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Morning Brief:
Scientific Review

22 May 2020

The purpose of the Morning Brief is to summarize and present key information, research articles and other relevant publications pertaining to critical care and COVID-19.

Stellenbosch University Research Response Team

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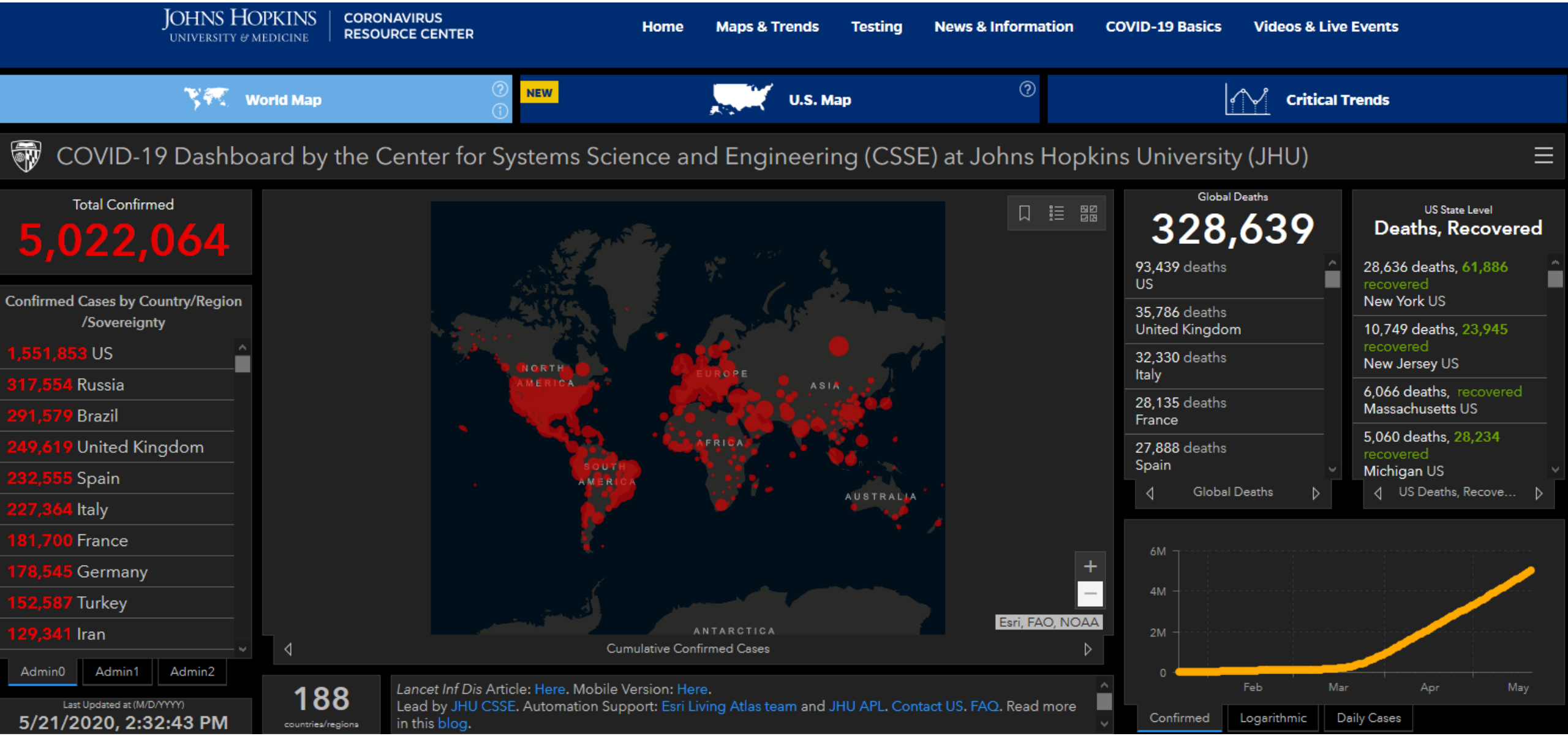
Content of the brief

- Global Statistics
- South African Statistics
- Topics:
  - Brief reports



Source: https://coronavirus.jhu.edu/map.html

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South African Statistics

As of today, the total number of confirmed COVID-19 cases in South Africa is **19 137**.

