Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Editorial

Neurological research & training after the easing of lockdown in countries impacted by COVID-19

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With the easing of lockdown restrictions following declining rates of COVID-19 infections, the biggest challenge for neurologists and neuroscientists in the most severely affected countries is likely to be the protracted transition to a new normal. While the neurological impact of COVID-19 is now well recognized, especially among healthcare workers and vulnerable groups [1,2] the challenges of restarting clinical and laboratory research, and allowing clinical study coordinators and laboratory staff back on-site are enormous and deserve greater attention (Table 1).

The first practical consideration is the need to maintain social distancing between staff members to deter and curb the spread of COVID-19. Most institutions will have to operate with reduced staff numbers who will function under staggered work schedules. As the roadmap to ease restrictive measures may also vary between different institutions and between collaborating countries involved in any given project, the slow and stepwise nature of return to normalcy will inevitably impede the work of the scientific community as a whole.

The opening of non-COVID-19 related clinical trials brings forth its own challenges. In many countries such as the United Kingdom, Italy, USA, China, and Singapore, non-COVID-19 trials were suspended during the acute phase of COVID-19 lockdown and are being re-started in various nation-specific “recovery” programmes. However, staff capacity remains an issue specifically where investigators have been deployed to COVID-19 studies while older and more vulnerable researchers are assigned to non-clinical support facilities. Delays in starting new trials therefore is inevitable given that such trials will be only prioritized after the large number of “suspended” studies are reopened with newly implemented safety protocols.

Risk assessment of clinical studies for neurological patients have to be made depending on the nature of the trials (experimental vs repurposing of established drugs vs natural history studies), participant profile (old vs young, presence of comorbidities), setting (acute intervention vs long term therapy), outcome measures (non-invasive neuroimaging vs invasive angiography) and location (inpatient vs outpatient). Research risks should still be incorporated into consent forms and ethics documents even if they cannot be quantified. Potential medico-legal implications must be considered in situations where participants may be subjected to additional risk either from accidental exposure to COVID-19 during clinical trials or from confounding comorbidities and other inherent individual factors.

For acute interventional trials such as in stroke patients, there may be a need to modify protocols to facilitate prompt clinical assessment while continuing all existing precautionary measures that mitigate COVID-19 risk for both patients and staff. Research workflow should incorporate important considerations raised by relevant scientific bodies on the optimal measures for stroke and dementia care or treatment modalities for various neurological conditions during COVID-19, with an emphasis on maintaining smooth care delivery while taking into account safety, ethical and logistic issues [3–5].

Unless community spread of COVID-19 is totally eradicated, patients with mild to moderate COVID-19 infection burden can present initially with symptoms ranging from common neurological signs to rarer neurological syndromes such as hyposmia and ageusia [6]. Furthermore, common neurological conditions for clinical trials may themselves represent risk factors for mortality in COVID-19-affected patients [7] and long-term neurological consequences caused by COVID-19 are still unknown. It is likely that such symptoms may add to those of chronic or degenerative neurological conditions, contributing to enrich or complicate the picture. Specific examples include the observation that dementia subjects infected with COVID-19 may present atypically [7] and that recent onset hyposmia, anxiety or fatigue which are well recognized symptoms of Parkinson's disease may masquerade as COVID-19 infection. Hence the recruitment of prospective subjects for research in any field in the post-COVID-19 world will need a higher level of vigilance and a heightened index of suspicion.

COVID-19-induced restrictions have led to a rapid emergence of telemedicine in clinical consultations. In patients who are not mentally competent to give consent, remote consent taken from an authorized representative may be a necessary alternative. This is especially critical in endovascular stroke trials where time is of the essence and subjects are often not able to give written consent in the nick of time. Another option would be to geographically limit the studies to certain locales or settings, thereby minimizing movement to and from acute hospitals. This has been demonstrated for certain dementia studies that are being conducted primarily in nursing homes or other community housing facilities with medical care where investigators focus manpower and expertise on a specific location to reduce the number of study visits of subjects to hospitals [5]. However, examination of patients for delivery

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Table 1
Challenges and solutions for post-COVID-19 research and training.

