Undiagnosed comorbidities among individuals hospitalised with COVID-19 in South African public hospitals

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Background. Previous studies have reported comorbid disease, including hypertension, diabetes mellitus, chronic cardiac and renal disease, malignancy, HIV, tuberculosis (TB) and obesity, to be associated with COVID-19 mortality. National demographic surveys have reported a high proportion of undiagnosed and untreated comorbid disease in South Africa (SA).

Objectives. To determine the number of individuals with previously undiagnosed HIV, TB and non-communicable diseases (NCDs) among patients hospitalised with COVID-19, and the level of medical control of these chronic diseases.

Methods. We conducted a sentinel surveillance study to collect enhanced data on HIV, TB and NCDs among individuals with COVID-19 admitted to 16 secondary-level public hospitals in six of the nine provinces of SA. Trained surveillance officers approached all patients who met the surveillance case definition for inclusion in the study, and consenting patients were enrolled. The data collection instrument included questions on past medical history to determine the self-reported presence of comorbidities. The results of clinical and laboratory testing introduced as part of routine clinical care for hospitalised COVID-19 patients were collected for the study, to objectively determine the presence of hypertension, diabetes, HIV and TB and the levels of control of diabetes and HIV.

Results. On self-reported history, the most prevalent comorbidities were hypertension (n=1 658; 51.5%), diabetes (n=855; 26.6%) and HIV (n=603; 18.7%). The prevalence of self-reported active TB was 3.1%, and that of previous TB 5.5%. There were 1 254 patients admitted with COVID-19 (39.0%) who met the body mass index criteria for obesity. On clinical and laboratory testing, 87 patients were newly diagnosed with HIV, 29 with TB, 215 with diabetes and 40 with hypertension during their COVID-19 admission. There were 151/521 patients living with HIV (29.0%) with a viral load >1 000 copies/mL and 309/570 (54.2%) with a CD4 count <200 cells/µL. Among 901 patients classified as having diabetes, 777 (86.2%) had a glycated haemoglobin (HbA1c) level \geq 6.5%.

Conclusion. The study revealed a high prevalence of comorbid conditions among individuals with COVID-19 admitted to public hospitals in SA. In addition, a significant number of patients had previously undiagnosed hypertension, diabetes, HIV and active TB, and many had poorly controlled chronic disease, as evidenced by high HbA1c levels in patients with diabetes, and high viral loads and low CD4 levels in patients with HIV. The findings highlight the importance of strengthening health systems and care cascades for chronic disease management, which include prevention, screening for and effectively treating comorbidities, and ensuring secure and innovative supplies of medicines in primary healthcare during the COVID-19 pandemic.

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South Africa (SA) experienced four COVID-19 waves and reported 3 472 436 laboratory-confirmed COVID-19 cases and 91 228 deaths by 3 January 2022.^[1] Apart from older age, male sex and non-white race, important factors associated with COVID-19 mortality in SA were comorbid diseases, including hypertension, diabetes, chronic cardiac and renal disease, malignancy, HIV, tuberculosis (TB) and obesity.^[2] In addition, a high prevalence of multimorbidity – non-communicable disease (NCD), HIV and tuberculosis – has been reported among patients admitted with COVID-19.^[2] Studies have also demonstrated an increased risk of COVID-19 mortality among

patients with poorly controlled diabetes $^{[3]}$ and people living with HIV (PLWH) with a low CD4 count. $^{[2]}$

SA has a high burden of NCDs and chronic infectious diseases such as HIV and TB. The estimated number of PLWH in 2018 was 7.7 million, with 2 million not on treatment.^[4] In addition, the estimated number of people with TB was >300 000, with 59% co-infected with HIV.^[5] According to the national demographic survey and other studies, a high proportion of people in SA have undiagnosed NCDs, and among those with known NCDs, a high proportion have poorly controlled disease.^[6,7] The burden of undiagnosed and poorly controlled chronic diseases can be attributed to patient factors (health literacy, health-seeking behaviour, stigma), health system factors (poor access to health services, poor quality of care) and upstream socioeconomic determinants of health.

With a high burden of HIV, TB and NCDs in SA, and a high proportion of undiagnosed and untreated comorbid disease, which are well-documented risk factors for COVID-19 mortality, it is important to determine the prevalence of comorbidities among hospitalised patients with COVID-19. The objectives of this study were to determine the number of individuals with previously undiagnosed HIV, TB and NCDs among patients hospitalised with COVID-19, and the levels of medical control of these chronic diseases. We also compared the characteristics of patients enrolled in the study with those reported to the national hospital surveillance system.