Case Data

Province	Total cases for 21 May 2020	Percentage total
Eastern Cape	2324	12,1
Free State	184	1,0
Gauteng	2453	12,8
KwaZulu-Natal	1693	8,8
Limpopo	121	0,6
Mpumalanga	95	0,5
North West	77	0,4
Northern Cape	37	0,2
Western Cape	12153	63,5
Unknown	0	0,0
Total	**19137**	**100,0**

Province	Deaths
Eastern Cape	50
Free State	6
Gauteng	27
KwaZulu Natal	46
Limpopo	3
Mpumalanga	0
North West	1
Northern Cape	1
Western Cape	235
Total	**369**

Testing Data

A total of **525 433** tests have been conducted to date with **18 572** tests done in the past 24 hours

Sources: https://sacoronavirus.co.za

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Articles of Interest

Original Investigation ONLINE FIRST FREE

May 5, 2020

Association of Use of Angiotensin-Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers With Testing Positive for Coronavirus Disease 2019 (COVID-19)

Neil Mehta, MBBS[1]; Ankur Kalra, MD[2,3]; Amy S. Nowacki, PhD[4]; et al

Author Affiliations | Article Information

JAMA Cardiol. Published online May 5, 2020. doi:10.1001/jamacardio.2020.1855

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Ohio and Florida, US

Investigated the association between ACEi or ARB use and testing positive for Covid-19

18 472 patients tested for COVID-19

Mean (SD) age was 49 (21) years, 7384 (40%) were male

Hypertension (7312 [40%]), diabetes (3478 [19%]), coronary artery disease (2179 [12%]), chronic obstructive pulmonary disease (2186 [12%]), and heart failure (1879 [10%])

2285 (12.4%) were taking either ACEIs or ARBs

Positive COVID-19 test in 1735/18 472 patients (9.4%)

421 (24.3%) admitted to the hospital

161 (9.3%) were admitted to an intensive care unit

111 (6.4%) required mechanical ventilation

Overlap propensity score weighting

- no significant association of ACEI and/or ARB use with COVID-19 test positivity (overlap propensity score–weighted odds ratio, 0.97; 95% CI, 0.81-1.15)
- Significant associations for hospital admission and ICU admission – see next slide

Of 1705 with outcome data, 3.8% on ACEi/ARBs died vs 2.1% not on Rx, no stats done

Retrospective cohort study
Overlap propensity score weighting – method to address confounding
Multivariable logistic regression model containing patient age, sex, and presence of hypertension, diabetes, coronary artery disease, heart failure, and chronic obstructive pulmonary disease

Mehta N, Kalra A, Nowacki AS, et al. Association of Use of Angiotensin-Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers With Testing Positive for Coronavirus Disease 2019 (COVID-19). *JAMA Cardiol.* Published online May 05, 2020. doi:10.1001/jamacardio.2020.1855

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Limitations
Low absolute numbers of events (table 3)
No info on duration of use
Potentially lower threshold to admit patients on ACEis or ARBs

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Table 3. Overlap Propensity Score-Weighted Characteristics and Clinical Outcomes Among ACEI and ARB Usage Groups in Patients Who Tested Positive for SARS-CoV-2

Table 3. Overlap Propensity Score-Weighted Characteristics and Clinical Outcomes Among ACEI and ARB Usage Groups in Patients Who Tested Positive for SARS-CoV-2

