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MORNING BRIEF

Scientific Review

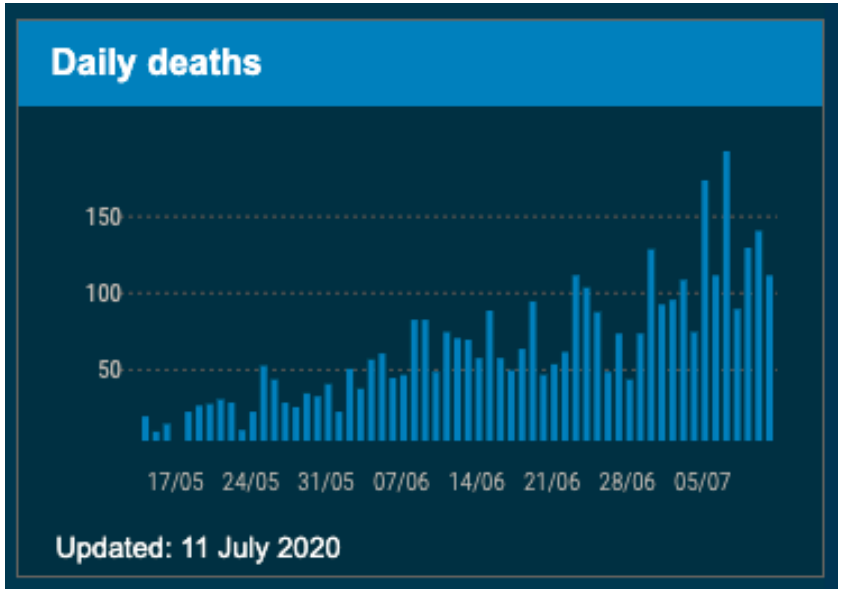
13 July 2020

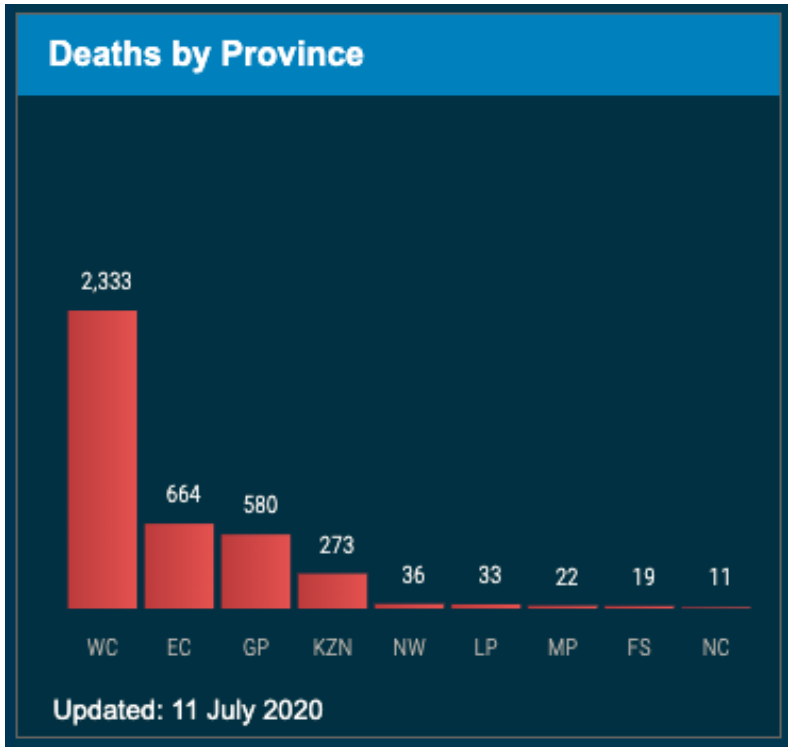
The purpose of the Morning Brief is to summarize and present key information, research articles and other relevant publications pertaining to critical care and COVID-19.

