BMJ Open

Risk factors for hospitalisation and death from COVID-19: a prospective cohort study in South Sudan and Eastern Democratic Republic of the Congo

Eva Leidman ,[1,2] Shannon Doocy,[2] Grace Heymsfield,[1] Abdou Sebushishe,[3] Eta Ngole Mbong,[4] Jennifer Majer,[5] The IMC-CDC COVID-19 Research Team, Iris Bollemeijer[5]

To cite: Leidman E, Doocy S, Heymsfield G, *et al*. Risk factors for hospitalisation and death from COVID-19: a prospective cohort study in South Sudan and Eastern Democratic Republic of the Congo. *BMJ Open* 2022;**12**:e060639. doi:10.1136/bmjopen-2021-060639

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2021-060639).

Received 05 January 2022
Accepted 11 April 2022

For numbered affiliations see end of article.

Correspondence to
Eva Leidman;
eleidman@cdc.gov

ABSTRACT

Objectives Our study described demographic characteristics, exposures and symptoms, and comorbidities to evaluate risk factors of hospitalisation and mortality among cases in Juba, South Sudan (SSD) and North and South Kivu in eastern Democratic Republic of the Congo (DRC).

Design Prospective observational cohort of COVID-19 cases.

Methods Individuals presenting for care at one of five study facilities in SSD (n=1) or DRC (n=4) or referred from home-based care by mobile medical teams between December 2020 and June 2021 were eligible for enrolment. Demographic characteristics, COVID-19 exposures, symptoms at presentation, as well as acute and chronic comorbidities, were evaluated using a standard questionnaire at enrolment. Disease progression was characterised by location of care using mixed-effects regression models.

Results 751 individuals were eligible for enrolment. Among cases followed to discharge or death (n=519), 375 were enrolled outpatients (75.7%). A similar number of cases were enrolled in DRC (n=262) and SSD (n=257). Overall mortality was 4.8% (95% CI: 3.2% to 6.9%); there were no outpatient deaths. Patients presenting with any symptoms had higher odds of hospitalisation (adjusted OR (AOR) 2.78, 95% CI 1.47 to 5.27) and all deaths occurred among symptomatic individuals. Odds of both hospitalisation and mortality were greatest among cases with respiratory symptoms; presence of low oxygen levels on enrolment was strongly associated with both hospitalisation (AOR 7.77, 95% CI 4.22 to 14.29) and mortality (AOR 25.29, 95% CI 6.42 to 99.54). Presence of more than one chronic comorbidity was associated with 4.96 (95% CI 1.51 to 16.31) times greater odds of death; neither infectious comorbidities evaluated, nor malnutrition, were significantly associated with increased mortality.

Conclusions Consistent with prior literature, older age, low oxygen level, other respiratory symptoms and chronic comorbidities were all risk factors for mortality. Patients presenting with these characteristics were more likely to be hospitalised, providing evidence of effective triage and referral.

Trial registration number NCT04568499.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ A prospective observational cohort study enrolled COVID-19 cases in South Sudan and the Democratic Republic of Congo to better characterise risk factors of hospitalisation and death.
⇒ Cases admitted for care at inpatient health facilities as well as cases managed by home-based care teams were enrolled in the study, such that the study population represent the spectrum of severity of COVID-19 cases.
⇒ Given barriers to case identification in both countries, particularly limited testing capacity, the study population represents only cases who interacted with the health system, the principal limitation of this study.

INTRODUCTION

Characterising risk factors for severe COVID-19 is critical for identifying individuals who may benefit from increased monitoring, hospitalisation or ventilator support, as well as those at increased risk of death.[1–3] Early identification and referral is particularly important in resource scarce contexts where access to inpatient care is limited. Risk factors for severe illness from COVID-19 with strong evidence supported by systematic reviews and meta-analyses include cancer, cerebrovascular disease, chronic kidney disease, chronic obstructive pulmonary disease, diabetes mellitus, cardiovascular disease, obesity, pregnancy and smoking.[4–7] Demographic risk

factors, including older age and male sex, have also been associated with poor prognosis.[1 2]

The evidence on risk factors for severe COVID-19 primarily includes case surveillance and studies conducted in higher income settings.[8] Consequently, less is known regarding how these risk factors, as well as undernutrition and exposure to infectious conditions more prevalent in lower resource settings, impact the severity of COVID-19. This evidence gap is particularly relevant given differences in the epidemiology of COVID-19 in Africa, where officially reported numbers of cases and deaths are lower than the Americas, Europe and Asia,[9] while case fatality rates are estimated to be higher. Modelled estimates of excess mortality for patients admitted for critical care in Africa are between 11 and 23 excess deaths per 100 admissions compared with the global average mortality from COVID-19.[10] This research aimed to characterise early symptoms, exposures, comorbidities and other risk factors associated with hospitalisation and death from COVID-19 in Juba, South Sudan (SSD) and North and South Kivu, Eastern Democratic Republic of Congo (DRC) to inform identification and triage of COVID-19 cases at higher risk of mortality in resource-poor and humanitarian settings in Africa.

METHODS

An observational cohort study enrolled COVID-19 cases between December 2020 and June 2021; the last cases were discharged in July 2021 in both countries. Five study facilities operated or supported by International Medical Corps (IMC) recruited patients, including a COVID-19 treatment centre in Juba, SSD and four health facilities in Eastern DRC. Study facilities in DRC included general public hospitals in Bukavu and Goma, as well as a public outpatient clinic and an non-governmental organization (NGO) operated health centre in Goma. Characteristics of the study facilities and care offered are described in online supplemental table. Availability of therapies for inpatients are presented by facility in a companion manuscript from this study focused on inpatient management.[11] Available therapies for outpatients were limited. Individuals presenting for care at a study facility or referred from home-based care by mobile medical teams in the facility catchment area were eligible. Cases with a positive real-time reverse transcription PCR (RT-PCR) or antigen test and inpatients not tested meeting the national suspect case definitions were eligible for enrolment. In DRC, a case met the syndromic case definition if they had one or more of the following sign(s) or symptom(s): fever, dry cough, headache, severe fatigue, sore throat, shortness of breath (SOB), dyspnoea (difficulty breathing), muscle or joint pain, or coryza (common cold). In SSD, suspect cases presented with acute onset of fever ≥38°C and cough, or an acute onset of any three or more signs or symptoms, including those in the DRC case definition as well as individuals with anorexia, nausea, vomiting, diarrhoea and altered mental status. Cases were excluded from analysis if they tested negative following enrolment, were lost to follow-up (before recovery or death), or were transferred to another facility for care.

Oral consent was obtained for eligible adults and parental consent for children <18 years. Additionally, assent was obtained for children 12–17 years. Participants receiving inpatient care were followed up daily, whereas outpatients were followed up weekly through home visits and/or phone interviews. All participants were followed until COVID-19 recovery, death or loss to follow-up. Inpatients were followed up daily whereas outpatient cases were followed weekly. Cases treated as inpatient were considered recovered if they were discharged alive from inpatient care. Patients treated at home were considered recovered if they met one of the following conditions: resolution of fever for at least 48 hours without the use of fever-reducing medications and with improvement of other symptoms; or asymptomatic at two sequential follow-up visits. For outpatients, three attempts to contact were made before an individual was considered lost to follow-up.