	All patients who tested positive, %[a]					
	ACEI		ARB		ACEI/ARB	
Characteristic	Yes	No	Yes	No	Yes	No
Count, No.	116	1619	98	1637	212	1523
Age, y	63	63	64	64	63	63
Male	57	57	58	58	55	55
Diabetes	51	51	48	48	46	46
CAD	21	21	23	23	22	22
Hypertension	97	97	92	92	93	93
COPD	12	12	16	16	14	14
HF	15	15	19	19	17	17
Admitted to hospital	54	39	53	41	53	36
OR (95% CI)	1.84 (1.22-2.79)		1.61 (1.04-2.50)		1.93 (1.38-2.71)	
Admitted to ICU	24	15	20	18	22	15
OR (95% CI)	1.77 (1.07-2.92)		1.16 (0.67-2.02)		1.64 (1.07-2.51)	
Use of ventilator	14	11	14	12	14	11
OR (95% CI)	1.35 (0.74-2.47)		1.12 (0.59-2.12)		1.32 (0.80-2.18)	

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; HF, heart failure; ICU, intensive care unit; OR, odds ratio; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

[a] Reported is either the overlap propensity score-weighted mean or proportion for each group.

Figure. Association of ACEI and ARB With Results of SARS-CoV-2 Testing (Primary Outcome) and Secondary Clinical Outcomes: Overlap Propensity Score Weighted-Analysis ORs With 95% CIs

Outcome	OR (95% CI)
Test positive	
ACEI vs no ACEI	0.89 (0.72-1.10)
ARB vs no ARB	1.09 (0.87-1.37)
ACEI/ARB vs no ACEI/ARB	0.97 (0.81-1.15)
Hospital admission	
ACEI vs no ACEI	1.84 (1.22-2.79)
ARB vs no ARB	1.61 (1.04-2.50)
ACEI/ARB vs no ACEI/ARB	1.93 (1.38-2.71)
ICU admission	
ACEI vs no ACEI	1.77 (1.07-2.92)
ARB vs no ARB	1.16 (0.67-2.02)
ACEI/ARB vs no ACEI/ARB	1.64 (1.07-2.51)
Use of ventilator	
ACEI vs no ACEI	1.35 (0.74-2.47)
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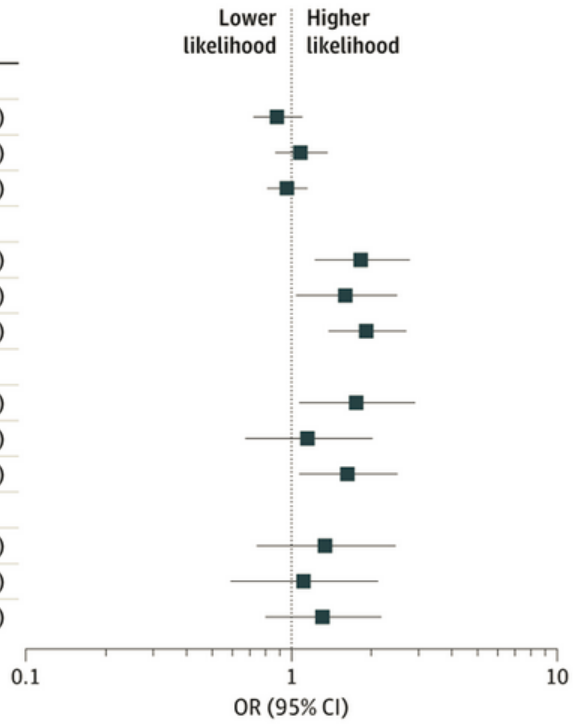
ACEI/ARB vs no ACEI/ARB	1.32 (0.80-2.18)



Mehta N, Kalra A, Nowacki AS, et al. Association of Use of Angiotensin-Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers With Testing Positive for Coronavirus Disease 2019 (COVID-19). *JAMA Cardiol.* Published online May 05, 2020. doi:10.1001/jamacardio.2020.1855

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France, n = 24, mean age 66y, 67% men

Awake, nonintubated, spontaneously breathing patients with COVID-19 and hypoxemic acute respiratory failure requiring oxygen supplementation

Arterial blood gases were performed just before PP, during PP, and 6 to 12 hours after resupination.