Methods

Study setting

The National Institute for Communicable Diseases (NICD) established DATCOV, a national hospital surveillance system for COVID-19, in late March 2020. DATCOV receives data from all 666 public and private hospitals in the country on hospital admissions for patients diagnosed with COVID-19 on polymerase chain reaction (PCR) or antigen testing. DATCOV collects limited data on NCDs in patients hospitalised with COVID-19. We therefore conducted a sentinel surveillance study to collect enhanced data on HIV, TB and NCDs among individuals admitted with COVID-19. Sixteen secondary-level public hospitals in six of the nine provinces in SA were selected because of their relatively high COVID-19 case numbers, and because some were already conducting surveillance for severe acute respiratory infections. Data were collected between 1 November 2020 and 30 June 2021, which included patients admitted during the second and third waves dominated by the SARS-CoV-2 Beta and Delta variants, respectively.

Sampling

For the purposes of this study, a COVID-19 case was defined as a person with a positive real-time reverse transcriptase PCR assay for SARS-CoV-2 or SARS-CoV-2 antigen test, who was \geq 18 years of age and admitted to the study site hospitals with a confirmed duration of stay in hospital of \geq 1 full day.

Sample size calculation accounted for the prevalence of diabetes, hypertension, TB and HIV, the proportion of mortality as an outcome for COVID-19 cases, an estimated contribution of diabetes, hypertension, TB and HIV to mortality, and clustering effect at the hospital level. The total sample size required was 3 080 COVID-19positive patients admitted to surveillance hospitals in SA. Trained surveillance officers, who were qualified nurses, approached all patients who met the surveillance case definition for inclusion in the study, and consenting patients were enrolled.

Data collection

Surveillance officers interviewed recruited participants and/or reviewed their patient medical records in order to administer the data collection instrument, which included questions on past medical history to determine the self-reported presence of comorbidities previously diagnosed and treated by a healthcare professional. Clinical and laboratory testing were introduced as part of routine clinical care for hospitalised COVID-19 patients at participating hospitals, and if not already conducted by the attending clinician were done by the surveillance officer. The following parameters were recorded for the study, to objectively determine the presence and level of control of comorbidities: (*i*) weight, height and calculation of the body mass index (BMI) to determine whether patients were overweight or obese; (*ii*) random and fasting blood glucose to determine the presence of diabetes; (*iii*) glycated haemoglobin (HbA1c) to determine the level of control of diabetes; (*iv*) blood pressure to determine the presence and control of hypertension; (*v*) fasting blood cholesterol to determine the presence of hypercholesterolaemia; (*vi*) sputum and Xpert MTB/RIF Ultra testing for TB diagnosis; and (*vii*) HIV enzyme-linked immunosorbent assay to determine the presence of HIV, and for those who were HIV positive, blood testing for CD4 and viral load to determine the levels of immunosuppression and viraemia (obtained either from tests conducted during admission).

The standardised case reporting form (CRF) was developed by the International Severe Acute Respiratory and emerging Infection Consortium (ISARIC). Data were entered and stored on a secure online Research Electronic Data Capture repository (REDCap, version 10.6.14; Vanderbilt University, USA) hosted by the University of Oxford on behalf of ISARIC.

Data analysis

Descriptive statistics such as frequencies and percentages were used for categorical variables, and continuous variables were expressed as medians and interquartile ranges (IQRs). Frequency distribution tables were used to describe demographics, prevalence of disease and complications, and completeness of data for both the study and DATCOV data. Categorical variables classifying the levels of disease control were constructed from the HbA1c, HIV CD4 count and HIV viral load laboratory results. A χ^2 test was used to compare categorical variables, and differences were reported as significant at *p*<0.05. Statistical analyses were performed using Stata software, version 15 (StataCorp, USA).

The dataset analysed for the manuscript and the data dictionary are available upon reasonable request from the corresponding author (WJ, at waasilaj@nicd.ac.za).

Ethical considerations

Ethical approval was obtained from local ethics boards (affiliated to the chosen hospitals), including the human research ethics committees of the University of the Witwatersrand, the University of Cape Town, the University of KwaZulu-Natal, North-West University, Walter Sisulu University and the University of the Free State. The National Department of Health (NDoH) NCD and TB directorates were collaborators on the study and provided letters of support encouraging hospitals to conduct screening laboratory tests on patients admitted with COVID-19. Permission was obtained from the National Health Research Database provincial research committees and from the management of the 16 hospitals.

