

UK-wide surveillance of neurological and neuropsychiatric complications of COVID-19: The first 153 patients

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Summary

Background

Increasingly, concerns regarding potential neurological complications of COVID-19 are being reported, mostly in small series. Larger studies have been limited by both geography and specialty. Consequently, the breadth of complications is not represented. Comprehensive characterisation of clinical syndromes is critical to rationally select and evaluate potential therapies.

Methods

During the exponential pandemic phase, we developed coordinated online portals for rapid notification across the spectrum of major UK neuroscience bodies, representing neurology, stroke, psychiatry, and intensive care. Evidence of infection and clinical case definitions were applied prospectively. Cases were compared to overall Government Public Health COVID-19 reporting.

Findings

The notification portals were live from 2nd April for ABN, 3rd April for BASP and 21st April for RCPsych, and data lock for this report was the 26th April 2020.

During this period, 153 cases were notified, from across the UK and with an exponential growth in reported cases which correlated with the same period of exponential growth as overall COVID-19 Public Health report data. Median (range) age was 71 (23-94) years. Complete clinical data for Clinical Case Definitions were available for 125 patients. Of whom 77/125 (62%) had a cerebrovascular event, of whom 57/77 (74%) had ischemic strokes, nine (12%) intracerebral haemorrhages, and one clinical diagnosis of CNS vasculitis.

The second most common group were 39/125 (31%) who had altered mental status, including nine/39 (23%) with encephalopathy and seven (18%) with encephalitis. The remaining 23/39 (59%) had a psychiatric diagnosis of whom 21/23 (92%) were new diagnoses. Of these psychiatric diagnoses, ten/23 (43%) were psychosis, six (26%) neurocognitive (dementia-like) syndrome, and four (17%) an affective disorder. Of cases with altered mental status, 18 (49%) were under 60 and 19 (51%) were over 60; whereas 13 (18%) cases of cerebrovascular events were under 60 relative to 61 (82%) cases in those over 60 years old ($p=0.001$).

Interpretation

This is the first nationwide, cross-specialty surveillance study of acute complications of COVID-19 in the nervous system. Alteration in mental status was common, reflecting encephalopathy/encephalitis and primary psychiatric diagnoses, often in young patients.

These data provide valuable and timely information urgently needed by clinicians, researchers, and funders to inform immediate steps in COVID-19 neuroscience research and health policy throughout the areas of neurology and neuropsychiatry

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RESEARCH IN CONTEXT

Evidence before this study

A PubMed search between January 1st 2020 and May 11th 2020 for “COVID-19 or SARS-CoV2” with “neurological or psychiatric” identified 133 and 371 publications, without language restrictions, respectively. However, focusing on those reporting data for the onset of new neurological or psychiatric diagnoses in hospitalised patients with confirmed or probable COVID-19 identified a more limited sub-set of baseline data. From a neurological perspective these publications included case reports or series (<10 patients) of stroke (6), encephalitis (5), seizures (1), cranial neuropathies (2), and posterior reversible encephalopathy syndrome (1). A larger series of 214 patients from Wuhan reported neurological symptoms in 78 patients. However, many of these symptoms were vague, such as ‘dizziness’ or ‘headache’, although a sub-set of 13 patients had a cerebrovascular diagnosis. One study from France reported patients with COVID-19 related acute respiratory distress syndrome of whom 8 had neurological manifestations, including 2 with strokes.

Many publications addressing the mental health impacts of COVID-19 on the general population, health care workers, or those with pre-existing psychiatric diagnoses were identified. However, cases of new-onset psychiatric diagnoses in hospitalised patients with confirmed or probable COVID-19 were limited to a few case reports. In the large Wuhan study acute psychiatric diagnoses are not described. In the French study, although a dysexecutive syndrome is reported in 14 patients and 26 are described as confused, limited information is available with regards to what the psychiatric diagnoses were, and this cohort represents only the severe end of the respiratory spectrum.

Added value of this study

By working across the clinical neuroscience communities of neurology, neuropsychiatry, stroke, and neurointensive care we were able to identify acute presentations of new-onset complications of COVID-19 reflecting the spectrum of the burden of disease. Whilst, ischaemic stroke was common in our cohort of 153, mainly confirmed COVID-19 patients, we identified a large group of patients with altered mental status, reflecting both neurological and psychiatric diagnoses, such as encephalitis and psychosis respectively. Although altered mental status was identified across all age groups, interestingly there was a large number of younger patients with this presentation.

Implications of all the available evidence

Our work highlights the importance of interdisciplinary work in the clinical neurosciences field in the era of COVID-19. Clinicians should be alert to the possibility of patients with COVID-19 developing these complications and, conversely, of the possibility of COVID-19 in patients presenting with acute neurological and psychiatric syndromes. These findings should direct future research to establish the role of viral neurotropism, host immune responses, and genetic factors in the development of these complications so that clinical management strategies can be developed.

