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Neurological manifestations of COVID-19 in adults and children

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Different neurological manifestations of coronavirus disease 2019 (COVID-19) in adults and children and their impact have not been well characterized. We aimed to determine the prevalence of neurological manifestations and in-hospital complications among hospitalized COVID-19 patients and ascertain differences between adults and children. We conducted a prospective multicentre observational study using the International Severe Acute Respiratory and emerging Infection Consortium (ISARIC) cohort across 1507 sites worldwide from 30 January 2020 to 25 May 2021. Analyses of neurological manifestations and neurological complications considered unadjusted prevalence estimates for predefined patient subgroups, and adjusted estimates as a function of patient age and time of hospitalization using generalized linear models.

Overall, 161 239 patients (158 267 adults; 2972 children) hospitalized with COVID-19 and assessed for neurological manifestations and complications were included. In adults and children, the most frequent neurological manifestations at admission were fatigue (adults: 37.4%; children: 20.4%), altered consciousness (20.9%; 6.8%), myalgia (16.9%; 7.6%), dysgeusia (7.4%; 1.9%), anosmia (6.0%; 2.2%) and seizure (1.1%; 5.2%). In adults, the most frequent in-hospital neurological complications were stroke (1.5%), seizure (1%) and CNS infection (0.2%). Each occurred more frequently in intensive care unit (ICU) than in non-ICU patients. In children, seizure was the only neurological complication to occur more frequently in ICU versus non-ICU (7.1% versus 2.3%, $P < 0.001$).

Stroke prevalence increased with increasing age, while CNS infection and seizure steadily decreased with age. There was a dramatic decrease in stroke over time during the pandemic. Hypertension, chronic neurological disease and the use of extracorporeal membrane oxygenation were associated with increased risk of stroke. Altered consciousness was associated with CNS infection, seizure and stroke. All in-hospital neurological complications were associated with increased odds of death. The likelihood of death rose with increasing age, especially after 25 years of age.

In conclusion, adults and children have different neurological manifestations and in-hospital complications associated with COVID-19. Stroke risk increased with increasing age, while CNS infection and seizure risk decreased with age.

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Introduction

Since the beginning of the coronavirus disease 2019 (COVID-19) pandemic in 2020, the medical community has had concerns about its neurological effects. COVID-19 is associated with a range of neurological manifestations such as altered consciousness, fatigue, seizures and altered sense of smell and taste. In addition, in-hospital neurological complications such as stroke, CNS infection and seizures have been reported in both adults and children with acute COVID-19.[1–3] Evidence regarding the neurological effects of COVID-19 has evolved over time but was initially based on the early report from Wuhan, China, that 36% of patients had neurological manifestations.[4] That report was followed by multicentre cohort studies,[5–8] comprehensive reviews and meta-analyses[2,3,9,10] and emerging evidence on CNS involvement of the virus.[11–13] Despite many reports during the pandemic, limited data exist on the prevalence of different neurological manifestations and complications in adults and children with COVID-19. Therefore, a robust, large-scale epidemiological study is needed on the prevalence, risk factors and outcomes in adults and children with COVID-19. We sought to characterize neurological manifestations of COVID-19 among hospitalized adults and children in a large, international registry, with the aim of (i) determining the prevalence of neurological diagnoses, risk factors and associations with outcomes; (ii) differences between adults and children; and (iii) trends over time.

Here, we present data on the prevalence of neurological manifestations and complications from an international cohort of hospitalized COVID-19 patients registered in the International Severe Acute Respiratory and emerging Infection Consortium (ISARIC) COVID-19 database. This repository collects data from 1507 sites across 61 countries. The primary aim was to describe different neurological manifestations present on admission and in-hospital neurological complications in children and adults. The secondary aims included risk factors, outcomes and trends over time for in-hospital neurological complications.

Materials and methods

Study design

We conducted a retrospective analysis of a multicentre, international observational dataset to ascertain the prevalence and characteristics of neurological manifestations at hospital admission and the occurrence of neurological complications during hospitalization. Data were collected according to the ISARIC-WHO Clinical Characterization Protocol (CCP), a prospective study of hospitalized patients that aims to characterize emerging infections.[14] Study sites aimed to enroll as many hospitalized individuals with COVID-19 as possible, according to locally available resources. Individuals with laboratory-confirmed severe acute respiratory distress syndrome coronavirus-2 (SARS-CoV-2) infection and hospitalized [or admitted to the intensive care unit (ICU) according to site implementation] were enrolled. A small number of sites recruited only patients admitted to ICU (Supplementary Table 1). Where resource constraints limited recruitment, sites were advised to utilize recruitment strategies to minimize bias.

Of these individuals, 261 161 were evaluated, as of 25 May 2021, for neurological manifestations and in-hospital neurological complications by clinical teams at study sites. The study was approved by the World Health Organization Ethics Review Committee

(RPC571 and RPC572). Local ethics approval was obtained for each participating country and site according to local requirements. Informed consent was taken in most settings, according to locally approved procedures, or waivers were granted. De-identified data were submitted to the ISARIC database by direct entry to Research Electronic Data Capture (REDCap, version 8.11.11, Vanderbilt University, Nashville, TN) hosted by the University of Oxford or by secure file transfer when locally managed data collection systems were used. All data submitted to the ISARIC data platform were harmonized to the CDISC SDTM standard (Study Data Tabulation Model; version 1.7, Clinical Data Interchange Standards Consortium, Austin, TX). Available data included demographics, comorbidities, signs and symptoms, clinical assessments, laboratory data, medications, procedures and outcomes. Glasgow Coma Score (GCS) was collected as part of the neurological baseline variable at admission. The study protocol and case report forms (CRFs) are available online http://isaric.org/research/covid-19-clinical-research-resources/ (ISARIC CCP and ISARIC CRF, respectively).

Cohorts

The study cohort for analysis included all patients of any age enrolled in the ISARIC/WHO global database with laboratory-confirmed COVID-19 infection who were hospitalized between 30 January 2020 and 25 May 2021. Children were defined as those less than 18 years of age. Completed analyses reported outcomes for all patients, in addition to stratification by critical care, defined as admission to ICU at any time during hospitalization. We excluded patients who were missing information on hospital admission and discharge dates, ICU admission or neurological manifestations/complications (Fig. 1). Availability of data on neurological variables is summarized in Supplementary Table 1. Cohort characteristics by geographic region and income classification are summarized in Supplementary Table 2. A detailed description of characteristics for all patients included in this dataset is available online (https://doi.org/10.1101/2020.07.17.20155218).

Selected characteristics documented at hospital admission and during hospitalization were summarized for all patients and grouped by whether patients were admitted to the ICU. In addition to ICU admission, we assessed the severity of critical illness and outcomes when invasive mechanical ventilation or extracorporeal membrane oxygenation (ECMO) was needed for support.

Definitions

Neurological manifestations of COVID-19 at admission that were reported in CRFs included altered consciousness, fatigue, anosmia, dysgeusia, myalgia and seizure at admission. CRF-reported in-hospital neurological complications were CNS infection (meningitis/encephalitis), new seizures during hospitalization and stroke.

Outcomes

The primary outcome was the description of neurological manifestations present on admission and in-hospital neurological complications in children and adults. The secondary outcome was in-hospital mortality, accounting for associations with known risk factors, trends over time and in-hospital neurological complications.

Statistical analysis

All continuous variables are summarized as medians with interquartile ranges (IQRs). Categorical variables are reported as frequencies with percentages. Summaries of data completeness per variable are given in Supplementary Table 3.