Data on sociodemographic characteristics, COVID-19 exposures and symptoms, self-reported health history, anthropometric measurements and SARS-COV-2 tests (RT-PCR and/or antigen) were collected at enrolment by research nurses using a standard data collection instrument. Anthropometric measures of mid-upper arm circumference, weight, height and oedema were assessed using standard procedures.[12] Malaria was evaluated using a rapid diagnostic test if ordered per the facility's standard operating procedures. Other infectious diseases—HIV and Tuberculosis (TB)—were self-reported. Haemoglobin A1c (HbA1c) was measured using an at home test kit for individuals who reported history of diabetes. Oxygen saturation, pulse rate and perfusion index were evaluated using the Masimo Rad 57 or Multi-parameter Patient Monitor (Both devices were used in DRC. The Multi-parameter Patient Monitor -YK8000K was used in SSD throughout the study).[13 14] Haemoglobin concentration was evaluated using either a HemoCue 301 or Masimo Rad 57 device. (Masimo devices were used at facilities in DRC between April and June 2021. The HemoCue was used between December 2020 and April 2021 in DRC and throughout the study in SSD.) Anaemia and nutritional status were classified based on WHO cut-offs.[15–18] Cut-offs for other clinical conditions, including poorly controlled diabetes (HbA1c >8.0%) and low oxygen levels (<94%) were defined to align with national treatment guidelines and case definitions.

In DRC, data were recorded on paper and subsequently uploaded to CommCare, a secure online data collection platform for collecting longitudinal patient data, and in SSD, data were directly entered. Analyses were conducted using R (V.4.0.4). Distributions of continuous variables were compared by country of enrolment and hospitalisation status using Kruskal-Wallis test, Fisher's exact test was used for categorical parameters. All demographic characteristics, COVID-19 exposures, symptoms, vital signs

and comorbidities evaluated as risk factors for hospitalisation and mortality are presented in tables 1 and 2; parameters are presented as they were parameterised in models. Parameters that were significant at p<0.1 in unadjusted models were evaluated in generalised linear mixed models (GLMM) for mortality and hospitalisation; patients were considered hospitalised if ever admitted into inpatient care while enrolled in the study. Two-level GLMMs were fitted using a logit link to account for the expected correlation in outcomes within health facilities which may be observed given differences in access to medication, staffing or quality of care available at each facility. Given the large number of risk factors of interest, separate models were built for each risk factor additionally adjusted for patient age, sex, country of enrolment and nationality as fixed effects; results are reported as adjusted ORs (AOR) with 95% CIs with a p value of <0.05 considered significant.

The study is registered with ClinicalTrials.gov (NCT04568499). The final datasets are archived on Humanitarian Data Exchange.[19]

Patient and public involvement

Patients with COVID-19 and their families were not involved in setting the research question, outcome measures, design and implementation of the study given the emergency nature of the study. However, patients and their families were involved in dissemination of the findings at interim points throughout the study which helped to inform triage, referral and care in the enrolling countries.

RESULTS

During the study period, 751 individuals were eligible per the study protocol of which 592 (78.8%) consented to participate (figure 1). Among cases followed to discharge (n=519), 375 were enrolled as outpatients (75.7%) of which all were confirmed cases and 144 were enrolled inpatient (24.3%) of which 137 were confirmed and seven were suspect cases. Similar numbers of cases were followed to discharge (recovery or death) in SSD (n=257) and DRC (n=262). Patients were followed up for an average of 8.9 days for a total of 4630 days of follow-up time.

Patient demographics, exposure history, symptoms at enrolment and clinical history differed by country (table 1). SSD had significantly fewer nationals (58.3% vs 94.3%, p<0.001) and female cases (24.9% vs 41.6%, p<0.001). There was no significant difference in mean age by country, however, the proportion of individuals >65 years was slightly higher in DRC (9.9% vs 6.6%). Cases in SSD were more likely to work outside the home (35.8% vs 26.3%, p=0.020); otherwise, risk factors for exposure were similar. Cases in DRC were more likely to present with symptoms (92.7% vs 54.5%, p<0.001), likely a function of testing protocols. The majority of cases in SSD were identified by travel screening (53.4%), whereas in DRC most participants sought testing after experiencing COVID-19 like symptoms (53.4%). Overall, the most common symptoms were cough (52.4%), headache (43.4%), fatigue/malaise (38.3%) and runny nose (30.9%) (table 2).

Evaluating differences in characteristics of hospitalised patients was a primary aim given that a minority of cases (28.1%) ever received inpatient care. Participants in DRC were more likely to be hospitalised (34.0% vs 22.2%, p=0.003), likely due in part to differences in case identification by country. Hospitalised patients were older than outpatients (mean age 48.0 vs 37.7 years, p<0.001) and more likely to be a national of the country of enrolment (88.2% vs 72.0%, p<0.001). Hospitalised patients were also more likely than outpatients to have been tested due to COVID-19 like symptoms (60.9% vs 31.7%, p<0.001), and for almost all symptoms assessed, a significantly higher proportion of cases among inpatients self-reported experiencing the symptom than among outpatient (table 2).

The prevalence of infectious comorbidities (ie, malaria, TB and/or HIV) overall was low (5.4%), however, hospitalised cases were more likely to present with one or more of the assessed infectious comorbidities (15.1% vs 2.2%, p<0.001); all confirmed malaria cases (n=7) were hospitalised. Chronic comorbidities were more prevalent, with 44.1% of persons presenting with at least one chronic comorbidity and 15.4% presenting with two or more chronic comorbidities. Chronic comorbidities were more common among hospitalised patients (53.4% vs 40.5%, p<0.008). High blood pressure was the most frequently reported chronic comorbidity, with similar prevalence between inpatients and outpatients (p=0.65). Obesity and self-reported history of hypertension, diabetes and chronic cardiac disease all were significantly more prevalent among hospitalised cases (p<0.02 for all comparisons). Among individuals with diabetes history for whom HbA1c values were available (n=28), diabetes was poorly controlled (HbA1c >8.0%) for 32.1%; neither differences by country nor by hospitalisation were significant. Anaemia was also more common (25.0% vs 7.2%, p<0.001) among hospitalised cases.

Overall, the mortality proportion was 4.8% (95% CI 3.2% to 6.9%). The mortality proportion was 17.1% (95% CI 11.6% to 23.8%) among patients ever hospitalised; there were no outpatient deaths. All deceased individuals were symptomatic at enrolment and classified by clinical staff as acutely ill and non-ambulatory; as such, estimates are unadjusted for severity at enrolment. Mortality was higher in SSD (6.6%) than DRC (3.3%), and this difference was marginally significant (p=0.058). Regression models evaluated the aOR of hospitalisation (table 3) and mortality (table 4). Age and nationality were the only demographic characteristics significantly associated with hospitalisation and mortality. Odds of hospitalisation were 12.16 (95% CI 5.67 to 26.09) times greater among older individuals (≥65 years) compared with individuals <45 years of age; odds of mortality were 49.75 (95% CI 12.23 to 202.33) times greater for older adults. Nationals had 2.48 (95% CI 1.31 to 4.69) times

Table 1 Demographics characteristics and exposures of patients, by country and location of treatment