Introduction

At the turn of the year the World Health Organization was notified by clinicians in Wuhan, China, of a novel and severe respiratory virus, SARS-CoV-2. Cases of COVID-19 were quickly recognized as a significant global public health emergency and SARS-CoV-2 was declared a pandemic on March 11th, 2020. The neurological community were alerted to the high prevalence of anosmia and dysgeusia in early reports.^{1,2,3} Some of these early cohorts also featured non-specific neurological symptoms, such as dizziness and headache.⁴ However, it became increasingly apparent that severe neurological and neuropsychiatric presentations in association with COVID-19 were occurring; including a case of encephalitis in China in whom SARS-CoV-2 was identified in cerebrospinal fluid (CSF),⁵ a case of acute necrotizing encephalopathy in Japan⁶ and cerebrovascular disease.^{4,7}

During other pandemics of respiratory pathogens, including SARS, MERS, and H1N1 influenza, there were similar reports of patients with neurological complications.^{8,9} Either during the acute phase, thought to reflect direct viral cytopathy or a para-infectious cytokine storm, or occurring later as a post-infectious, likely cellular immune or antibody-mediated phenomena, classically manifest as Guillain-Barré syndrome.¹⁰ In addition, occasionally neuropsychiatric and psychiatric presentations have been reported in severe coronavirus infections.¹¹ Although acute neuropsychiatric presentations may reflect broader socioeconomic implications of the pandemic on mental health. Whilst the proportion who develop these complications may be relatively uncommon, these patients are often the most severely affected, necessitating protracted intensive care admission and often resulting in poor outcomes.⁸

Nevertheless, most published reports on neurological complications of COVID-19 are limited to individual cases or small case series.⁴⁻⁶ A few studies have demonstrated the benefits of identifying patients across centers,^{1,12} but have largely been limited to 2-3 hospitals and are therefore restricted by both geography and specialty, thereby not assessing the neurological and neuropsychiatric complications of COVID-19 presenting to clinicians across the clinical spectrum of neurology, stroke/acute medicine, psychiatry, and intensive care.

Consequently, many important questions remain for neurologists and psychiatrists. Including: How common are neurological and psychiatric complications in COVID-19 patients? What proportion affect the central versus peripheral nervous system, and are novel syndromes emerging? And who is at risk?

This breadth of early clinical presentations has not been represented, at least in part because patients may be primarily managed by a variety of clinical specialties, including neurologists, stroke or acute medical physicians, psychiatrists, or intensive care physicians. More comprehensive and integrated epidemiological characterisation is critical to understanding the mechanisms underlying these presentations, without which it would be impossible to rationally select, evaluate, and use appropriate therapies.

To answer these crucial questions, data need to be collated urgently through large-scale, national, dynamic, cross-specialty collaborative structures, to both inform best practice management guidelines and to direct research priorities.

Methods

Case notification

During the exponential phase of the pandemic we developed an online network of secure rapid-response case report portals comprising the Association of British Neurologists (ABN) Rare Diseases Ascertainment and Recruitment (ABN RaDAR),¹³ the British Association of Stroke Physicians (BASP)¹⁴ and the Royal College of Psychiatrists (RCPsych),¹⁵ in collaboration with the British Paediatric Neurology Association (BPNA),¹⁶ the NeuroAnaesthesia and Critical Care Society (NACCS),¹⁷ and key stakeholders. Reporting portals for fully anonymised details were hosted on the web platforms of these collaborating professional bodies and via a novel web portal. Members of these professional organisations were emailed on a weekly basis to remind them of the surveillance programmes and were invited to notify the central CoroNerve group of any cases of COVID-19 associated with any of the clinical case definitions (defined below) that they had seen through these portals.

Due to the clinical demands of the pandemic, we identified minimum clinical datasets that could be completed in under 5 minutes, to reflect the critical data required to determine the confidence in the diagnosis of COVID-19, demography, geography, and the nature of the clinical syndrome. Physicians were encouraged to report cases prospectively and we also allowed for recent cases to be notified retrospectively when assigned a confirmed date of admission or initial clinical assessment, to identify cases occurring prior to notification portals being available. Patients were not randomised. Awareness was increased through social platforms during the peak of the pandemic, including professional webinars, recorded online presentations, and social media. The ABN portal was launched on the 2nd April, the BASP on the 3rd April, and the RCPsych on the 21st April 2020. Data lock for this report was on the 26th April 2020. Given the propensity for hospitalisation with COVID-19 to older demographic groups, older cases were defined as those aged >60 years old and younger cases as those <60 years old.

Evidence of covid19

Evidence of SARS-CoV2 infection was defined as ‘Confirmed COVID-19’ if polymerase chain reaction (PCR) of respiratory samples (e.g. nasal/throat swab) or cerebrospinal fluid (CSF) was positive or if serology was positive for anti-SARS-CoV2 IgM/IgG. Cases were defined as ‘Probable’ if a chest radiograph or chest computed tomography (CT) were consistent with COVID-19 but PCR and serology were negative or not performed. Cases were defined as ‘Possible’ if COVID-19 was suspected on clinical grounds by the notifying clinician, but PCR, serology, and chest imaging were negative or not performed.