We analysed neurological manifestations reported at hospital admission and neurological complications during hospitalization using all available data collected as prespecified fields in study CRFs (Table 1). For analyses of neurological manifestations and neurological complications, we considered unadjusted prevalence estimates for predefined patient subgroups and adjusted estimates as a function of patient age and time of hospitalization (month/year) using generalized linear models (GLMs). All GLMs assumed a binary response (yes/no) and fixed effects for age, sex, month/year of hospitalization and contributing study site as a potential confounder (Fig. 1). Age and month/year of hospitalization were treated as continuous variables and modelled via polynomial terms

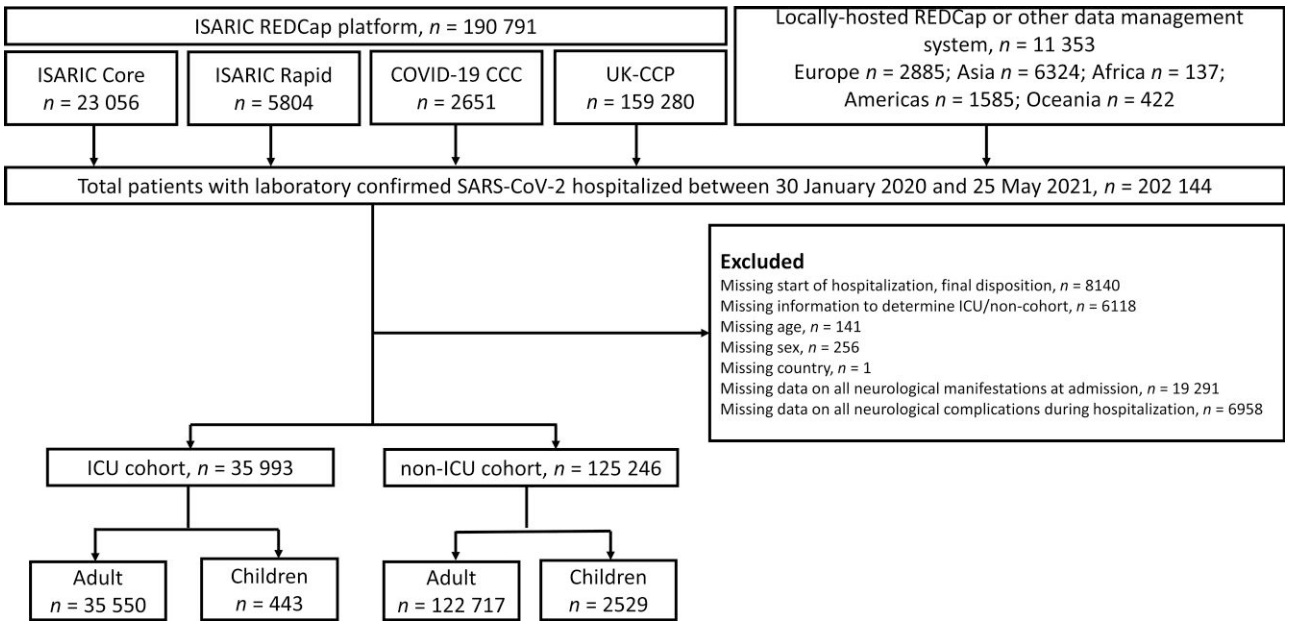

Figure 1 Origin of study cohorts and breakdown of subgroups (ICU, non-ICU, adult and children).

Table 1 Characteristics reported at hospital admission and clinical outcomes of all, ICU and non-ICU admitted COVID-19 patients

	All patients (*n* = 161 239)	ICU cohort (*n* = 35 993)		Non-ICU cohort (*n* = 125 246)	
		Adult (*n* = 35 550)	Children (*n* = 443)	Adult (*n* = 122 717)	Children (*n* = 2529)
Demographics					
Age, median (IQR), years	69 (54–81)	61 (51–71)	6 (1–14)	73 (56–83)	7 (1–14)
Sex, male, *n* (%)	91 380 (56.7)	23 270 (65.5)	249 (56.2)	66 463 (54.2)	1398 (55.3)
Time from first symptom of COVID-19 to hospitalization, median (IQR), days	5 (1–8)	6 (2–9)	2 (1–6)	4 (1–8)	2 (1–5)
Ethnicity, *n* (%)					
Black	4937 (3.1)	1789 (5.0)	45 (10.2)	2992 (2.4)	111 (4.4)
Caucasian	101 887 (63.2)	14 681 (41.3)	132 (29.8)	85 959 (70.0)	1115 (44.1)
Southeast Asian	19 724 (12.2)	8684 (24.4)	100 (22.6)	10 219 (8.3)	721 (28.5)
Mixed ethnicity	874 (0.5)	167 (0.5)	11 (2.5)	648 (0.5)	48 (1.9)
Other	5923 (3.7)	1 829 (5.1)	32 (7.2)	3926 (3.2)	136 (5.4)
Comorbidities reported at hospital admission					
Asthma, *n* (%)	19 386 (12.2)	4134 (11.8)	25 (5.7)	15 082 (12.5)	146 (5.8)
Chronic cardiac disease, *n* (%)[a]	43 821 (27.7)	6451 (18.4)	47 (10.7)	37 242 (31.0)	81 (3.2)
Chronic kidney disease, *n* (%)[b]	23 255 (14.7)	2995 (8.5)	11 (2.5)	20 198 (16.8)	52 (2.1)
Chronic neurological disorder, *n* (%)[c]	17 199 (10.9)	2372 (6.8)	53 (12.0)	4646 (12.2)	128 (5.1)
Chronic pulmonary disease, *n* (%)[d]	22 624 (14.3)	2 935 (8.4)	14 (3.2)	19 631 (16.3)	44 (1.8)
Dementia,[e] *n* (%)	17 543 (11.6)	596 (1.8)	0 (0)	16 942 (14.6)	5 (0.2)
Diabetes mellitus, *n* (%)	47 406 (29.8)	11 839 (33.7)	53 (12.1)	35 362 (29.2)	153 (6.1)
GCS at admission, median (IQR)	15 (15–15)	15 (15–15)	15 (15–15)	15 (15–15)	15 (15–15)
Hypertension, *n* (%)	61 601 (45.2)	14 456 (46.3)	26 (6.4)	47 058 (45.9)	61 (2.7)
Liver disease, *n* (%)	5044 (3.1)	1122 (3.2)	7 (1.6)	3901 (3.2)	14 (0.6)
Obesity, *n* (%)	19 117 (13.7)	6833 (21.6)	18 (4.5)	12 217 (11.7)	49 (2.1)
Smoking, *n* (%)[f]	38 071 (39.8)	6514 (36.0)	10 (3.6)	31 477 (41.9)	70 (3.2)
Mechanically ventilated, *n* (%)	19 130 (12.1)	18 614 (53.2)	153 (34.9)	18 767 (52.9)	363 (0.3)
Outcome, *n* (%)					
Continued hospitalization	5216 (3.2)	3030 (8.5)	28 (6.3)	2138 (1.7)	20 (0.8)
Died	38 847 (24.1)	11 568 (32.5)	33 (7.4)	27 213 (22.2)	33 (1.3)
Discharged	105 770 (65.6)	18 225 (51.3)	337 (76.1)	84 859 (69.2)	2349 (92.9)
Transferred to other facility	11 406 (7.1)	2727 (7.7)	45 (10.2)	8507 (6.9)	127 (5.0)
Time from hospitalization to outcome, median (IQR), days					
Continued hospitalization	28 (6–37)	7 (4–28)	9 (3–28)	37 (29–61)	34 (31–64)
Death	11 (6–20)	12 (7–20)	7 (5–16)	11 (6–20)	9 (4–15)
Discharged	9 (5–17)	13 (8–24)	9 (4–14)	9 (5–16)	4 (2–11)
Transfer to other facility	15 (8–28)	16 (7–34)	5 (3–13)	15 (9–27)	9 (4–12)

See Supplementary Table 2 for a summary of data completeness on baseline characteristics.
[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 m^2 or history of kidney transplantation.
[c]Chronic neurological disorder: any of cerebral palsy, multiple sclerosis, motor neuron disease, muscular dystrophy, myasthaenia gravis, Parkinson's disease, stroke, severe learning difficulty.
[d]Chronic pulmonary disease: chronic bronchitis, chronic obstructive pulmonary disease, emphysema, cystic fibrosis, bronchiectasis, interstitial lung disease, pre-existing requirement for long-term oxygen therapy; not asthma.
[e]Clinical diagnosis of dementia.
[f]Smokers included current and former smokers.

up to an order of 3 with model selection performed using Akaike's Information Criterion. Model estimates were summarized as marginal effects and uncertainty was reported by 95% CIs.

Unadjusted odds ratios (ORs) with 95% CIs were calculated for neurological complications when we compared ICU to non-ICU cohorts in Table 2. Adjusted ORs (aORs) from multivariable analyses accounted for prespecified variables and determined the association between covariates and neurological complications.