Results

From 1 November 2020 to 30 June 2021, of the 9 671 admissions that were reported to DATCOV, a total of 3 217 hospitalised patients with COVID-19 were enrolled from 16 surveillance sites (see Table 1 for comparison of all admissions and study participants). The median (IQR) age of participants was 56 (42 - 66) years, and most (n=1 664; 51.7%) were aged 40 - 65 years. The majority of the patients were female (n=1 832; 57.0%). Of the 3 217 participants recruited, 2 356 (73.2%) were black African, 487 (15.1%) were coloured, 142 (4.4%) were Indian, 202 (6.3%) were white and 28 (0.9%) were classified as other race group (Table 2).

The most commonly reported symptoms on admission among study participants were shortness of breath (n=2 308; 71.7%), cough

	DATCOV all	Study enrolled
	admissions	admissions
Characteristic	(N=9 671), n (%)	(N=3 217), n (%)
Age (years)		
18 - 39	2 524 (26.1)	662 (20.6)
40 - 64	4 356 (45.0)	1 664 (51.7)
≥65	2 735 (28.3)	890 (27.7)
Sex		
Male	4 123 (42.6)	1 384 (43.0)
Female	5 535 (57.2)	1 832 (56.9)
Comorbidities	5 061 (52.3)	2 769 (86.1)
Received supplemental oxygen	4 702 (48.6)	2 443 (75.9)
Received invasive ventilation	553 (5.7)	228 (7.1)
Ever in ICU	842 (8.8)	371 (11.5)
Died	3 337 (34.5)	680 (21.1)

Table 1. Comparison of all admissions reported to DATCOV

(n=2 070; 64.4%), fatigue (n=1 359; 42.2%), fever (n=1 342; 41.7%), chest pain (n=864; 26.9%), muscle aches (n=720; 22.4%) and sore throat (n=474; 14.7%), while 216 (6.7%) had no symptoms. The most commonly reported COVID-19 complications among study participants during admission were pneumonia (n=2 487; 77.3%), acute respiratory distress syndrome (*n*=457; 14.2%), anaemia (*n*=108; 3.4 %) and acute renal failure (*n*=105; 3.3%) (Table 2).

During the course of the admission, 371 participants (11.5%) were admitted to an intensive care unit (ICU). Most participants (n=2 443; 75.9%) received supplemental oxygen during their stay in hospital, and 228 (7.1%) required invasive mechanical ventilation. Of the participants, 2 487 (77.3%) were discharged alive and 680 (21.1%) died, while 39 (1.3%) were still in hospital when the study ended or were transferred to other facilities for step-down care (Table 2).

Prevalence of comorbidities

On self-reported history, the most prevalent comorbidities were hypertension (n=1 658; 51.5%), diabetes (n=855; 26.6%) and HIV (n=603; 18.7%). The prevalence of self-reported active TB was 3.1% (n=100) and that of previous TB 5.5% (n=176). There were 1 254 patients (39.0%) who met the BMI criteria for obesity. A total of 183 participants (5.7%) reported being current smokers (Table 3).

On clinical and laboratory testing, a number of patients were newly diagnosed with HIV, TB, diabetes and hypertension (Table 4). The TB GeneXpert test was conducted on 1 531 participants (47.6%), as the remaining patients were unable to produce sputum or the test was not conducted for other reasons. Of those tested, 89 (5.8%) had positive results, and 29/89 (32.6%) were newly diagnosed. Among 2 851 participants who had an HIV test, 685 (24.0%) tested positive, and of these, 87 (12.7%) were newly diagnosed. A total of 2 954 participants were tested for diabetes or prediabetes; 1 028 (34.8%) were classified as diabetic, with 215 (20.9%) being newly diagnosed. A total of 1 698 (52.8%) participants were classified as hypertensive, with 40 (2.4%) being newly diagnosed.