Stellenbosch University Research Response Team

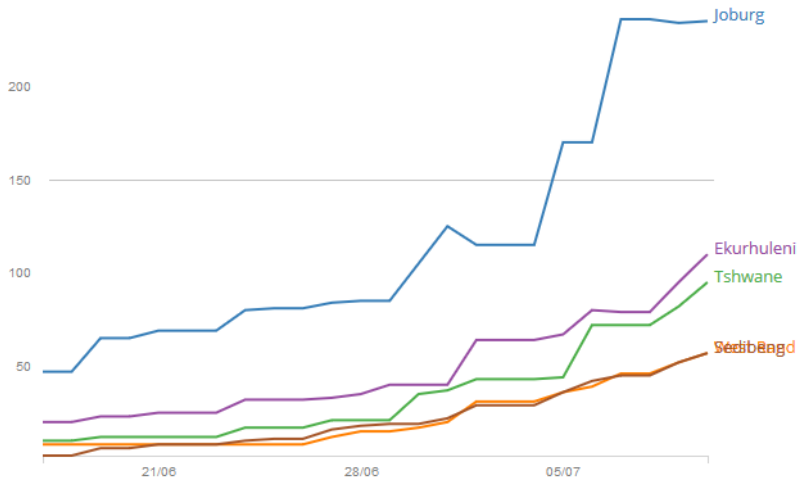
Content

Statistics
Brief reports – OPENsafely and corticosteroids



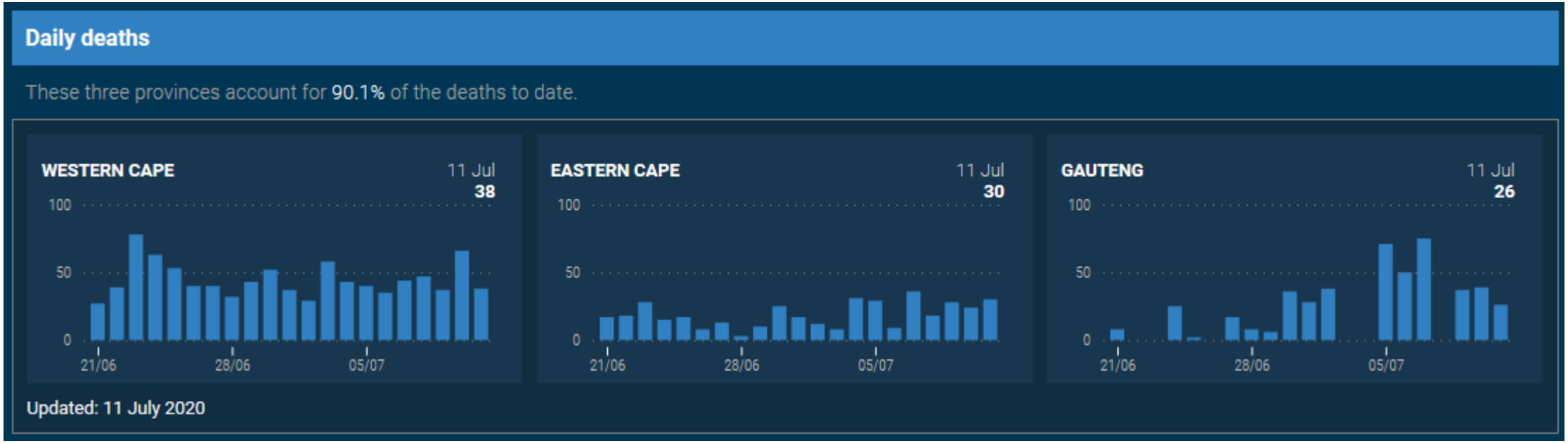


Cumulative covid-19-related deaths in Gauteng's districts

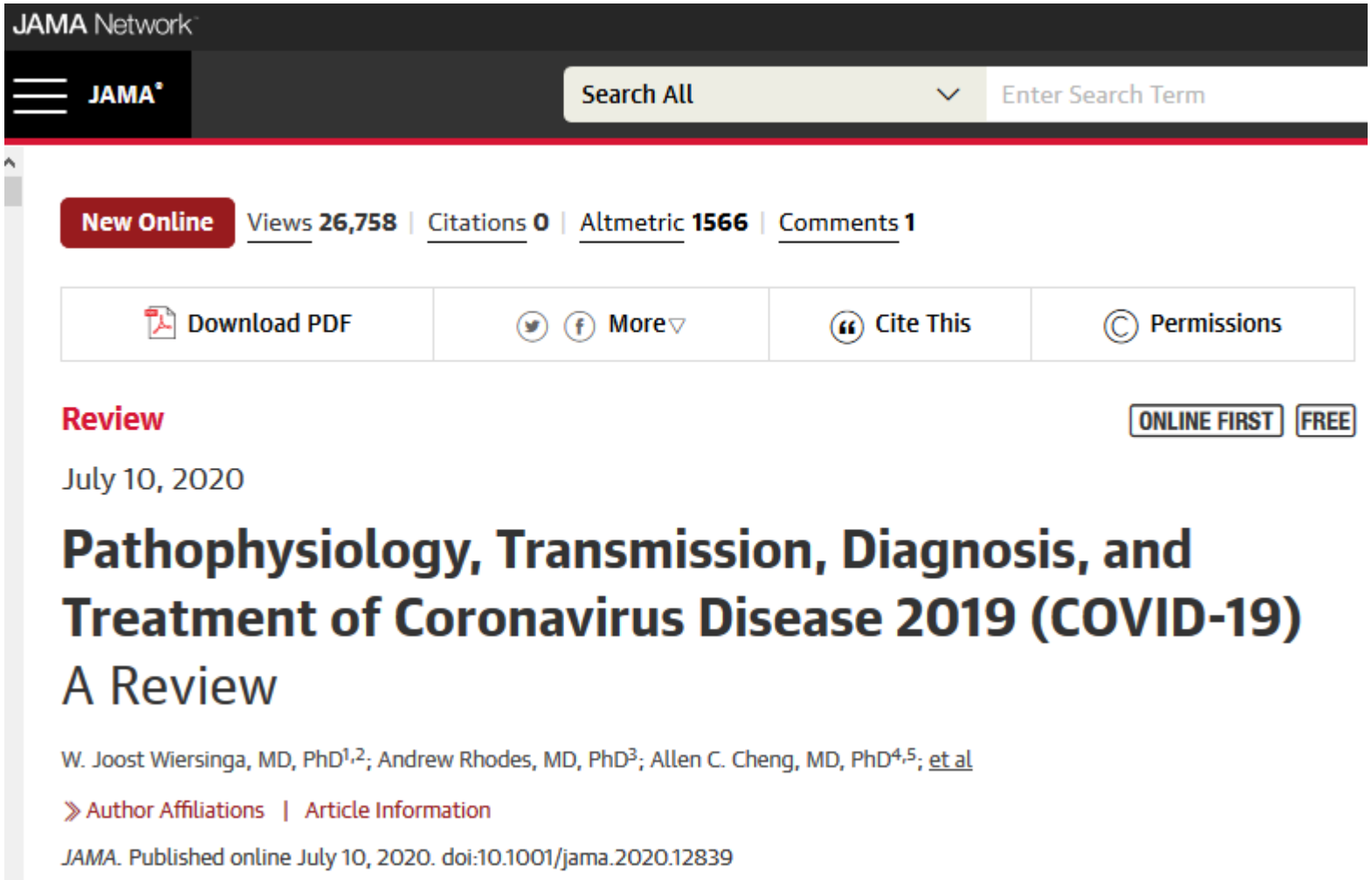


The cumulative deaths in Johannesburg announced by the Gauteng Department of Health for 9 July are lower than the deaths announced for 8 July. No reason was given for the decrease in the media statement.

https://mediahack.co.za/datastories/coronavirus/dashboard/



Recommended read:



TREATMENT COMPARISONS

We report below the forest plots for the main treatment comparisons.