Secondary analysis and missing data

We examined associations between neurological complications and in-hospital mortality and used unadjusted analyses to investigate the cumulative incidence of death and discharge up to 100 days from hospitalization. In multivariable analysis, we used logistic regression models to examine associations with the odds of in-hospital mortality based on recorded final disposition. For multivariable analyses, missing data on independent variables were assumed missing at random and values were imputed by Multiple Imputing using Chained Equations (MICE). To account for differences in data collection across CRFs, MICE was applied independently to each study cohort. Completeness of data included in multivariable analyses of variables is reported in Supplementary Table 3. Unadjusted cumulative incidence functions were computed for patients with reported stroke, in-hospital seizures and CNS infection. Functions were further computed for a matched subset of controls, defined as patients who did not experience any neurological complications during hospitalization. Controls were matched based on study cohort, month/year of hospitalization, geographical subregion, sex and age (5-year

Table 2 Neurological manifestations reported at hospital admission and neurological complications reported during hospitalization of all, ICU and non-ICU admitted COVID-19 patients

	All patients[a] (*n* = 161 239)	ICU cohort[a] (*n* = 35 993)	Non-ICU cohort[a] (*n* = 125 246)	Unadjusted OR[b] (95% CI)	*P*-value
Neurological manifestations reported at hospital admission					
Altered consciousness					
Children	161/2365 (6.80)	50/418 (12)	111/1947 (5.70)	2.25 (1.55–3.18)	<0.001
Adults	30 569/146 269 (20.90)	3687/34 052 (10.80)	26 882/112 217 (24.00)	0.39 (0.37–0.40)	<0.001
Anosmia					
Children	48/2135 (2.20)	3/312 (0.96)	45/1823 (2.50)	0.38 (0.09–1.06)	0.110
Adults	6589/110 315 (6.00)	1637/26 022 (6.30)	4952/84 293 (5.90)	1.08 (1.01–1.14)	0.013
Dysgeusia					
Children	39/2068 (1.90)	4/299 (1.30)	35/1769 (2.00)	0.67 (0.20–1.70)	0.445
Adults	8028/108 491 (7.40)	1814/25 387 (7.10)	6214/83 104 (7.50)	0.95 (0.90–1.01)	0.077
Fatigue					
Children	548/2680 (20.40)	122/401 (30.40)	426/2279 (18.70)	1.90 (1.50–2.41)	<0.001
Adults	54 205/145 029 (37.40)	12 380/33 395 (37.10)	41 825/111 634 (37.50)	0.98 (0.96–1.01)	0.191
Myalgia					
Children	191/2526 (7.60)	48/376 (12.80)	143/2150 (6.70)	2.05 (1.44–2.89)	<0.001
Adults	23 638/139 538 (16.90)	6428/32 379 (19.90)	17 210/107 159 (16.10)	1.29 (1.25–1.34)	<0.001
Seizure					
Children	124/2403 (5.20)	28/429 (6.50)	96/1974 (4.90)	1.37 (0.87–2.80)	0.160
Adults	1558/142 554 (1.10)	267/33 685 (0.79)	1291/108 869 (1.20)	0.67 (0.58–0.76)	<0.001
Neurological complications reported during hospitalization					
CNS infection[c]					
Children	10/2962 (0.34)	3/438 (0.68)	7/2524 (0.28)	2.49 (0.65–8.62)	0.147
Adults	342/157 456 (0.22)	162/35 047 (0.46)	180/122 409 (0.15)	3.66 (3.04–4.42)	<0.001
Seizure[d]					
Children	88/2965 (3.0)	31/439 (7.10)	57/2526 (2.30)	4.42 (3.02–6.47)	<0.001
Adults	1558/157 524 (0.99)	468/35 073 (1.30)	1090/122 451 (0.89)	1.68 (1.52–1.84)	<0.001
Stroke[e]					
Children	3/2864 (0.10)	2/405 (0.49)	1/2459 (0.04)	18.63 (2.75–364.82)	0.009
Adults	2273/152 325 (1.50)	591/33 266 (1.80)	1682/119 059 (1.40)	1.39 (1.29–1.51)	<0.001

Non-ICU = patients not admitted to the ICU at any point during hospitalization.
[a]Unadjusted OR compares the groups ICU and non-ICU.
[b]Data are presented as *n*/total *n* (%). Total *n* differs for each category because of missing data.
[c]CNS infection includes meningitis or encephalitis.
[d]Seizure regardless of cause (e.g. febrile or due to epilepsy).
[e]Stroke may be a clinical diagnosis, with or without supportive radiological findings.

age bands); up to 10 matched controls per patient with a reported neurological complication.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

The data that underpin this analysis are highly detailed clinical data on individuals hospitalised with COVID-19. Due to the sensitive nature of these data and the associated privacy concerns, they are available via a governed data access mechanism following review of a data access committee. Data can be requested via the IDDO COVID-19 Data Sharing Platform (http://www.iddo.org/covid-19). The Data Access Application, Terms of Access and details of the Data Access Committee are available on the website. Briefly, the requirements for access are a request from a qualified researcher working with a legal entity who have a health and/or research remit; a scientifically valid reason for data access which adheres to appropriate ethical principles. The full terms are at https://www.iddo.org/document/covid-19-data-access-guidelines. A small subset of sites who contributed data to this analysis have not agreed to pooled data sharing as above. In the case of requiring access to these data, please contact the corresponding author in the first instance who will look to facilitate access.

Results

Our primary study cohort included 161 239 patients (158 267 adults and 2972 children) with acute COVID-19 infection, of which 35 993 (22.3%) patients were admitted to an ICU and 125 246 (77.7%) were hospitalized in non-ICU beds (Fig. 1 and Supplementary Fig. 1). Among the ICU cohort, 15 961 (44.3%) were admitted to the ICU on the same day as initial COVID-19 hospitalization. Demographic characteristics and comorbidities of the COVID-19 cohort are summarized in Table 1. Overall, 56.7% were male and median age was 69 years (IQR = 54–81). The median time from symptom onset to hospitalization was 5 days (IQR = 1–8). After hospitalization, 65.6% of patients were discharged alive and 24.1% died; the remaining patients were transferred to other facilities for further treatment (7.1%) or had recovered from COVID-19 but remained hospitalized (3.2%). Among the ICU cohort (*n* = 35 993), more than half of all patients (52.3%) were admitted to the ICU on the first day of admission (Supplementary Table 4). ICU patients were younger than non-ICU patients (61 versus 73 years) and had a higher frequency of obesity (21.4% versus 11.4%; Table 1). Additional characteristics of the ICU cohort, including the use of invasive mechanical ventilation and ECMO, are presented in Supplementary Table 4.

