

generative pathology, mirroring the acceleration of beta-amyloid and tau pathology caused by other neurotropic viruses such as HIV and herpes viruses.

Extensive future work will be needed to map out the mechanisms and prevalence of long-term “cognitive COVID”. *In vivo* and *in vitro* lab studies can evaluate the interaction of viral and neurodegenerative proteins and any potential synergistic effect on synaptic and neuronal function, while large scale longitudinal epidemiological studies will be required to identify the demographic, genetic and psychosocial risk factors of COVID-19-related cognitive decline, and to differentiate between direct and indirect effects of the infection. Targeted cognitive testing, focusing on the functions of vulnerable brain regions, will help differentiate cognitive dysfunction directly due to the infection from that associated with depression and other mental health issues.

Lessons learned during the first stage of the pandemic have improved acute clinical outcomes. As the second stage unfolds, it is imperative that attention now focus on the implications of

COVID-19 infection for long-term cognitive impairment and dementia risk, to aid prospective detection and intervention with pharmacological and public health strategies.

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Post-traumatic stress disorder in the aftermath of COVID-19 pandemic

Post-traumatic stress disorder (PTSD) is a potentially debilitating mental health disorder which affects an important minority of people exposed to events involving actual or threatened death, serious injury or sexual violence. The COVID-19 pandemic is unfortunately providing multiple opportunities for people to experience traumatic situations which may lead to PTSD.

Imagine the previously fit person who rapidly goes from an active lifestyle to a chemical induced coma, surviving only after weeks on a mechanical ventilator. Or the nurse who volunteers to join a rapidly assembled intensive care team with minimal preparatory training, and faces the stark reality that many of those cared for end up dying alone, with relatives being unable to visit the unit¹. These situations have a high potential to induce PTSD. Indeed, it has been reported that up to 20% of intensive care unit survivors go on to develop PTSD². On the other hand, there is evidence that repeated exposure to traumatic events in health care workers can lead to the development of PTSD even if the staff member cannot identify which specific traumatic event caused him/her to become unwell³.

Whilst PTSD must follow trauma exposure, other factors substantially influence the likelihood of developing this condition. Comprehensive meta-analyses of risk factors for PTSD consistently find that the nature of the post-trauma environment is a more important predictor than pre-traumatic factors such as childhood adversity, or demographic factors such as gender or ethnicity. In particular, there is strong evidence that psychological stress experienced during the initial post-exposure period, as well as the availability and quality of post-trauma social support, are highly influential determinants⁴. Whilst we know that social support is highly protective against the development of PTSD,

social distancing restrictions are making it more difficult for people to access non-professional support, so that the onset of PTSD after trauma exposure may become more likely.

Another important risk factor for PTSD is moral injury, which is defined as the psychological distress, including feelings of deep shame and guilt, resulting from doing, or not preventing, events that someone believes are “wrong”. Many health care workers are likely to experience morally injurious events during this pandemic. Feeling unable to deliver high-quality care, or having to make hard choices about who will and who will not receive a given intervention due to shortage of available equipment, have become somewhat commonplace, especially when the rates of hospitalization are high. Moral injury is also a relevant concept outside of work environments, especially when people are concerned about having infected loved ones who have died. Moral injury is important as it can predispose people to developing PTSD⁵ as well as making it less likely that they will seek treatment if they do.

Within organizational settings, a number of approaches have been tried to prevent the onset of PTSD. Pre-employment, or pre-role, psychological health screening aims to identify higher risk individuals, so they can either not be employed in trauma-exposed roles or be provided with extra support to mitigate the risk. However, there is consistent evidence that this approach is ineffective. It may indeed be harmful, by providing employers with false reassurance that screened personnel are resilient to trauma and will not develop PTSD⁶. Whilst health care managers understandably may wish to exclude vulnerable staff from dealing with the most severe COVID-19 patients, in order to protect their mental health, the reality is that the state of the current evidence base on screening is unsatisfactory and this practice cannot be recommended.

Another approach that has been shown to be ineffective, and indeed potentially harmful, is the use of psychological debriefing, or post-trauma counselling, delivered in the days after a traumatic event has occurred. Well-accepted PTSD management guidelines are clear in recommending against the use of such approaches⁷. This evidence is highly relevant during the current pandemic, when mental health professionals want to support their “front-line” physical health colleagues, or assist individuals recovering from serious COVID-19 infection. Whilst both aspirations are laudable, it is important to avoid causing harm.

On the other hand, there is strong evidence that training supervisors to implement supportive and empathetic communication techniques with their team members is highly beneficial to employees’ post-trauma mental health and is associated with a reduction in their sickness absence⁸. Good evidence also exists that formal peer support programs can protect the mental health of trauma-exposed employees⁹. Furthermore, it may be useful to ensure that trauma-exposed staff are actively monitored, provided with time away from trauma-prone workplaces, and encouraged to engage in reflective practice protecting them against the onset of moral injury.

For people who do develop PTSD, there are some evidence-based treatments available. Whilst demand for these interventions is likely to be high, given the scale of the pandemic, it remains highly important that evidence-based approaches are utilized. Most evidence exists for trauma-focused cognitive behavioral psychotherapy and eye movement desensitization and reprocessing⁶. Most people will experience substantial improvement from 8 to 12 sessions of cognitive behavioral psychotherapy, although

those with more complex presentations of PTSD are likely to require more prolonged treatment. For those who do not accept or respond to psychotherapy, antidepressant medications may help, and they may be especially useful for people who present a comorbid depressive disorder.

As with other mental health conditions, it is important that treatment for PTSD begins early on, before people lose their self-esteem, important relationships or employment, or develop other mental health disorders, including substance misuse. Given the likely increased global incidence of PTSD as a result of the pandemic, the routine use of the effective preventive measures and the dissemination of the evidence-based psychotherapies outlined above should be seen as a priority.

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Prioritizing COVID-19 vaccination for people with severe mental illness

In the global race for a safe and effective COVID-19 vaccination, there are still many challenges that need to be addressed. One of these is being the initial scarcity of doses and the associated ethical considerations as to whom they should be distributed first.

Recently, the National Academies of Sciences, Engineering, and Medicine have proposed an ethical framework for equitable allocation of COVID-19 vaccine in the US¹. The World Health Organization, as well as several other entities, have produced similar frameworks. In the prioritization of vaccines, these frameworks endorse three universal ethical principles. A first principle concerns minimizing harm and maximizing benefit: an effective vaccine should reduce deaths, disease burden, and societal and economic disruption, and have a minimal side effect profile. The second principle advocates prioritizing populations that may experience disproportionately greater health burdens as a result of the COVID-19 pandemic: some groups are at higher risk of being infected with, dying of or having lasting sequelae of COVID-19, due to their age, profession, medical status or socioeconomic

factors. The third principle relates to equal respect for every person, and requires that, in allocation and priority-setting, individuals are considered and treated as having equal dignity and worth. Individuals who, because of vulnerability or structural inequalities, would face barriers to accessing a vaccine, should be offered an equal opportunity to be vaccinated as compared to more privileged groups².

People of all ages with comorbid and underlying physical conditions, such as cardiovascular diseases, chronic obstructive pulmonary disease, type 2 diabetes mellitus, chronic kidney disease, obesity, immunodeficiency and cancer, are particularly vulnerable to morbidity and mortality due to COVID-19. The risk of premature death or severe morbidity in these patients is significant enough for the US National Academies of Sciences, Engineering, and Medicine to prioritize these patients in the allocation of vaccines¹.

Even without factoring COVID-19 into the calculation, people with severe mental illness, including schizophrenia, major depressive disorder and bipolar disorder, have a two to three times