Please choose a Treatment Comparison:

- Remdesivir vs Placebo
- Dexamethasone vs Standard Care
- Lopinavir + Ritonavir vs Standard care
- Lopinavir + Ritonavir + Ribavirin + Interferon-b-1b vs Lopinavir + Ritonavir
- Umifenovir vs Standard care
- Hydroxychloroquine vs Standard care
- Chloroquine vs Standard Care
- Umifenovir vs Lopinavir + Ritonavir
- Favipiravir vs Umifenovir
- a-Lipoic acid vs Placebo
- Novaferon + Lopinavir + Ritonavir vs Lopinavir + Ritonavir
- Novaferon + Lopinavir + Ritonavir vs Novaferon
- Novaferon vs Lopinavir + Ritonavir
- Baloxavir marboxil vs Lopinavir + Ritonavir or Darunavir/Cobicistat + Umifenovir + Interferon-a
- Favipiravir vs Baloxavir marboxil
- Favipiravir vs Lopinavir + Ritonavir or Darunavir/Cobicistat + Umifenovir + Interferon-a
- Colchicine vs Standard Care
- Convalescent plasma vs Standard care
- Hydroxychloroquine vs Chloroquine
- Ruxolitinib vs Vitamin C
- Interferon β-1a vs Standard care

https://covid-nma.com/living_data/index.php

Comparisons for which there are at least one randomised clinical trial available

International Journal of Antimicrobial Agents
Available online 4 July 2020, 106077
In Press, Journal Pre-proof

Corticosteroid therapy for patients with CoVID-19 pneumonia: a before-after study

Firouzé BANI-SADR [a], Maxime HENTZIEN [a], Madeline PASCARD [b], Yohan N'GUYEN [a], Amélie SERVETTAZ [a], Laurent ANDREOLETTI [c], Lukshe KANAGARATNAM [b], Damien JOLLY [b]

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https://doi.org/10.1016/j.ijantimicag.2020.106077

Two periods at 1 hospital in France:
- before period from March 3rd to 20th (n= 85)
- after period (n=172) from March 26th to April 14th 2020.

Compared rates of death (primary outcome)

ICU admission and/or death before ICU admission
- ICU admission alone was not considered as an outcome, since did not exclude patients aged over 80 years and/or with comorbidities, who were less likely to have access to ICU care.

Average of 2-3 days between dyspnea onset and ICU admission - corticosteroid treatment as soon as the patient has shortness of breath or needs oxygen therapy

protocol since 27 March 2020
- Prednisone or methylprednisolone
- 1 mg/kg equivalent per day (0.5 mg/kg for patients also receiving antiviral therapy with ritonavir due to drug interactions) for 3 to 4 weeks, according to the severity of pneumonia

Protocol also included
- antiviral therapy (lopinavir plus ritonavir or darunavir plus ritonavir)
- and/or hydroxychloroquine
- empiric broad-spectrum antibiotic treatment for 14 days
- preventive anticoagulation
- For 14 to 21 days

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Results

85 in before period, 172 in after period (transition period excluded = 62)

11/85 (12.9%) on steroids in before group

119/172 (69.2%) on steroids in after group

mean duration of follow-up was 16.0 ± 7.0 days

Risk of death

Multivariate analysis adjusted for age, National Early Warning score and institutionalization status

(HR = 0.47; 95% CI 0.23 - 0.97; p=0.04)

Risk of ICU admission and/or death before ICU

Multivariate analysis adjusted for age, National Early Warning score and institutionalization status

(HR=0.37 95% CI 0.21 - 0.64; p=0.0005)