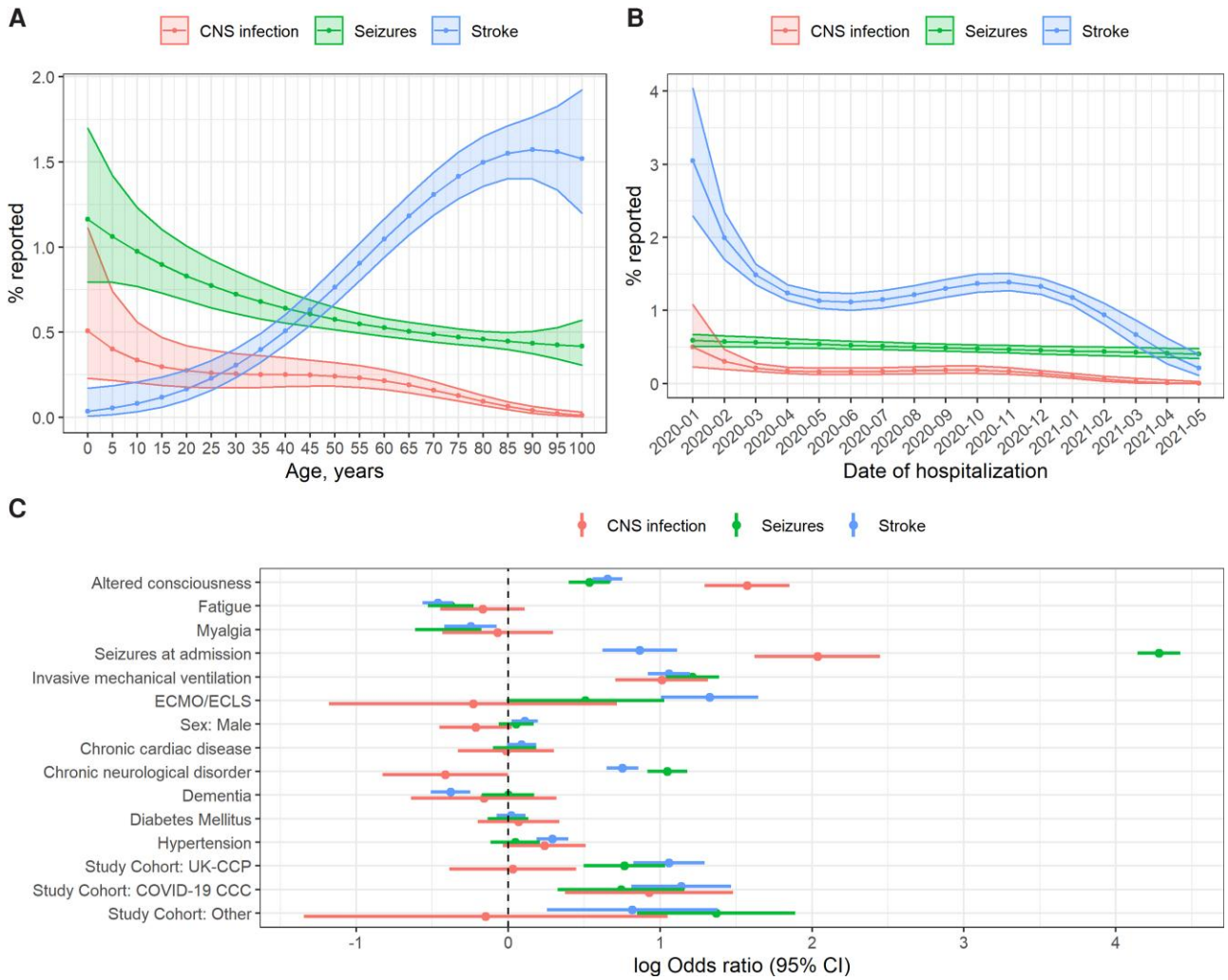

Figure 2 Results of multivariable analysis of neurological complications. (**A**) Age trends. (**B**) Trends over time. (**C**) Forest plot for remaining fixed effects, including confounders. Raw values (**C**) are presented in Supplementary Table 5. UK-CCP = United Kingdom Clinical Characterization Protocol; COVID-19 CCC = COVID-19 Critical Care Consortium.

Neurological manifestation at presentation

Adults versus children

Fatigue was the most commonly reported neurological manifestation of acute COVID-19 at admission (adults: 37.4%; children: 20.4%). All neurological manifestations were more frequent in adults than in children, except for seizures (adults: 1.1%; children: 5.2%). One in 20 children presented with a seizure, a frequency approximately 5 times greater than that in adults (Table 2). Notably, altered consciousness was substantially more common in adults (20.9%) than in children (6.8%), and prevalence increased with age (Table 2 and Supplementary Fig. 2).

ICU versus non-ICU

Altered consciousness, fatigue and myalgia were more prevalent in children admitted to the ICU than in children admitted to a non-ICU floor ($P < 0.001$), whereas anosmia, dysgeusia and seizure were similarly present in both cohorts. Surprisingly, adults with COVID-19 infection requiring ICU admission were less likely to present with altered consciousness than those on non-ICU floors (10.8 versus 24.0%; OR = 0.39; 95% CI = 0.37–0.40, $P < 0.001$) and less likely to have seizure (0.8 versus 1.2%; OR = 0.67; 95% CI = 0.58–0.76, $P < 0.001$) as their initial neurological presentation (Table 2).

In-hospital neurological complications

Adults versus children

In-hospital neurological complications (CNS infection, seizure and stroke) were rare in both adults and children. In the overall cohort, 0.22% (95% CI = 0.20–0.24%) had CNS infection, 1.0% (95% CI = 0.98–1.10%) experienced seizures and 1.5% (95% CI = 1.4–1.5%) suffered acute stroke during the index hospitalization with COVID-19. Again, seizure was more frequent in children (3.0%) than in adults (1.0%; Table 2); reported in-hospital seizures decreased with increasing age (Fig. 2). The frequency of stroke increased with increasing age. In contrast, CNS infection and seizure proportions steadily decreased with increasing age (Fig. 2).

ICU versus non-ICU

In children, ICU patients ($n = 443$) were more likely than non-ICU patients ($n = 2529$) to have in-hospital neurological complications, whereas the frequency of neurological complications was not as

distinct in ICU and non-ICU adult cohorts (Table 2). Notably, ICU patients who received ECMO had a higher prevalence of stroke (ECMO: 7.2%; non-ECMO: 1.6%; OR = 4.68; 95% CI = 3.48–6.28, $P < 0.001$) and seizure (ECMO: 2.8%; non-ECMO: 1.4%; OR = 2.02; 95% CI = 1.30–3.14, $P < 0.001$; Supplementary Table 5) than those who did not receive ECMO.

Risk factors for in-hospital neurological complications

Chronic neurological disorder was associated with all neurological complications (CNS infection, seizures and stroke; Fig. 2). Specifically, underlying hypertension (aOR = 1.38; 95% CI = 1.25–1.52) and chronic neurological disease (aOR = 1.34; 95% CI = 1.21–1.48) increased the odds of acute stroke (Supplementary Table 6). Among initial neurological manifestations, only altered consciousness and seizure at presentation were consistently associated with in-hospital neurological complications (Fig. 2). In other words, patients with acute COVID-19 infection who developed neurological complications more frequently presented with altered consciousness and seizure at admission. As expected, seizure at initial presentation had a strong effect on recurrent seizures (aOR = 69.42; 95% CI = 60.67–79.43; Supplementary Table 6). Altered consciousness at hospital admission was strongly associated with CNS infection (aOR = 5.31; 95% CI = 4.01–7.04) and moderately associated with seizures (aOR = 1.77; 95% CI = 1.55–2.03) and stroke (aOR = 1.95; 95% CI = 1.77–2.15; Supplementary Table 6).

Neurological complications were reported more often among patients who received invasive mechanical ventilation during hospitalization versus patients who did not. The adjusted odds of stroke (aOR = 3.77; 95% CI = 2.74–5.19) indicated higher incidence of stroke reported among ECMO patients, as reflected in unadjusted estimates (Supplementary Table 5). The reported incidence of all complications decreased over time, most notably for stroke, which decreased from 3.5% at the start of the initial COVID-19 outbreak (95% CI = 2.63–4.55) to 0.25% by the end of the study time frame (95% CI = 0.13–0.46; Fig. 2). Steady declines in seizure and CNS infection were also observed; however, absolute changes were small in line with low baseline incidence (seizure: 0.64 to 0.44%; CNS infection: 0.63 to 0.004%).

Mortality

Overall, mortality was significantly higher in adults than in children (24.5% versus 2.2%, OR = 14.3, 95% CI = 11.3–18.4, $P < 0.001$). This contrast held true in both ICU (adults versus children: 32.5% versus 7.4%, OR = 5.99, 95% CI = 4.27–8.71, $P < 0.001$) and non-ICU settings (adults versus children: 22.2% versus 1.3%, OR = 21.6, 95% CI = 15.6–31.0, $P < 0.001$). Death was more frequent for patients admitted to the ICU than for those not admitted to the ICU (32.2% versus 21.8%, OR = 1.71, 95% CI = 1.67–1.76, $P < 0.001$; Table 1). The likelihood of death rose steadily with increasing age, especially after 25 years of age, in both ICU and non-ICU patients, although mortality at any age was lower in non-ICU patients (Supplementary Fig. 3). As the COVID-19 pandemic progressed from 2020 to 2021, mortality in the non-ICU cohort decreased significantly but changed little for ICU patients (Supplementary Fig. 2).

Among ICU patients with neurological complications, the cumulative probability of death increased over the first 30 days of ICU admission (Fig. 3, Supplementary Table 7 and Supplementary Fig. 4). In non-ICU patients with stroke, the cumulative probabilities of death and discharge were similar regardless of admission duration (Fig. 3).

Discussion

In this study to characterize neurological manifestations of COVID-19 among hospitalized adults and children in the ISARIC registry, we found that non-specific symptoms of fatigue and altered consciousness were the most common at admission. Altered consciousness was 3.5 times less common in children than in adults, whereas seizure (as an initial manifestation) was 5 times more frequent in children. Altered consciousness and seizure at admission were strong risk factors for in-hospital neurological complications after adjusting for covariates (Fig. 2). Although there are limited data in CSF or imaging data to establish the causality or direction association, an important clinical implication of this analysis is that the possibility of CNS infection should be considered for patients presenting with seizures or altered consciousness at the time of hospital admission for COVID-19. Neurological manifestations on presentation, such as anosmia, ageusia, fatigue and myalgia, were more common in adults admitted to the ICU than in those admitted to a non-ICU floor. However, caution is needed when interpreting these results, as these non-specific neurological symptoms are reported in up to 80% of surveyed patients with COVID-19.[7,8]

In-hospital neurological complications were infrequent in our cohort, with 1.5% for strokes, 1.0% for seizures and 0.2% for CNS infections. These rates are in keeping with prior data on adults with COVID-19.[7,8] Authors of the Global Consortium Study of Neurologic Dysfunction in COVID-19, which used detailed definitions of neurological complications for hospitalized patients, reported a 3% incidence of strokes, 1% incidence of seizures and <1% incidence of CNS infection.[7,8] In the International Multicentre Coronavirus Disease 2019 Critical Care Consortium Study, acute stroke was reported in 2.2% of patients, with haemorrhagic stroke being the dominant type in ICU patients. That study also noted that this risk was 10 times higher in the subset of patients receiving ECMO.[7,8]

Overall mortality was lower in our study cohort at 24.1%, likely because the proportion of patients who required ICU care was relatively lower (22.3%) compared to a systematic review and meta-analysis of 24 983 patients demonstrating 32% ICU admission and 39% in-hospital mortality.[15] Although neurological complications were not common in our study, they have been noted to be the most strongly associated with reduced ability for self-care and worse functional outcome on hospital discharge.[16] In our study, such complications were also associated with in-hospital mortality in our multivariable model estimates (Supplementary Table 7). Therefore, given the high prevalence of COVID-19, neurological complications will be a substantial global public health and social care burden in the near future.