	All participants		By enrolment country			By location of treatment		
			DR Congo, N=262	S sudan, N=257	p value	Ever Hospitalised, n=146	Never hospitalised, N=373	
	N	n (%)	n (%)	n (%)		N (%)	n (%)	P value
Age (years) (mean, SD)	519	40.6±15.6	40.2±17.8	41.1±12.9	0.45	48.0±18.8	37.7±13.0	**<0.001**
Age categories (years)	519				**<0.001**			**<0.001**
<18		21 (4.0)	20 (7.6)	1 (0.4)		5 (3.4)	16 (4.3)	
18–44		308 (59.3)	139 (53.1)	169 (65.8)		58 (39.7)	250 (67.0)	
45–64		147 (28.3)	77 (29.4)	70 (27.2)		51 (34.9)	96 (25.7)	
65+		43 (8.3)	26 (9.9)	17 (6.6)		32 (21.9)	11 (2.9)	
Sex	519				**<0.001**			0.27
Male		346 (66.7)	153 (58.4)	193 (75.1)		92 (63.0)	254 (68.1)	
Female		173 (33.3)	109 (41.6)	64 (24.9)		54 (37.0)	119 (31.9)	
Nationality	516				**<0.001**			**<0.001**
National (DRC/SSD)		395 (76.6)	247 (94.3)	148 (58.3)		127 (88.2)	268 (72.0)	
African country		68 (13.2)	8 (3.1)	60 (23.6)		7 (4.9)	61 (16.4)	
Non-African country		53 (10.3)	7 (2.7)	46 (18.1)		10 (6.9)	43 (11.6)	
Study site	519							**0.004**
Juba		257 (49.5)	–	257 (100.0)		57 (39.0)	200 (53.6)	
North Kivu		173 (33.3)	173 (66.0)	–		64 (43.8)	109 (29.2)	
South Kivu		89 (17.1)	89 (34.0)	–		25 (17.1)	64 (17.2)	
Reason for testing	491				**<0.001**			**<0.001**
COVID-19 symptoms		196 (39.9)	127 (53.4)	69 (27.3)		84 (60.9)	112 (31.7)	
Known COVID-19 exposure		71 (14.5)	33 (13.9)	38 (15.0)		12 (8.7)	59 (16.7)	
Travel		211 (43.0)	76 (31.9)	135 (53.4)		40 (29.0)	171 (48.4)	
Other		13 (2.6)	2 (0.8)	11 (4.3)		2 (1.4)	11 (3.1)	
Risk of exposure								
Work outside the home	519	161 (31.0)	69 (26.3)	92 (35.8)	**0.02**	57 (39.0)	104 (27.9)	**0.01**
Healthcare worker	516	48 (9.3)	29 (11.1)	19 (7.5)	0.15	8 (5.6)	40 (10.8%)	0.07
Visit to healthcare facility*	517	188 (36.4)	85 (32.6)	103 (40.2)	0.07	64 (43.8)	124 (33.4%)	**0.03**
Caring for COVID-19 patient	506	14 (2.8)	6 (2.4)	8 (3.2%)	0.58	3 (2.1%)	11 (3.0%)	0.77
Contact with a COVID-19 case	262	80 (30.5%)	48 (35.6%)	32 (25.2%)	0.07	15 (26.3%)	65 (31.7%)	0.43

Values in bold indicate statistically significant results.
*As a healthcare worker and/or as a care provider to a family/ friend/ caregiver, within the past 4 weeks.
DRC, Democratic Republic of the Congo; SSD, South Sudan.

Table 2 Symptoms, comorbidities and risk factors reported at enrolment, by country and location of treatment

	All patients		By enrolment country			By location of treatment		
			DR Congo, N=262	S sudan, N=257		Ever Hospitalised N=146	Never Hospitalised N=373	
	N	n (%)	n (%)	n (%)	P value	n (%)	n (%)	P value
Primary outcomes								
Ever hospitalised	519	146 (28.1)	89 (34.0)	57 (22.2)	**0.003**	–	–	–
Died	519	25 (4.8)	8 (3.1)	17 (6.6)	0.06	25 (17.1)	0 (0.0)	**<0.001**
Symptoms (self-reported)								
Symptomatic	519	383 (73.8)	243 (92.7)	140 (54.5)	**<0.001**	131 (89.7)	252 (67.6)	**<0.001**
Cough	519	272 (52.4)	176 (67.2)	9 (37.4)	**<0.001**	104 (71.2)	168 (45.0)	**<0.001**
Sore throat	518	127 (24.5)	54 (20.7)	73 (28.4)	**0.04**	52 (35.9)	75 (20.1)	**<0.001**
Runny nose	518	160 (30.9)	106 (40.6)	54 (21.0)	**<0.001**	54 (37.2)	106 (28.4)	0.05
Shortness of breath	519	96 (18.5)	51 (19.5)	45 (17.5)	0.57	76 (52.1)	20 (5.4)	**<0.001**
Wheezing	519	18 (3.5)	12 (4.6)	6 (2.3)	0.16	14 (9.6)	4 (1.1)	**<0.001**
Chest pain	518	110 (21.2)	63 (24.1)	47 (18.3)	0.10	63 (43.4)	47 (12.6)	**<0.001**
Headache	518	225 (43.4)	154 (59.0)	71 (27.6)	**<0.001**	77 (53.1)	148 (39.7)	**0.006**
Muscle/joint pain	518	111 (21.4)	63 (24.1)	48 (18.7)	0.13	50 (34.5)	61 (16.4)	**<0.001**
Fatigue/malaise	519	199 (38.3)	136 (51.9)	63 (24.5)	**<0.001**	88 (60.3)	111 (29.8)	**<0.001**
Vomiting/nausea	519	41 (7.9)	31 (11.8)	10 (3.9)	**<0.001**	22 (15.1)	19 (5.1)	**<0.001**
Abdominal pain	519	60 (11.6)	35 (13.4)	25 (9.7)	0.20	24 (16.4)	36 (9.7)	**0.03**
Chills	519	61 (11.8)	42 (16.0)	19 (7.4)	**0.002**	24 (16.4)	37 (9.9)	**0.04**
Loss of taste/smell	515	87 (16.9)	48 (18.6)	39 (15.2)	0.30	25 (17.2)	62 (16.8)	0.89
Loss of appetite	519	17 (3.3)	12 (4.6)	5 (1.9)	0.09	8 (5.5)	9 (2.4)	0.10
Clinical presentation								
Fever (>37.5°C)	518	68 (13.1)	45 (17.2)	23 (9.0)	**0.006**	20 (13.7)	48 (12.9)	0.81
Hypothermia (≤35.0°C)	518	30 (5.8)	23 (8.8)	7 (2.7)	0.003	10 (6.8)	20 (5.4)	0.52
Low oxygen level (<94%)	481	91 (18.9)	55 (24.1)	36 (14.2)	**0.006**	64 (43.8)	27 (8.1)	**<0.001**
Appearance at enrolment	519				**<0.001**			**<0.001**
Acutely ill: non-ambulatory		79 (15.2)	49 (18.7)	30 (11.7)		79 (54.1)	0 (0.0)	
Acutely ill: ambulatory		145 (27.9)	133 (50.8)	12 (4.7)		24 (16.4)	121 (32.4)	
Healthy looking		295 (56.8)	80 (30.5)	215 (83.7)		43 (29.5)	252 (67.6)	
Infectious comorbidities								