Comorbid disease control

Of 685 PLWH, 553 (80.7%) were on antiretroviral therapy, 521 (76.1%) had a viral load result available, and 570 (83.2%) had a CD4 cell count available (during admission or within the past 6 months). There were

Characteristics	Participants
Age (years), median (IQR)	56 (42 - 66)
Age group (years), n (%)	
<40	662 (20.6)
40 - 64	1 664 (51.7)
≥65	890 (27.7)
Unknown	1 (0.03)
Sex, <i>n</i> (%)	
Female	1 832 (57.0)
Male	1 384 (43.0)
Not specified	1 (0.03)
Race group, <i>n</i> (%)	
White	202 (6.3)
Black	2 356 (73.2)
Coloured	487 (15.1)
Indian	142 (4.4)
Other	28 (0.9)
Unknown	2 (0.1)
Symptoms on admission, n (%)	
No symptoms	216 (6.7)
Shortness of breath	2 308 (71.7)
Cough	2 070 (64.4)
Fatigue/malaise	1 359 (42.2)
Fever	1 342 (41.7)
Chest pain	864 (26.9)
Muscle aches (myalgia)	720 (22.4)
Headache	531 (16.5)
Sore throat	474 (14.7)
Joint pain (arthralgia)	425 (13.2)
Complications, <i>n</i> (%)	
Pneumonia	2 487 (77.3)
Acute respiratory distress syndrome	457 (14.2)
Anaemia	108 (3.4)
Acute renal injury	105 (3.3)
Received supplemental oxygen, n (%)	2 443 (75.9)
Received invasive ventilation, <i>n</i> (%)	228 (7.1)
Treated in intensive care unit, n (%)	371 (11.5)
Outcome	
Discharged alive	2 487 (77.3)
Died	680 (21.1)
Transferred out or still in hospital	39 (1.3)
IQR = interquartile range.	

Table 2. Baseline characteristics among enrolled patients with COVID-19 admitted to study hospitals, 1 November

151/521 PLWH (29.0%) with a viral load >1 000 copies/mL; 25.6% of patients with known HIV and 58.5% of patients with newly diagnosed HIV had severe viraemia. There were 309/570 PLWH (54.2%) with a CD4 count <200 cells/µL; 58.2% of patients with known HIV and 25.0% of patients with newly diagnosed HIV were immunocompromised. A total of 2 289 participants (77.5%) had HbA1c results, of whom 901 were classified as diabetic. Of these, 777 (86.2%) had an HbA1c level ≥6.5%; 85.6% patients with known diabetes and 88.4% of patients with newly diagnosed diabetes were poorly controlled (Table 5).

Treatment and outcomes

On comparing patients admitted with pre-existing comorbidities and those with newly diagnosed comorbidities, there were generally no differences in terms of treatment with oxygen, ventilation, intensive care and mortality. The only statistically significant differences were among patients with hypertension, where treatment with supplemental oxygen was required by 83.7% of those with pre-existing comorbidities compared with 65.0% of those with newly diagnosed comorbidities (p=0.002), and among patients with diabetes, where ventilation was required by 13.0% of those with newly diagnosed comorbidities compared with 6.8% of those with pre-existing comorbidities (p=0.01), and treatment in an ICU was required by 19.1% of those with newly diagnosed comorbidities (p=0.02), and treatment in an ICU was required by 19.1% of those with pre-existing comorbidities (p=0.02) (Table 6).

Discussion

The study revealed a high prevalence of comorbid conditions among individuals admitted to public hospitals in SA with COVID-19. In addition, a significant number of patients had previously undiagnosed hypertension, diabetes, HIV and active TB. Many patients had poorly controlled chronic disease, as evidenced by high HbA1c levels in diabetics, and high viral

Table 3. Prevalence of self-reported comorbidities among enrolled patients with COVID-19 admitted to study hospitals, 1 November 2020 - 30 June 2021 (*N*=3 217)

Comorbidities/risk factors	n (%)
Hypertension	1 658 (51.5)
Diabetes	855 (26.6)
HIV	603 (18.7)
Active tuberculosis	100 (3.1)
Previous tuberculosis	176 (5.5)
Chronic pulmonary disease	57 (1.8)
Asthma	112 (3.5)
Chronic renal failure	70 (2.2)
Chronic liver disease	9 (0.3)
Chronic neurological disorder	33 (1.0)
Asplenia	4 (0.1)
Malignancy	50 (1.6)
Obesity	1 254 (39.0)
Hypercholesterolaemia	67 (2.4)
Current smoker	183 (5.7)
Obesity Hypercholesterolaemia	1 254 (39.0) 67 (2.4)

loads and low CD4 cell counts in PLWH. The study was able to identify previously undiagnosed TB and diabetes because the study sites performed routine HbA1c and TB GeneXpert tests on all participants.