Clinical case definitions

Broad clinical syndromes associated with COVID-19 were classified as a ‘Cerebrovascular event’ (defined as an acute ischemic, haemorrhagic, or thrombotic vascular event involving the brain parenchyma or sub-arachnoid space), ‘Altered Mental Status’ (defined as an acute alteration in personality, behavior, cognition, or consciousness),¹⁸ ‘Peripheral Neurology’ (defined as involving nerve roots, peripheral nerves, neuromuscular junction, or muscle), or ‘Other’ (with free text boxes for those not meeting these syndromic presentations). Data were collected on the specific clinical case definitions within these broad presentations, reflecting: A cerebrovascular event: Ischaemic stroke, intracerebral or subarachnoid hemorrhage, cerebral venous sinus thrombosis, or cerebral vasculitis.

Altered Mental Status: Encephalopathy, encephalitis (defined as encephalopathy with evidence of inflammation in the CNS (CSF white cell count >5/μl, protein >0.45g/dL, or

MRI consistent with inflammation), seizures (clinical or electroencephalographic evidence), and neuropsychiatric syndromes notified through psychiatrists/neuropsychiatrists: psychosis, neurocognitive (dementia-like syndrome), personality change, catatonia, mania, anxiety/depression, chronic fatigue syndrome, and post-traumatic stress disorder. Peripheral Neurology: Guillain-Barré syndrome, Miller Fisher syndrome, brachial neuritis, myasthenia gravis, peripheral neuropathy, myopathy, myositis (defined as myopathy with evidence of inflammation e.g. by magnetic resonance imaging or biopsy of muscle with elevated creatine kinase), and critical illness neuromyopathy.

When patients met more than one specific clinical case definition (e.g. seizures and encephalitis) the underlying aetiological diagnosis was considered primary and complications of that diagnosis considered secondary features (e.g. encephalitis and seizures respectively). Where there was discrepancy in classification this was resolved through discussion with senior authors (BDM, IG, RHT,). Chi squared analysis was conducted for group-wise comparisons and R-square for linear correlation, using GraphPad Prism^(c) (v7). Full details are available on: www.coronerve.com.

Additional data collection

By asking the reporting physician to submit their contact details at the time of notification (including a National Health Service email address) we established both confirmation of the veracity of the data, and the creation of a log for subsequent sample collection and longitudinal follow-up studies, through linkage with existing platforms including co-recruitment into the International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC) Clinical Characterization Protocol which was also recorded.¹⁹ Data collected were compared relative to the geographic, demographic, and temporal presentation of overall cases of COVID-19 as reported by national Government Public Health bodies representing each of the regions of the UK (Public Health England, Health Protection Scotland, Public Health Wales, and the Public Health Agency- Northern Ireland).

The UK Health Research Authority formally confirmed this approach was compliant with regulations regarding anonymized surveillance of routine clinical practice in pandemic conditions, as initiated by the local attending clinician.

Role of the funding source

The funders of the CoroNerve Study Management Group had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

In the first three weeks of submission portals accepting notifications, the *CoroNerve* Studies platforms received notification of 153 unique cases meeting the clinical case definitions by clinicians in the UK. The physician contact details for future studies were provided by all who completed the notification. Cases were geographically dispersed across the UK as were overall laboratory-confirmed cases of patients with COVID-19 reported by Government Public Health bodies during the same time period (Appendix). The data of the admitting medical units were available for 152/153 cases. Of these 26/152 (17%) were tertiary care hospitals, 125 (82%) were secondary care hospitals, and one was primary care. Overall, 75/153 (49%) cases were notified through BASP, 53 (35%) through ABN/*CoroNerve.com*, and 25 (16%) through RCPsych portals. Overall, cases were reported retrospectively for 24/153 (16%) cases and the remaining were reported prospectively. The BPNA surveillance network was not available for notifications during the first three weeks the other notification portals were live. Data on the reporting physician's specialty were available for 150 cases and 61/150 (41%) were stroke physicians, 39 (26%) neurologists, 26 (17%) psychiatrists or neuropsychiatrists, 23 (15%) acute medicine and other physicians, and one General Practitioner.

Complete clinical datasets were available for 125/153 (82%) cases. The dates of admission or initial clinical assessment were available for 112/125 (90%) of reported cases and correlated with the national case identification data of all laboratory-confirmed patients with COVID-19 reported by Government Public Health bodies over this same time period reflecting the exponential phase of infection; R-square Goodness of Fit 0.819 and 0.744 respectively, $p < 0.0001$ (Figure 1).

Overall, the median (range) age was 71 (23-94) years, which broadly reflected the national data collected through Government Public Health bodies over the same timeframe, although for some centiles an older population may be over represented within this cohort (Figure 2). Data were available for sex for 117/153 (76%) of cases, as this question was not included in the original RaDAR web portal, reflecting 28 (19%) cases, and this question was not answered in the *CoroNerve* portal in eight (5%) cases. Therefore, data regarding sex were available for 117/125 (94%) of cases for whom these data were requested and 44 (38%) were female.

