

Supplemental Material

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Supplemental Table 1: Data availability on neurological manifestations and complication by contributing study/database.

Availability was defined based on data collection for prespecified fields in study case report forms.

Study ID	ISARIC REDCap platform				Locally-hosted REDCap or other data management system					
	CVCCPUK (UK-CCP)	CVVECMO (COVID-19 CCC)	CVVCORE (ISARIC Core)	CVRAPID (ISARIC Rapid)	CVTDWXD	CVPRQTA	CVPSICL	CVKBQEI	CVKMNLG	CVCSXGF
Total patients analysed	129,946	2,377	15,104	5,520	1,457	6,190	99	26	123	397
ICU	20,748	2,377	8,955	2,233	1,104	198	15	16	37	397
Non-ICU	109,198	0	6,149	3,287	353	5,992	84	10	86	0
Neurological manifestations at hospitalisation										
Alternated consciousness										
Fatigue										
Anosmia										
Dysguesia										
Myalgia										
Seizures										
Neurological complications during hospitalisation										
Stoke ^a										
CNS infection ^b										
Seizures ^c										

^a Stroke may be a clinical diagnosis, with or without supportive radiological findings

^b CNS infection includes meningitis or encephalitis

^c Seizure regardless of cause (e.g. febrile or due to epilepsy)

Supplemental Table 2: Cohort summary by geographic region and income classification showing the number of patients analysed by major geographic region and subregion.

Characteristic	Number of patients
Geographic region	
Sub-region	
Africa	
Sub-Saharan Africa	119
Americas	
Latin America and the Caribbean	2,508
Northern America	5,853
Asia	
Eastern Asia	97
South-eastern Asia	6,648
Southern Asia	6,964
Western Asia	343
Europe	
Eastern Europe	905
Northern Europe	131,227
Southern Europe	1,497
Western Europe	4,666
Oceania	
Australia and New Zealand	412
Income classification	
High	145 006
Upper middle	9,081
Low middle	7,053
Low	99

Supplemental Table 3: Data completeness summary for baseline characteristics, neurological manifestations, and neurological complications

Data completeness on variables used to defined inclusion/exclusion criteria (age, sex, clinical outcome) are not reported.

Characteristic	All patients (n=161,239)	ICU cohort (n = 35,993)	Non-ICU cohort (n = 125,246)
Baseline characteristics			
Age, years	100%	100%	100%
Sex	100%	100%	100%
Days from first symptom of COVID-19 to hospitalisation	78.2%	86.4%	75.8%
Ethnicity	82.7%	76.3%	84.5%
Asthma	98.2%	98.7%	98.0%
Chronic Cardiac Disease ^a	98.2%	98.7%	98.0%
Chronic Kidney Disease ^b	98.1%	98.7%	97.9%
Chronic Neurological Disorder ^c	97.9%	98.6%	97.7%
Chronic Pulmonary Disease ^d	98.2%	98.7%	98.1%
Dementia ^e	94.1%	92.6%	94.6%
Diabetes	98.6%	98.9%	98.5%
Former/Current Smoker	59.4%	51.1%	61.7%
Hypertension	84.6%	87.8%	83.7%
Liver Disease	99.7%	99.5%	99.8%
Obesity	86.3%	89.1%	85.6%
GCS at admission	39.8%	54.1%	35.7%
Neurological manifestations at hospitalisation ^f			
Altered consciousness	92.2%	95.8%	91.2%
Anosmia	69.7%	73.2%	68.8%
Dysgeusia	68.6%	71.4%	67.8%
Fatigue	91.6%	93.9%	91.0%
Myalgia	88.1%	91.0%	87.3%
Seizure	89.9%	94.8%	88.5%
Neurological complications during hospitalisation ^f			
Stroke	96.2%	93.5%	97.0%
CNS infection	99.5%	98.6%	99.8%
Seizures	99.5%	98.7%	99.8%
Final disposition			
Outcome	100%	100%	100%
Days from hospitalisation to outcome	100%	100%	100%

Where ICU, intensive care unit; GCS, Glasgow coma scale.

^a Chronic cardiac disease: any of coronary artery disease, heart failure, congenital heart disease, cardiomyopathy, or rheumatic heart disease, not hypertension.

