≥3    | 182,911          | 89,011 (47.7%)              | 73,900 (41.1%)           |         |
| Unknown | 3,913           | 2,162 (11.5%)               | 1,751 (9.7%)             |         |

Among people living with HIV, the three most frequent symptoms were cough (62.1%), fever (55.7%), and shortness of breath (51.9%). All clinical signs and symptoms, except fever and sore throat, were more frequent among people living with HIV compared with people who were HIV-negative (appendix 2 p 3). Creatinine and bilirubin...
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tuberculosis, malignant neoplasms, chronic kidney disease, cardiac disease, pulmonary disease, and corticosteroid use. Other factors associated with severe or critical presentation were age older than 45 years (compared with individuals <18 years), chronic cardiac disease, diabetes, and malignancy (appendix 2 p 7). The increased odds of severe or critical disease and risk of mortality in people living with HIV compared with non-HIV were consistent in models adjusting for underlying condition burden (number of underlying conditions, rather than individual conditions; appendix 2 pp 8–9).

Among people with severe presentation, the median time from hospital admission to death was shorter in people living with HIV (19 days, IQR 6–49) compared with HIV-negative individuals (23 days, 10–51; p<0.0001).

Conversely, among people with mild or moderate presentation, the median time from hospital admission to mortality was longer in people living with HIV (80 days, 14–not estimable) compared with who who were HIV-negative (32 days, 15–102; p<0.0026).

Overall, 9773 (5%) of 194,221 patients had received corticosteroids during hospitalisation. Of those, 1229 (7.5%) were people living with HIV and 8544 (4.8%) were HIV-negative (p<0.0001). Among patients with severe COVID-19 who received corticosteroids, people living with HIV were more likely to die compared with who who were HIV-negative (aHR 1.25, 95% CI 1.04–1.50).

Three exploratory subgroup analyses were done to assess the impact of geographical region, ART use, and viral load status on mortality and severity. Compared with who who were HIV-negative, people living with HIV were more likely to die from COVID-19 in the WHO African region (aHR 1.28, 95% CI 1.24–1.33), but not in the WHO European region (aHR 1.05, 0.77–2.94) or WHO region of the Americas (aHR 1.18, 0.76–1.82), after adjusting for age, sex, underlying conditions, and clinical presentation.

In an exploratory subgroup analysis assessing the effect of ART on mortality in a subset of 9097 patients from South Africa reporting ART information, both people living with HIV on ART (aHR 1.48, 95% CI 1.24–1.33) and not on ART (aHR 1.79, 1.48–2.16) had a significantly higher risk of death compared with who who were HIV-negative, people living with HIV on ART (aHR 1.48, 95% CI 1.24–1.33), but not in the WHO European region (aHR 1.50, 0.77–2.94) or WHO region of the Americas (aHR 1.18, 0.76–1.82), after adjusting for age, sex, underlying conditions, and clinical presentation.