Of those with complete notification data, 114/125 (93%) met the criteria for 'Confirmed SARS-CoV2 infection', 5 (4%) for 'Probable SARS-CoV2 infection', and 4 (3%) for 'Possible SARS-CoV2 infection'. Of the whole cohort with complete data, 77/125 (62%) presented with the broad clinical syndrome of a cerebrovascular event, of whom 57/77 (74%) had suffered an ischemic stroke, nine (12%) an intracerebral hemorrhage, and a clinical diagnosis of CNS vasculitis was reported in one case with an unusual, and otherwise unexplained, infarct of the corpus callosum and imaging appearances suggestive of vasculitis; however, the full angiographic report and pathological confirmation were not provided (Figure 3). Beyond cerebrovascular events, 39/125 (31%) of patients presented with altered mental status, representing nine/39 (23%) patients with encephalopathy and a further seven (18%) with both clinical symptoms/signs of encephalopathy and with evidence of CNS inflammation meeting the clinical case definition for encephalitis; all of whom met the criteria for confirmed SARS-CoV2 infection.

Of these cases with altered mental status, the remaining 23/39 (59%) fulfilled the clinical case definitions for psychiatric diagnoses as classified by the notifying psychiatrist/neuropsychiatrist. Only two/23 (9%) were exacerbations of existing enduring mental illness, while 21 (92%) were not exacerbations of long-term psychopathology. Ten/23 (43%) of these cases had new-onset psychosis, six (26%) had a neurocognitive (dementia-like) syndrome, and four (17%) had an affective disorder, after exclusion of known dementia and/or delirium.

Age data were available for 74/77 (96%) of patients with cerebrovascular events and 37/39 (95%) patients with altered mental status. Of these cases with altered mental status, 18/37 (49%) were under 60 years old and 19/37 (51%) were over 60; whereas 13/74 (18%) cases of cerebrovascular events were under 60 years old relative to 61/74 (82%) cases in those over 60 ($p=0.001$) (Figure 4).

Discussion

To our knowledge, this is the first systematic, nationwide surveillance study of the breadth of acute complications of COVID-19 in the nervous system, undertaken through rapid mobilisation of UK professional bodies reflecting neurology, stroke/acute medicine, psychiatry, and intensive care. Cases notified by the professional membership of these bodies were obtained from across the UK, and the exponential rise in cases of neurological and psychiatric complications of COVID-19 occurred during the exponential rise in overall COVID-19 cases reported by Government Public Health bodies. Future studies, particularly those assessing genetic and associated risk factors, would benefit from attempting to obtain notification of all cases of infection admitted to every hospital as a denominator, or a cohort of COVID-19 patients without neurological or psychiatric complications as control groups. However, given the time pressure on busy clinical teams during the pandemic we decided to focus our notification structure on those patients with neurological or psychiatric complications of infection. Cases were reported from physicians spanning the specialties, and almost all met the case definition of confirmed SARS-CoV2 infection. Cerebrovascular events in COVID-19 patients, which are well described elsewhere, were also identified as a major group within our cohort. However, interestingly, a large proportion of cases of acute alteration in mental status were identified reflecting neurological syndromic diagnoses, such as encephalopathy and encephalitis and also primary psychiatric syndromic diagnoses, such as psychosis. Whilst cerebrovascular events and altered mental status were identified across all age groups, our cohort confirms that cerebrovascular events predominate in older patients, but these early data identify that acute alterations in mental status were disproportionately over represented in younger patients in our cohort. These rates of neurological and psychiatric complications of COVID-19 cannot be widely extrapolated to the mildly affected/asymptomatic infection cases, especially those in the community, but give a broad national perspective on complications severe enough to require hospitalisation.

This approach to case ascertainment has the potential for reporting bias and requires validation through detailed prospective clinic-epidemiologic data collection; and plans for these studies should be developed in advance of the next pandemic so that they can be mobilized early in the phase of disease spread. It is possible that a more ‘engaged’ professional membership or those more used to submitting data to surveillance studies through this approach could potentially be over-represented. However, this was the first major national study using this approach for clinicians reflecting our largest cohorts, i.e.

British Association of Stroke Physicians and Royal College of Psychiatrists. In addition, the present study included *a priori* considerations to determine the strength of the evidence for SARS-CoV2 infection, and data collection was informed by clear clinical case definitions. Moreover, in this cohort we conclude that this is unlikely to have resulted in systematic over-ascertainment bias for psychiatric/neuropsychiatric presentations. In particular 41% of cases were reported by Stroke Physicians, and the RCPsych web portal was launched 18 days later than the other neurological, stroke, ICU/general portals, yet we observed a large number of psychiatric/neuropsychiatric notifications. Indeed, as many patients are managed on ITU with sedative and paralytic medications, which can both mask and also contribute to iatrogenic complications it may be that our cohort under-represents the rate of neurological/psychiatric symptoms. As we specifically identified moderate-severe complications of COVID-19 as they were reported for in-patient cases by neurologists and psychiatrists, this cohort may well under-represent milder out-patients symptoms, such as reduced taste/smell. Furthermore, future hypothesis-testing studies building on our findings to infer causal relationships between infection and neurological/neuropsychiatric presentations should adhere to basic principles, such the criteria for causation outlined by Bradford-Hill as they pertain to pandemic respiratory infection and effects on the brain.²¹