^b Chronic kidney disease: chronic estimated glomerular filtration rate < 60 mL/min/1.73 m² or history of kidney transplantation.

^c Chronic neurologic disease: any of cerebral palsy, multiple sclerosis, motor neuron disease, muscular dystrophy, myasthenia gravis, Parkinson's disease, stroke, severe learning difficult

^d Chronic pulmonary disease: chronic obstructive pulmonary disease (chronic bronchitis, chronic obstructive pulmonary disease (COPD), emphysema), cystic fibrosis, bronchiectasis, interstitial lung disease

^e Dementia: Clinical diagnosis of dementia

^f Across all study case report forms. See Supplemental Table 1 for data availability for all neurological variables by study.

Supplemental Table 4: Baseline characteristics of the ICU cohort. Categorical variables are reported as frequencies (%); continuous variables are reported as medians (inter-quartile range)

Characteristic	ICU cohort
Admitted to ICU on the same day as hospitalization	15,961 (52.3%)
Treatment during ICU admission	
Invasive mechanical ventilation (IMV)	18,767 (52.9%)
Extra-corporal membrane oxygenation (ECMO)	770 (2.2%)
Days from ICU to outcome	
Death	9 (5 – 16)
Discharged	7 (4 – 14)
Continued hospitalization	6 (3 – 14)
Transferred	10 (4 – 21)

Supplemental Table 5: Neurological complications in ICU patients stratified by IMV and ECMO/ECLS use. Estimates are reported as estimate percentages and 95% confidence intervals. OR: Odds ratio; CI: Confidence interval; ECMO/ELCS: Extracorporeal Membrane Oxygenation/Extracorporeal Life Support

Received at any time during hospitalisation	Yes Cases/Total Estimate (95% CI)	No Cases/Total Estimate (95% CI)	Unadjusted OR Estimate (95% CI) p-value
CNS infection			
Invasive mechanical ventilation	129/18,481 0.7 (0.59 to 0.83)	33/16,443 0.2 (0.14 to 0.28)	3.5 (2.38-5.13) <0.001
ECMO/ECLS	6/752 0.8 (0.36 to 1.8)	151/33,760 0.45 (0.38 to 0.52)	1.79 (0.79-4.06) 0.164
Seizure (In-hospital)			
Invasive mechanical ventilation	353/18,482 1.9 (1.7 to 2.1)	144/16,467 0.87 (0.74 to 1)	2.21 (1.82-2.68) <0.001
ECMO/ECLS	21/752 2.8 (1.8 to 4.2)	474/33,784 1.4 (1.3 to 1.5)	2.02 (1.3-3.14) <0.001
Stroke			
Invasive mechanical ventilation	407/17,329 2.3 (2.1 to 2.6)	173/15,772 1.1 (0.95 to 1.3)	2.17 (1.81-2.59) <0.001
ECMO/ECLS	52/718 7.2 (5.6 to 9.4)	525/31,971 1.6 (1.5 to 1.8)	4.68 (3.48-6.28) <0.001

Supplemental Table 6: Multivariable model estimates for reported neurological complications during hospitalisation.
Estimates are reported as an odds ratio (OR) with 95% confidence interval.

Parameter	CNS infection	Seizure	Stroke
Intercept	0.001 (0.000 – 0.002)	0.002 (0.001 – 0.003)	0.003 (0.002 – 0.004)
Altered consciousness	4.82 (3.64 to 6.37)	1.70 (1.49 to 1.95)	1.92 (1.74 to 2.12)
Chronic cardiac disease	0.99 (0.72 to 1.35)	1.04 (0.91 to 1.20)	1.09 (0.99 to 1.20)
Chronic neurological disorder	0.66 (0.44 to 1.0)	2.85 (2.5 to 3.25)	2.12 (1.9 to 2.36)
Dementia	0.85 (0.53 to 1.37)	1 (0.84 to 1.19)	0.68 (0.60 to 0.78)
Diabetes Mellitus	1.07 (0.82 to 1.4)	1.0 (0.87 to 1.14)	1.02 (0.93 to 1.12)
Hypertension	1.27 (0.97 to 1.66)	1.05 (0.89 to 1.23)	1.34 (1.20 to 1.48)
Fatigue/Malaise	0.84 (0.64 to 1.11)	0.68 (0.59 to 0.80)	0.63 (0.57 to 0.69)
Myalgia	0.93 (0.65 to 1.34)	0.67 (0.54 to 0.84)	0.78 (0.66 to 0.93)
Seizures at admission	7.66 (5.06 to 11.58)	72.54 (62.98 to 83.56)	2.38 (1.86 to 3.04)
Sex: Male	0.807 (0.64 to 1.02)	1.05 (0.94 to 1.18)	1.12 (1.02 to 1.22)
Invasive mechanical ventilation	2.75 (2.03 to 3.73)	3.36 (2.82 to 4.01)	2.88 (2.51 to 3.31)

