

# THE LANCET

## Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

**This online publication has been corrected. The corrected version first appeared at [thelancet.com](https://www.thelancet.com) on June 24, 2021.**

Supplement to: The 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.

# SUPPLEMENTARY MATERIAL

**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**

The ACCCOS Investigators

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## Supplementary Material S2. Definitions document

### ACCCOS CRF DEFINITIONS

Ability to provide invasive ventilation

At time of admission the Unit had the resources to provide invasive mechanical ventilation

Active TB

Current diagnosis of pulmonary or extrapulmonary tuberculosis (either empiric or microbiological diagnosis) whether currently on treatment or not.

Admission delayed due to lack of resources (e.g. bed, staffing etc)

Admission to critical care delayed by more than one hour because of the non-availability of a bed, ventilator, staff or any other resource required to provide critical care.

Age

Age in years on day of referral to the Critical Care Unit

Antiretroviral therapy

Currently on an antiretroviral therapy program

Cancer

Diagnosis of cancer in the last 12 months (whether treated with surgery, radiotherapy or chemotherapy, or not) with the exclusion of non-melanomatous skin cancers.

Cardiorespiratory arrest

Cardiac arrest requiring cardiopulmonary resuscitation

Cardiovascular support

Intravenous fluid, inotrope or vasoconstrictor to maintain blood pressure or cardiac output

Chronic/ malaria within 3 months

Chronic malaria (with anaemia or splenomegaly) OR previous treatment for malaria (either as inpatient or outpatient) within the last 3 months.

Chronic kidney disease

Diagnosis of chronic kidney disease (stable abnormal renal function with documentation of serum creatinine) whether on dialysis or not

Chronic liver disease

Confirmation of one of the following: chronic jaundice, cirrhosis, portal hypertension with ascites and/or splenomegaly

Chronic lung disease

Diagnosis of airways disease (asthma, COPD [emphysema, chronic bronchitis], bronchiectasis), having previously been prescribed inhaler therapy OR pulmonary fibrosis OR post-infectious lung disease.

CNS

Central Nervous system

Congestive heart failure

Diagnosis of CHF with hospitalisation in the last 12 months

Coronary artery disease

History of previous myocardial infarction, OR currently on anti-anginal medication.

COVID-19 positive.

An internationally accepted positive test for the presence of the SARS-CoV-2 virus in nasopharyngeal or bronchial secretions.

CPAP

Continuous positive airway pressure of at least 5-10cmH<sub>2</sub>O via face-mask or helmet

Critical Care Unit

An Intensive Care Unit or High Care unit that manages critically ill patients

Current smoker

Current smoker (daily) of any tobacco product (cigarettes, pipes or cigars).

CVS

Cardiovascular system

Decision to limit therapy

A decision was made to not provide additional therapy (e.g. ventilation, adrenaline, dialysis) because of bad prognosis but to continue with current therapy.

Diabetes mellitus

Diagnosis of diabetes on oral medication OR insulin with or without diabetic complications

Elective Intubation

A planned intubation while the patient is stable

Emergency Department:

An area of the hospital where newly admitted patients are triaged and /or managed including an epidemic triage area

Emergency Intubation

Immediate intubation required for an acute deterioration

GCS

Glasgow coma score out of 15

Haem

Haematological system

HCU

High Care Unit. A patient area that provides a level of care between that of an ICU and a general ward but not usually invasive ventilation.

HFNO

High flow nasal oxygen humidified to 37°C and at a flow of 45-60L/min with variable inspired oxygen concentrations from 40-100%

HIV/AIDS

Diagnosis of HIV infection, whether on antiretroviral therapy or not.

Hypertension

Diagnosis of hypertension, whether on treatment or not.

ICU

Intensive care unit. A patient area that provides invasive ventilation, other organ support and monitoring.

Inotropes/Vasopressors

Catecholamines such as dobutamine, dopamine, adrenaline (epinephrine), Noradrenaline (norepinephrine), ephedrine, phenylephrine, vasopressin and its analogs, milrinone.

Dialysis

Renal replacement therapy for acute kidney injury e.g. Intermittent haemodialysis, Sustained low efficiency daily dialysis (SLEDD) or continuous venous-venous haemodialysis (CVVHD)

Invasive ventilation

Intermittent positive pressure ventilation via an endotracheal tube or tracheostomy

NIV

Non-invasive ventilation. Positive pressure mechanical ventilation via a face mask/helmet or nasal mask delivering pressure supported breaths and/or mandatory ventilatory support e.g. CPAP with PSV (pressure support ventilation) or Non-invasive SIMV (synchronized intermittent mandatory ventilation)

No Critical Care beds

A High Care or Intensive Care bed not available due to insufficient space, equipment or staff

Nurse to patient ratio

The average number of patients managed by one nurse (day and night) (number entered can have 1 decimal place)

Organ support indication to "other area", HCU or ICU

Choose none, one or many of the listed organ systems requiring support when referred to Critical Care

Other

Any other form of active organ support

"Other Area for critical care"

An area set up to manage the overflow of CoVID-19 patients requiring critical care.

Patient refused care

Patient or surrogate declined invasive ventilation or admission to critical care

Physician available on site 24/7

A doctor was on-site at all times exclusively for the patients in the critical care unit

Proned on mechanical ventilation

Turning the patient to lie front (ventral surface) down on the bed while intubated and ventilated

Quick SOFA

Quick sequential organ failure assessment. A score devised to screen for sepsis in emergency departments and wards.<sup>1</sup>



#### Renal support

Any form of haemodialysis or peritoneal dialysis

Repurposed/experimental Covid-19 drug therapy

The use of any drug for presumed antiviral effect including subjects on a blinded study that includes a placebo

Resp Rate

Respiratory rate

Respiratory support

Oxygen mask >40%, continuous positive airway pressure (CPAP), high flow nasal oxygen (HFNO), non-invasive ventilation

SBP

Systolic blood pressure

SOFA score

Sequential organ failure assessment score. See bottom of CRF for details <sup>2</sup>

#### Steroid Therapy

Corticosteroids administered while in critical care except when used to treat septic shock or a pre-existing condition (e.g. Asthma)

#### Stroke or Transient ischaemic attack

Known cerebrovascular disease with previous stroke (independent of extent of neurological deficit), or previous transient ischaemic attack.

#### Suspected COVID-19 infection

As qRT-PCR testing was not available at all participating hospitals, patients were also included based on either clinical or radiological findings. Clinical diagnosis consistent with SARS-CoV-2 infection was made by a senior physician and based on clinical presentation of symptoms highly suspicious for SARS-CoV-2 infection, including cough, fever, and/or myalgia.<sup>3</sup> Radiological diagnosis was based on computed tomography (CT) of the chest, with typical findings in keeping with locally implemented protocols.

#### Therapeutic anticoagulation

Any anticoagulant exceeding normal doses used for thromboembolic prophylaxis or to prevent dialysis circuit clotting.<sup>4</sup>

Too sick for Critical Care

Admission refused because subject assessed to be too ill to benefit from critical care

Too well for Critical Care

Admission refused because subject likely to survive without Critical Care

Withdrawal of Life support

A life sustaining treatment was stopped (e.g. mechanical ventilation, inotropes) because of bad prognosis

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## Supplementary Material S3. Statistical analysis plan

### Primary outcome

The primary outcome is in-hospital mortality in adult patients referred to intensive care or high-care units following suspected or known COVID-19 infection in Africa.

### Statistical analysis plan for primary objective

We will present the incidence and 95% CI for these data.

### Secondary outcomes

To determine the risk factors (resources, comorbidities and interventions) associated with mortality in adult patients with suspected or known COVID-19 infection in Africa.

The research questions to be addressed are the following. In patients with suspected or known COVID-19 infection in Africa;

1. What are the critical care resources associated with survival?
2. What patient comorbidities and other risk factors are associated with in-hospital mortality?
3. What hospital interventions are associated with in-hospital survival?

### Statistical analysis plan

Categorical variables will be described as proportions and compared using chi-square tests, Fisher's exact tests, Pearson's chi-square tests or chi-square tests with Yates correction, as appropriate. Continuous variables will be described as mean and standard deviation if normally distributed or otherwise median and interquartile range (IQR). Comparisons of continuous variables between groups will be performed using unpaired t-tests or one-way ANOVA as appropriate. Univariate analysis will be performed to test for risk factors associated with in-hospital death.

The main model will only include patients with complete outcome data (i.e. patients who are still in hospital receiving therapy, and have not reached the outcome definition of death, discharge, or in-hospital at 30 days will be excluded). Generalized linear mixed models using a logit link will be used to identify independent risk factors for the binary outcome of mortality. We will use a three-level generalized mixed model, with patients being at the first level, hospital at the second and country at the third level, to account for the expected correlation in outcomes within hospitals and countries. We will exclude patients with missing values for potential risk predictors, and only use a complete case analysis if there are <5% of the dataset with incomplete potential clinical risk predictors.<sup>8</sup> All risk factors will be entered into the model, unless the number of reported deaths is insufficient to provide 10 events (deaths) per variable.<sup>7</sup> Should the events per variable be <10, then variables with a univariate association of  $p < 0.05$ , and variables with biological plausibility and a low rate of missing data will be used.