Despite data notification across the specialties, many cerebrovascular events were identified as has been reported in other cohorts and case reports of acute COVID-19 complications.^{4,22,23} The pathophysiological mechanisms require further study, but there is a potential biological rationale for a vasculopathy, with a report of SARS-CoV2 endothelitis in organs outside of the cerebral vasculature²⁴ and cerebrovascular events,²⁵ in addition to coagulopathy; along with conventional stroke risk during sepsis.²⁶⁻²⁸ However, comprehensive studies with clear control groups including those hospitalised with COVID-19 but without cerebrovascular events and also those with cerebrovascular events but who are negative for COVID-19 are required to address this issue.

Confirmation of the link between COVID-19 and new acute psychiatric/neuropsychiatric complications in younger patients will require detailed prospective longitudinal studies. Understanding this relationship will require systematic participant evaluation, characterisation of immune host responses, exploration of genetic associations, and comparison with appropriate controls (including patients hospitalized with COVID-19 who do not experience acute neuropsychiatric features).

Alteration in mental status is common in patients admitted to hospital with severe infection, especially in those requiring intensive care management. However, this typically predominates in older groups which may reflect an unmasking of latent neurocognitive degenerative disease, and/or multiple medical co-morbidities, often in association with sepsis, hypoxia, and the requirement for polypharmacy and sedative medications. In this study we observed a disproportionate number of neuropsychiatric presentations in younger patients, and a predominance of cerebrovascular complications in the older patients, which may reflect the state of health of the cerebral vasculature and associated risk factors, exacerbated by critical illness, in the older cohort.²⁸ The larger number of cases of altered mental status may reflect increased access to neuropsychiatry/psychiatry review for younger patients, and increased attribution of altered mental status to delirium in the older groups. Nevertheless, that acute alterations in mental status are being increasingly recognised in patients hospitalised with COVID-19 certainly warrants study. Importantly, the exclusion of iatrogenic factors, such as sedatives and antipsychotics, need to be quantified in future modelling studies. In our study, whilst the majority of cases with psychiatric diagnoses were

determined as new by the notifying psychiatrist/neuropsychiatrist, we cannot exclude the possibility that these were undiagnosed prior to the patient developing COVID-19.

The population reported reflects a snap-shot of cases of acute neurological/psychiatric complications/associations with COVID-19 in hospitalised adults. Larger, ideally prospective, studies should identify the broader cohort of COVID-19 patients both in and outside of hospitals, with capture-recapture analysis and health record linkage to determine clearer estimates of the prevalence of these complications and also those at risk. In addition, community studies are required to identify those at risk of both COVID-19 and these complications, although this will require wide-spread serological testing.

The importance of data sharing is increasingly recognized as fundamental to facilitate rapidly responsive clinical research and is particularly critical during an international emergency such as that due to SARS-CoV2. The *CoroNerve* Studies Group has been made possible by open collaboration between several UK institutions. We anticipate there will be added value to sharing data more widely, across European and global partners, particularly those in low and middle-income countries; the Brain Infections Global COVID-Neuro network is supporting data collection in such countries through freely available case record forms.²⁹ Such wide collaboration is likely to be even more important for characterising rarer or novel COVID-19-associated neurological syndromes. It is critical that these ‘enriched’ populations reflecting less common, but nevertheless severe, disease are studied in close collaboration with larger surveillance efforts, such as the ISARIC-CCP, to identify at risk groups, determine the strength of relative risk factors, and have adequate controls for mechanistic studies.

This early nation-wide, dynamic, clinician-reported cohort approach provides valuable and timely information urgently needed by clinicians, researchers, and funders to inform the next immediate steps in neuroscience COVID-19-related research and health policy planning. In particular, these national data begin to better characterise the spectrum of neurological and neuropsychiatric complications which need to be addressed. This multi-disciplinary, coordinated approach should be emulated in the detailed national mechanistic studies of COVID-19 and the brain which are desperately needed, to distinguish the role of the virus and the host-inflammatory response versus the broader socioeconomic effects of the pandemic.³⁰

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Declaration of Interest

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Author Statement

BDM, RHT, IG, SP, RK, AV, MAE, and NT form the CoroNerve Study Management Team AV and BDM drafted the initial manuscript and the document was edited and approved by all co-authors.

The authors are committed to open science; for the wider advancement of scientific research, the broader data from these studies will be made available at the end of these studies wherever possible, within the terms of participant consent and when not otherwise limited by intellectual property rights or on-going collaborative research.

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Figure 1.