ECMO/ECLS	0.79 (0.31 to 2.05)	1.66 (0.99 to 2.80)	3.77 (2.74 to 5.19)
Study cohort: ISARIC Core (reference)	1 (-)	1 (-)	1 (-)
Study cohort: CCP-UK	1.03 (0.68 to 1.57)	2.15 (1.64 to 2.81)	2.88 (2.28 to 3.64)
Study cohort: COVID-19 CCC	2.53 (1.45 to 4.39)	2.10 (1.38 to 3.20)	3.13 (2.25 to 4.34)
Study cohort: Other	0.86 (0.26 to 2.85)	3.93 (2.34 to 6.62)	2.26 (1.29 to 3.97)

Supplementary Table 7: Multivariable model estimates for in-hospital mortality, ICU and non-ICU cohorts. Estimates are reported as an odds ratio (OR) with 95% confidence interval. Age and time polynomial effects are presented in Supplemental Figure 1.*ICU cohort only

Parameter	ICU cohort	non-ICU cohort
Intercept (Mean age = 60 years)	0.09 (0.08 to 0.1)	0.04 (0.04 to 0.05)
Stroke	1.57 (1.31 to 1.88)	1.63 (1.46 to 1.81)
Seizures (in-hospital)	1.04 (0.83 to 1.3)	1.5 (1.3 to 1.73)
CNS infection	1.19 (0.79 to 1.78)	2.98 (2.07 to 4.28)
Invasive mechanical ventilation*	4.31 (4.05 to 4.6)	–
ECMO/ECLS*	1.39 (1.18 to 1.65)	–
Sex: Male	1.16 (1.1 to 1.23)	1.4 (1.36 to 1.44)
Ethnicity: Caucasian (reference)	1 (–)	1 (–)
Ethnicity: Black	0.78 (0.69 to 0.89)	0.98 (0.88 to 1.11)
Ethnicity: Unknown	0.92 (0.85 to 0.99)	0.99 (0.94 to 1.04)
Ethnicity: Other	0.98 (0.87 to 1.11)	0.92 (0.82 to 1.02)
Ethnicity: Southeast Asian	1.46 (1.35 to 1.57)	1.01 (0.93 to 1.1)
Chronic cardiac disease (not hypertension)	1.16 (1.08 to 1.25)	1.23 (1.19 to 1.27)
Chronic kidney disease	1.48 (1.35 to 1.63)	1.34 (1.3 to 1.39)
Chronic pulmonary disease (not asthma)	1.68 (1.53 to 1.83)	1.49 (1.44 to 1.55)
Diabetes Mellitus	1.2 (1.13 to 1.27)	1.19 (1.15 to 1.23)
Obesity	1.01 (0.94 to 1.09)	1.08 (1.02 to 1.14)

Hypertension	0.97 (0.89 to 1.05)	0.89 (0.85 to 0.92)
Study cohort: ISARIC Core (reference)	1 (--)	1 (--)
Study cohort: CCP-UK	1.82 (1.69 to 1.96)	2.9 (2.61 to 3.23)
Study cohort: COVID-19 CCC*	1.52 (1.35 to 1.7)	–
Study cohort: Other	0.88 (0.74 to 1.05)	0.25 (0.17 to 0.36)

Supplemental Table 8: Additional reports neurological complications based on free-text entries.