	Before (N=85) n (%) or mean ± SD		After (N=172) n (%) or mean ± SD		p
Received corticosteroids	11	12.9	119	69.2	<0.0001
Age	70.1	±15.1	71.8	±16.4	0.44
Male sex	46	54.1	51.7	41.7	0.72
Charlson comorbidity score	1.8	±2.0	2.05	±1.94	0.42
Dementia	8	9.4	33	19.2	0.04
Nursing home resident	8	9.4	47	27.3	0.001
Time from symptom onset to hospitalization (days)	5.8	±4.2	7.5	±4.9	0.009
Diagnosis by positive PCR	80	94.1	143	83.1	0.01
Diagnosis by chest CT scan	5	5.9	29	16.9	
Risk factor of severity	71	83.5	156	90.7	0.09
- Immunocompromised	11	12.9	22	12.8	0.97
- Cardiovascular disease	41	48.2	94	54.7	0.33
- Complicated diabetes	7	8.2	23	13.4	0.23
- Cirrhosis	1	1.2	3	1.7	0.99
- Chronic respiratory disease	22	25.9	32	18.6	0.18
- Chronic renal disease	4	4.7	16	9.3	0.20
- Cancer	7	8.2	10	5.8	0.46
- BMI>40	2	2.4	13	7.7	0.15
- National Early Warning Score	6.2	3.8	6.9	3.2	0.12
Biological characteristics					
- Lymphocyte count G/L	1.1	±0.56	1.1	±1.0	0.73
- Lymphopenia<1G/L	43	51.2	91	53.9	0.69
- Neutrophil count, G/L	5.0	±3.6	5.6	±4.0	0.26
- C-reactive protein, mg/L	98.0	±90.2	89.9	±77.1	0.46
- Serum creatinine, □mol/L	103.5	±106.2	137.7	±174.3	0.05
Treatment use with expected antiviral activity	63	75.0	135	79.4	0.43
- Lopinavir	46	54.8	13	7.9	<0.0001
- Darunavir	27	32.5	133	78.2	<0.0001
- Hydroxychloroquine	11	13.3	10	6.0	0.049
Antibiotic therapy	80	95.2	162	95.9	0.99
Evolution					
- Required oxygen therapy	52	61.9	125	76.7	0.01
- Maximum oxygen flow in medical ward †	5.0	±7.6	5.7	±5.2	0.48
- Death	17	20.0	31	18.0	0.70
- ICU admission and/or Death	29	34.1	40	23.6	0.07

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Limitations

Potential confounders:

- General improvement in care over time
- Anti-viral effect of other drugs?
- No safety data reported

nature

https://doi.org/10.1038/s41586-020-2521-4

Accelerated Article Preview

OpenSAFELY: factors associated with COVID-19 death in 17 million patients

Received: 15 May 2020

Accepted: 1 July 2020

Accelerated Article Preview Published online 8 July 2020

Elizabeth J. Williamson, Alex J. Walker, Krishnan Bhaskaran, Seb Bacon, Chris Bates, Caroline E. Morton, Helen J. Curtis, Amir Mehrkar, David Evans, Peter Inglesby, Jonathan Cockburn, Helen I. McDonald, Brian MacKenna, Laurie Tomlinson, Ian J. Douglas, Christopher T. Rentsch, Rohini Mathur, Angel Y. S. Wong, Richard Grieve, David Harrison, Harriet Forbes, Anna Schultze, Richard Croker, John Parry, Frank Hester, Sam Harper, Rafael Perera, Stephen J. W. Evans, Liam Smeeth & Ben Goldacre