Our study showed that the cumulative probability of in-hospital mortality increased most acutely in the first 30 days for ICU patients who had in-hospital neurological complications and was most pronounced for those with stroke. However, it continued increasing up to 100 days after hospital admission, emphasizing the importance of vigilant neurological evaluation for patients with long hospitalizations (Fig. 3) as large vessel occlusion in acute ischaemic stroke is common (>20%)[17] and early detection with standardized neuromonitoring may improve the neurological outcome in ICU patients.[18] Also, it is important to note that the rate of change in the cumulative probability curves decreased over time, indicating the risk and hazard of neurological complications are high early in the disease course. In a previous study that used a 31-day follow-up, the increased frequency of

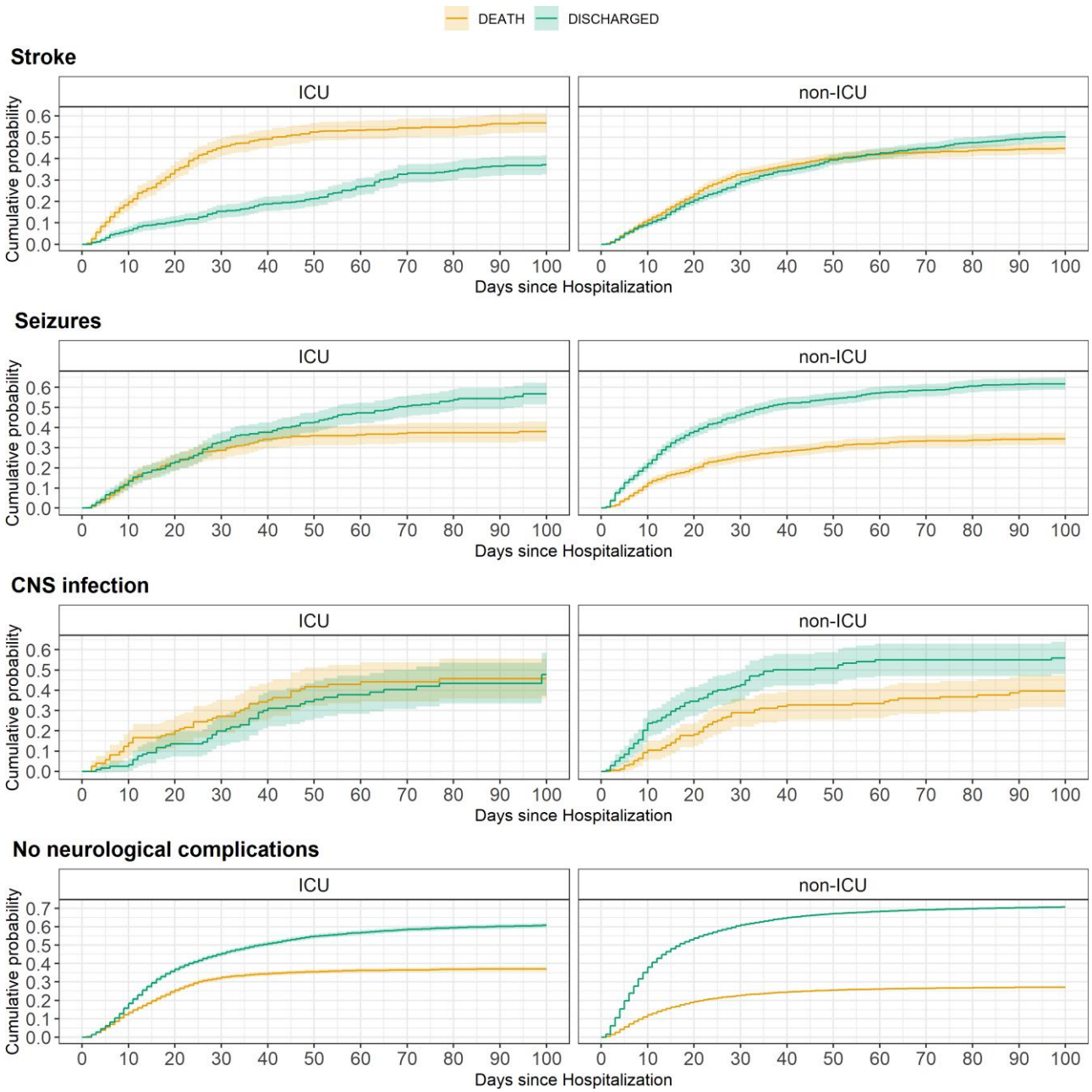

Figure 3 Cumulative probability (unadjusted, days) for in-hospital mortality (death) and discharge alive from hospital (discharge) for patients who developed neurological complications. Results are stratified by ICU and non-ICU cohorts.

ischaemic stroke was 10 times higher than normal in the 14 days after a COVID-19 diagnosis, and the risk remained up to 6 times higher than normal at 31 days.[14,19] The risk of acute myocardial infarction was also assessed to be 5 times higher in the 14 days after a COVID-19 diagnosis. The authors postulated that the underlying mechanisms may include cytokine-mediated plaque destabilization and hypercoagulability.[14,19] This is likely in line with the fact that early variants were associated with more severe illness requiring hospitalization and ICU admission.[20]

Notably, our study showed a dramatic decline in stroke frequency whereas seizure frequency remained steady over time (Fig. 2). Several possible explanations might account for the decrease in stroke frequency during the pandemic. Treatment of COVID-19 changed rapidly after the initial clinical experience, such as with widespread use of high-intensity thromboprophylaxis and avoidance of mechanical ventilation (with the concomitant need for more sedation), for example. Global trends in these management approaches may have reduced the impact of COVID-19-related coagulopathy or reduced hypotension and shock associated with aggressive use of mechanical ventilation. Another possibility is that early variants of SARS-CoV-2 had greater inflammatory and coagulopathy effects. Other explanations are that resources for neuroimaging became reduced as the pandemic progressed, with parallel reductions in surveillance for stroke, or that the initial population of patients enrolled in the registry had a greater baseline risk of stroke, before public health messages about high-risk,

vulnerable groups taking extra precautions against contracting COVID-19 became widespread. More research is needed to better understand the factors related to this strong trend.

Evidence regarding the neurological effects of COVID-19 in children is more limited than that for adults. Our study included 2365 patients younger than 18 years and noted a different profile and frequency of neurological manifestations in this cohort. Except for seizures, all neurological manifestations and complications were less frequent in children than in adults. Interestingly, we showed a linear decrease in the prevalence of seizures as age increased. This finding is likely consistent with paediatric seizures where febrile seizure or CNS infection related seizures are more common in younger age.[21] A similar pattern was observed for CNS infection, which decreased with age, whereas the prevalence of stroke increased sharply with increasing age (Fig. 2). A prevalence study in the UK paediatric and adolescent population (<18 years) identified neurological and psychological complications in 52 cases of 1334 children linked to COVID-19.[6] The authors reported a 0.4% incidence of CNS infection and 0.07% incidence of transient ischaemic attack.