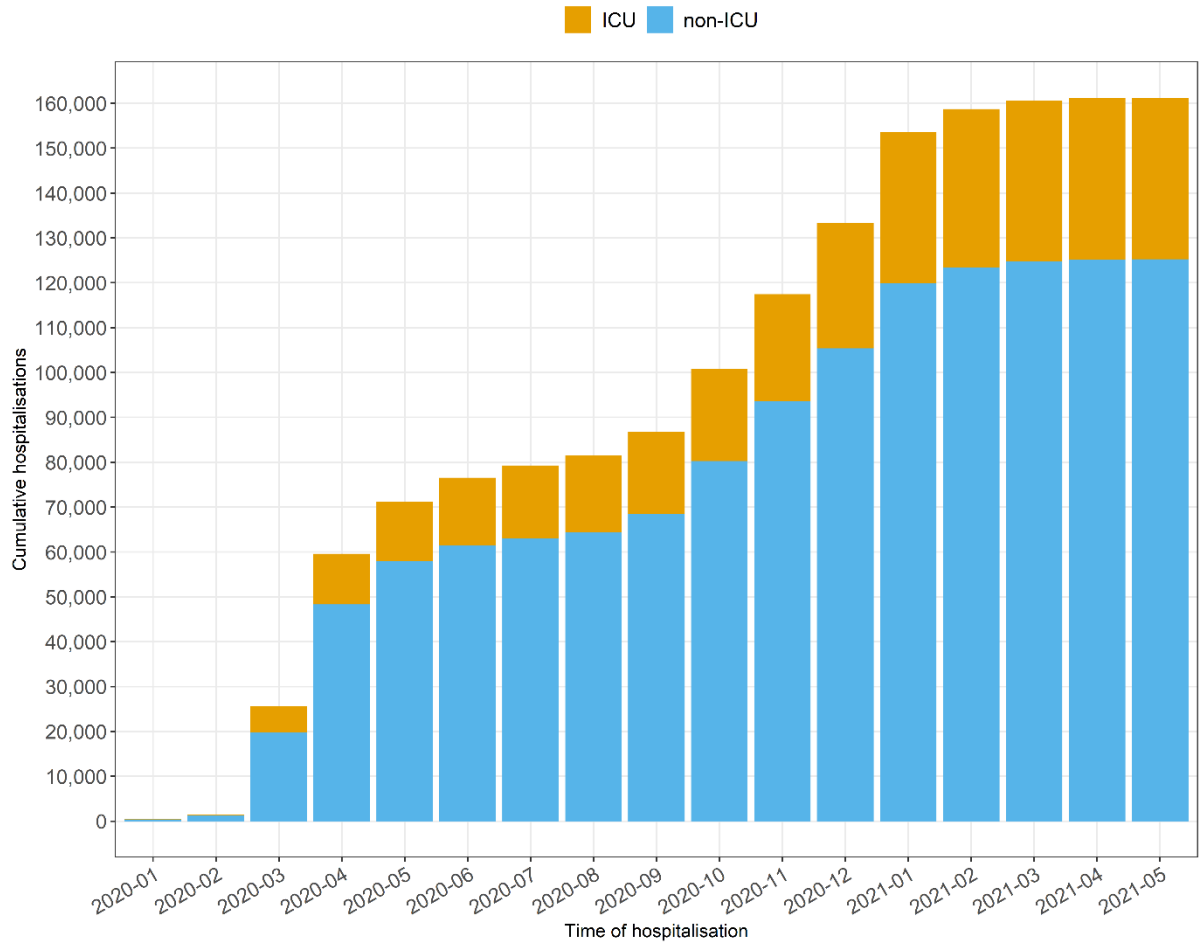
Notes for main text as relevant:

- Across all records, we identified 52,801 free-text complications for 34,214 patients: 33,767 adults, 447 children.
- 77% of all free-text complications were recorded in the non-ICU cohort (26,365 vs. 7,849 in the ICU cohort).
- All almost free-text entries were from studies contributing to the ISARIC REDCap platform (n = 33,714 patients).