Finally, risk factors for in-hospital mortality and severity among people living with HIV were then determined. Among people living with HIV the most significant risk factor for in-hospital mortality was severe or critical presentation (aHR 1.86, 95% CI 1.82–1.90), followed by chronic kidney disease, diabetes, malignant neoplasms, tuberculosis, male sex, and hypertension.
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| Characteristics          | Total | Death (n=3913) | Discharged alive (n=12166) | p value |
|---------------------------|-------|----------------|-----------------------------|---------|
| **Asthma**                |       |                |                             |         |
| Yes                       | 890   | 181 (6.5%)     | 709 (7.3%)                  | 0.186   |
| No                        | 11640 | 2589 (93.5%)   | 9051 (92.7%)                | -       |
| Unknown                   | 3549  | 1143 (3.2%)    | 2406 (2.7%)                 | -       |
| **Chronic kidney disease**|       |                |                             |         |
| Yes                       | 658   | 275 (10.1%)    | 383 (4.1%)                  | <0.001  |
| No                        | 11193 | 2449 (89.9%)   | 8944 (95.9%)                | -       |
| Unknown                   | 4028  | 1189 (3.1%)    | 2839 (3.1%)                 | -       |
| **Malignant neoplasm**    |       |                |                             |         |
| Yes                       | 183   | 70 (2.7%)      | 113 (1.3%)                  | <0.0001 |
| No                        | 11411 | 2569 (97.3%)   | 8842 (98.7%)                | -       |
| Unknown                   | 4485  | 1274 (2.9%)    | 3211 (3.5%)                 | -       |
| **Chronic liver disease** |       |                |                             |         |
| Yes                       | 81    | 11 (11.0%)     | 70 (11.6%)                  | 0.851   |
| No                        | 620   | 89 (9.0%)      | 531 (88.3%)                 | -       |
| Unknown                   | 15378 | 3813 (24.8%)   | 11565 (24.7%)               | -       |
| **Chronic neurological disorder** |       |                |                             |         |
| Yes                       | 19    | 5 (9.4%)       | 14 (5.5%)                   | 0.281   |
| No                        | 288   | 48 (90.6%)     | 240 (94.5%)                 | -       |
| Unknown                   | 15772 | 3860 (24.3%)   | 11912 (24.3%)               | -       |
| **Comorbidity burden**    |       |                |                             |         |
| None                      | 5725  | 946 (27.3%)    | 4779 (43.2%)                | <0.0001 |
| 1-2                       | 7623  | 2172 (62.6%)   | 5452 (49.3%)                | -       |
| ≥3                        | 1208  | 371 (10.7%)    | 837 (7.5%)                  | -       |
| Unknown                   | 1523  | 425 (1.2%)     | 1098 (1.3%)                 | -       |
| **Severity of illness on admission** |       |                |                             |         |
| Mild or moderate illness  | 9778  | 1675 (43.3%)   | 8103 (68.7%)                | <0.0001 |
| Severe or critical illness| 5889  | 2196 (56.7%)   | 3693 (33.3%)                | -       |
| Unknown                   | 16413 | 3931 (2.4%)    | 12482 (1.3%)                | -       |
| **Admission to ICU**      |       |                |                             |         |
| Yes                       | 344   | 227 (6.5%)     | 117 (1.5%)                  | <0.0001 |
| No                        | 10600 | 2992 (92.9%)   | 7608 (98.5%)                | -       |
| Unknown                   | 5135  | 694 (1.2%)     | 4441 (1.2%)                 | -       |

ART=antiretroviral therapy. BMI=body-mass index. ICU=intensive care unit. Column percentages are calculated excluding unknown categories.

Table 2: Characteristics, underlying conditions, therapeutics, and outcomes among people living with HIV hospitalised with suspected or confirmed COVID-19, by outcome status

Increase in age category was associated with increased mortality risk (table 4). Among people living with HIV, factors significantly associated with severe or critical COVID-19 at admission were chronic cardiac disease, male sex, and age 45–75 years (appendix 2 p 10).

In an exploratory analysis assessing the impact of ART and viral load on clinical outcomes, people living with HIV on ART were 17% less likely to die (p=0·048) and 40% less likely to be admitted with severe disease than those not on ART (p<0·0001). Among people living with HIV, individuals with viral load of less than 1000 copies per mL were 15% less likely to die while in the hospital and 45% less likely to be admitted with severe disease compared with those with viral load of more than 1000 copies per mL (p<0·0001).

Discussion

This analysis found that people living with HIV had 15% greater odds of being admitted to hospital with a severe or critical COVID-19 presentation and, once hospitalised, were 38% more likely to die in hospital than people who were HIV-negative. Among people with severe presentation, the median time from hospital admission to death was shorter in people living with HIV. Among people hospitalised with COVID-19, underlying conditions were more frequent in people living with HIV than people who were HIV-negative, putting them at increased risk of poor outcomes. We found that older age, tuberculosis, and pulmonary diseases were associated with increased risk of in-hospital mortality. Other factors associated with an increased risk of mortality were diabetes, kidney diseases, and malignancies, in line with other reports.10,26 Our exploratory analyses showed that the use of ART or viral load suppression were associated with a reduced risk of poor outcomes among people living with HIV; however, HIV infection remained a risk factor for severity and mortality regardless of ART and viral load suppression status.

The independent association between HIV infection and poor COVID-19 outcomes suggests that the mechanisms for the more severe COVID-19 course in people living with HIV might reside with the HIV disease pathophysiology. Helper-cell lymphopenia is known to contribute to immunosuppression and thus increases the risk of opportunistic infections.27 We also know that people living with HIV—despite adequate treatment—can have a higher propensity to chronic inflammation, underlying immune dysregulation, and cytokine storm due to key cytokines IL-6, IL-1, and TNF-a, and, to a lesser extent, IL-10 and GM-CSFs.28,29 The increased immune activation and persistent, chronic inflammation associated with HIV infection are major players in the accelerated aging process.

The role of immune depression or dysregulation needs to be further investigated to explain the intersection between the two infections, and the mechanisms behind the increased risk of severe or fatal COVID-19 in people living with HIV.