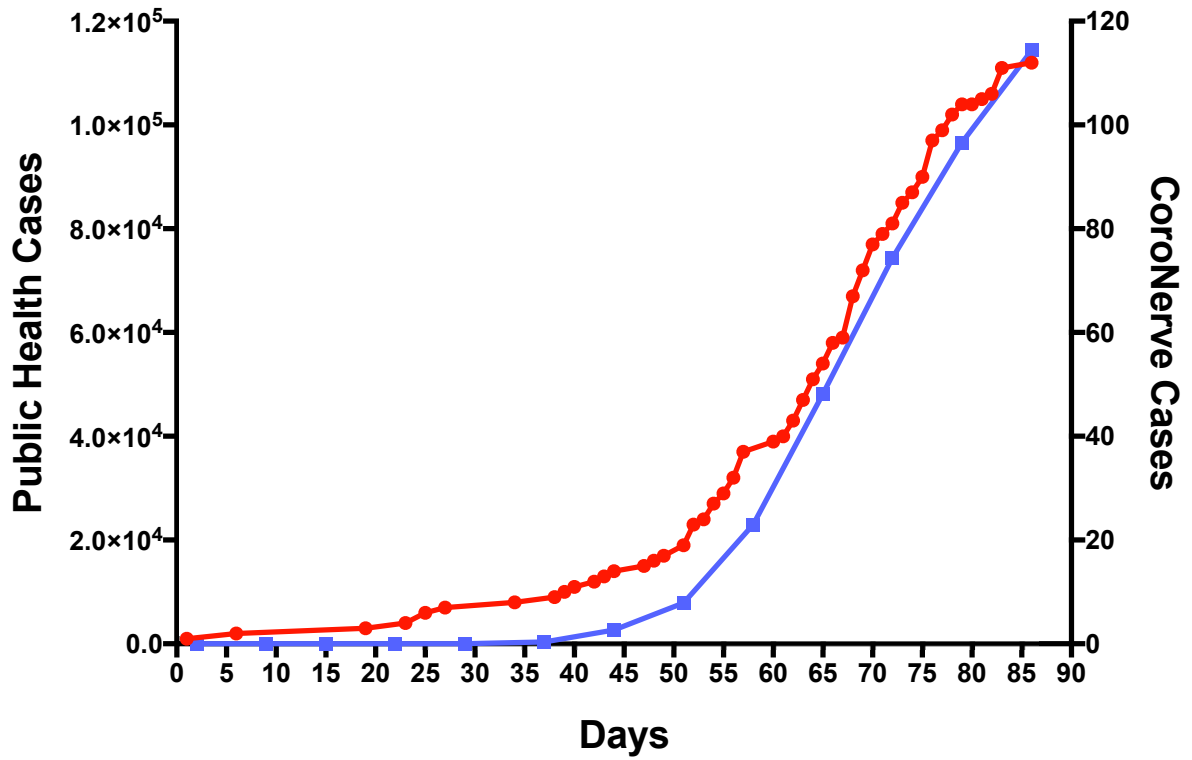


Figure 1. Temporal distribution of the date of admission/first assessment for cases notified to the *CoroNerve* Studies Group (red) relative to those identified by Government Public Health bodies of the UK administrations (blue).

Figure 2.