Variables to be considered for inclusion in the model;

- i. Age
- ii. Sex
- iii. BMI
- iv. COVID-19 positive or suspected (sensitivity only known positive)
- v. Coronary artery disease
- vi. Congestive heart failure
- vii. Hypertension
- viii. Stroke or Transient ischaemic attack
- ix. Diabetes mellitus
- x. Cancer
- xi. Current smoker
- xii. Chronic Lung Disease
- xiii. Active TB
- xiv. Chronic Liver Disease
- xv. HIV/AIDS (no, yes, yes on anti-retrovirals)
- xvi. Chronic/previous malaria
- xvii. Chronic kidney disease
- xviii. Cardiorespiratory arrest in 24 hours prior to critical care referral
- xix. Quick SOFA score on referral
- xx. SOFA score on referral/ admission

- xxi. Was admission delayed due to lack of resources (e.g. bed, staffing etc)
- xxii. Nurse to patient ratio
- xxiii. Ability to provide invasive ventilation for patient if required
- xxiv. Physician available on site 24/7 for patient
- xxv. Indication for admission (number of organ system support i.e. none, one, two, three or more)
- xxvi. Respiratory support (None, Oxygen mask, HFNO, CPAP)
- xxvii. Proned (None, not ventilated, on mech ventilation)
- xxviii. Ventilation (None, Non-invasive ventilation, Invasive ventilation)
- xxix. Intubation (no, yes elective, yes emergency)
- xxx. Inotropes/ vasoconstrictors
- xxxi. Dialysis
- xxxii. Therapeutic anticoagulation
- xxxiii. Steroid therapy
- xxxiv. Repurposed/ experimental Covid-19 drug therapy
- xxxv. ECMO

Collinearity will be assessed using the variance inflation factor. If collinearity is detected, then variables will either be excluded or combined. The model fit will be evaluated.

Results of the logistic regression will be reported as adjusted odds ratios (OR) with 95% confidence intervals (CI). The models will be assessed through the use of sensitivity analyses to explore possible interacting factors and examine any effect on the results.

A single final analysis is also planned at the end of the study.

Univariate and multivariate statistical analyses will be performed using the Statistical Package for the Social Sciences (SPSS) version 24 (SPSS Inc., Chicago, IL, USA).

#### Sensitivity analyses for the secondary outcome

1. Analysis of confirmed Covid-19 positive patients only
2. Analysis which excludes all patients who had withdrawal of life support or decision to limit therapy

#### Additional analyses

Description of participating sites will include the following;

1. Number of hospital beds
2. Number of critical care beds allowing invasive ventilation
3. Number of critical care and high-care beds not allowing invasive ventilation
4. Nurse to patient ratio for critical care patients during the day
5. Nurse to patient ratio for critical care patients during the night
6. Number of specialist intensivists managing patients in critical care unit
7. Number of other specialist doctors managing patients in critical care unit
8. Number of non-specialist doctors managing patients in critical care unit
9. Doctor to patient ratio for critical care patients
10. Doctor on site in the critical care unit after hours
11. How many extra ventilators could be used for a critical care surge?
12. ICU type ventilators
13. Operating room type ventilators
14. ECMO
15. Proning during mechanical ventilation
16. Pulse oximetry for all, some or no patients
17. Ability to do arterial blood gases

#### Supplementary Material S4. Data missingness for the secondary outcome

	Missing (n)	Missing (%)	Valid (n)
Body mass index	1544	49.2%	1596
Prone ventilation	314	10.0%	2826
Admission delayed due to lack of resources (e.g. bed staffing etc)	193	6.1%	2947
Steroid therapy	129	4.1%	3011
Nurse to patient ratio	78	2.5%	3062
Quick SOFA score	71	2.3%	3069
Current smoker	62	2.0%	3078
Therapeutic anticoagulation	56	1.8%	3084
Physician onsite 24 hours a day for 7 days per week	56	1.8%	3084
HIV/ AIDS	56	1.8%	3084
Active tuberculosis	56	1.8%	3084
Chronic kidney disease	55	1.8%	3085
Inotropes/ vasoconstrictors	54	1.7%	3086
Cardiorespiratory arrest in 24 hours prior to critical care referral	54	1.7%	3086
Chronic liver disease	54	1.7%	3086
Congestive heart failure	53	1.7%	3087
Chronic lung disease	52	1.7%	3088
Cancer	52	1.7%	3088
Stroke or transient ischaemic attack	52	1.7%	3088
Chronic malaria/ malaria within 3 months	51	1.6%	3089
Diabetes	50	1.6%	3090
Coronary artery disease	47	1.5%	3093
Respiratory support	43	1.4%	3097
Number of organs requiring support	36	1.1%	3104
Hypertension	36	1.1%	3104

**Supplementary Material S5. Sensitivity analysis 1: Generalised linear mixed model with full dataset for mortality. Control are patients alive in hospital and alive and discharged.**

Dataset	Original (n=1299)				Imputed (n=3140)				Imputed (n=2995)				Imputed (n=2710)			
Sensitivity	Full dataset				Full dataset				Confirmed SARS-CoV-2 positive				Confirmed SARS-CoV-2 positive and no limitation of therapy			
	Odds ratio	2-5% CI	97-5% CI	p-value	Odds ratio	2-5% CI	97-5% CI	p-value	Odds ratio	2-5% CI	97-5% CI	p-value	Odds ratio	2-5% CI	97-5% CI	p-value
Intercept	0.01	0.00	0.03	<0.001	0.01	0.00	0.04	<0.001	0.01	0.00	0.04	<0.001	0.01	0.00	0.04	<0.001
Age (years)	1.03	1.02	1.04	<0.001	1.03	1.02	1.04	<0.001	1.03	1.02	1.04	<0.001	1.03	1.02	1.04	<0.001
Male	0.76	0.53	1.10	0.14	0.86	0.69	1.06	0.15	0.88	0.71	1.09	0.24	0.84	0.66	1.06	0.14
<i>Body mass index</i>																
<25	Reference															
25-29.9	1.30	0.81	2.07	0.27	1.12	0.78	1.61	0.52	1.13	0.79	1.63	0.49	1.14	0.77	1.69	0.50
30-34.9	1.61	0.91	2.83	0.10	1.06	0.73	1.53	0.77	1.07	0.73	1.55	0.73	0.99	0.63	1.55	0.96
35-39.9	1.74	0.83	3.65	0.14	1.16	0.74	1.81	0.51	1.17	0.75	1.84	0.48	1.24	0.73	2.09	0.42
>40	1.89	0.86	4.16	0.11	1.11	0.66	1.86	0.70	1.08	0.61	1.92	0.77	1.06	0.58	1.93	0.85
Coronary artery disease	0.69	0.36	1.31	0.26	0.80	0.54	1.19	0.27	0.84	0.56	1.26	0.40	0.81	0.52	1.26	0.35
Congestive heart failure	1.15	0.61	2.18	0.66	0.93	0.63	1.38	0.71	0.99	0.66	1.48	0.96	0.86	0.55	1.34	0.49
Hypertension	0.85	0.57	1.26	0.41	0.95	0.76	1.19	0.65	0.94	0.75	1.17	0.58	0.94	0.74	1.19	0.61
Stroke or transient ischaemic attack	0.79	0.39	1.62	0.52	1.04	0.63	1.69	0.89	1.05	0.63	1.75	0.84	0.69	0.39	1.23	0.21
Diabetes	1.02	0.69	1.50	0.92	1.25	1.01	1.56	0.04	1.23	0.98	1.54	0.07	1.22	0.96	1.56	0.10
Cancer	1.50	0.55	4.14	0.43	1.62	0.90	2.91	0.11	1.43	0.78	2.62	0.24	1.41	0.72	2.77	0.32
Current smoker	0.75	0.37	1.54	0.44	0.59	0.35	1.01	0.06	0.59	0.34	1.01	0.06	0.52	0.28	0.96	0.04
Chronic lung disease	0.72	0.38	1.36	0.32	0.96	0.65	1.42	0.85	0.94	0.63	1.40	0.75	1.02	0.66	1.57	0.93
Active tuberculosis	0.68	0.17	2.78	0.59	1.86	0.85	4.06	0.12	1.72	0.77	3.86	0.19	1.88	0.81	4.38	0.14
Chronic liver disease	5.62	1.73	18.27	0.004	3.48	1.48	8.18	0.004	3.38	1.43	8.00	0.01	3.18	1.28	7.86	0.01
HIV/AIDS	2.48	1.21	5.07	0.01	1.91	1.31	2.79	<0.001	1.89	1.28	2.77	0.001	1.80	1.19	2.72	0.01
Chronic malaria/ malaria within 3 months	1.45	0.42	5.03	0.55	1.06	0.52	2.15	0.88	1.08	0.51	2.27	0.84	1.21	0.57	2.56	0.61
Chronic kidney disease	1.37	0.73	2.56	0.33	1.89	1.28	2.78	0.001	1.83	1.24	2.71	0.002	1.85	1.21	2.83	0.005