WHO recommends the use of corticosteroids in severely ill COVID-19 patients.30 In this sample, corticosteroid use was infrequent in both people living with HIV and people who were HIV-negative with severe presentation, indicating the need to increase the access to this therapeutic. We also found that tuberculosis and pulmonary diseases were associated with increased risk of in-hospital mortality, but not of severe presentation; this inconsistency might be explained by selection bias in the criteria or timing of hospitalisation (ie, people with tuberculosis or pulmonary diseases with initial symptoms of COVID-19 might access the hospital earlier
or be triaged for an early admission, thus reducing the likelihood of severe presentation at admission). Of note, in our dataset, severity status was assessed within the first 24 h of hospital admission.

Our findings have important public health implications. We found that underlying conditions are common and more frequent among people living with HIV than the general population. Alongside the response to COVID-19, it is thus critical to maintain access to essential health services for this vulnerable group. These include supporting people living with HIV to stay as healthy as possible, regularly access and take their ART medications to achieve viral load suppression, and prevent, diagnose, and manage underlying conditions and co-infections. HIV infection cannot be adequately managed if it is not diagnosed in the first place. Concerningly, large decreases in HIV testing services have been seen across countries. The Global Fund reported that HIV testing declined by 41% in LMICs and referrals for diagnosis and treatment declined by 37% between April and September, 2020, compared with the same period in 2019.31 Concerted efforts are needed to put in place an HIV testing catch-up plan. The increased risk of poor outcomes in people living with HIV hospitalised for COVID-19 should prompt countries to consider including this population as a priority group for COVID-19 vaccination according to the epidemiological context. Informed by these findings, the WHO Strategic Advisory Group of Experts on Immunization (SAGE) has included people living with HIV as a risk group requiring priority consideration for vaccination of COVID-19 in the context of limited supply.32 Countries are already moving in this direction: an informal WHO survey of 100 countries found that 40 have an immunisation policy that prioritises vaccination for people living with HIV.33

Our analysis has several strengths. We were able to pool patient-level data from a large number of facilities using standardised data collection tools, providing sufficient statistical power to support a number of different analyses to assess risk factors for adverse outcomes. There are also

| HIV status | Hazard ratio (95% CI) | p value |
|------------|-----------------------|---------|
| HIV-negative (ref) | 1.38 (1.34–1.41) | <0.0001 |
| HIV positive | 1.38 (1.34–1.41) | <0.0001 |

| Sex | Hazard ratio (95% CI) | p value |
|-----|-----------------------|---------|
| Female (ref) | 1.11 (1.04–1.18) | 0.0061 |
| Male | 1.11 (1.04–1.18) | 0.0061 |

| Age group, years | Hazard ratio (95% CI) | p value |
|-----------------|-----------------------|---------|
| ≤18 years (ref) | 1.07 (1.05–1.09) | <0.0001 |
| >18–45 | 1.38 (1.34–1.41) | <0.0001 |
| >45–65 | 2.50 (2.28–2.74) | <0.0001 |
| >65–75 | 2.50 (2.28–2.74) | <0.0001 |
| >75 years | 3.16 (2.86–3.48) | <0.0001 |

| Severity at admission | Hazard ratio (95% CI) | p value |
|-----------------------|-----------------------|---------|
| Mild or moderate (ref) | 1.07 (1.05–1.09) | <0.0001 |
| Severe or critical | 1.38 (1.34–1.41) | <0.0001 |

| Tuberculosis | None (ref) | 1.10 (1.04–1.16) | 0.003 |
| Tuberculosis | 1.07 (1.04–1.09) | <0.0001 |

| Diabetes | None (ref) | 1.39 (1.36–1.43) | <0.0001 |
| Diabetes | 1.07 (1.05–1.09) | <0.0001 |

| Chronic pulmonary disease | None (ref) | 1.03 (1.01–1.05) | 0.02 |
| Chronic pulmonary disease | 1.03 (1.01–1.05) | 0.02 |

| Chronic kidney disease | None (ref) | 1.58 (1.56–1.61) | <0.0001 |
| Chronic kidney disease | 1.58 (1.56–1.61) | <0.0001 |

| Malignant neoplasms | None (ref) | 1.14 (1.09–1.20) | <0.0001 |
| Malignant neoplasms | 1.14 (1.09–1.20) | <0.0001 |

Covariates that did not pass covariate selection criteria and not included in the full model: asplenia, asthma, chronic cardiac, liver and neurological diseases, smoking, hypertension, obesity, antiretroviral therapy, and steroid use.