Challenges	Solutions
Maintain physical distancing (within and between laboratories)	● Reopen trial units and laboratories at a reduced capacity ● All staff on-site to wear a mask to prevent the risk of transmission of COVID-19 ● All research staff who can work effectively from home, should continue to telecommute
Limitation of all large gatherings (laboratory meetings/scientific conferences)	● Video conferencing ● Virtual networking sessions ● Online symposia ● *E*-posters
Clinical study challenges (new clusters of infections, risk of subjects in clinical areas, lack of research staff, restriction of research space, limited neuroimaging slots, hiring freezes, re-deployment of study team members, litigation, stress/anxiety/depression)	● Interventional studies (e.g stroke) to adopt stricter recruitment protocols to protect subjects and staff against COVID-19 ● Research for subjects with cognitive or physical impairment carried out in specific locations to minimise movements • Negotiate with sponsors to extend intervals for investigations (such as neuroimaging) • Neuroimaging to be carried out after office hours • Schedule study patients at the same time as regular appointments • Defer non-essential biochemical tests ● Remote consent taking with subject and investigator training • Legal advice on medico-legal liability for high risk subjects ● Research coordinators to cross cover different studies and work on staggered schedule ● Opening of administrative areas for subject assessment • Dedicated transport and transfer of subjects to avoid clinical areas • Separate isolation rooms for subjects with COVID-19 related symptoms ● Calibrated return based on a tiered framework depending on prevailing community transmission risk ● Counselling and emergency hotlines for research staff and study subjects
Laboratory study challenges (risk of staff exposure in clinical areas, restriction of research space with physical distancing, reductions in number of animal experiments, disruptions to protocols that require continuous drug challenges or monitoring, changes to experimental design especially on aging animals, problems with maintenance of precious lines and animals.)	● Staggered work schedule ● Prioritize select key experiments ● Freezing of breeding pairs of animals • Modify experimental protocol (by increasing time intervals for evaluations) ● Research staff to share common lines and tissues ● Postpone animal experiments (such as neurobehavioral evaluations) by focusing on in vitro experiments ● Appoint key personnel to cross cover for time-sensitive drug treatment of cell lines ● Cryopreservation of cell lines for longitudinal experiments ● Downsizing of multi-well cell culture batches ● Stagger the harvesting of cell lines for analyses
Prioritization of research activities	● COVID-19 studies: All ongoing and new projects should be prioritized in the order of therapeutics / vaccines, diagnostics, and epidemiology ● Non-COVID-19 studies (clinical trials): life-saving interventions (e.g acute strokes) and neurology trials for diseases with rapid progression such as motor neuron disease and progressive multiple sclerosis can continue, other studies involving human subjects can be restarted in phases, ● Non-COVID-19 studies (basic science): to be assessed on a case-by-case basis depending on specific requirements (such as neural stem cell transplant studies in non human primates)
Program continuity for students (PhD/MD-PhD/Neurology residents)	● Academic institutions should consider system-wide adjustment to graduate degree timelines • Create academic time specifically for data analysis and manuscript/thesis writing • Delay or suspend research activities for Neurology residents ● Extend duration of funded support to graduate students ● Crisis counselling for postdoctoral students/residents ● Mitigate financial impact on students (eg. repurpose funds previously budgeted for travel) ● Free remote access to national and international academic meetings and courses
Early-career scientists (post-doctoral/pre-tenure positions)	● Institutions to consider extension of tenure clocks ● Budget additional funds for graduate students ● Creation of new positions that would allow postdoctoral fellows to continue career advancements
Future funding resources Financial barriers	● Governments to strengthen their commitment to fund biomedical research ecosystems especially non-COVID-19 neurological programmes ● Governments to ease financial barriers (such as lifting restrictions of regional insurance coverage by the state/city or allowing global coverage) ● Joint international research funding initiatives

of scale-based assessments may be difficult without face-to-face attendance and therefore, in many setups, additional ethical and clinical validation of scales delivered virtually will need to be obtained.

For training, PhD students who lost precious experimental data during the lockdown may face significant impediments in progressing toward earning their degrees. Even earlier in the pipeline, students who have been accepted into graduate schools are having to postpone entry into their programs. Uncertainty about research scholarships and career choices looms large. In some universities, courses are being rebranded for online delivery but acceptance among students needs to be determined. Budding clinical-investigators in MD-PhD students share the same concerns where delayed and out-of-phase clinical residency trainings could pose a major problem in their career advancement. In addition, loss of revenue for universities in some countries and shrinking economic forecasts will affect students and teachers alike. Global mobility restrictions bear an understated yet significant impact on cross-country fellowship training, delaying the entry and return of existing fellows. Early-career scientists including postdoctoral or pre-tenure positions, will all need to face the insecurities associated with the application of grants, fellowships and jobs post-COVID-19 [8]. Neurology residents and clinical fellows have faced a substantial decrease of contact with patients resulting in a negative impact on their training. It may be necessary to postpone or delay residency-related research activities and possibly even waive certain academic requirements. On a positive note, many participants who registered for free (among 42,000 attendees) at the recent European Academy of Neurology meeting in May 2020 were residents, fellows and students [9], suggesting that free access to international academic teaching and research meetings for trainees is likely to be a norm in the near future.

Until a vaccine for COVID-19 becomes available, researchers will have to recognize the challenges, and explore possible solutions (Table 1). However, details in efforts to address the obstacles will be highly dependent on the prevalence of infections and other local and geopolitical factors and constraints and the economic stimulatory measures in the respective countries. What is certain though is that neurological research and training will never be the same in the post-COVID era and hopefully the evolving changes will augment the ability of the medical community to better handle the next pandemic.

Declaration of Competing Interest

Nil

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