<b>Cardiorespiratory arrest in 24 hours prior to critical care referral</b>	1.53	0.48	4.85	0.47	4.43	2.25	8.73	<0.001	4.34	2.20	8.57	<0.001	4.99	2.44	10.22	<0.001
<i>Quick SOFA score</i>																
<b>0 risk factor</b>	Reference															
<b>1 risk factor</b>	1.75	0.87	3.51	0.12	1.44	1.01	2.04	0.04	1.37	0.96	1.97	0.08	1.37	0.92	2.04	0.12
<b>2 risk factors</b>	2.97	1.40	6.26	0.004	2.00	1.33	2.99	<0.001	1.96	1.30	2.96	0.002	1.86	1.18	2.92	0.01
<b>3 risk factors</b>	7.08	2.69	18.64	<0.001	3.66	2.12	6.33	<0.001	3.74	2.14	6.56	<0.001	3.40	1.87	6.17	<0.001
<b>Admission delayed due to lack of resources (e.g. bed, staffing etc)</b>	2.07	1.11	3.84	0.02	2.14	1.42	3.22	<0.001	2.21	1.45	3.37	<0.001	2.29	1.46	3.60	<0.001
<b>Physician available on site 24/7 for patient</b>	0.98	0.44	2.19	0.96	0.84	0.50	1.42	0.51	0.81	0.47	1.38	0.43	0.97	0.50	1.86	0.93
<b>Nurse to patient ratio</b>	1.28	0.93	1.76	0.13	1.31	0.98	1.74	0.07	1.27	0.95	1.70	0.10	1.56	1.09	2.25	0.02
<i>Respiratory support</i>																
<b>None</b>	Reference															
<b>Oxygen mask</b>	1.17	0.46	2.97	0.75	1.28	0.74	2.20	0.37	1.31	0.75	2.28	0.35	1.33	0.72	2.45	0.37
<b>High flow nasal oxygenation</b>	1.19	0.43	3.29	0.74	2.72	1.46	5.08	0.002	2.71	1.43	5.15	0.001	2.57	1.23	5.36	0.01
<b>CPAP</b>	3.63	1.35	9.72	0.01	3.93	2.13	7.26	<0.001	3.92	2.09	7.36	<0.001	4.06	2.02	8.18	<0.001
<b>Invasive mechanical ventilation</b>	14.56	5.68	37.28	<0.001	15.27	8.51	27.37	<0.001	15.35	8.43	27.95	<0.001	20.89	10.75	40.61	<0.001
<i>Organ systems requiring support at admission</i>																
<b>No organ system</b>	Reference															
<b>One organ system</b>	0.88	0.31	2.46	0.80	0.93	0.56	1.52	0.76	1.01	0.60	1.69	0.98	0.95	0.55	1.64	0.86
<b>Two organ systems</b>	1.21	0.40	3.67	0.74	0.93	0.54	1.58	0.78	0.97	0.56	1.69	0.93	0.91	0.51	1.63	0.75
<b>Three organ systems</b>	1.69	0.49	5.81	0.40	1.49	0.76	2.93	0.25	1.71	0.85	3.44	0.14	1.56	0.75	3.28	0.24
<b>Four organ systems</b>	1.20	0.22	6.73	0.83	2.99	0.88	10.18	0.08	2.97	0.87	10.20	0.08	3.30	0.83	13.12	0.09
<i>Prone ventilation</i>																
<b>No proning</b>	Reference															
<b>On spontaneous ventilation</b>	0.58	0.35	0.95	0.03	0.82	0.61	1.09	0.17	0.85	0.63	1.14	0.27	0.91	0.66	1.25	0.56
<b>Invasive mechanical ventilation</b>	1.24	0.65	2.35	0.52	1.42	0.88	2.30	0.15	1.38	0.85	2.24	0.18	1.22	0.75	1.98	0.42
<b>Inotropes/ vasoconstrictors</b>	4.90	3.04	7.89	<0.001	3.67	2.77	4.86	<0.001	3.57	2.68	4.75	<0.001	3.80	2.81	5.15	<0.001
<b>Therapeutic anticoagulation</b>	1.18	0.67	2.07	0.58	1.18	0.85	1.63	0.33	1.17	0.84	1.63	0.35	1.27	0.90	1.80	0.18
<b>Steroid therapy</b>	0.77	0.40	1.47	0.43	0.55	0.37	0.81	0.003	0.52	0.35	0.79	0.002	0.50	0.32	0.77	0.002

CI=confidence interval CPAP=continuous positive airway pressure HIV=human immunodeficiency virus AIDS=acquired immunodeficiency syndrome SOFA=sequential organ failure assessment score

**Supplementary Material S6. Sensitivity analysis 2: Generalised linear mixed model with full dataset for mortality. Control are patients alive and discharged.**

Dataset	Original (n=1299)				Imputed (n=3140)				Imputed (n=2995)				Imputed (n=2710)			
Sensitivity	Full dataset				Full dataset				Confirmed SARS-CoV-2 positive				Confirmed SARS-CoV-2 positive and no limitation of therapy			
	Odds ratio	2-5% CI	97-5% CI	p-value	Odds ratio	2-5% CI	97-5% CI	p-value	Odds ratio	2-5% CI	97-5% CI	p-value	Odds ratio	2-5% CI	97-5% CI	p-value
Intercept	0.00	0.00	0.03	<0.001	0.02	0.00	0.05	<0.001	0.01	0.00	0.05	<0.001	0.01	0.00	0.04	<0.001
Age (years)	1.04	1.03	1.06	<0.001	1.03	1.03	1.04	<0.001	1.03	1.03	1.04	<0.001	1.03	1.02	1.04	<0.001
Male	0.78	0.51	1.18	0.23	0.86	0.68	1.09	0.21	0.88	0.70	1.12	0.31	0.83	0.64	1.07	0.14
<i>Body mass index</i>																
<25	Reference															
25-29.9	1.37	0.80	2.35	0.25	1.19	0.80	1.75	0.37	1.18	0.80	1.74	0.39	1.21	0.79	1.84	0.37
30-34.9	1.47	0.77	2.80	0.24	1.04	0.69	1.57	0.85	1.05	0.70	1.58	0.81	0.99	0.60	1.61	0.96
35-39.9	1.22	0.52	2.88	0.64	1.02	0.61	1.72	0.94	1.02	0.61	1.71	0.93	1.09	0.61	1.94	0.77
>40	2.02	0.83	4.93	0.12	1.10	0.59	2.03	0.76	1.07	0.55	2.08	0.83	1.08	0.54	2.15	0.81
Coronary artery disease	0.65	0.31	1.39	0.27	0.71	0.46	1.09	0.12	0.73	0.47	1.13	0.15	0.69	0.43	1.12	0.14
Congestive heart failure	1.21	0.58	2.50	0.62	0.89	0.58	1.37	0.61	0.92	0.59	1.41	0.69	0.78	0.48	1.27	0.32
Hypertension	0.86	0.55	1.36	0.52	1.02	0.80	1.30	0.87	1.01	0.79	1.29	0.95	1.00	0.77	1.30	0.99
Stroke or transient ischaemic attack	1.07	0.47	2.44	0.87	1.59	0.91	2.77	0.10	1.66	0.94	2.94	0.08	1.12	0.59	2.12	0.73
Diabetes	1.13	0.73	1.76	0.58	1.32	1.04	1.69	0.02	1.29	1.01	1.65	0.04	1.30	1.00	1.70	0.05
Cancer	1.88	0.50	6.99	0.35	2.04	1.05	3.98	0.04	1.83	0.92	3.63	0.08	1.71	0.80	3.64	0.16
Current smoker	0.51	0.22	1.20	0.12	0.60	0.33	1.09	0.09	0.60	0.33	1.10	0.10	0.57	0.29	1.14	0.11
Chronic lung disease	0.90	0.41	1.96	0.79	0.98	0.64	1.51	0.94	0.97	0.63	1.51	0.90	1.10	0.68	1.78	0.69
Active tuberculosis	0.76	0.14	4.03	0.75	2.61	1.07	6.38	0.03	2.48	0.98	6.32	0.06	2.77	1.06	7.21	0.04
Chronic liver disease	10.66	2.62	43.28	<0.001	4.11	1.61	10.47	0.003	4.00	1.56	10.28	0.004	3.78	1.43	10.04	0.01
HIV/AIDS	2.04	0.93	4.50	0.08	1.83	1.21	2.75	0.004	1.81	1.20	2.75	0.005	1.71	1.10	2.67	0.02
Chronic malaria/ malaria within 3 months	0.98	0.30	3.27	0.98	1.06	0.48	2.35	0.89	1.12	0.49	2.55	0.78	1.22	0.54	2.76	0.63
Chronic kidney disease	1.04	0.52	2.08	0.92	1.70	1.12	2.57	0.01	1.65	1.09	2.51	0.02	1.68	1.06	2.65	0.03
Cardiorespiratory arrest in 24 hours prior to critical care referral	1.30	0.35	4.80	0.69	4.07	1.97	8.42	<0.001	4.01	1.93	8.30	<0.001	4.52	2.09	9.79	<0.001
<i>Quick SOFA score</i>																