Severe illness requiring ICU admission was closely associated with in-hospital neurological complications. Invasive mechanical ventilation and especially extracorporeal support were associated with elevated risks of neurological complications (Supplementary Table 5). The risk of stroke was 8.3% among those receiving extracorporeal support, substantially higher than the 4.5% frequency reported in the Extracorporeal Life Support Registry among patients receiving veno-venous ECMO for non-COVID-19 acute respiratory distress syndrome (ARDS).[22]

Limitations

The spectrum of neurological manifestations and complications of COVID-19 is broader than the CRF terms included in the patient registry. Patient recruitment strategies varied between sites and were subject to staff and resource limitations, introducing the possibility of recruitment bias in some sites. Challenges exist in defining and capturing neurological manifestations[1] and in establishing causation,[23] especially in complex ICU patients with ARDS and when COVID-19 therapies can have iatrogenic neurological side effects. For analysis of neurological manifestations, we used data available at the time of hospital admission; however, data availability on neurological complications was limited to reports at any time during hospitalization. Having neurological manifestations at admission such as seizure or altered consciousness may have biased clinicians to investigate and find more in-hospital neurological complications. The use of sedative and analgesic drugs within the ICU setting may have influenced the reporting of these variables. Additional information on the timing of neurological complications would have allowed for more detailed analysis on the risk of complications over the course of hospitalization and time-dependent associations with mortality, as well as the timing of invasive ventilation and ECMO relative to the development of complications.[8] Certain variables such as GCS and smoking status where there is a large missingness in data should be interpreted carefully. Also, the absence of control patients without COVID-19 in the ISARIC dataset prevented estimation of specificity or positive and negative predictive values. Future studies need to more rigorously apply standardized definitions, report temporal relationships and exclude alternate aetiologies to better differentiate primary COVID-19 neurological sequelae from associated comorbidities and iatrogenic causes. Additionally, it is essential that ongoing research into neurological complications of COVID-19 record vaccination status, the temporal relationship between presentation and neurological complications and the specific COVID-19 variant affecting the patient. Finally, we did not investigate Guillain-Barré syndrome (GBS), as it was not part of the CRF. However, it is of particular relevance given the COVID-19 vaccine hesitancy worldwide. GBS is reported to occur at 145 excess cases per 10 million people after a positive SARS-CoV-2 test, which is greater than the 38 excess cases of GBS per 10 million people receiving ChAdOx1 nCoV-19 vaccinations.[24]

Conclusions

We report a low but not insignificant prevalence of neurological complications that can be anticipated in hospitalized patients with COVID-19. This study adds to the body of evidence that adults and children have different neurological manifestations and in-hospital complications after acute COVID-19 infection. Stroke risk increased with increasing age, while CNS infection and seizure risk decreased with age. The results of this study can assist in healthcare planning given the long-term impact of these complications.

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Competing interests

The authors report no competing interests.

Supplementary material

Supplementary material is available at *Brain* online.

Appendix 1

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Further information is provided in the Supplementary material.

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Laffey, Marie Lagrange, Fabrice Laine, Olivier Lairez, Antonio Lalueza, Marc Lambert, François Lamontagne, Marie Langelot-Richard, Vincent Langlois, Eka Yudha Lantang, Marina Lanza, Cédric Laouénan, Samira Laribi, Delphine Lariviere, Stéphane Lasry, Naveed Latif, Odile Launay, Didier Laureillard, Yoan Lavie-Badie, Andy Law, Teresa Lawrence, Cassie Lawrence, Minh Le, Clément Le Bihan, Cyril Le Bris, Georges Le Falher, Lucie Le Fevre, Quentin Le Hingrat, Marion Le Maréchal, Soizic Le Mestre, Gwenaël Le Moal, Vincent Le Moing, Hervé Le Nagard, Paul Le Turnier, Ema Leal, Marta Leal Santos, Todd C. Lee, Heng Gee Lee, Biing Horng Lee, Yi Lin Lee, Su Hwan Lee, James Lee, Gary Leeming, Laurent Lefebvre, Bénédicte Lefebvre, Benjamin Lefevre, Sylvie LeGac, Jean-Daniel Lelievre, François Lellouche, Adrien Lemaignen, Véronique Lemee, Anthony Lemeur, Gretchen Lemmink, Ha Sha Lene, Jenny Lennon, Rafael León, Marc Leone, Michela Leone, Quentin Lepiller, François-Xavier Lescure, Olivier Lesens, Mathieu Lesouhaitier, Amy Lester-Grant, Yves Levy, Bruno Levy, Claire Levy-Marchal, Erwan L'Her, Gianluigi Li Bassi, Ali Liaquat, Geoffrey Liegeon, Kah Chuan Lim, Wei Shen Lim, Chantre Lima, Lim Lina, Bruno Lina, Andreas Lind, Guillaume Lingas, Sylvie Lion-Daolio, Samantha Lissauer, Keibun Liu, Marine Livrozet, Patricia Lizotte, Antonio Loforte, Navy Lolong, Leong Chee Loon, Diogo Lopes, Anthony L. Loschner, Paul Loubet, Bouchra Loufti, Guillame Louis, Silvia Lourenco, Lee Lee Low, Marije Lowik, Jia Shyi Loy, Jean Christophe Lucet, Carlos Lumbreras Bermejo, Carlos M. Luna, Olguta Lungu, Liem Luong, Nestor Luque, Dominique Luton, Nilar Lwin, Ruth Lyons, Olavi Maasikas, Oryane Mabiala, Moïse Machado, Gabriel Macheda, Guillermo Maestro de la Calle, Rafael Mahieu, Sophie Mahy, Ana Raquel Maia, Lars S. Maier, Mylène Maillet, Thomas Maitre, Maximilian Malfertheiner, Nadia Malik, Paddy Mallon, Fernando Maltez, Denis Malvy, Victoria Manda, Laurent Mandelbrot, Julie Mankikian, Edmund Manning, Aldric Manuel, Ceila Maria Sant`Ana Malaque, Flávio Marino, Daniel Marino, Samuel Markowicz, Ana Marques, Catherine Marquis, Brian Marsh, Laura Marsh, Megan Marshal, John Marshall, Celina Turchi Martelli, Emily Martin, Guillaume Martin-Blondel, Ignacio Martin-Loeches, Martin Martinot, João Martins, Ana Martins, Nuno Martins, Caroline Martins Rego, Gennaro Martucci, Olga Martynenko, Eva Miranda Marwali, Marsilla Marzukie, David Maslove, Sabina Mason, Sobia Masood, Basri Mat Nor, Moshe Matan, Meghena Mathew, Daniel Mathieu, Mathieu Mattei, Romans Matulevics, Laurence Maulin, Michael Maxwell, Thierry Mazzoni, Natalie Mc Evoy, Lisa Mc Sweeney, Colin McArthur, Colin McArthur, Anne McCarthy, Aine McCarthy, Colin McCloskey, Rachael McConnochie, Sherry McDermott, Sarah E. McDonald, Aine McElroy, Samuel McElwee, Victoria McEneany, Allison McGeer, Chris McKay, Johnny McKeown, Kenneth A. McLean, Paul McNally, Bairbre McNicholas, Elaine McPartlan, Edel Meaney, Cécile Mear-Passard, Maggie Mechlin, Maqsood Meher, Ferruccio Mele, Luis Melo, Joao Joao Mendes, Ogechukwu Menkiti, Kusum Menon, France Mentré, Alexander J. Mentzer, Noémie Mercier, Emmanuelle Mercier, Antoine Merckx, Mayka Mergeay-Fabre, Blake Mergler, Laura Merson, António Mesquita, Osama Metwally, Agnès Meybeck, Dan Meyer, Alison M. Meynert, Vanina Meysonnier, Amina Meziane, Mehdi Mezidi, Céline Michelanglei, Isabelle Michelet, Vladislav Mihnovit, Hugo Miranda-Maldonado, Nor Arisah Misnan, Tahira Jamal Mohamed, Nik Nur Eliza Mohamed, Asma Moin, David Molina, Elena Molinos, Brenda Molloy, Mary Mone, Agostinho Monteiro, Claudia Montes, Giorgia Montrucchio, Shona C. Moore, Sarah Moore, Lina Morales Cely, Lucia Moro, Ben Morton, Catherine Motherway, Ana Motos, Hugo Mouquet, Clara Mouton Perrot, Julien Moyet, Aisha Kalsoom Mufti, Ng Yong Muh, Dzawani Muhamad, Jimmy Mullaert, Fredrik Müller, Karl Erik Müller, Syed Muneeb, Nadeem Munir, Aisling Murphy, Lorna Murphy, Aisling Murphy, Marlène Murris, Srinivas Murthy, Himed Musaab, Himasha Muvindi, Gugapriyaa Muyandy, Dimitra Melia Myrodia, Farah Nadia Mohd-Hanafiah, Dave Nagpal, Alex Nagrebetsky, Nageswaran Narayanan, Rashid Nasim Khan, Nadège Neant, Raul Neto, Emily Neumann, Pauline Yeung Ng, Wing Yiu Ng, Anthony Nghi, Duc Nguyen, Orna Ni Choileain, Niamh Ni Leathlobhair, Alistair Nichol, Prompak Nitayavardhana, Nurul Amani Mohd Noordin, Marion Noret, Nurul Faten Izzati Norharizam, Lisa Norman, Mahdad Noursadeghi, Karolina Nowicka, Saad Nseir, Jose I Nunez, Nurnaningsih Nurnaningsih, Elsa Nyamankolly, Fionnuala O Brien, Annmarie O Callaghan, Annmarie O'Callaghan, Giovanna Occhipinti, Derbrenn OConnor, Max O'Donnell, Tawnya Ogston, Takayuki Ogura, Sophie O'Halloran, Katie O'Hearn, Shinichiro Ohshimo, Agnieszka Oldakowska, João Oliveira, Larissa Oliveira, Piero L. Olliaro, David S.Y. Ong, Jee Yan Ong, Wilna Oosthuyzen, Anne Opavsky, Peter Openshaw, Saijad Orakzai, Claudia Milena Orozco-Chamorro, Jamel Ortoleva, Javier Osatnik, Linda O'Shea, Miriam O'Sullivan, Siti Zubaidah Othman, Nadia Ouamara, Rachida Ouissa, Eric Oziol, Maïder Pagadoy, Justine Pages, Mario Palacios, Amanda Palacios, Massimo Palmarini, Giovanna Panarello, Prasan Kumar Panda, Hem Paneru, Lai Hui Pang, Mauro Panigada, Nathalie Pansu, Aurélie Papadopoulos, Rachael Parke, Melissa Parker, Briseida Parra, Taha Pasha, Jérémie Pasquier, Bruno Pastene, Fabian Patauner, Mohan Dass Pathmanathan, Luís Patrão, Patricia Patricio, Juliette Patrier, Lisa Patterson, Rajyabardhan Pattnaik, Mical Paul, Christelle Paul, Jorge Paulos, William A. Paxton, Jean-François Payen, Kalaiarasu Peariasamy, Miguel Pedrera Jiménez, Florent Peelman, Nathan Peiffer-Smadja, Vincent Peigne, Mare Pejkovska, Paolo Pelosi, Ithan D. Peltan, Rui Pereira, Daniel Perez, Luis Periel, Thomas Perpoint, Antonio Pesenti, Vincent Pestre, Lenka Petrou, Michele Petrovic, Ventzislava Petrov-Sanchez, Frank Olav Pettersen, Gilles Peytavin, Scott Pharand, Walter Picard, Olivier Picone, Carola Pierobon, Djura Piersma, Carlos Pimentel, Raquel Pinto, Catarina Pires, Isabelle Pironneau, Lionel Piroth, Riinu Pius, Laurent Plantier, Hon Shen Png, Julien Poissy, Ryadh Pokeerbux, Maria Pokorska-Spiewak, Sergio Poli, Georgios Pollakis, Diane Ponscarme, Jolanta Popielska,