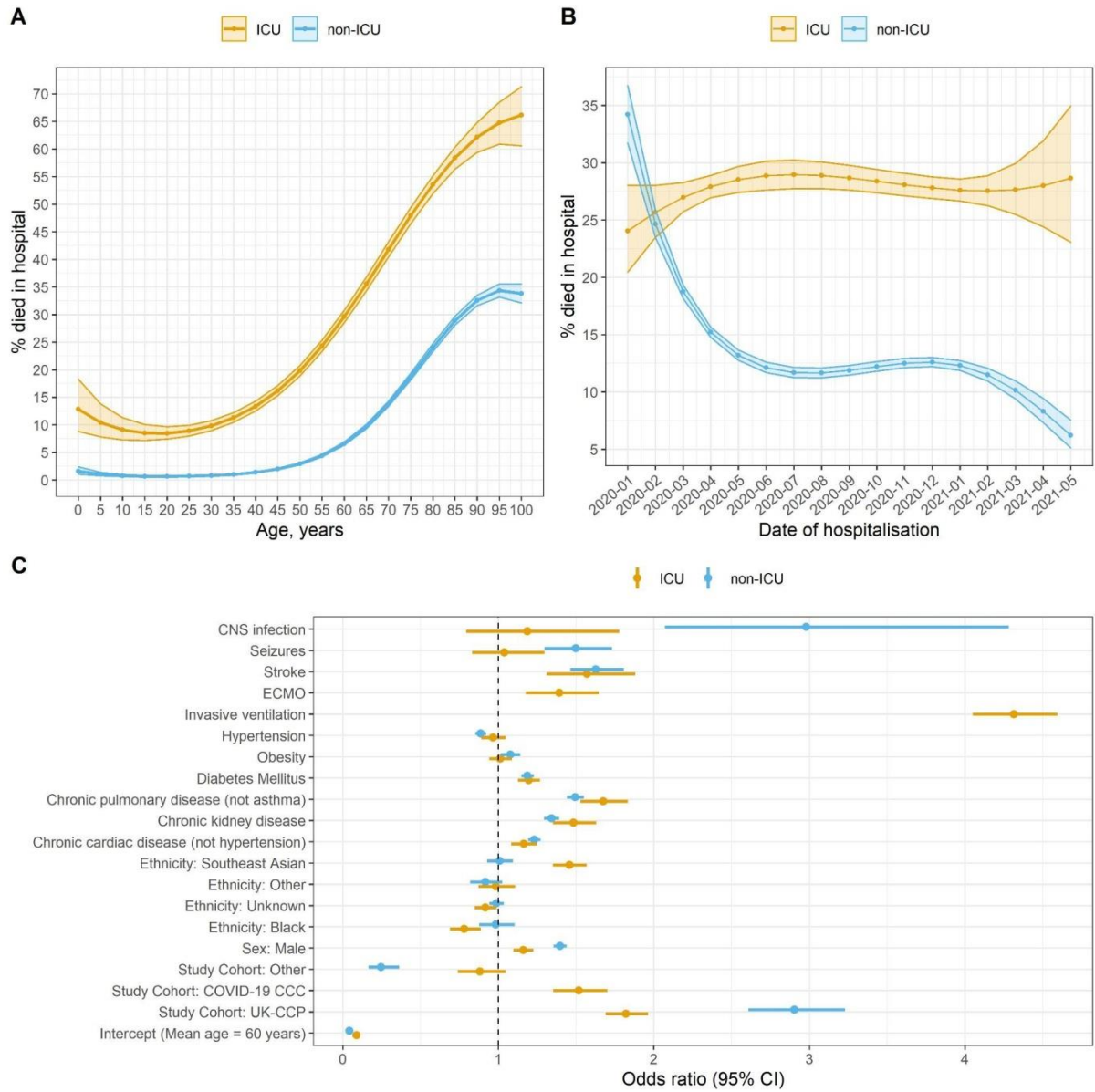
Complication	Number of records ^a
Delirium	2,250
Encephalopathy	135