Table 3: Risk factors for in-hospital mortality in the overall sample of patients hospitalised with suspected or confirmed COVID-19

| Sex | Hazard ratio (95% CI) | p value |
|-----|-----------------------|---------|
| Female (ref) | 1.07 (1.05–1.09) | <0.0001 |
| Male | 1.07 (1.05–1.09) | <0.0001 |

| Age group, years | Hazard ratio (95% CI) | p value |
|-----------------|-----------------------|---------|
| ≤18 (ref) | 1.38 (1.34–1.41) | <0.0001 |
| >18–45 | 1.38 (1.34–1.41) | <0.0001 |
| >45–65 | 2.50 (2.28–2.74) | <0.0001 |
| >65–75 | 2.50 (2.28–2.74) | <0.0001 |
| >75 | 3.16 (2.86–3.48) | <0.0001 |

| Severity at admission | Hazard ratio (95% CI) | p value |
|-----------------------|-----------------------|---------|
| Mild or moderate (ref) | 1.07 (1.05–1.09) | <0.0001 |
| Severe or critical | 1.38 (1.34–1.41) | <0.0001 |

| Tuberculosis | None (ref) | 1.10 (1.04–1.16) | 0.003 |
| Tuberculosis | 1.07 (1.04–1.09) | <0.0001 |

| Diabetes | None (ref) | 1.39 (1.36–1.43) | <0.0001 |
| Diabetes | 1.07 (1.05–1.09) | <0.0001 |

| Hypertension | None (ref) | 1.07 (1.05–1.09) | <0.0001 |
| Hypertension | 1.07 (1.05–1.09) | <0.0001 |

| Chronic kidney disease | None (ref) | 1.41 (1.31–1.52) | <0.0001 |
| Chronic kidney disease | 1.41 (1.31–1.52) | <0.0001 |

| Malignant neoplasms | None (ref) | 1.24 (1.12–1.38) | 0.0003 |
| Malignant neoplasms | 1.24 (1.12–1.38) | 0.0003 |

Covariates that did not pass covariate selection criteria and not included in the full model: asplenia, asthma, chronic cardiac, liver and neurological diseases, smoking, hypertension, obesity, antiretroviral therapy, and steroid use.

Table 4: Risks factors for in-hospital mortality among people living with HIV hospitalised with suspected or confirmed COVID-19

41% in LMICs and referrals for diagnosis and treatment declined by 37% between April and September, 2020, compared with the same period in 2019.31 Concerted efforts are needed to put in place an HIV testing catch-up plan. The increased risk of poor outcomes in people living with HIV hospitalised for COVID-19 should prompt countries to consider including this population as a priority group for COVID-19 vaccination according to the epidemiological context. Informed by these findings, the WHO Strategic Advisory Group of Experts on Immunization (SAGE) has included people living with HIV as a risk group requiring priority consideration for vaccination of COVID-19 in the context of limited supply.32 Countries are already moving in this direction: an informal WHO survey of 100 countries found that 40 have an immunisation policy that prioritises vaccination for people living with HIV.33

Our analysis has several strengths. We were able to pool patient-level data from a large number of facilities using standardised data collection tools, providing sufficient statistical power to support a number of different analyses to assess risk factors for adverse outcomes. There are also
In conclusion, we report, to our knowledge, the largest multicountry analysis to date exploring the association between HIV infection and clinical outcomes in people hospitalised with COVID-19, using a large dataset from LMICs. This analysis will be updated regularly, and as of April 1, 2022, the WHO Platform included 621,441 total patients, of whom 37,453 were people living with HIV. WHO encourages countries and stakeholders to support the generation of evidence-based interventions, including optimised vaccination strategies for subpopulations, by contributing their data through the WHO Global Platform for COVID-19.

Contributors
SB conceived the Article, developed the analysis plan, and wrote the first draft. RS did the statistical analysis. SST developed the analysis plan and did the analysis. JD developed the analysis plan and contributed to the review. SN contributed to the writing. WJ, RF, RH, LR, NF, and MD provided input into the manuscript. SST and RS directly accessed and verified the underlying data reported in the manuscript. SB, RS, SST, and JD had full access to all the data in the study. All authors had final responsibility for the decision to submit for publication.

Declaration of interests
RH received funding from the Wellcome Trust, Canadian Institute of Health Research, UK Research and Innovation/Medical Research Council, and International COVID-19 Data Alliance–Health Data Research UK. All other authors declare no competing interests.

Data sharing
All relevant documents related to the WHO Clinical Platform, including the statistical analysis plan, CRF, data dictionary, and terms of use, can be found on the WHO Global Clinical Platform webpage.27 Data submitted to the WHO Platform are the property of the individual Ministries of Health. All data outputs will be published in an open access format on the webpage.

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The views presented in this Article are those of the authors and do not reflect those of the WHO or the Pan American Health Organization.

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