Continued

Table 2 Continued

	All patients		By enrolment country			By location of treatment		
			DR Congo, N=262	S sudan, N=257		Ever Hospitalised N=146	Never Hospitalised N=373	
	N	n (%)	n (%)	n (%)	P value	n (%)	n (%)	P value
Malaria* confirmed	90	7 (7.8)	6 (8.8)	1 (4.5)	**0.003**	7 (11.5)	0 (0.0)	**<0.001**
Suspected		44 (48.9)	28 (41.2)	16 (72.7)		15 (24.6)	29 (100.0)	
Negative		39 (43.3)	34 (50.0)	5 (22.7)		39 (63.9)	0 (0.0)	
Tuberculosis†	518	4 (0.8)	1 (0.4)	3 (1.2)	0.37	2 (1.4)	2 (0.5)	0.32
HIV†	291	5 (1.7)	4 (4.0)	1 (0.5)	0.05	2 (2.9)	3 (1.3)	0.33
Any infectious co-morbidity	296	16 (5.4)	11 (10.5)	5 (2.6)	**0.004**	11 (15.1)	5 (2.2)	**<0.001**
Chronic comorbidities								
Diabetes‡	519	40 (7.7)	20 (7.6)	20 (7.8)	0.95	28 (19.2)	12 (3.2)	**<0.001**
High blood pressure (>130/80)	508	163 (32.1)	56 (22.0)	107 (42.1)	**<0.001**	48 (33.6)	115 (31.5)	0.65
Chronic cardiac disease history‡	514	18 (3.5)	13 (5.0)	5 (2.0)	0.06	12 (8.5)	6 (1.6)	**<0.001**
Chronic pulmonary disease‡	518	9 (1.7)	2 (0.8)	7 (2.7)	0.10	2 (1.4)	7 (1.9)	>0.99
Current smoker‡	515	21 (4.1)	4 (1.5)	17 (6.7)	**0.003**	3 (2.1)	18 (4.8)	0.16
Hypertension‡	518	77 (14.9)	39 (14.9)	38 (14.8)	0.99	42 (29.0)	35 (9.4)	**<0.001**
Any chronic comorbidity	519	229 (44.1)	84 (32.1)	145 (56.4)	**<0.001**	78 (53.4)	151 (40.5)	**0.008**
≥2 chronic comorbidities	519	80 (15.4)	37 (14.1)	4 (16.7)	0.41	43 (29.5)	37 (9.9)	**<0.001**
Nutritional status†	470				0.79			**0.02**
Obese		84 (17.9)	48 (19.4)	36 (16.1)		23 (21.5)	61 (16.8)	
Overweight		166 (35.3)	85 (34.4)	81 (36.3)		32 (29.9)	134 (36.9)	
Normal weight		203 (43.2)	106 (42.9)	97 (43.5)		43 (40.2)	160 (44.1)	
Underweight		17 (3.6%)	8 (3.2)	9 (4.0)		9 (8.4)	8 (2.2)	
Anaemia status§								
Anaemic	213	26 (12.2)	19 (9.6)	7 (46.7)	**<0.001**	15 (25.0)	11 (7.2)	**<0.001**

Values in bold indicate statistically significant results.
*RDTs were performed for inpatients suspected of having malaria by clinical staff; routine testing was not available. Suspected malaria refers to cases for whom no RDT was performed, who received antimalarial medications taken prior to enrolment, and who reported chills and/or fever (measured or reported).
†Obesity: in adults BMI ≥30, in children up to 19 years old: BMI-for-age-z-score >3 SD. Overweight: in adults BMI <30 and ≥25, in children: BMI-for-age-z-score 2–2.99 SD Underweight: in adults: BMI <18.5, in children ≤2 SD children <5 (n=8) were excluded from this analysis, of them 0/7 with valid anthropometric measurements were malnourished by WHZ, and 2/7 were MAM by MUAC (≥11.5 cm and <12.5 cm).
‡Condition was self-reported by patient at enrolment.
§Children <12 years old: haemoglobin <110 g/L, children 12–15 years old: haemoglobin <120 g/L, non-pregnant women ≥15 years old: haemoglobin <120 g/L, pregnant women ≥15 years old: haemoglobin <110 g/L, males ≥15 years old: haemoglobin <130 g/L.
BMI, body mass index; MAM, moderate acute malnutrition; MUAC, mid-upper arm circumference; RDT, Rapid diagnostic test; WHZ, weight-for-height.

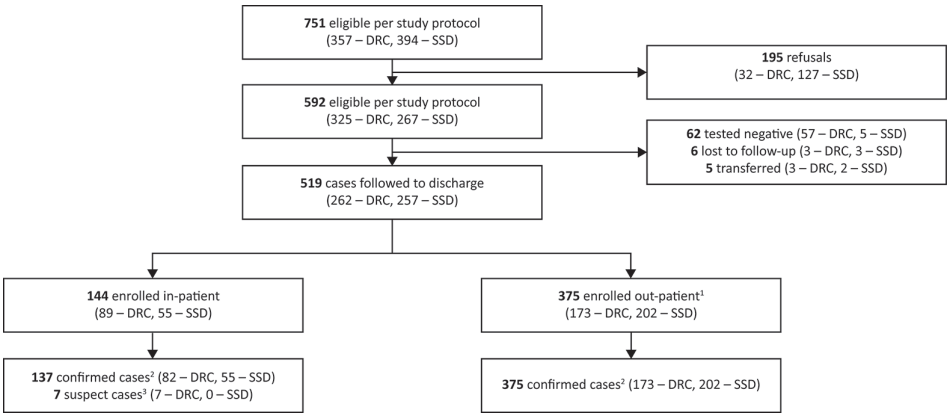

Figure 1 Study inclusion criteria flow chart. [1]Of the 375 individuals enrolled outpatient, 2 individuals in South Sudan were subsequently admitted for inpatient care. [2]Cases were confirmed by real-time reverse transcription PCR (RT-PCR) (90% of confirmed cases) or antigen tests (10% of confirmed cases). [3]National case definitions were used to classify individuals as suspect cases. Of the suspect cases followed to discharge (n=7), two were never tested, three did not receive their test results and two had specimens collected >3 days after enrolment. DRC, Democratic Republic of the Congo; SSD, South Sudan.

higher odds of hospitalisation and 8.90 (95% CI 1.87 to 42.39) times higher odds of mortality than patients who were not nationals of the country of enrolment.

Patients presenting with any symptoms had higher odds of hospitalisation (AOR 2.78, 95% CI 1.47 to 5.27) and all deaths occurred among symptomatic individuals. Hospitalisation and mortality AORs were significant for cough, fatigue, SOB, chest pain and wheezing. Joint pain, sore throat and nausea were significantly associated with hospitalisation but not mortality. Loss of appetite was significantly associated with mortality but not hospitalisation. The magnitude of the effect was greatest for respiratory symptoms: SOB (hospitalisation AOR 21.37, 95% CI 10.91 to 41.87; mortality AOR 36.45, 95% CI 7.69 to 172.87) and wheezing (hospitalisation AOR 8.34, 95% CI 2.42 to 28.67; mortality AOR 11.54, 95% CI 3.04 to 43.83). Consistently, presence of oxygen levels <94% at enrolment was strongly associated with both hospitalisation and death (hospitalisation AOR 7.77, 95% CI 4.22 to 14.29; mortality AOR 25.29, 95% CI 6.42 to 99.54). Among patients classified by research nurses as acutely ill and non-ambulatory on enrolment, all were hospitalised; this classification was the strongest risk factor for mortality (AOR 164.67, 95% CI 18.87 to 1437.13).