<b>0 risk factor</b>	Reference															
<b>1 risk factor</b>	1·67	0·78	3·58	0·19	1·41	0·96	2·07	0·08	1·36	0·92	2·00	0·12	1·33	0·87	2·02	0·18
<b>2 risk factors</b>	4·81	2·12	10·90	<0·001	2·39	1·53	3·72	<0·001	2·33	1·49	3·64	<0·001	2·25	1·38	3·67	0·001
<b>3 risk factors</b>	4·79	1·65	13·92	0·004	4·05	2·19	7·49	<0·001	4·42	2·35	8·30	<0·001	4·04	2·08	7·84	<0·001
<b>Admission delayed due to lack of resources (e.g. bed, staffing etc)</b>	2·27	1·15	4·50	0·02	2·01	1·29	3·15	0·002	2·14	1·35	3·39	0·001	2·22	1·37	3·59	0·001
<b>Physician available on site 24/7 for patient</b>	0·92	0·39	2·19	0·85	0·66	0·37	1·19	0·17	0·65	0·36	1·17	0·15	0·84	0·40	1·75	0·64
<b>Nurse to patient ratio</b>	1·30	0·90	1·87	0·16	1·39	0·98	1·98	0·06	1·38	0·97	1·96	0·08	1·58	1·04	2·41	0·03
<i>Respiratory support</i>																
<b>None</b>	Reference															
<b>Oxygen mask</b>	1·30	0·46	3·67	0·62	1·36	0·75	2·46	0·31	1·35	0·73	2·48	0·33	1·35	0·70	2·63	0·37
<b>High flow nasal oxygenation</b>	1·93	0·63	5·92	0·25	3·43	1·74	6·76	<0·001	3·28	1·64	6·57	<0·001	2·81	1·27	6·18	0·01
<b>CPAP</b>	4·79	1·59	14·39	0·01	4·85	2·47	9·51	<0·001	4·64	2·33	9·24	<0·001	4·57	2·13	9·78	<0·001
<b>Invasive mechanical ventilation</b>	31·89	10·90	93·26	<0·001	24·63	12·82	47·31	<0·001	23·86	12·26	46·42	<0·001	33·48	16·00	70·03	<0·001
<i>Organ systems requiring support at admission</i>																
<b>No organ system</b>	Reference															
<b>One organ system</b>	0·75	0·24	2·34	0·62	0·93	0·54	1·59	0·79	1·00	0·58	1·75	0·99	0·96	0·54	1·71	0·88
<b>Two organ systems</b>	1·14	0·33	3·89	0·83	0·86	0·49	1·53	0·62	0·90	0·50	1·62	0·71	0·87	0·47	1·62	0·66
<b>Three organ systems</b>	1·34	0·34	5·29	0·68	1·22	0·58	2·56	0·59	1·38	0·65	2·95	0·40	1·29	0·58	2·86	0·53
<b>Four organ systems</b>	0·75	0·10	5·91	0·79	2·87	0·66	12·47	0·16	3·06	0·69	13·52	0·14	3·97	0·69	23·00	0·12
<i>Prone ventilation</i>																
<b>No proning</b>	Reference															
<b>On spontaneous ventilation</b>	0·67	0·39	1·16	0·16	0·78	0·57	1·07	0·13	0·82	0·59	1·13	0·21	0·88	0·62	1·25	0·48
<b>Invasive mechanical ventilation</b>	2·63	1·15	5·99	0·02	1·82	1·03	3·22	0·04	1·81	1·02	3·23	0·04	1·69	0·93	3·05	0·08
<b>Inotropes/ vasoconstrictors</b>	6·90	3·83	12·43	<0·001	4·43	3·20	6·11	<0·001	4·31	3·10	5·99	<0·001	4·57	3·23	6·46	<0·001
<b>Therapeutic anticoagulation</b>	1·26	0·66	2·42	0·48	1·15	0·79	1·67	0·46	1·13	0·78	1·65	0·51	1·22	0·82	1·81	0·33
<b>Steroid therapy</b>	0·65	0·32	1·32	0·23	0·50	0·33	0·75	0·001	0·49	0·32	0·75	0·001	0·46	0·29	0·73	0·001

CI=confidence interval CPAP=continuous positive airway pressure HIV=human immunodeficiency virus AIDS=acquired immunodeficiency syndrome SOFA=sequential organ failure assessment score



**Supplementary Material S7. Sensitivity analysis 3: Generalised linear mixed model with full dataset for mortality. Variable ‘cardiorespiratory arrest in 24 hours before admission’ not entered into the GLMM.**

Dataset	Imputed (n=3140)				Imputed (n=3140)			
Sensitivity	Full dataset (Control alive in hospital and alive and discharged)				Full dataset (Control alive and discharged)			
	Odds ratio	2.5% CI	97.5% CI	p-value	Odds ratio	2.5% CI	97.5% CI	p-value
Intercept	0.02	0.01	0.05	<0.001	0.02	0.01	0.05	<0.001
Age (years)	1.03	1.02	1.04	<0.001	1.03	1.03	1.04	<0.001
Male	0.86	0.70	1.06	0.16	0.86	0.68	1.09	0.21
<i>Body mass index</i>								
<25	Reference							
25-29.9	1.12	0.77	1.63	0.53	1.19	0.80	1.78	0.38
30-34.9	1.06	0.73	1.52	0.76	1.05	0.70	1.56	0.82
35-39.9	1.19	0.77	1.85	0.44	1.05	0.63	1.75	0.85
>40	1.11	0.66	1.86	0.68	1.11	0.60	2.03	0.73
Coronary artery disease	0.80	0.54	1.18	0.26	0.70	0.46	1.08	0.11
Congestive heart failure	0.94	0.64	1.39	0.76	0.90	0.59	1.38	0.62
Hypertension	0.96	0.77	1.19	0.71	1.03	0.81	1.31	0.80
Stroke or transient ischaemic attack	1.03	0.64	1.68	0.89	1.57	0.90	2.71	0.11
Diabetes	1.24	0.99	1.54	0.06	1.31	1.03	1.66	0.03
Cancer	1.70	0.95	3.06	0.08	2.17	1.11	4.24	0.02
Current smoker	0.63	0.37	1.07	0.09	0.64	0.35	1.15	0.14
Chronic lung disease	0.94	0.64	1.39	0.77	0.97	0.63	1.49	0.88
Active tuberculosis	1.99	0.91	4.34	0.09	2.82	1.15	6.91	0.02
Chronic liver disease	3.25	1.39	7.59	0.01	3.81	1.50	9.65	0.005
HIV/AIDS	1.88	1.29	2.75	0.001	1.80	1.20	2.72	0.005
Chronic malaria/ malaria within 3 months	1.08	0.53	2.18	0.84	1.05	0.48	2.30	0.91
Chronic kidney disease	1.99	1.35	2.92	<0.001	1.81	1.20	2.73	0.01
<i>Quick SOFA score</i>								
0 risk factor	Reference							
1 risk factor	1.44	1.01	2.04	0.04	1.42	0.97	2.08	0.07
2 risk factors	1.99	1.33	2.98	<0.001	2.40	1.54	3.73	<0.001
3 risk factors	3.93	2.28	6.77	<0.001	4.34	2.35	8.02	<0.001

<b>Admission delayed due to lack of resources (e.g. bed staffing etc)</b>	2.11	1.40	3.16	<0.001	1.98	1.27	3.08	0.003
<b>Physician available on site 24/7 for patient</b>	0.83	0.49	1.41	0.50	0.66	0.37	1.18	0.16
<b>Nurse to patient ratio</b>	1.30	0.98	1.74	0.07	1.37	0.97	1.95	0.07
<i>Respiratory support</i>								
<b>None</b>	Reference							
<b>Oxygen mask</b>	1.24	0.72	2.12	0.44	1.32	0.73	2.39	0.35
<b>High flow nasal oxygenation</b>	2.65	1.42	4.92	0.002	3.38	1.72	6.64	<0.001
<b>CPAP</b>	3.82	2.08	7.04	<0.001	4.74	2.42	9.28	<0.001
<b>Invasive mechanical ventilation</b>	14.75	8.26	26.32	<0.001	23.84	12.47	45.58	<0.001
<i>Organ systems requiring support at admission</i>								
<b>No organ system</b>	Reference							
<b>One organ system</b>	0.90	0.55	1.47	0.67	0.89	0.52	1.52	0.68
<b>Two organ systems</b>	0.91	0.53	1.54	0.71	0.84	0.48	1.48	0.55
<b>Three organ systems</b>	1.49	0.76	2.92	0.25	1.21	0.58	2.51	0.61
<b>Four organ systems</b>	2.88	0.86	9.67	0.09	2.76	0.64	11.85	0.17
<i>Prone ventilation</i>								
<b>No proning</b>	Reference							
<b>On spontaneous ventilation</b>	0.82	0.62	1.09	0.17	0.79	0.57	1.09	0.14
<b>Invasive mechanical ventilation</b>	1.44	0.89	2.34	0.13	1.86	1.05	3.29	0.04
<b>Inotropes/ vasoconstrictors</b>	3.77	2.85	4.98	<0.001	4.57	3.31	6.30	<0.001
<b>Therapeutic anticoagulation</b>	1.16	0.84	1.61	0.37	1.13	0.78	1.64	0.51
<b>Steroid therapy</b>	0.54	0.36	0.79	0.002	0.49	0.32	0.73	<0.001