Andra-Maris Post, Douwe F. Postma, Pedro Povoa, Diana Póvoas, Jeff Powis, Sofia Prapa, Sébastien Preau, Christian Prebensen, Jean-Charles Preiser, Anton Prinssen, Mark G. Pritchard, Gamage Dona Dilanthi Priyadarshani, Lucia Proença, Sravya Pudota, Oriane Puéchal, Bambang Pujo Semedi, Mathew Pulicken, Gregory Purcell, Luisa Quesada, Vilmaris Quinones-Cardona, Víctor Quirós González, Else Quist-Paulsen, Mohammed Quraishi, Christian Rabaud, Ebenezer Rabindrarajan, Aldo Rafael, Marie Rafiq, Rozanah Abd Rahman, Ahmad Kashfi Haji Ab Rahman, Arsalan Rahutullah, Fernando Rainieri, Giri Shan Rajahram, Pratheema Ramachandran, Nagarajan Ramakrishnan, Ahmad Afiq Ramli, Blandine Rammaert, Grazielle Viana Ramos, Asim Rana, Ritika Ranjan, Christophe Rapp, Aasiyah Rashan, Thalha Rashan, Ghulam Rasheed, Menaldi Rasmin, Indrek Rätsep, Cornelius Rau, Tharmini Ravi, Ali Raza, Andre Real, Stanislas Rebaudet, Sarah Redl, Brenda Reeve, Attaur Rehman, Liadain Reid, Liadain Reid, Dag Henrik Reikvam, Renato Reis, Jonathan Remppis, Martine Remy, Hongru Ren, Hanna Renk, Anne-Sophie Resseguier, Matthieu Revest, Oleksa Rewa, Luis Felipe Reyes, Tiago Reyes, Maria Ines Ribeiro, David Richardson, Denise Richardson, Laurent Richier, Siti Nurul Atikah Ahmad Ridzuan, Jordi Riera, Ana L Rios, Asgar Rishu, Patrick Rispal, Karine Risso, Nicholas Rizer, Chiara Robba, André Roberto, Stephanie Roberts, David L. Robertson, Olivier Robineau, Ferran Roche-Campo, Paola Rodari, Simão Rodeia, Bernhard Roessler, Pierre-Marie Roger, Emmanuel Roilides, Amanda Rojek, Juliette Romaru, Roberto Roncon-Albuquerque Jr, Mélanie Roriz, Manuel Rosa-Calatrava, Michael Rose, Dorothea Rosenberger, Nurul Hidayah Mohammad Roslan, Andrea Rossanese, Matteo Rossetti, Bénédicte Rossignol, Patrick Rossignol, Stella Rousset, Carine Roy, Benoît Roze, Desy Rusmawatiningtyas, Clark D. Russell, Maria Ryan, Maeve Ryan, Steffi Ryckaert, Mazankowski Heart Institute Ryckaert, Aleksander Rygh Holten, Isabela Saba, Sairah Sadaf, Valla Sahraei, Maximilien Saint-Gilles, Pranya Sakiyalak, Nawal Salahuddin, Leonardo Salazar, Jodat Saleem, Gabriele Sales, Stéphane Sallaberry, Charlotte Salmon Gandonniere, Hélène Salvator, Olivier Sanchez, Angel Sanchez-Miralles, Vanessa Sancho-Shimizu, Gyan Sandhu, Zulfiqar Sandhu, Pierre-François Sandrine, Oana Sandulescu, Marlene Santos, Shirley Sarfo-Mensah, Bruno Sarmento Banheiro, Benjamine Sarton, Sree Satyapriya, Rumaisah Satyawati, Egle Saviciute, Parthena Savvidou, Yen Tsen Saw, Justin Schaffer, Tjard Schermer, Arnaud Scherpereel, Marion Schneider, Stephan Schroll, Michael Schwameis, Janet T. Scott, James Scott-Brown, Nicholas Sedillot, Tamara Seitz, Jaganathan Selvanayagam, Mageswari Selvarajoo, Caroline Semaille, Malcolm G. Semple, Rasidah Bt Senian, Eric Senneville, Claudia Sepulveda, Filipa Sequeira, Tânia Sequeira, Ary Serpa Neto, Pablo Serrano Balazote, Ellen Shadowitz, Syamin Asyraf Shahidan, Mohammad Shamsah, Shaikh Sharjeel, Pratima Sharma, Catherine A. Shaw, Victoria Shaw, Ashraf Sheharyar, Haixia Shi, Mohiuddin Shiekh, Nobuaki Shime, Keiki Shimizu, Sally Shrapnel, Hoi Ping Shum, Nassima Si Mohammed, Ng Yong Siang, Jeanne Sibiude, Atif Siddiqui, Louise Sigfrid, Piret Sillaots, Catarina Silva, Rogério Silva, Maria Joao Silva, Benedict Sim Lim Heng, Wai Ching Sin, Punam Singh, Budha Charan Singh, Pompini Agustina Sitompul, Karisha Sivam, Vegard Skogen, Sue Smith, Benjamin Smood, Coilin Smyth, Michelle Smyth, Michelle Smyth, Morgane Snacken, Dominic So, Tze Vee Soh, Joshua Solomon, Tom Solomon, Emily Somers, Agnès Sommet, Rima Song, Myung Jin Song, Tae Song, Jack Song Chia, Azlan Mat Soom, Alberto Sotto, Edouard Soum, Marta Sousa, Ana Chora Sousa, Maria Sousa Uva, Vicente Souza-Dantas, Alexandra Sperry, B. P. 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Tedder, Tze Yuan Tee, João Teixeira, Marie-Capucine Tellier, Sze Kye Teoh, Vanessa Teotonio, François Téoulé, Pleun Terpstra, Olivier Terrier, Nicolas Terzi, Hubert Tessier-Grenier, Adrian Tey, Alif Adlan Mohd Thabit, Zhang Duan Tham, Suvintheran Thangavelu, Vincent Thibault, Simon-Djamel Thiberville, Benoît Thill, Jananee Thirumanickam, Shaun Thompson, David Thomson, Emma C. Thomson, Surain Raaj Thanga Thurai, Ryan S. Thwaites, Paul Tierney, Vadim Tieroshyn, Jean-François Timsit, Bharath Kumar Tirupakuzhi Vijayaraghavan, Noémie Tissot, Jordan Zhien Yang Toh, Maria Toki, Kristian Tonby, Sia Loong Tonnii, Margarida Torres, Antoni Torres, Hernando Torres-Zevallos, Michael Towers, Tony Trapani, Théo Treoux, Cécile Tromeur, Ioannis Trontzas, Tiffany Trouillon, Jeanne Truong, Christelle Tual, Sarah Tubiana, Helen Tuite, Jean-Marie Turmel, Lance C.W. Turtle, Anders Tveita, Pawel Twardowski, Makoto Uchiyama, PG Ishara Udayanga, Andrew Udy, Roman Ullrich, Alberto Uribe, Asad Usman, Timothy M. Uyeki, Cristinava Vajdovics, Luís Val-Flores, Amélie Valran, Stijn Van de Velde, Marcel van den Berge, Machteld Van der Feltz, Job van der Palen, Paul van der Valk, Nicky Van Der Vekens, Peter Van der Voort, Sylvie Van Der Werf, Laura van Gulik, Jarne Van Hattem, Carolien van Netten, Ilonka van Veen, Noémie Vanel, Henk Vanoverschelde, Pooja Varghese, Shoban Raj Vasudayan, Charline Vauchy, Shaminee Veeran, Aurélie Veislinger, Sebastian Vencken, Sara Ventura, Annelies Verbon, James Vickers, José Ernesto Vidal, César Vieira, Deepak Vijayan, Joy Ann Villanueva, Judit Villar, Pierre-Marc Villeneuve, Andrea Villoldo, Benoit Visseaux, Hannah Visser, Chiara Vitiello, Harald Vonkeman, Fanny Vuotto, Suhaila Abdul Wahab, Nadirah Abdul Wahid, Wan Fadzlina Wan Muhd Shukeri, Chih-Hsien Wang, Steve Webb, Jia Wei, Katharina Weil, Tan Pei Wen, Sanne Wesselius, Murray Wham, Bryan Whelan, Nicole White, Paul Henri Wicky, Aurélie Wiedemann, Surya Otto Wijaya, Keith Wille, Suzette Willems, Virginie Williams, Evert-Jan Wils, Calvin Wong, Xin Ci Wong, Yew Sing Wong, Teck Fung Wong, Gan Ee Xian, Lim Saio Xian, Kuan Pei Xuan, Ioannis Xynogalas, Siti Rohani Binti Mohd Yakop, Masaki Yamazaki, Yazdan Yazdanpanah, Nicholas Yee Liang Hing, Cécile Yelnik, Chian Hui Yeoh, Stephanie Yerkovich, Toshiki Yokoyama, Hodane Yonis, Obada Yousif, Saptadi Yuliarto, Akram Zaaqoq, Marion Zabbe, Masliza Zahid, Maram Zahran, Nor Zaila Binti Zaidan, Maria Zambon, Miguel Zambrano, Alberto Zanella, Konrad Zawadka, Nurul Zaynah, Hiba Zayyad, Alexander Zoufaly, David Zucman.