Infectious comorbidities (malaria, TB, HIV) were only associated with increased hospitalisation when analysed as a single aggregated risk factor for presence of any assessed coinfectious disease. Presence of confirmed or suspected malaria was associated with a decreased odds of death (AOR 0.14, 95% CI 0.02 to 0.91). History of diabetes and hypertension were both significantly associated with increased risk for hospitalisation and death (p<0.005 for all comparisons). Presence of more than one chronic comorbidity was associated with 3.11 (95% CI 1.62 to 5.96) times greater odds of hospitalisation and 4.96 (95% CI 1.51 to 16.31) odds of death. Underweight and anaemia were significantly associated with hospitalisation risk (underweight AOR 5.04, 95% CI: 1.63 to 15.57; anaemia AOR 10.69, 95% CI 3.32 to 34.41) but not mortality.

DISCUSSION

Consistent with reports from other African settings,[20 21] among our sample of 519 COVID-19 patients in Eastern DRC and Juba, there were nearly three times as many patients enrolled as outpatients. Outpatients ultimately experienced no deaths during the study period. Case fatality reported in our observational cohort study (4.8%) was consequently closer to estimates from national case surveillance in DRC (1.9%), SSD (1.1%) and Africa overall (2.4%) as well as studies of outpatients from other settings (1.3%) than estimates among hospitalised cases; among patients admitted to intensive care units in Africa, case fatality has been estimated to approach 50%.[22]

Given both supply and demand barriers to facility-based treatment, WHO recommends that in cases where it is not possible to isolate all laboratory confirmed cases in a healthcare facility, groups with the highest risk of poor outcomes should be prioritised.[23] Our study provides information about the profile of patients receiving home-based care in resource poor African settings that can inform case management strategies.

Age and nationality of patients receiving home-based care differed significantly from those receiving inpatient care and both characteristics were significantly associated with odds of mortality, consistent with prior research; however, sex was not associated with either hospitalisation or mortality. Older age has been well established as a strong predictor of severity and clinical outcomes from COVID-19,[24] and as such, referral of older individuals for inpatient care is recommended in national protocols and global guidance. Differences in both hospitalisation and survival by nationality, where SSD/DRC nationals faced increased risk compared with non-nationals, likely reflect differences in case identification, care seeking, as

Table 3 Unadjusted and adjusted odds of hospitalisation by select patient characteristics

	Unadjusted odds			Adjusted Odds*		
	Point estimate	95% CI	P value	Point estimate	95% CI	P value
Demographic characteristics						
Age (ref: age <45 years)			**<0.001**			**<0.001**
Age 45–64 years	2.24	(1.45 to 3.47)		2.42	(1.53 to 3.83)	
Age 65+ years	12.28	(6.04 to 26.76)		12.16	(5.67 to 26.09)	
Male sex (ref: female)	0.80	(0.53 to 1.19)	0.27	0.93	(0.59 to 1.46)	0.76
South Sudan (ref: DRC)	0.55	(0.38 to 0.82)	**0.003**	0.77	(0.45 to 1.33)	0.35
National (ref: non-nationals)	2.90	(1.67 to 5.05)	**<0.001**	2.48	(1.31 to 4.69)	**0.005**
Primary reason for testing						
COVID-19 like symptoms (ref: other)†	3.35	(2.22 to 5.04)	**<0.001**	2.59	(1.62 to 4.16)	<0.001
Clinical presentation at enrolment						
Low oxygen level (<94%)	8.90	(5.34 to 14.85)	**<0.001**	7.77	(4.22 to 14.29)	**<0.001**
Symptoms at enrolment (self-reported)						
Symptomatic (ref: asymptomatic)	4.19	(2.36 to 7.46)	**<0.001**	2.78	(1.47 to 5.27)	**0.002**
Cough	3.02	(2.00 to 4.56)	**<0.001**	2.27	(1.43 to 3.62)	**<0.001**
Fatigue/malaise	3.58	(2.40 to 5.34)	**<0.001**	2.80	(1.77 to 4.41)	**<0.001**
Shortness of breath	19.16	(11 to 33.39)	**<0.001**	21.37	(10.91 to 41.87)	**<0.001**
Chest pain	5.33	(3.4 to 8.35)	**<0.001**	4.48	(2.71 to 7.43)	**<0.001**
Wheezing	9.78	(3.16 to 30.25)	**<0.001**	8.34	(2.42 to 28.67)	**<0.001**
Joint pain	2.69	(1.74 to 4.17)	**<0.001**	2.08	(1.25 to 3.46)	**0.005**
Loss of appetite	2.34	(0.89 to 6.2)	0.07	1.52	(0.52 to 4.42)	0.44
Runny nose	1.49	(1.00 to 2.24)	0.05	1.43	(0.91 to 2.25)	0.12
Sore throat	2.22	(1.45 to 3.39)	**<0.001**	2.29	(1.43 to 3.68)	**<0.001**
Headache	1.72	(1.17 to 2.53)	**0.006**	1.36	(0.88 to 2.12)	0.17
Nausea	3.31	(1.73 to 6.31)	**<0.001**	2.88	(1.42 to 5.85)	**0.003**
Abdominal pain	1.84	(1.06 to 3.21)	**0.032**	1.73	(0.95 to 3.17)	0.07
Diarrhoea	2.21	(0.93 to 5.24)	0.07	2.44	(0.94 to 6.29)	0.07
Chills	1.79	(1.03 to 3.11)	**0.04**	1.83	(0.91 to 3.70)	0.09
Exposure						
Visit to healthcare facility	1.55	(1.05 to 2.3)	**0.03**	1.41	(0.91 to 2.18)	0.12
Worked outside the home	1.66	(1.11 to 2.48)	**0.01**	2.56	(1.61 to 4.06)	**<0.001**
Healthcare worker	0.49	(0.22 to 1.07)	0.07	0.46	(0.20 to 1.06)	0.07
Comorbidities						
Any infectious comorbidity	7.74	(2.59 to 23.1)	**<0.001**	4.92	(1.46 to 16.62)	**0.01**
Diabetes	7.14	(3.52 to 14.48)	**<0.001**	5.08	(2.28 to 11.32)	**<0.001**

Continued

Table 3 Continued

	Unadjusted odds			Adjusted Odds*		
	Point estimate	95% CI	P value	Point estimate	95% CI	P value
Chronic cardiac disease	5.63	(2.07 to 15.31)	**<0.001**	3.65	(1.21 to 11.04)	**0.02**
Hypertension	3.94	(2.39 to 6.49)	**<0.001**	2.65	(1.45 to 4.85)	**0.002**
Chronic comorbidities (ref: none)‡			**<0.001**			**0.002**
One chronic comorbidity	1.00	(0.63 to 1.6)		1.19	(0.70 to 2.05)	
Two or more chronic comorbidities	3.79	(2.27 to 6.39)		3.11	(1.62 to 5.96)	
Nutrition						
BMI§			**0.02**			**0.01**
Obesity (ref: normal weight)	1.40	(0.78 to 2.52)		1.00	(0.52 to 1.95)	
Overweight (ref: normal weight)	0.89	(0.53 to 1.48)		0.70	(0.39 to 1.25)	
Underweight (ref: normal weight)	4.19	(1.52 to 11.78)		5.04	(1.63 to 15.57)	
Anaemic¶	4.30	(1.84 to 10.04)	**<0.001**	10.69	(3.32 to 34.41)	**<0.001**