CI=confidence interval CPAP=continuous positive airway pressure HIV=human immunodeficiency virus AIDS=acquired immunodeficiency syndrome SOFA=sequential organ failure assessment score

## Supplementary Material S8. Search Strategy For COVID-19 Critical Care Mortality Meta-Analysis

1	(Betacoronavirus OR Betacoronaviruses)
2	(Corona Virus OR Corona Viruses OR Coronavirus OR Coronaviruses)
3	(COVID OR COVID19 OR COVID-19)
4	(CoV OR CoV2 OR HCoV-19 OR nCoV OR 2019nCoV)
5	(Severe Acute Respiratory Syndrome CoV OR severe acute respiratory syndrome coronavirus 2 OR SARS CoV 2 OR SARS-CoV-2 OR SARSCoV OR SARS-CoV OR SARS2)
6	(Intensive care OR intensive care unit* OR ICU*)
7	(ITU* or intensive treatment* OR intensive treatment unit*)
8	critical care.
9	critical* ill*
10	1 or 2 or 3 or 4 or 5
11	6 or 7 or 8 or 9
12	10 and 11
13	Limit 12 to yr= "2020"

### Databases used in the literature search:

MEDLINE via Ovid (*ab,ti*), Embase via Ovid (*ab,ti*), Cochrane Library (*ab,ti,kw*), *Africa-Wide Information* via EBSCOhost (*af*), *SciELO Citation Index* via *Web of Science* (*ab,ti,au,kw*).

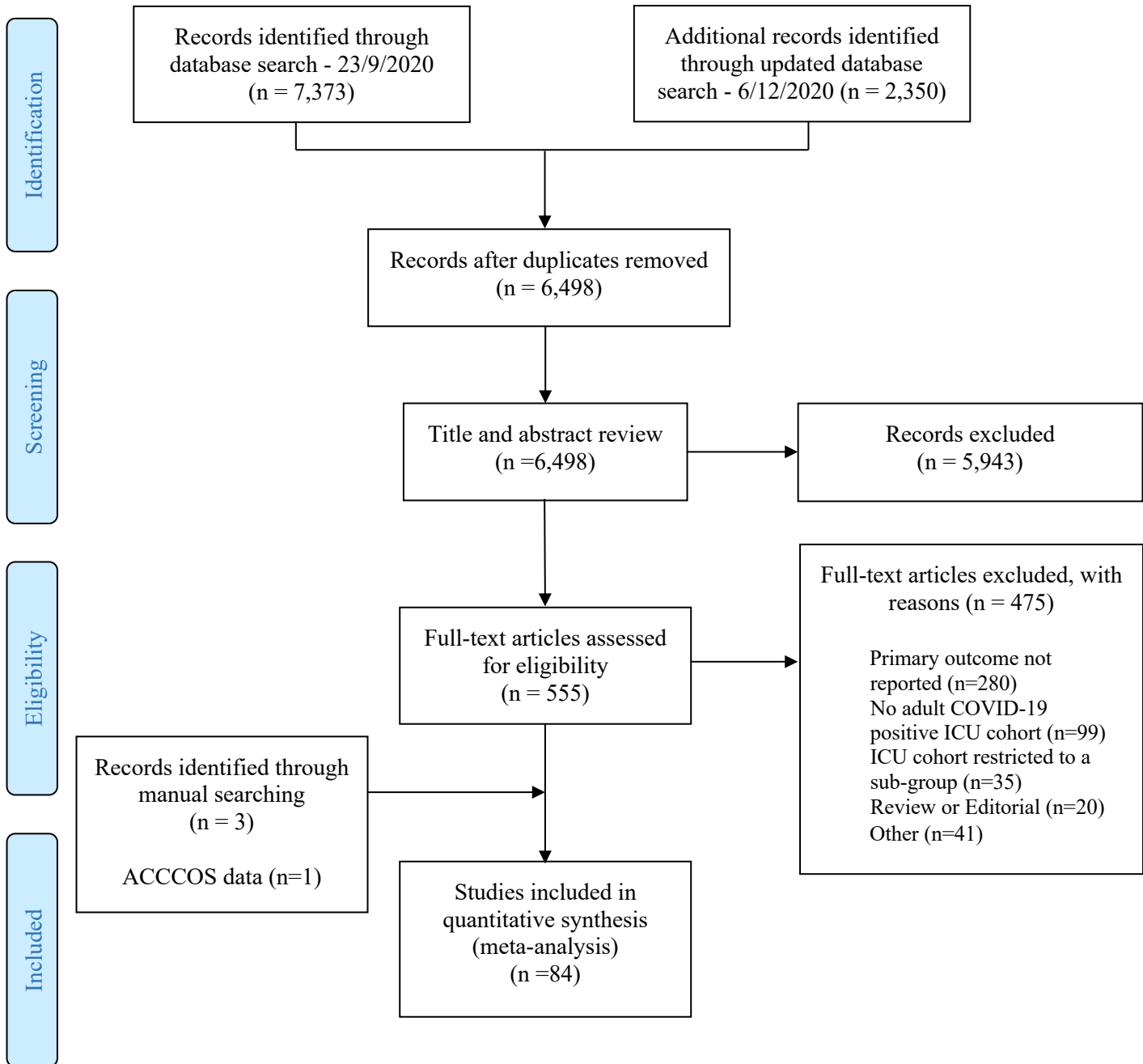
### Search date:

Original search: 1st January 2020 to 23rd September 2020.  
Updated search: 23<sup>rd</sup> September 2020 to 6<sup>th</sup> December 2020.

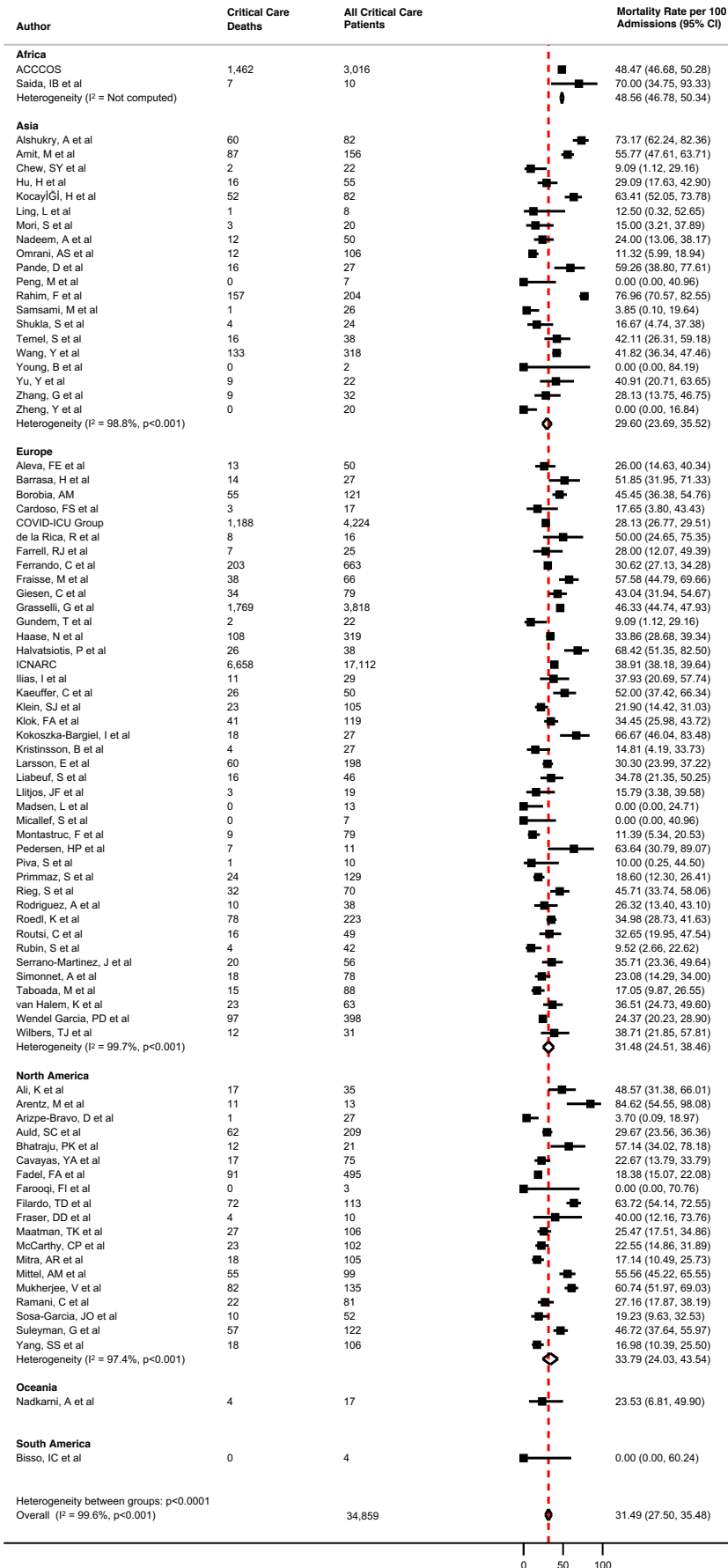
### Meta-Analysis Protocol:

PROSPERO CRD42020212347

**Supplementary Material S9. PRISMA Flow Diagram For COVID-19 Critical Care Mortality Meta-Analysis**



# Supplementary Material S10. Meta-Analysis of definitive COVID-19 Critical Care Outcomes



### Supplementary Material S11. Excess COVID-19 critical care mortality in Africa

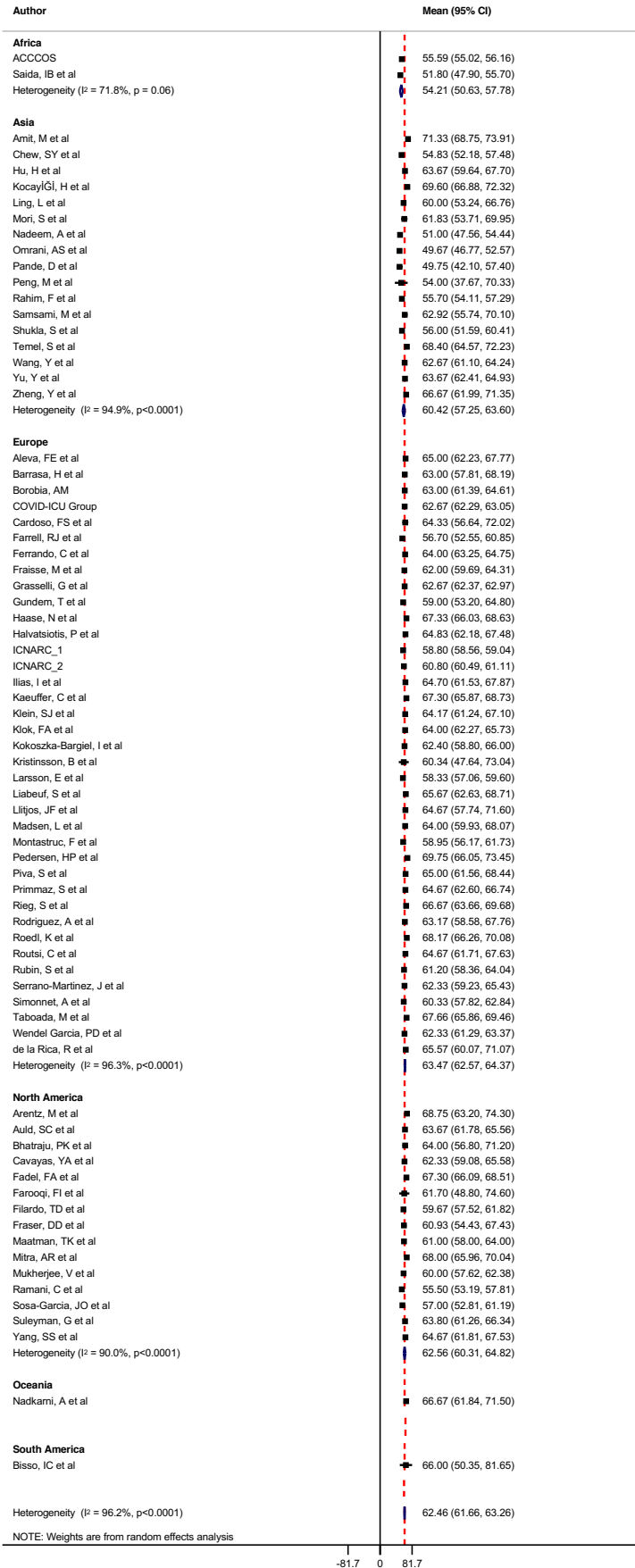
	<b>2·5% CI</b>	<b>97·5% CI</b>	<b>Africa 2·5% CI</b>	<b>Africa 97·5% CI</b>	<b>Best case scenario</b>	<b>Worst case scenario</b>
Global	27·5	35·5	46·8	50·3	11·3	22·8
Asia	23·7	35·5	46·8	50·3	11·3	26·6
Europe	24·5	38·5	46·8	50·3	8·3	25·8
North America	24	43·5	46·8	50·3	3·3	26·3

CI confidence interval

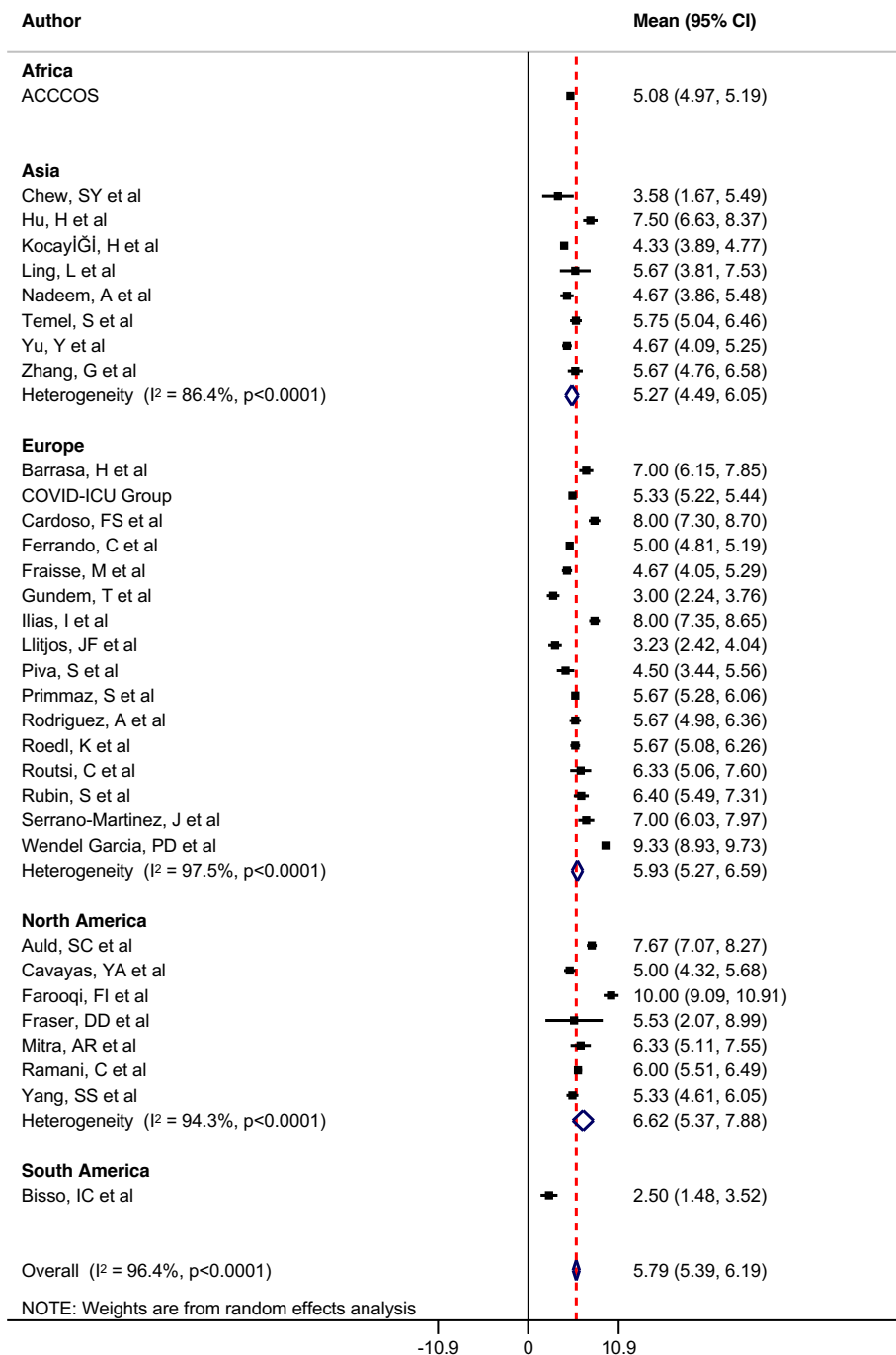
Data source: Meta-analysis Supplementary Material S10

Methodology: ‘Best case scenario’ assumes that the true mortality of the non-African region is represented by the upper confidence interval for mortality, and the true mortality in Africa is represented by the lower confidence interval for mortality. ‘Worst case scenario’ assumes that the true mortality of the non-African region is represented by the lower confidence interval for mortality, and the true mortality in Africa is represented by the upper confidence interval for mortality.