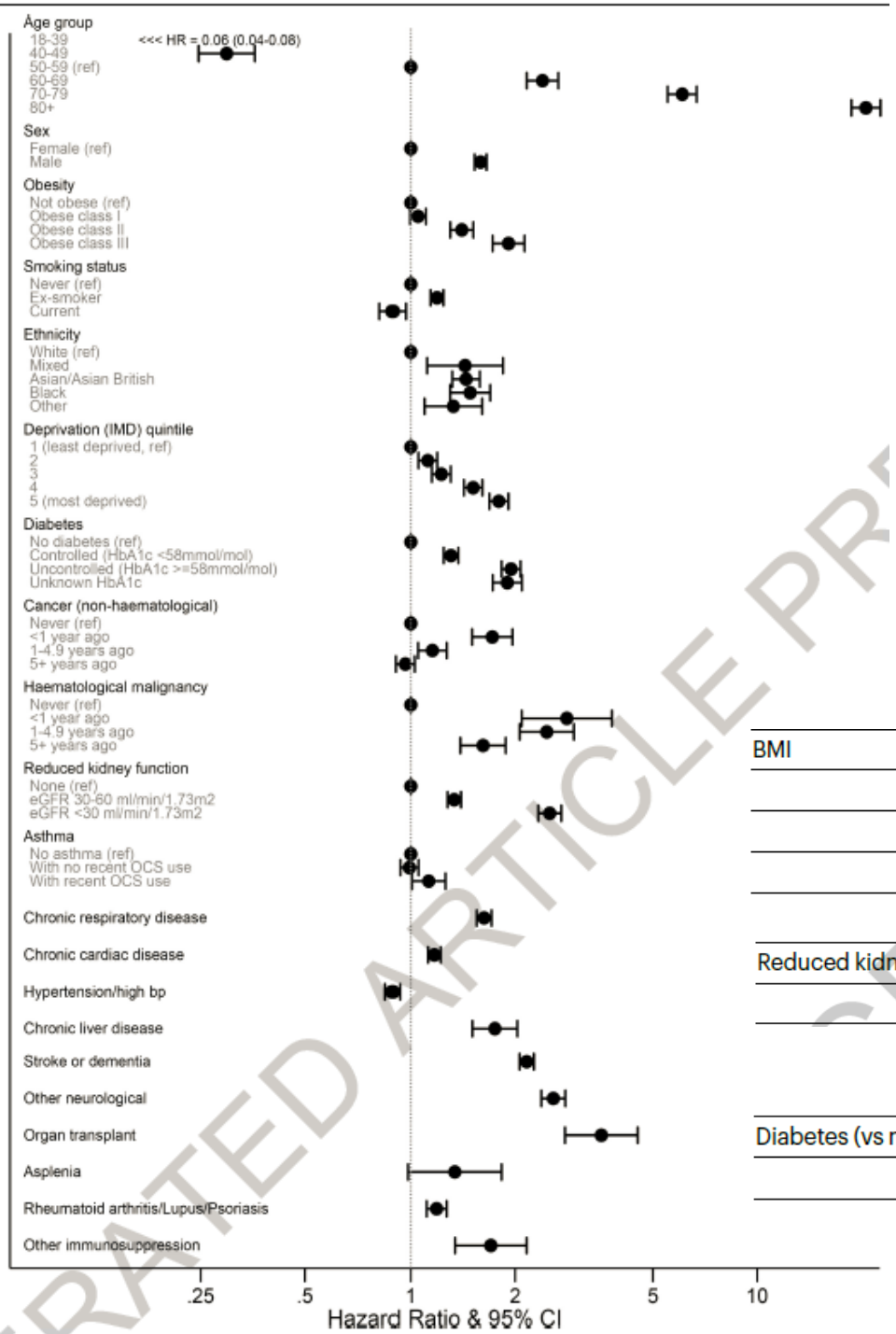

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Fig. 3 | Estimated Hazard Ratios (shown on a log scale) for each potential risk factor from a multivariable Cox model. Error bars represent limits of the 95% confidence interval for the hazard ratio. Obese class I: 30-34.9kg/m^2, class II: 35-39.9kg/m^2, class III: >=40kg/m^2. OCS = oral corticosteroid. All HRs are adjusted for all other factors listed other than ethnicity. Ethnicity estimates are from a separate model among those with complete ethnicity data, and are fully adjusted for other covariates. Total n = 17,278,392 for non-ethnicity models, and 12,718,279 for ethnicity model.

BMI	Not obese	1.00 (ref)	1.00 (ref)
	30-34.9kg/m2 (Obese class I)	1.23 (1.17-1.30)	1.05 (1.00-1.11)
	35-39.9kg/m2 (Obese class II)	1.81 (1.68-1.95)	1.40 (1.30-1.52)
	≥40 kg/m2 (Obese class III)	2.66 (2.39-2.95)	1.92 (1.72-2.13)
Reduced kidney function (vs none)****	Estimated GFR 30-60	1.56 (1.49-1.63)	1.33 (1.28-1.40)
	Estimated GFR <30	3.48 (3.23-3.75)	2.52 (2.33-2.72)
Diabetes (vs none)***	With HbA1c<58 mmol/mol	1.58 (1.51-1.66)	1.31 (1.24-1.37)
	With HbA1c>=58 mmol/mol	2.61 (2.46-2.77)	1.95 (1.83-2.07)
	With no recent HbA1c measure	2.27 (2.06-2.50)	1.90 (1.72-2.09)

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