Values in bold indicate statistically significant results.
*Individual risk factor models adjusted for age, sex, country of enrolment and (non)national status (fixed effects) and facility (random effect).
†Included travel, close contact with a confirmed case or other reason.
‡Self-reported history of diabetes, chronic cardiac disease, chronic pulmonary disease, hypertension, asthma, current smoking or a blood pressure at enrolment of >130/80.
§Obesity: in adults BMI ≥30, in children up to 19 years old: BMI-for-age-z-score >3 SD. Overweight: in adults BMI <30 and ≥25, in children: BMI-for-age-z-score 2–2.99 SD underweight: in adults: BMI <18.5, in children ≤2 SD children <5 (n=8) were excluded from this analysis, of them 0/7 with valid anthropometric measurements were malnourished by WHZ, and 2/7 were MAM by MUAC (≥11.5 cm and <12.5 cm).
¶Children<12 years old: haemoglobin <110 g/L, children 12–15 years old: haemoglobin <120 g/L, non-pregnant women ≥15 years old: haemoglobin <120 g/L, pregnant women ≥15 years old: haemoglobin <110 g/L, males ≥15 years old: haemoglobin <130 g/L.
BMI, body mass index; DRC, Democratic Republic of the Congo; MAM, moderate acute malnutrition; MUAC, mid-upper arm circumference; WHZ, weight-for-height.

well as sociodemographic characteristics of these populations, as explored in the qualitative research that complemented this study.[11] The finding of no sex differences is in contrast with prior meta-analysis that have found men at higher risk of severe disease; however, a 2021 study of inpatients in Africa similarly found no sex differences in mortality.[10 24 25] It is possible that greater differences in exposure and care seeking by gender in these settings confound the association between sex and severity.

In addition to age, current WHO guidance recommends that individuals who smoke, are obese or have a history of cardiovascular disease, diabetes mellitus, chronic lung disease, are at greater risk for poor outcomes from COVID-19 and should be referred for inpatient care.[23] However, neither individuals who smoked, were obese or had chronic lung disease in our study were significantly more likely to be treated inpatient, suggesting a potential opportunity to improve triage and referral. Interestingly, study subjects classified as being underweight and anaemic were both more likely to be hospitalised but did not face increased risk of death. However, anthropometric measurements frequently could not be collected for patients who were non-ambulatory at admission; the association between availability of anthropometric measurements and clinical severity of COVID-19 at admission may be confounding this effect. Evidence regarding anaemia and poor COVID-19 outcomes from prior meta-analyses is mixed.[26 27] We did not observe the 'j-shape' relationship between body mass index and mortality reported in prior meta-analysis.[28] Additionally, consistent with prior literature,[29] history of hypertension was strongly associated with increased risk of both hospitalisation and mortality, suggesting the need to screen for hypertension at initial patient consultation.

Triage of patients at risk of severe outcomes remains predominantly based on history of chronic conditions given the preponderance of evidence related to these conditions. While several cohort studies and case series suggest that individuals with HIV are at increased risk of severe outcomes,[1] and that TB and malaria may confer an increased risk of COVID-19 coinfection,[30 31] evidence on infectious comorbidities is more limited than that for chronic comorbidities. Given higher prevalence of these conditions in our target populations in DRC

Table 4 Unadjusted and adjusted odds of mortality by select patient characteristics

	Unadjusted odds			Adjusted Odds*		
	Point estimate	95% CI	P value	Point estimate	95% CI	P value
Demographic characteristics						
Age (ref: age <45 years)			**<0.001**			**<0.001**
Age 45–64 years	8.79	(2.41 to 32.0)		11.42	(3.06 to 3.06)	
Age 65+ years	37.35	(11.02 to 171.55)		49.75	(12.23 to 202.33)	
Male sex (ref: female)	1.62	(0.63 to 4.13)	0.31	2.11	(0.73 to 6.15)	0.17
South Sudan (ref: DRC)	2.25	(0.95 to 5.31)	**0.06**	5.79	(0.89 to 37.83)	0.07
National (ref: non-nationals)	3.68	(0.85 to 15.83)	**0.08**	8.9	(1.87 to 42.39)	**0.006**
COVID-19 testing						
COVID-19 symptoms (ref: other reason)†	17.58	(4.07 to 75.87)	**<0.001**	13.44	(2.83 to 63.76)	**0.001**
Clinical presentation at enrolment						
Acutely ill: non-ambulatory‡	191.56	(25.43 to 1443.3)	**<0.001**	164.67	(18.87 to 1437.13)	**<0.001**
Low oxygen level (<94%)	41.13	(11.98 to 141.16)	**<0.001**	25.29	(6.42 to 99.54)	**<0.001**
Symptoms at enrolment (self-reported)						
Symptomatic (ref: asymptomatic)						
Cough	5.08	(1.72 to 15.02)	**0.003**	3.33	(1.03 to 10.79)	**0.05**
Fatigue/malaise	7.04	(2.6 to 19.08)	**<0.001**	7.09	(2.26 to 22.25)	**<0.001**
Shortness of breath	66.32	(15.31 to 287.34)	**<0.001**	36.45	(7.69 to 172.87)	**<0.001**
Chest pain	11.21	(4.55 to 27.62)	**<0.001**	6.37	(2.32 to 17.51)	**<0.001**
Loss of taste/smell	2.45	(1.02 to 5.87)	**0.05**	1.59	(0.56 to 4.54)	0.39
Wheezing	12.68	(4.3 to 37.42)	**<0.001**	11.54	(3.04 to 43.83)	**<0.001**
Joint pain	2.16	(0.93 to 5.02)	0.08	1.10	(0.42 to 2.90)	0.84
Loss of appetite	7.05	(2.12 to 23.47)	**0.001**	5.17	(1.13 to 23.69)	**0.04**
Exposure						
Visit to healthcare facility	2.77	(1.22 to 6.29)	0.02	2.08	(0.78 to 5.55)	0.14
Comorbidities						
Confirmed/suspect malaria (ref: negative)	0.33	(0.09 to 1.19)	0.09	0.14	(0.02 to 0.91)	**0.04**
History of diabetes	12.60	(5.26 to 30.2)	<0.001	4.49	(1.59 to 12.63)	**0.004**
History of hypertension	7.26	(3.17 to 16.61)	<0.001	2.82	(1.06 to 7.49)	**0.04**
High blood pressure (>130/80)	2.85	(1.27 to 6.43)	0.01	1.66	(0.64 to 4.32)	0.30
No of chronic comorbidities (ref: none)§			<0.001			**0.005**
One chronic comorbidity	1.57	(0.42 to 5.94)		0.80	(0.19 to 3.32)	
Two or more chronic comorbidities	14.25	(5.36 to 44.87)		4.96	(1.51 to 16.31)	

Values in bold indicate statistically significant results.
*Individual risk factor models adjusted for age, sex, country of enrolment and (non)national status (fixed effects) and facility (random effect).
†Included travel, close contact with a confirmed case or other reason.
‡General appearance at enrolment classified by clinical staff at enrolment.
§Self-reported history of diabetes, chronic cardiac disease, chronic pulmonary disease, hypertension, asthma, current smoking, or a blood pressure at enrolment of >130/80.
DRC, Democratic Republic of the Congo.

(HIV=1.2%,[32] TB=0.3%,[33] malaria=32.6%[34]) and SSD (HIV=2.5%,[35] TB=0.1%,[36] malaria=27.2%[34]) than in high-income countries, gathering evidence on these conditions was a core aim of this study. However, our final samples of individuals with HIV (n=5), TB (n=4) and suspected (n=44) or confirmed (n=7) malaria were all small. Given these small samples, presence of infectious comorbidities was only a significant predictor of hospitalisation when

pooled. Malaria was significantly negatively associated with mortality, however, findings should be interpreted with caution given potential biases in case identification given universal testing was not conducted as part of the study protocol.