# Supplementary Material S12. Meta-Analysis of mean ‘age’ of definitive COVID-19 Critical Care Outcomes studies



### Supplementary Material S13. Meta-Analysis of mean ‘SOFA score’ of definitive COVID-19 Critical Care Outcomes studies





### Supplementary Material S14. COVID-19 Critical Care Mortality Meta-Analysis Summary Table

First author (surname, initial)	Sites	Country	Region	Cohort type	Recruitment start (date)	Recruitment end (date)	Final follow-up (date)	Age (years)	Sequential Organ Failure Assessment (SOFA) Score	Total patients in Critical Care cohort (n)	Alive Critical Care discharge (n)	In Critical Care mortality (n)
Mean (SD); Median (IQR)*; Median (range)**												
<b>AFRICA</b>												
ACCCOS	Multiple	Continental	-	Prospective	07/05/20	18/12/20	18/12/20	55.59 (16.11)	5.08 (3.21)	3085	1554	1462
Saida, IB et al <sup>1</sup>	Single	Tunisia	Sousse	Retrospective	11/03/20	07/05/20	07/05/20	51.8 (6.3)	-	10	3	7
<b>ASIA</b>												
Alshukry, A et al <sup>2</sup>	Single	Kuwait	Kuwait City	Retrospective	24/02/20	24/05/20	24/05/20	-	-	82	22	60
Amit M, et al <sup>3</sup>	Multiple	Israel	National	Retrospective	05/03/20	27/04/20	08/05/20	72 (60-82)*	-	156	69	87
Chew, SY et al <sup>4</sup>	Single	Singapore	-	Retrospective	07/02/20	07/06/20	30/06/20	54.5 (51-59)*	2.5 (1.25-7)*	22	20	2
Hu, H et al <sup>5</sup>	Single	China	Hubei	Retrospective	08/01/20	12/03/20	12/03/20	63 (54-74)*	7.5 (3.3)	55	39	16
Kocaylğlı, H et al <sup>6</sup>	Single	Turkey	Sakarya	Unclear	19/03/20	13/04/20	18/04/20	69.6 (14.1)	4 (3-6)*	103	30	52
Ling, L et al <sup>7</sup>	Multiple	Hong Kong	National	Retrospective	22/01/20	11/02/20	09/03/20	64 (42-70)**	6 (4-7)*	8	7	1
Mori, S et al <sup>8</sup>	Single	Japan	Tokyo	Retrospective	10/03/20	02/06/20	28/06/20	58 (51.5-76)*	-	22	17	3
Nadeem, A et al <sup>9</sup>	Single	United Arab Emirates	Abu Dhabi	Retrospective	31/03/20	10/05/20	20/06/20	51 (13)	4 (3-7)*	55	38	12
Omri, AS et al <sup>10</sup>	Multiple	Qatar	National	Retrospective	28/02/20	17/04/20	17/06/20	49.5 (39.5-60)	-	108	94	12
Pande, D et al <sup>11</sup>	Single	India	New Delhi	Unclear	20/04/20	03/05/20	Discharge	50 (9-90)**	-	27	11	16
Peng, M et al <sup>12</sup>	Single	China	Shenzhen	Unclear	20/01/20	06/02/20	25/02/20	56 (41-65)*	-	7	7	0
Rahim, F et al <sup>13</sup>	Single	Pakistan	Peshawar	Unclear	01/04/20	31/08/20	31/08/20	55.7 (11.6)	-	204	47	157
Samsami, M et al <sup>14</sup>	Single	Iran	Tehran	Retrospective	23/03/20	23/04/20	23/04/20	63.56 (50.7-74.5)*	-	26	25	1
Shukla, U et al <sup>15</sup>	Single	India	Maharashtra	Retrospective	01/04/20	14/05/20	14/05/20	54 (50-64)*	-	24	20	4
Temel, S et al <sup>16</sup>	Single	Turkey	Kayseri	Retrospective	20/03/20	22/04/20	22/04/20	68.4 (13.4)	5 (1-12)**	47	22	16
Wang Y, et al <sup>17</sup>	Single	China	Hubei	Unclear	25/01/20	25/02/20	28 days	64 (52-72)*	-	344	185	133
Young, B et al <sup>18</sup>	Multiple	Singapore	National	Unclear	23/01/20	03/02/20	25/02/20	-	-	2	2	0

Yu, Y et al <sup>19</sup>	Multiple	China	Hubei	Prospective	26/02/20	27/02/20	09/04/20	64 (57-70)*	4 (2-8)*	226	13	9
Zhang G, et al <sup>20</sup>	Single	China	Hubei	Retrospective	02/01/20	10/02/20	15/02/20	-	5 (4-8)*	44	23	9
Zheng, Y et al <sup>21</sup>	Single	China	Hangzhou	Retrospective	22/01/20	05/03/20	05/03/20	66 (58-76)*	-	34	20	0
<b>EUROPE</b>												
Aleva, FE et al <sup>22</sup>	Single	Netherlands	s-Hertogenbosch	Unclear	09/03/20	07/04/20	20/06/20	65 (10)	-	50	37	13
Barrasa, H et al <sup>23</sup>	Single	Spain	Vitoria	Prospective	04/03/20	31/03/20	06/04/20	63 (51-75)*	7 (3)	48	13	14
Borobia, AM et al <sup>24</sup>	Single	Spain	Madrid	Unclear	25/02/20	19/04/20	19/04/20	64 (54-71)*	-	237	66	55
Cardoso,FS et al <sup>25</sup>	Single	Portugal	Lisbon	Unclear	10/03/20	Unclear	10/04/20	67 (52-74)*	8 (7-9)*	20	14	3
COVID-ICU Group <sup>26</sup>	Multiple	France, Switzerland, Belgium	-	Prospective	25/02/20	04/05/20	90-day	63 (54-71)*	5 (3-8)*	4224	3036	1188
de la Rica, R et al <sup>27</sup>	Single	Spain	Palma de Mallorca	Retrospective	15/03/20	31/03/20	28/04/20	65.57 (12.87)	-	21	8	8
Farrell, RJ et al <sup>28</sup>	Single	Ireland	Dublin	Unclear	13/03/20	01/05/20	01/05/20	56.7 (11.8)	-	31	18	7
Ferrando, C et al <sup>29</sup>	Multiple	Andorra and Spain	-	Prospective	12/03/20	26/05/20	26/05/20	64 (56-72)*	5 (3-7)*	960	460	203
Fraisse, M et al <sup>30</sup>	Single	France	Argenteuil	Retrospective	06/03/20	22/04/20	06/05/20	61 (55-70)*	4 (3-7)*	92	28	38
Giesen, C et al <sup>31</sup>	Single	Spain	Madrid	Retrospective	27/02/20	29/06/20	29/06/20	-	-	83	45	34
Grasselli, G et al <sup>32</sup>	Multiple	Italy	Lombardy	Retrospective	20/02/20	22/04/20	30/05/20	63 (56-69)*	-	3909	2049	1769
Gundem, T et al <sup>33</sup>	Single	Norway	Ullevål	Unclear	05/03/20	28/05/20	28/05/20	Mean (range) 59 (25-78)	Mean (range) 3 (0-7)	22	20	2
Haase, N et al <sup>34</sup>	Multiple	Denmark	National	Retrospective	10/03/20	19/05/20	16/06/20	68 (59-75)*	-	323	211	108
Halvatsiotis, P et al <sup>35</sup>	Multiple	Greece	National	Retrospective	10/03/20	13/04/20	13/04/20	65.5 (56-73)*	-	90	12	26
ICNARC <sup>36</sup>	Multiple	UK	England, Wales and Northern Ireland	Retrospective	01/03/20	31/08/20	17/12/20	58.8 (12.7)	-	10935	6622	4311
					01/09/20	17/12/20	17/12/20	60.8 (13.7)	-	7677	3832	2347
Ilias, I et al <sup>37</sup>	Single	Greece	Athens	Unclear	20/03/20	03/05/20	29/05/20	64.7 (9.7)	8 (2)	36	18	11
Kaeuffer, C et al <sup>38</sup>	Multiple	France	Alsace	Prospective	20/03/20	20/03/20	7-days	67.3 (13.4)	-	335	24	26
Klein, SJ et al <sup>39</sup>	Multiple	Austria	Tyrol	Unclear	09/03/20	04/06/20	17/07/20	64 (54-74.5)*	-	106	82	23
Klok, FA et al <sup>40</sup>	Multiple	Netherlands	National	Unclear	07/03/20	05/04/20	22/04/20	64 (12)	-	184	78	41
Kokoszka-Bargiel, I et al <sup>41</sup>	Single	Poland	Silesian District	Retrospective	10/03/20	10/06/20	10/06/20	62.4 (10.4)	-	32	9	18
Kristinsson, B et al <sup>42</sup>	Multiple	Iceland	National	Prospective	14/03/20	13/04/20	06/05/20	64 (37-80)**	-	27	23	4