Similar to other studies, the most prevalent comorbidities in our study were hypertension, diabetes and obesity.^[8-11] Our prevalence rates for HIV were higher than in other international studies, ranging from 0.5% to 7.5%,^[11,12-14] but similar to prevalences of HIV reported in SA studies.^[10,15] In some studies, comorbidities such as chronic cardiac disease, asthma and chronic pulmonary disease were noted to be highly prevalent,^[16,17] which was not the case in the present study, where these conditions had prevalence rates <5%. These diseases could have been missed owing to poor historical records of pre-existing medical conditions. The differences in prevalence of comorbidities are also possibly related to the fact that only secondary-level public hospitals were sampled.

We also found that a higher proportion of patients with newly diagnosed diabetes required ventilation and treatment in an ICU compared with those with previously diagnosed diabetes. It is likely that these patients had poor control of diabetes and poorer overall health status, which would explain their more severe disease. This finding is in keeping with other studies that showed worse outcomes among patients with poorly controlled diabetes.^[3]

The finding of previously undiagnosed comorbidities and poorly controlled chronic diseases on admission to hospital for COVID-19 may be related to disruption of routine health services during the pandemic. Studies have shown that routine health services in SA were negatively affected during the COVID-19 pandemic, particularly in the weeks during which the country adopted high levels of national restrictions on movement.^[18,19] These restrictions resulted in reduced active screening for comorbid diseases, as evidenced by the reduction in GeneXpert testing in SA, particularly during the pandemic wave periods.^[20] National restrictions may also have affected access to healthcare for people with chronic medical conditions, and they may not have had routine follow-up visits or monitoring investigations, or collected their medication from primary healthcare facilities. However, it must be noted that the high level of undiagnosed and poorly controlled comorbid disease is probably not related solely to strained routine health services during lockdowns, as the issue of poor screening for and treatment of comorbidities predates the COVID-19 pandemic.[21]

Table 4. Prevalence of pre-existing and newly diagnosed comorbidities among enrolled patients with COVID-19 admitted to study hospitals, 1 November 2020 - 30 June 2021

Comorbidities	Pre-existing comorbidities, n/N (%)	Newly diagnosed comorbidities, <i>n</i> / <i>N</i> (%)	Total comorbidities, <i>n</i> / <i>N</i> (%)
Hypertension	1 658/3 217 (51.5)	40/1 698 (2.4)	1 698/3 217 (52.8)
Diabetes	855/3 217 (26.6)	215/2 954 (7.3)	1 070/3 217 (33.3)
HIV	603/3 217 (18.7)	87/2 851 (3.1)	690/3 217 (21.5)
Active tuberculosis	100/3 217 (3.1)	29/1 531 (1.9)	129/3 217 (4.0)

Table 5. Disease control for patients with HIV and those with diabetes among enrolled patients with COVID-19 and with laboratory results available admitted to study hospitals, 1 November 2020 - 30 June 2021

	Pre-existing comorbid disease,	Newly diagnosed comorbid disease,	Total comorbid disease,
Test/lab result	n/N (%)	n/N (%)	n/N (%)
HIV disease control			
VL >1 000 copies/mL	120/468 (25.6)	31/53 (58.5)	151/521 (29.0)
CD4 count <200 cells/µL	292/502 (58.2)	17/68 (25.0)	309/570 (54.2)
Diabetes control			
HbA1c ≥6.5%	602/703 (85.6)	175/198 (88.4)	777/901 (86.2)
VL = viral load; HbA1c = glycated haemog	obin.		

		Pre-existing comorbidities,	Newly diagnosed comorbidities,	
Comorbidity	Characteristics	n/N (%)	n/N (%)	<i>p</i> -value
Hypertension	Received supplemental oxygen	1 388/1 658 (83.7)	26/40 (65.0)	0.002
	Received invasive ventilation	140/1 658 (8.4)	3/40 (7.5)	0.86
	Treated in ICU	204/1 658 (12.3)	4/ 40 (10.0)	0.74
	Outcome			0.67
	Discharged alive	1 205/1 658 (72.6)	34/40 (85.0)	
	Died	436/1 658 (26.3)	6/40 (15.0)	
	Transferred out or still in hospital	17/1 658 (1.1)	-	
Diabetes	Received supplemental oxygen	695/855 (81.3)	177/215 (82.3)	0.29
	Received invasive ventilation	58/855 (6.8)	28/215 (13.0)	0.01
	Treated in ICU	104/855 (12.2)	41/215 (19.1)	0.02
	Outcome			0.06
	Discharged alive	621/855 (72.6)	157/215 (73.0)	
	Died	225/855 (26.3)	54/215 (25.1)	
	Transferred out or still in hospital	8/855 (0.8)	4/215 (1.9)	
HIV	Received supplemental oxygen	402/598 (67.2)	57/87 (65.5)	0.84
	Received invasive ventilation	25/598 (4.1)	5/87 (5.7)	0.49
	Treated in ICU	44/598 (7.4)	10/87 (11.5)	0.17
	Outcome			0.07
	Discharged alive	495/598 (82.8)	66/87 (75.9)	
	Died	82/598 (13.7)	21/87 (24.1)	
	Transferred out or still in hospital	18/598 (3.0)	-	
Active	Received supplemental oxygen	70 /100 (70.0)	20/29 (69.0)	0.91
tuberculosis	Received invasive ventilation	1/100 (1.0)	2/29 (6.9)	0.06
	Treated in ICU	7/100 (7.0)	3/29 (10.3)	0.55
	Outcome			0.52
	Discharged alive	81/100 (81.0)	25/29 (86.2)	
	Died	19/100 (19.0)	14/29 (13.8)	
	Transferred out or still in hospital	-	-	