Patients presenting with evidence of respiratory symptoms were at greatest risk of death. Individuals with low oxygen levels and clinical assessment of non-ambulatory (generally in respiratory distress) had 25 and 164 times greater odds of mortality, respectively. These data suggest these high-risk individuals were being successfully triaged for inpatient care, potentially due to ability to measure oxygen among outpatients using pulse oximeters made available by the study. In August 2020, WHO revised guidance on home-based management to recommend use of home pulse oximetry as a safe, non-invasive tool for early identification of low oxygen levels in patients with initially mild or moderate COVID-19.[23] This approach is not yet universal practice in many low-income settings including SSD and DRC and this research suggests a need to advocate for their adoption and scale-up in resource-poor settings. Self-reported respiratory symptoms at admission (SOB, wheezing and chest pain) were also associated with increased odds of mortality which is indicative of the need for a standardised approach to respiratory assessment in outpatient screening. The strength of the associations between respiratory symptoms and mortality may be informative to improve patient triaged in these settings.

Our study is subject to five principal limitations. First, the study population reflects only patients with COVID-19 who interacted with the health system; given many barriers to case identification (including weak surveillance systems, limited COVID-19 testing capacity and suboptimal care seeking behaviours) the cases identified for recruitment are a subset of COVID-19 cases and may not be representative of all the caseload in the target population.[37] In particular, while both countries had similar national protocols for prioritisation of specimens for testing, a much larger proportion of specimens tested in SSD were among travellers; the larger proportion of travellers, most of whom were asymptomatic or had only mild symptoms, in SSD than in DRC is reflected in our sample. Second, among eligible individuals, 76.7% in SSD and 15.6% in DRC could not be reached given invalid or missing phone numbers and addresses; identification and enrolment of outpatients was particularly challenging, and limitations likely resulted in further sampling bias. Third, operational factors during the research led to a smaller sample size than planned, reducing power; these included insecurity and the 22 May 2021 eruption of Mt. Nyiragongo in DRC as well as a health worker strike in SSD. Fourth, infectious comorbidities were self-reported, potentially resulting in underdetection; these conditions were rarely observed in the final sample and the study lacked power to adequately assess their relationship with adverse COVID-19 outcomes. Finally, to ensure rigorous supervision the study sites were all operated or supported by IMC and may therefore be better resourced than other health facilities in the two countries.

CONCLUSIONS

Risk factors for mortality observed in our study were generally consistent with those identified in the current WHO guidance on clinical evaluation of COVID-19 patients for risk factors of severe disease based on evidence from higher-income settings.[23] Individuals who were older, presenting with low oxygen levels, or reporting a history of diabetes, chronic cardiac disease or hypertension were more likely to be hospitalised suggesting successful triage and referral of patients at increased risk of death. Individuals with evidence of respiratory distress—as reported by the patient, evaluated by clinical staff, or presenting with low oxygen—were at greatest risk of mortality. Given small samples, evaluation of individual infectious comorbidities, anaemia and wasting is limited; however, pooled data suggest increased risk of hospitalisation but not mortality.

The evaluation of risk factors for severe COVID-19 presented in this study may be informative for developing locally adapted tools for improving patient triage and referral, to support efforts to reduce morbidity and mortality in these settings. Similar tools to support community case managers in identifying children at greatest need for clinical management have been effective for childhood illnesses.[38] Triage and referral efforts may be most impactful where mobile medical teams are provided equipment to evaluate oxygen levels and assess symptoms of respiratory distress.

Author affiliations
[1]Division of Global Health Protection, Centers for Disease Control and Prevention, Atlanta, Georgia, USA
[2]International Health, Johns Hopkins University Bloomberg School of Public Health, Baltimore, Maryland, USA
[3]International Medical Corps, Juba, South Sudan
[4]International Medical Corps, Kinshasa, The Democratic Republic of the Congo
[5]International Medical Corps, Santa Monica, California, USA

Acknowledgements We are immensely grateful for the efforts of the IMC data collection team including Joseph Bongomin and Sinjaro Madol in South Sudan, and Dr. Fiz Mussa Bashizi, Dr. Jean Marie Kashosi, Numbi Sabiti Cyprien, Matabaro Cirhuza Jean-Paul, Bienvenu Kambale, Dr. Mulinganya Guy and Dr. Matata Ngilima Sebastien in Democratic Republic of Congo (DRC). The study would not have been possible without the support of the Ministry of Health (MoH), in particular the local health authorities in North Kivu and South Kivu provinces in DRC and the Ministry of Health focal Point Dr. Richard Lako in SSD. We also would like to express our gratitude to the NGOs and actors engaged in COVID-19 control in SSD and DRC, in particular those involved in laboratory diagnosis, surveillance and case management staff, for their efforts to ensure timely sharing of case data which facilitated study enrolment. We would like to acknowledge JHSPH faculty member Mija Ververs; Dr. Dayan Woldemichael and Katja Ericson from IMC HQ and IMC operations staff in DRC and SSD. Finally, our deepest appreciation goes to key informants and study participants who volunteered to engage at an especially difficult personal time; their generosity has furthered our understanding of COVID-19 impacts in some of the most underserved settings globally.

Collaborators IMC-CDC COVID-19 Research Team. The study team included Deepak Kumar, Kelechi Udoh from IMC S South Sudan, Dugsiye Ahmed, Arsene Baleke, from IMC DR Congo, and Aimee Summers from the US CDC.

Contributors EL, SD, AS, ENM, JM and IB made substantial contributions to the conception or design of the work. ENM and JM contributed to acquisition, and EL,

SD, GH, contributed to analysis and interpretation of data for the work. EL and SD drafting the manuscript; GH, AS, ENM, JM and IB revising it critically for important intellectual content. All authors gave final approval of the version to be published and agree to be accountable for the accuracy or integrity of the work. EL and SD both serve as guarantors for this work.

Funding Funded by USAID (award 72OFDA20GR0221).

Disclaimer The findings and conclusions are those of the authors and do not necessarily represent the official position of their respective institutions.

Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Ethics approval This study was reviewed and approved by the Johns Hopkins University Institutional Review Board (IRB number: IRB00000758), the South Sudan Ministry of Health Ethics Committee, the University of Kinshasa School of Public Health, and the US CDC.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available in a public, open access repository. Data are available in the Humanitarian Data Exchange (https://data.humdata.org/).