References

1. Ellul MA, Benjamin L, Singh B, *et al*. Neurological associations of COVID-19. *Lancet Neurol*. 2020;19:767-783.
2. Hassett CE, Gedansky A, Migdady I, Bhimraj A, Uchino K, Cho SM. Neurologic complications of COVID-19. *Cleve Clin J Med*. 2020;87:729-734.
3. Panda PK, Sharawat IK, Panda P, Natarajan V, Bhakat R, Dawman L. Neurological complications of SARS-CoV-2 infection in children: A systematic review and meta-analysis. *J Trop Pediatr*. 2021;67:fmaa070.
4. Mao L, Jin H, Wang M, *et al*. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. *JAMA Neurol*. 2020;77:683-690.
5. Kremer S, Lersy F, Anheim M, *et al*. Neurologic and neuroimaging findings in patients with COVID-19: A retrospective multicenter study. *Neurology*. 2020;95:e1868-e1882.
6. Ray STJ, Abdel-Mannan O, Sa M, *et al*. Neurological manifestations of SARS-CoV-2 infection in hospitalised children and adolescents in the UK: a prospective national cohort study. *Lancet Child Adolesc Health*. 2021;5:631-641.
7. Chou SH, Beghi E, Helbok R, *et al*. Global incidence of neurological manifestations among patients hospitalized with COVID-19—A report for the GCS-NeuroCOVID Consortium and the ENERGY Consortium. *JAMA Netw Open*. 2021;4:e2112131.
8. Cho SM, Premraj L, Fanning J, *et al*. Ischemic and hemorrhagic stroke among critically ill patients with coronavirus disease 2019: An international Multicenter Coronavirus Disease 2019 Critical Care Consortium study. *Crit Care Med*. 2021;49:e1223-e1233.
9. Pezzini A, Padovani A. Lifting the mask on neurological manifestations of COVID-19. *Nat Rev Neurol*. 2020;16:636-644.
10. Huth SF, Cho SM, Robba C, *et al*. Neurological manifestations of coronavirus disease 2019: A comprehensive review and meta-analysis of the first 6 months of pandemic reporting. *Front Neurol*. 2021;12:664599.
11. Meinhardt J, Radke J, Dittmayer C, *et al*. Olfactory transmucosal SARS-CoV-2 invasion as a port of central nervous system entry in individuals with COVID-19. *Nat Neurosci*. 2021;24:168-175.
12. Thakur KT, Miller EH, Glendinning MD, *et al*. COVID-19 neuropathology at Columbia University Irving Medical Center/New York Presbyterian Hospital. *Brain*. 2021;144:2696-2708.
13. Lou JJ, Movassaghi M, Gordy D, *et al*. Neuropathology of COVID-19 (neuro-COVID): Clinicopathological update. *Free Neuropathol*. 2021;2:2.
14. Dunning JW, Merson L, Rohde GGU, *et al*. Open source clinical science for emerging infections. *Lancet Infect Dis*. 2014;14:8-9.
15. Abate SM, Ahmed Ali S, Mantfardo B, Basu B. Rate of intensive care unit admission and outcomes among patients with coronavirus: A systematic review and meta-analysis. *PLoS One*. 2020;15:e0235653.
16. Drake TM, Riad AM, Fairfield CJ, *et al*. Characterisation of in-hospital complications associated with COVID-19 using the ISARIC WHO clinical characterisation protocol UK: A prospective, multicentre cohort study. *Lancet*. 2021;398:223-237.
17. Kihira S, Schefflein J, Mahmoudi K, *et al*. Association of coronavirus disease (COVID-19) with large vessel occlusion strokes: A case-control study. *AJR Am J Roentgenol*. 2021;216:150-156.
18. Ong CS, Etchill E, Dong J, *et al*. Neuromonitoring detects brain injury in patients receiving extracorporeal membrane oxygenation support. *J Thorac Cardiovasc Surg*. Published online 30 October 2021.
19. Ermis U, Rust MI, Bungenberg J, *et al*. Neurological symptoms in COVID-19: A cross-sectional monocentric study of hospitalized patients. *Neurol Res Pract*. 2021;3:17.
20. Lin L, Liu Y, Tang X, He D. The disease severity and clinical outcomes of the SARS-CoV-2 variants of concern. *Front Public Health*. 2021;9:775224.
21. Mallick AA, Ganesan V, Kirkham FJ, *et al*. Childhood arterial ischaemic stroke incidence, presenting features, and risk factors: A prospective population-based study. *Lancet Neurol*. 2014;13:35-43.
22. Cho SM, Canner J, Caturegli G, *et al*. Risk factors of ischemic and hemorrhagic strokes during venovenous extracorporeal membrane oxygenation: Analysis of data from the Extracorporeal Life Support Organization registry. *Crit Care Med*. 2021;49:91-101.
23. Watson CJ, Thomas RH, Solomon T, Michael BD, Nicholson TR, Pollak TA. COVID-19 and psychosis risk: Real or delusional concern? *Neurosci Lett*. 2021;741:135491.
24. Patone M, Handunnetthi L, Saatci D, *et al*. Neurological complications after first dose of COVID-19 vaccines and SARS-CoV-2 infection. *Nat Med*. 2021;27:2144-2153.