Responders = 20% increase in partial pressure of arterial O2 during PP, compared to before

O2 supplementation: 67% on < 4 L/min, 33% on > 4 L/min or HFNC

tolerance of PP: 4 less than 1 hour, 5 1 - 3 hours, 15 more than 3 hours

6 = responders (25%)

3 = persistent responders, remained improved after re-supination

no significant difference in mean PaO2 before PP and after resupination.

5 patients required invasive mechanical ventilation during 10 day follow-up.

4 of them were the group who could not sustain PP for more than an hour

Research Letter

ONLINE FIRST FREE

May 15, 2020

Use of Prone Positioning in Nonintubated Patients With COVID-19 and Hypoxemic Acute Respiratory Failure

Xavier Elharrar, MD[1]; Youssef Trigui, MD[1]; Anne-Marie Dols, MD[2]; et al

» Author Affiliations | Article Information

JAMA. Published online May 15, 2020. doi:10.1001/jama.2020.8255

Prospective, single-center, before-after study

Conclusion

63% were able to tolerate PP more than 3 hours

Oxygenation improved substantially in only 25% and in very few after resupination

Authors speculate that a trial of PP may be a mechanism to select patients who will do well, or it may be useful in a subset

Limitations

Small, limited follow-up, not randomised

Elharrar X, Trigui Y, Dols A, et al. Use of Prone Positioning in Nonintubated Patients With COVID-19 and Hypoxemic Acute Respiratory Failure. *JAMA.* Published online May 15, 2020. doi:10.1001/jama.2020.8255

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Research Letter

ONLINE FIRST FREE

May 15, 2020

Respiratory Parameters in Patients With COVID-19 After Using Noninvasive Ventilation in the Prone Position Outside the Intensive Care Unit

Chiara Sartini, MD[1]; Moreno Tresoldi, MD[2]; Paolo Scarpellini, MD[3]; et al

» Author Affiliations | Article Information

JAMA. Published online May 15, 2020. doi:10.1001/jama.2020.7861

Cross-sectional, single-center

Italy, n = 15, mean age 59 y, 13/15 men

Mild to moderate ARDS who had saturation less than 94% on face mask with high-c concentration, applying 10 cm H_2O continuous positive airway pressure and 0.6 fra of inspired oxygen (FIO_2) – in poor response to NIV, trial of PP used, continued if improvement in first hour

Study measurements taken on 1 day on all eligible patients on NIV and PP, regardless of when NIV and PP started

3 time points: before NIV, during NIV in pronation (60 minutes after start), and 60 minutes after NIV end

Results

NIV duration median of 5 days (interquartile range [IQR], 3-10 days)

Compared with baseline, all patients had a reduction in respiratory rate during and after pronation ($P < .001$ for both)

All patients had an improvement in SpO_2 and PaO_2:FIO_2 during pronation ($P < .001$ for both)

12 patients (80%) had an improvement in SpO_2 and PaO_2:FIO_2 after pronation

2 (13.3%) had the same value; and 1 (6.7%) had worsened

At the 14-day follow-up, 9 patients were discharged home, 1 improved and stopped pronation, 3 continued pronation, 1 patient was intubated and admitted to ICU, and 1 patient died.