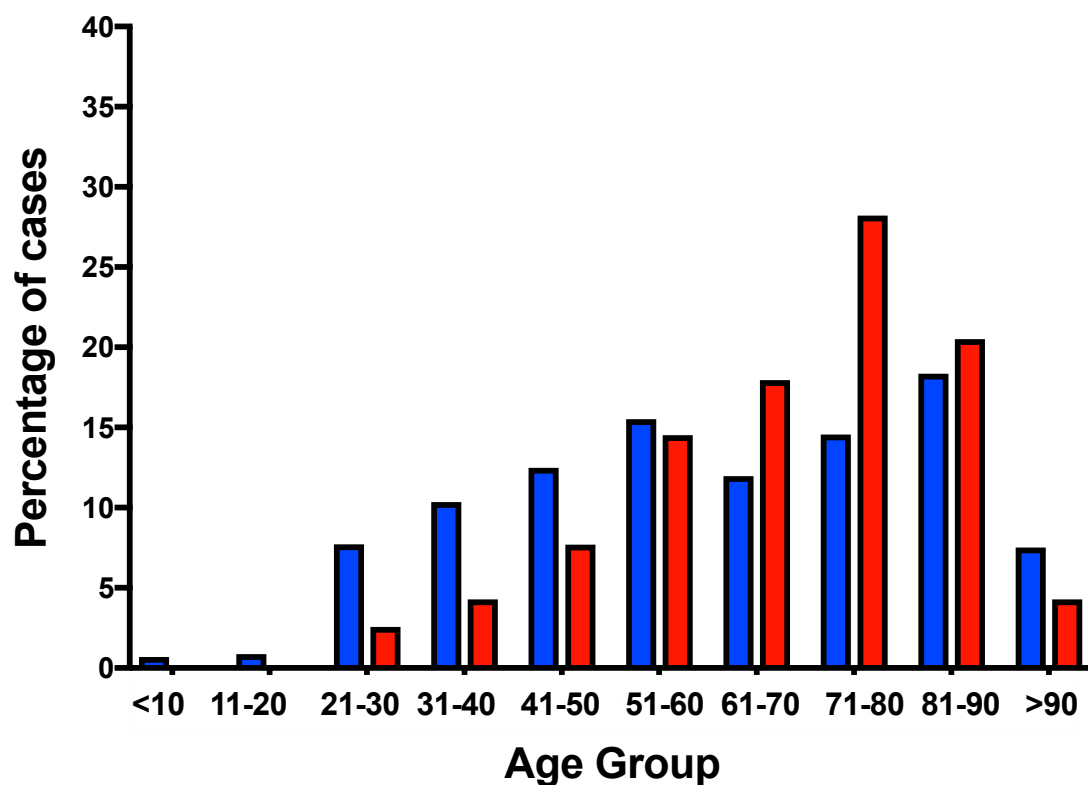


Figure 2. Age distribution of all cases notified to the *CoroNerve* studies surveillance programme (red) relative to national data collected by Government Public Health bodies of the UK administrations (blue) within the first 3 weeks of *CoroNerve* accepting notifications.

Figure 3.

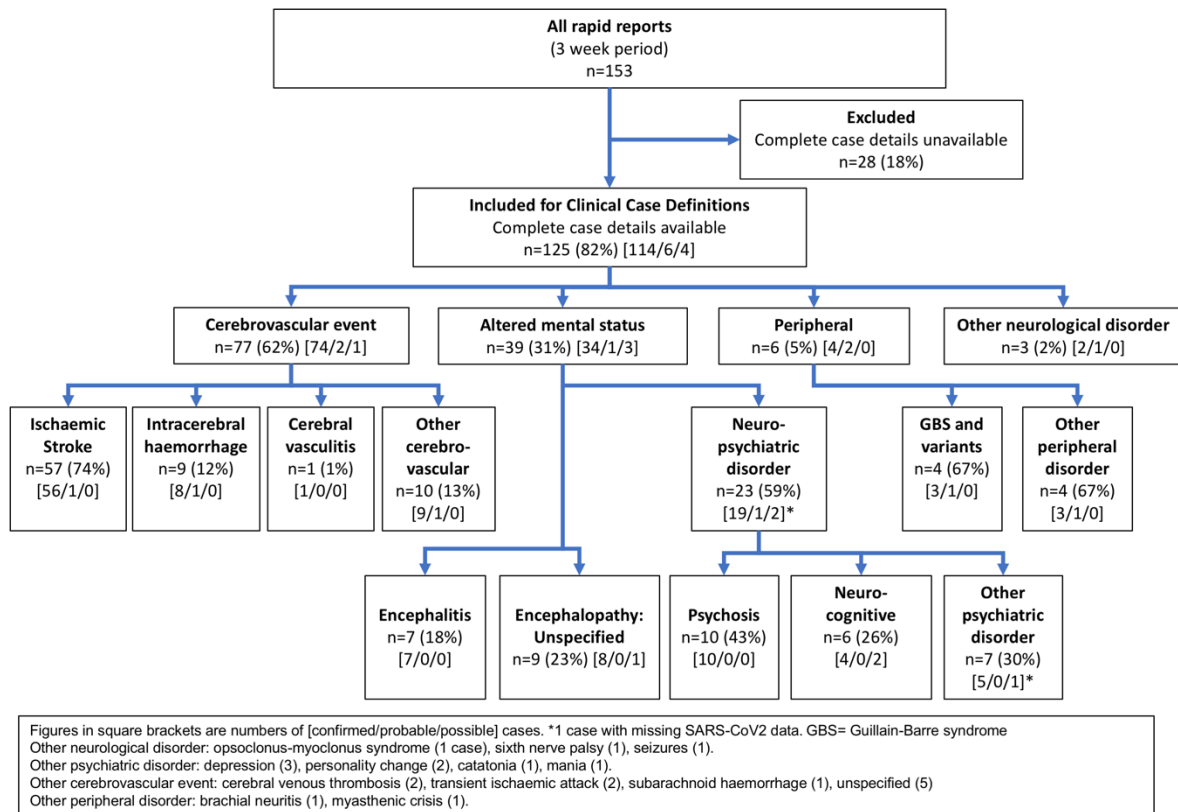


Figure 3: Number (percentage) of broad and specific clinical case definitions notified in the dataset, including evidence for SARS-CoV2 within each grouping, according to the clinical case definition (Format: ‘Confirmed/Probable/Possible’).

Figure 4.