^a See Supplementary Data 1 for list of all records returned by complication

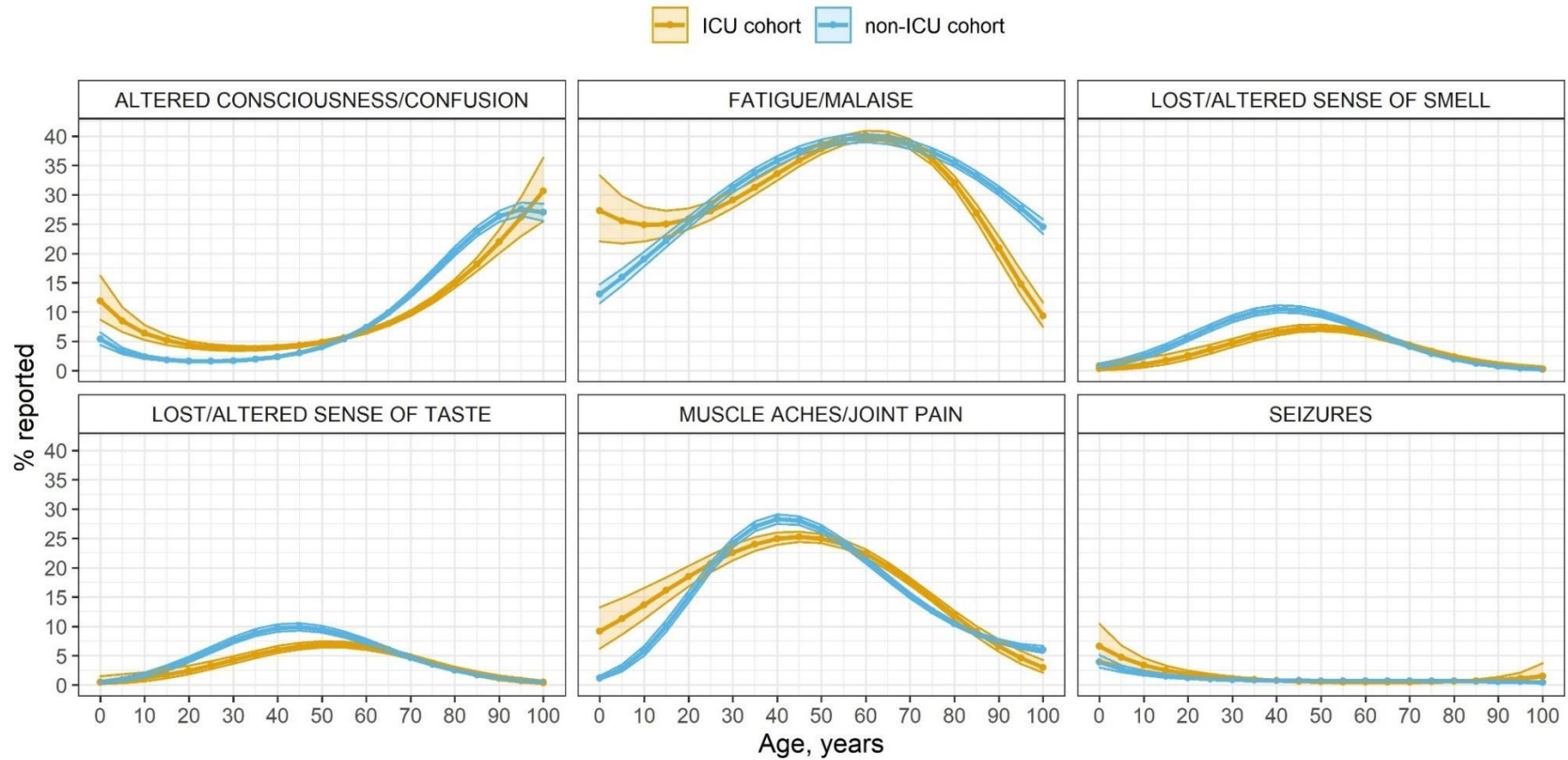
Supplemental Figure 1: Cumulative COVID-19 hospitalisations over time summarised by month and year of hospital admission. Cumulative numbers are stratified by ICU and non-ICU cohort



Supplemental Figure 2: Results of multivariable analysis for in-hospital mortality based on final disposition (logistic regression/Binomial GLM). Covariate associations are displayed as odds ratios (OR) with 95% confidence intervals.



Supplemental Figure 3: Estimated age-related prevalence of reported neurological manifestations at hospital admission. Model estimates are stratified by ICU and non-ICU cohorts and plotted per 10-year age increase. Estimate uncertainty is presented as 95% confidence intervals.



Supplemental Figure 4: Stacked probability plot, final disposition up to 100 days following hospitalisation with SARS-CoV-2 infection. Stratification by ICU, non-ICU cohorts; all hospitalised patients