Conclusion

PP feasible

Unclear whether intubation was avoided or delayed

Limitations

Small, majority men, not randomised, selection bias – duration of illness and severity

P-value reported, but not effect size

Sartini C, Tresoldi M, Scarpellini P, et al. Respiratory Parameters in Patients With COVID-19 After Using Noninvasive Ventilation in the Prone Position Outside the Intensive Care Unit. *JAMA.* Published online May 15, 2020. doi:10.1001/jama.2020.7861

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Cochrane Library

Cochrane Database of Systematic Reviews

Convalescent plasma or hyperimmune immunoglobulin for people with COVID-19: a rapid review (Review)

Valk SJ, Piechotta V, Chai KL, Doree C, Monsef I, Wood EM, Lamikanra A, Kimber C, McQuilten Z, So-Osman C, Estcourt LJ, Skoetz N

Rapid living systematic review – monthly search update
Included Covid-19 studies, any type, evaluating convalescent plasma or hyperimmune immunoglobulin

Included eight studies (seven case-series, one prospectively planned, single-arm intervention study) with total 32 participants (range 1 to 10)

Identified 48 ongoing studies evaluating convalescent plasma (47 studies) or hyperimmune immunoglobulin (one study), of which 22 are randomised.

Overall risk of bias of the eight included studies was high

- study design
- small number of participants
- poor reporting
- varied type of participants with different severities of disease, comorbidities, and types of previous or concurrent treatments

All outcomes rated as very low certainty, reported results narratively.

All studies reported mortality, no deaths in included studies, follow-up ranged from 3 to 37 days

Finding: not enough evidence for the intervention's effect on mortality, improvement of clinical symptoms, ICU stay, duration of mechanical ventilation

No studies reported grade of adverse events – 2 reported adverse events presumably grade 3 or 4 - 1 fever, 1 severe anaphylactic shock

Valk, SJ et al. Convalescent plasma or hyperimmune immunoglobulin for people with COVID-19: a rapid review. Cochrane Database of Systematic Reviews 2020, Issue 5. Art. No.: CD013600. DOI: 10.1002/14651858.CD013600.

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Two nested cohorts from Global Tuberculosis Network (GTN) study

Cohort A

49 patients with TB and COVID-19 from 26 centres in Belgium, Brazil, France, Italy, Russia, Singapore, Spain, and Switzerland

Cohort B

20 cases admitted to a single reference hospital located in Northern Italy

All consecutive cases with TB and covid-19 included

68/69 male, median age 70y (range 45 – 82)

43/69 migrants (younger, lower mortality rate)

All had at least 2 comorbidities, 1 HIV co-infected (70y, died)

In 67/69 Covid-19 diagnosis 7 – 75 days after TB diagnosis

Mortality 8/69 (11.6%) (A: 14%, B: 5%)

6 age above 70y, 1 45y (alcohol abuse, liver disease), 1 66y (alcohol abuse, COPD, liver disease)

6 of patients who died had nosocomial SARS-Cov-2 infection

Pulmonology
Available online 14 May 2020
In Press, Journal Pre-proof

Brief Communication

Tuberculosis, COVID-19 and migrants: preliminary analysis of deaths occurring in 69 patients from two cohorts

Ilaria Motta [a, j], Rosella Centis [b, j], Lia D'Ambrosio [c, j], José-María García-García [d, j], Delia Goletti [e, j], Gina Gualano [f, j], Filippo Lipani [a, j], Fabrizio Palmieri [f, j], Adrián Sánchez-Montalvá [g, h, i, j], Emanuele Pontali [j], Giovanni Sotgiu [m, j], Antonio Spanevello [n, o, j], Claudia Stochino [p, j], Eva Tabernero [q, j], Marina Tadolini [r, j], Martin van den Boom [s, j], Simone Villa [t, j], Dina Visca [n, o, j], Giovanni Battista Migliori [b, j]

Cross-sectional report of larger TB cohort study

Limitations

Small numbers

Generalisability unclear

Ilaria Motta et al, Tuberculosis, COVID-19 and migrants: preliminary analysis of deaths occurring in 69 patients from two cohorts (2020), doi: https://doi.org/10.1016/j.pulmoe.2020.05.002

This summary was prepared by Dr E Maasdorp as part of the daily brief to the TBH ICU team.