Larsson, E et al <sup>43</sup>	Single	Sweden	Stockholm	Unclear	09/03/20	20/04/20	30/04/20	59 (51-65)*	-	260	138	60
Liabeuf, S et al <sup>44</sup>	Single	France	Amiens	Retrospective	28/02/20	30/03/20	14/04/20	66 (57-74)*	-	69	30	16
Litijos, JF et al <sup>45</sup>	Multiple	France	-	Retrospective	19/03/20	11/04/20	Unclear	68 (51.5-74.5)*	3 (2-4.7)*	26	16	3
Madsen, LW et al <sup>46</sup>	Single	Denmark	Odense	Prospective	10/03/20	21/04/20	01/05/20	63 (60-69)*	-	13	13	0
Micallef, S et al <sup>47</sup>	Single	Malta	National	Retrospective	07/03/20	24/04/20	30-days	-	-	7	7	0
Montastruc, F et al <sup>48</sup>	Single	France	Toulouse	Unclear	10/03/20	21/04/20	21/04/20	63.4 (20-89)**	-	96	70	9
Pedersen, HP et al <sup>49</sup>	Single	Denmark	Zealand	Retrospective	11/03/20	01/04/20	16/04/20	69.5 (56-84)**	-	17	4	7
Piva, S et al <sup>50</sup>	Single	Italy	Lombardy	Prospective	02/03/20	13/03/20	Unclear	64 (59-72)*	3.5 (3-7)*	33	9	1
Primmaz, S et al <sup>51</sup>	Single	Switzerland	Geneva	Prospective	09/03/20	19/05/20	Unclear	64 (57-73)*	6 (4-7)*	129	105	24
Rieg, S et al <sup>52</sup>	Single	Germany	Freiburg	Retrospective	25/02/20	08/05/20	19/06/20	65 (59-76)*	-	70	38	32
Rodriguez, A et al <sup>53</sup>	Multiple	Spain	Tarragona	Prospective	14/03/20	15/04/20	28 days	65.5 (52-72)*	6 (4-7)*	43	28	10
Roedel, K et al <sup>54</sup>	Multiple	Germany	Hamburg	Retrospective	01/02/20	03/06/20	03/06/20	69 (58-77.5)*	5 (3-9)*	223	145	78
Routsis, C et al <sup>55</sup>	Single	Greece	Athens	Prospective	11/03/20	27/04/20	16/06/20	64 (58-72)*	7 (3-9)*	50	33	16
Rubin, S et al <sup>56</sup>	Multiple	France	Bordeaux	Unclear	03/03/20	14/04/20	Unclear	61.2 (12.2)	6.4 (3.9)	71	38	4
Serrano-Martinez, J et al <sup>57</sup>	Single	Spain	Grenada	Retrospective	12/03/20	01/05/20	01/05/20	63 (54-70)*	8 (4-9)*	59	36	20
Simonnet, A et al <sup>58</sup>	Single	France	Lille	Retrospective	27/02/20	05/04/20	06/04/20	60 (51-70)*	-	124	60	18
Taboada, M et al <sup>59</sup>	Multiple	Spain	Galicia	Prospective	21/03/20	19/04/20	06/05/20	69 (61-73)*	-	97	73	15
van Halem, K et al <sup>60</sup>	Single	Belgium	Hasselt	Retrospective	11/03/20	15/04/20	15/04/20	-	-	63	40	23
Wendel Garcia, PD et al <sup>61</sup>	Multiple	Continental	-	Prospective	Unclear	22/04/20	22/04/20	63 (53-71)*	9 (6-13)*	639	301	97
Wilbers, TJ et al <sup>62</sup>	Single	Netherlands	Arnhem	Retrospective	16/03/20	10/05/20	13/05/20	-	-	37	19	12
<b>NORTH AMERICA</b>												
Ali, K et al <sup>63</sup>	Single	USA	Texas	Unclear	01/03/20	15/05/20	15/05/20	64	-	35	18	17
Arentz, M et al <sup>64</sup>	Single	USA	Washington State	Unclear	20/02/20	05/03/20	17/03/20	70 (43-92)**	-	21	2	11
Arizpe-Bravo, D et al <sup>65</sup>	Single	Mexico	Puebla City	Retrospective	15/03/20	15/07/20	15/07/20	54*	-	28	26	1
Auld, SC et al <sup>66</sup>	Multiple	USA	Georgia	Retrospective	06/03/20	17/04/20	07/05/20	64 (54-73)*	7 (5-11)*	217	147	62
Bhatraju, PK et al <sup>67</sup>	Multiple	USA	Seattle	Unclear	24/02/20	09/03/20	23/03/20	64 (18)	-	24	9	12

Cavayas, YA et al <sup>68</sup>	Single	Canada	Montreal	Retrospective	20/03/20	13/05/20	27/07/20	62 (53-72)*	5 (3-7)*	75	58	17
Fadel, FA et al <sup>69</sup>	Single	USA	Ohio	Retrospective	15/03/20	01/06/20	29/06/20	67.3 (13.7)	-	495	404	91
Farooqi, FI et al <sup>70</sup>	Single	USA	Florida	Unclear	Unclear	Unclear	Unclear	61.7 (11.4)	10 (0.8)	3	3	0
Filardo, TD et al <sup>71</sup>	Single	USA	New York	Retrospective	09/03/20	08/04/20	30-days	60 (51-68)*	-	135	41	72
Fraser, DD et al <sup>72</sup>	Single	Canada	Ontario	Unclear	Unclear	Unclear	Unclear	61 (54.8-67)*	4.5 (2.8-9.3)*	10	6	4
Maatman, TK et al <sup>73</sup>	Multiple	USA	Indianapolis	Retrospective	12/03/20	31/03/20	06/05/20	61 (16)	-	109	79	27
McCarthy, CP et al <sup>74</sup>	Multiple	USA	Massachusetts	Retrospective	07/03/20	30/03/20	24/06/20	-	-	103	79	23
Mitra, AR et al <sup>75</sup>	Multiple	Canada	Vancouver	Retrospective	21/02/20	14/04/20	05/05/20	69 (60-75)*	6 (2-11)*	117	87	18
Mittel, AM et al <sup>76</sup>	Single	USA	New York	Retrospective	24/03/20	14/05/20	14/05/20	Median (SD) 63 (12.6)	-	133	44	55
Mukherjee, V et al <sup>77</sup>	Single	USA	New York	Retrospective	10/03/20	07/04/20	18/05/20	59 (51-70)*	-	137	53	82
Ramani, C et al <sup>78</sup>	Single	USA	Virginia	Unclear	Unclear	Unclear	30/07/20	55.5 (11.9)	6 (2.5)	102	59	22
Sosa-Garcia, JO et al <sup>79</sup>	Single	Mexico	Mexico City	Retrospective	20/03/20	05/06/20	05/06/20	58 (46-67)*	MEXSOFA 7 (5-8)	56	42	10
Suleyman, G et al <sup>80</sup>	Multiple	USA	Michigan	Retrospective	09/03/20	27/03/20	30-day	63.8 (15.4)	-	141	65	57
Yang, SS et al <sup>81</sup>	Single	Canada	Quebec	Retrospective	05/03/20	21/05/20	04/08/20	66 (54-74)*	5 (3-8)*	106	88	18
<b>OCEANIA</b>												
Nadkarni, A et al <sup>82</sup>	Single	Australia	Adelaide	Unclear	24/03/20	13/04/20	23/04/20	67 (60-73)*	-	18	13	4
<b>SOUTH AMERICA</b>												
Bisso, IC et al <sup>83</sup>	Single	Argentina	Buenos Aires	Unclear	15/03/20	15/04/20	15/04/20	71 (52-75)*	2 (2-3.5)*	7	4	0

## Supplementary Material S15. COVID-19 Critical Care Mortality Meta-Analysis Reference List

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### Supplementary Material S16. Case fatality rate for Covid-19 infection as of 11 December 2020

Region	Total cases (n)	Total deaths (n)	Case fatality rate	2·5% CI	97·5% CI	Cases per 100 000 population
Africa	2344616	55662	2·37%	2·35%	2·39%	57
Asia	18909807	309745	1·64%	1·63%	1·64%	405
Europe	19588248	451198	2·30%	2·30%	2·31%	849
North America	18359411	439095	2·39%	2·38%	2·40%	483
Oceania	30905	943	3·05%	2·86%	3·24%	22
South America	11847866	338096	2·85%	2·84%	2·86%	1766
World	142163148	3189508	2·24%	2·24%	2·25%	140

CI confidence interval

Data source: Ritchie H, Ortiz-Ospina E, Beltekian D, et al. Mortality Risk of COVID-19. 2020. Available from <https://ourworldindata.org/mortality-risk-covid> (accessed 14 December 2020)

**Interpretation:** Although the case fatality rate for COVID-19 in Africa is similar to North America, the low number of cases reported per 100 000 population, may represent under reporting of asymptomatic, infected patients through inadequate testing. This would lead to a lower case fatality rate, than that which is reported in the table. It is therefore possible that that the overall mortality in Africa following COVID-19 infection may be lower than the global mortality rate.