Table 6. Treatment and outcomes of patients with pre-existing and newly diagnosed comorbidities among enrolled patients with COVID-19 admitted to study hospitals, 1 November 2020 - 30 June 2021

ICU = intensive care unit.

The present study also revealed a level of under-reporting in the national COVID-19 hospital surveillance. While study participants were similar in age and sex to all admissions reported to DATCOV, they had a higher prevalence of comorbidities, which may be due to under-reporting in DATCOV, and the newly diagnosed disease in the study. While similar proportions of study participants were treated in ICUs or received invasive mechanical ventilation, 76% received supplemental oxygen compared with 49% of participants reported to DATCOV. Study participants also had a lower CFR than all admissions to study hospitals in DATCOV, because the surveillance officers had very limited access to patients who had severe disease and died early during their admission, and therefore could not be enrolled in the study. In-hospital mortality was 21%, which was similar to the 24% rate reported from the national surveillance^[2] and other studies ranging from 13% to 26%.^[22-24]

Study strengths and limitations

A strength of the study was the ability to collect more complete data on comorbidities compared with the DATCOV national hospital surveillance, owing to the placement of trained surveillance officers to conduct data collection. The study in collaboration with the NDoH encouraged screening of patients admitted with COVID-19 and was able to document underlying comorbidities more accurately than is routinely done in public hospitals. The study had a few limitations. While we aimed to recruit only patients admitted for COVID-19 and not those admitted for other reasons

who had incidental positive SARS-CoV-2 tests, some patients in the latter category may have been included. Of the patients, 6.7% were admitted with no symptoms. Selection of hospitals and participants may have introduced a potential bias. The study included a sample of provincial and regional public hospitals from six provinces, and may therefore not be representative of all hospitals in SA. There may have been an overestimation of the prevalence of diseases such as HIV compared with the national population prevalence, because the prevalence of HIV is higher among public sector patients. Also, the data may have not represented SA's income level diversity, as it did not include private sector patients, who are generally considered to be of higher economic status. Lastly, since the sample consisted of individuals admitted with a positive SARS-CoV-2 test, and presumably more severe COVID-19 disease, the results may not be generalisable to patients without COVID-19 or with less severe COVID-19 because of potential collider bias.

Conclusion

The study identified previously undiagnosed NCDs and chronic infectious diseases among patients admitted with COVID-19 that place these patients at risk of severe disease and poor COVID-19 outcomes. These individuals would benefit from COVID-19 prevention programmes such as vaccine prioritisation, as well as early referral and treatment for acute COVID-19. The findings highlight the importance of strengthening health systems and care cascades for disease management, which include prevention, screening, and effective treatment of comorbidities. Ensuring secure and innovative supplies of medicines in primary healthcare during the COVID-19 pandemic is critical, including antiretrovirals, TB treatment and chronic medications, so that patients' chronic diseases are optimally treated even during periods when routine health services are disrupted. A further recommendation is for the government to strengthen risk communication and community engagement during the pandemic, to ensure that health service users are aware that they should continue to access primary healthcare services, and obtain and regularly take their chronic medications.

The study has also shown the importance of establishing sentinel surveillance studies to complement routine surveillance. They ensure high-quality and more detailed data collection to answer research questions that national surveillance systems may not be able to. Studies like this need to be developed, approved and initiated at the start of a pandemic in time to inform case management and public health policy. The study points to the importance of forward planning and investment in preparedness studies.

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The corresponding author (WJ) had full access to all the data in the study and had final responsibility for the decision to submit for publication. **Conflicts of interest.** None.

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