ORCID iD

Eva Leidman http://orcid.org/0000-0002-4191-5931

REFERENCES

1 Centers for Disease Control and Prevention. Science Brief: Evidence used to update the list of underlying medical conditions that increase a person's risk of severe illness from COVID-19, 2021. Available: https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/underlying-evidence-table.html#print [Accessed 21 Jul 2021].
2 Zhou F, Yu T, Du R, *et al*. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020a;395:1054–62.
3 Nandy K, Salunke A, Pathak SK, *et al*. Coronavirus disease (COVID-19): a systematic review and meta-analysis to evaluate the impact of various comorbidities on serious events. *Diabetes Metab Syndr* 2020;14:1017–25.
4 Underlying medical conditions associated with high risk for severe COVID-19: information for healthcare providers. Available: https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html
5 Kalligeros M, Shehadeh F, Mylona EK, *et al*. Association of obesity with disease severity among patients with coronavirus disease 2019. *Obesity* 2020;28:1200–4.
6 Lippi G, Wong J, Henry BM. Hypertension in patients with coronavirus disease 2019 (COVID-19): a pooled analysis. *Pol Arch Intern Med* 2020;130:304–9.
7 Schlesinger S, Neuenschwander M, Lang A, *et al*. Risk phenotypes of diabetes and association with COVID-19 severity and death: a living systematic review and meta-analysis. *Diabetologia* 2021;64:1480–91.
8 Gupta M, Wahl B, Adhikari B, *et al*. The need for COVID-19 research in low- and middle-income countries. *Glob Health Res Policy* 2020;5:33.
9 WHO World Health Organization. Coronavirus (COVID-19) Dashboard, 2021. Available: http://covid19.who.int
10 African COVID-19 Critical Care Outcomes Study (ACCCOS) Investigators. Patient care and clinical outcomes for patients with COVID-19 infection admitted to African high-care or intensive care units (ACCCOS): a multicentre, prospective, observational cohort study. *Lancet* 2021;397:1885–94.
11 Doocy S, Bollemeijer I, *et al*, IMC-CDC COVID-19 Research Team. Clinical progression and outcomes of patients hospitalized with COVID-19 in humanitarian settings: a prospective cohort study in South Sudan and eastern Democratic Republic of the Congo. *Manuscript under review*.
12 National Health and Nutrition Examination Survey.. Anthropometry procedures manual, 2007. Available: https://www.cdc.gov/nchs/data/nhanes/nhanes_07_08/manual_an.pdf
13 Whitehead RD, Mei Z, Mapango C, *et al*. Methods and analyzers for hemoglobin measurement in clinical laboratories and field settings. *Ann N Y Acad Sci* 2019;1450:147–71.
14 Hiscock R, Kumar D, Simmons SW. Systematic review and meta-analysis of method comparison studies of Masimo pulse co-oximeters (Radical-7™ or Pronto-7™) and HemoCue® absorption spectrometers (B-Hemoglobin or 201+) with laboratory haemoglobin estimation. *Anaesth Intensive Care* 2015;43:341–50.
15 World Health Organization. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. WHO/NMH/NHD/MNM/11.1. Available: https://www.who.int/vmnis/indicators/haemoglobin.pdf
16 World Health Organization. Global health Observatory data Repository: body mass index (BMI). Available: https://apps.who.int/gho/data/node.main.BMIANTHROPOMETRY?lang=en
17 World Health Organization. Physical status: the use and interpretation of anthropometry, report of a who expert Committee. Geneva, Switzerland; 1995. https://apps.who.int/iris/handle/10665/37003
18 WHO Multicentre Growth Reference Group. *Child growth standards: Length/height-for-age, weight-for-age, weight-for-length, weight-for-height and body mass index-for-age: methods and development*. Geneva: World Health Organization, 2006. http://www.who.int/childgrowth/ standards/technical_report/en/
19 Leidman E, Doocy S, the IMC-CDC COVID-19 Research Team, Bollemeijer, *et al*. Data from: risk factors for hospitalization and death from COVID-19: a prospective cohort study in South Sudan and eastern Democratic Republic of the Congo, 2022. Humanitarian data exchange. Available: https://data.humdata.org/dataset/risk-factors-for-hospitalization-and-death-from-covid-19-in-humanitarian-settings
20 World Health Organization. Zambia's COVID-19 home-based care relieves health facilities, 2020. Available: https://www.afro.who.int/news/zambias-covid-19-home-based-care-relieves-health-facilities
21 World Health Organization. Home-based care boosts Nigeria's COVID-19 fight, 2021. Available: https://www.afro.who.int/news/home-based-care-boosts-nigerias-covid-19-fight
22 Halalau A, Odish F, Imam Z, *et al*. Epidemiology, clinical characteristics, and outcomes of a large cohort of COVID-19 outpatients in Michigan. *Int J Gen Med* 2021;14:1555–63.
23 World Health Organization. Interim guidance: home care for patients with suspected or confirmed COVID-19 and management of their contacts, 2020. Available: https://www.who.int/publications/i/item/home-care-for-patients-with-suspected-novel-coronavirus-(ncov)-infection-presenting-with-mild-symptoms-and-management-of-contacts
24 Pijls BG, Jolani S, Atherley A, *et al*. Demographic risk factors for COVID-19 infection, severity, ICU admission and death: a meta-analysis of 59 studies. *BMJ Open* 2021;11:e044640.
25 Biswas M, Rahaman S, Biswas TK, *et al*. Association of sex, age, and comorbidities with mortality in COVID-19 patients: a systematic review and meta-analysis. *Intervirology* 2021;64:36–47.
26 Taneri PE, Gómez-Ochoa SA, Llanaj E, *et al*. Anemia and iron metabolism in COVID-19: a systematic review and meta-analysis. *Eur J Epidemiol* 2020;35:763–73.
27 Hariyanto TI, Kurniawan A. Anemia is associated with severe coronavirus disease 2019 (COVID-19) infection. *Transfus Apher Sci* 2020;59:102926.
28 Huang H-K, Bukhari K, Peng CC-H, *et al*. The J-shaped relationship between body mass index and mortality in patients with COVID-19: a dose-response meta-analysis. *Diabetes Obes Metab* 2021;23:1701–9.
29 World Health Organization. COVID-19 science brief: hypertension and COVID-19, 2021. Available: https://www.who.int/publications/i/item/WHO-2019-nCoV-Sci_Brief-Hypertension-2021.1
30 Visca D, Ong CWM, Tiberi S, *et al*. Tuberculosis and COVID-19 interaction: a review of biological, clinical and public health effects. *Pulmonology* 2021;27:151–65.

31 Onosakponome EO, Wogu MN. The role of sex in Malaria-COVID19 coinfection and some associated factors in rivers state, Nigeria. *J Parasitol Res* 2020;2020:1–4.
32 Ministère du Plan et Suivi de la Mise en œuvre de la Révolution de la Modernité. MPSMRM/Congo, Ministère de la Santé Publique - MSP/Congo and ICF International. In: *Enquête Démographique et de Santé en République Démocratique du Congo 2013-2014*. Rockville, Maryland, USA: MPSMRM, MSP, and ICF International, 2014. https://dhsprogram.com/pubs/pdf/HF55/HF55.pdf
33 Centers for Disease Control and Prevention. Global HIV and TB: Democratic Republic of Congo country profile. Available: https://www.cdc.gov/globalhivtb/where-we-work/drc/drc.html
34 World Health Organization. World malaria report, 2020. Available: https://www.who.int/publications/i/item/9789240015791
35 Global AIDS Monitoring. Country progress report - South Sudan. Available: https://www.unaids.org/sites/default/files/country/documents/SSD_2020_countryreport.pdf
36 Centers for Disease Control and Prevention. Global HIV and TB: South Sudan country profile. Available: https://www.cdc.gov/globalhivtb/where-we-work/southsudan/southsudan.html
37 Majer J, Udoh K, Baleke A, *et al*. Operational challenges and considerations for COVID-19 research in humanitarian settings: a qualitative study of a project in eastern Democratic Republic of the Congo and South Sudan. Manuscript under review..
38 Gera T, Shah D, Garner P, *et al*. Integrated management of childhood illness (IMCI) strategy for children under five. *Cochrane Database Syst Rev* 2016:CD010123.