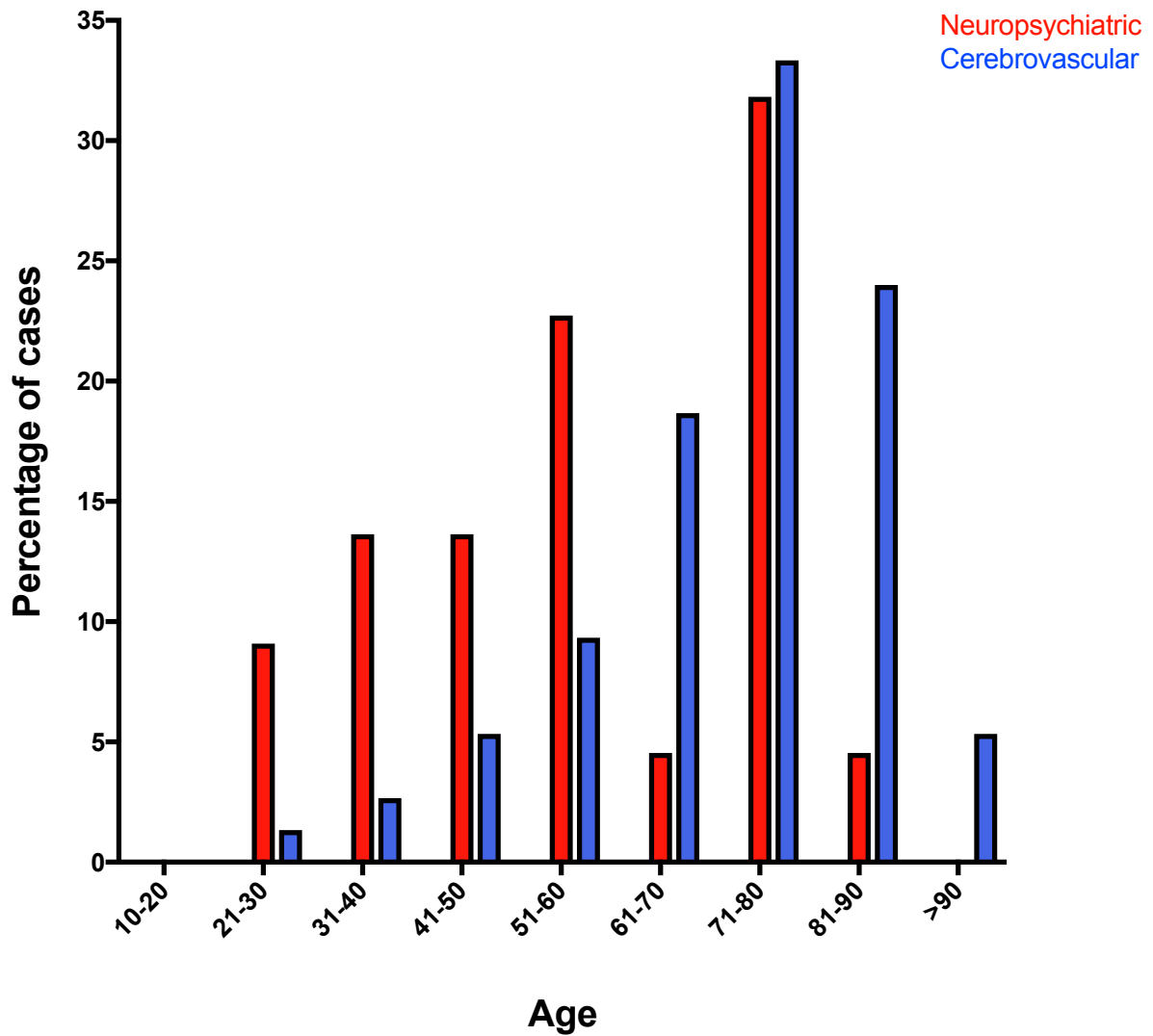
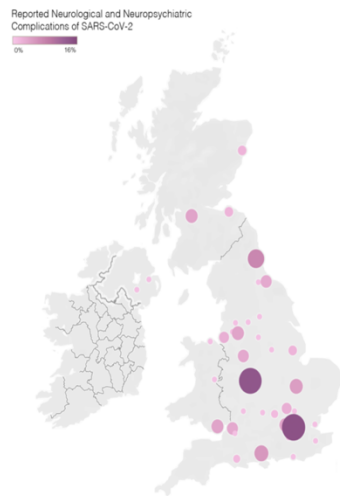


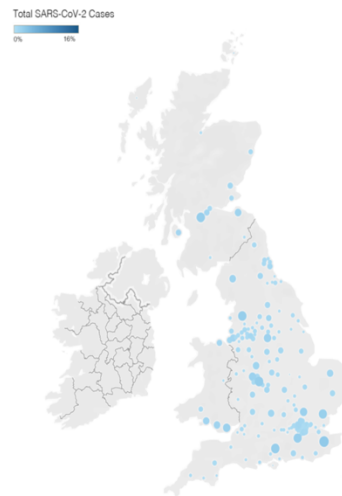
Figure 4. Age distribution of patients identified through the *CoroNerve* surveillance study meeting the clinical case definitions for cerebrovascular events (blue) and altered mental status (red).

APPENDIX

CoroNerve COVID-19 Neurology/Neuropsychiatry cases



Government Public Health COVID-19 cases



Appendix: Geographic distribution of the percentage of neurological and neuropsychiatric case notifications through the *CoroNerve* platforms (purple) relative to the percentage of overall COVID-19 cases reported by Government Public Health bodies of the UK administrations during the same time frame (blue).