Clozapine-related fever, tachycardia, or myocarditis can clinically overlap with COVID-19 infection.

Patients with schizophrenia are seven times more likely to die as a consequence of pneumonia compared to general population.[2]

Clozapine (and other antipsychotics) has been tied to an increased risk of pneumonia including COVID-19. A multitude of factors seem at play. Clozapine-induced sialorrhea and aspiration is contributory. Clozapine-related "diabesity" is a risk factor for COVID-19 infection. Immune-related mechanisms are also implicated. Smoking is highly comorbid in these patients with poor respiratory reservoir (e.g. *poor* housing and ventilation) can further complicate medical prognostication.

Viral infection, including COVID-19, are long known to incite a relapse in these patients either directly (inflammatory pathways) or indirectly acting as a proximal stressor (coronaphobia and infodemics).[3]

Furthermore, severe infections, as COVID-19, can inhibit CYP 450 1A2, through "cytokine storm" with resultant toxic levels. Metabolic ratio of clozapine to norclozapine can jump above three in these cases.

Prescribed medications for COVID-19 might be challenging with clozapine. Quinolones and macrolides antibiotics can inhibit CYP 450 1A2 and 3A4, respectively, for which clozapine is a substrate with possible toxicity. Macrolides can prolong QTc interval. Hydroxychloroquine might be associated with psychiatric side effects. QTc prolongation is a definite risk, as well as seizures and neutropenia especially when co-prescribed with clozapine. Remdesivir-reported hepatotoxicity can be mistaken for ubiquitous clozapine-related transaminitis.[4]

"Neurocovid"-associated delirium can be mistaken for neuroleptic malignant syndrome (NMS) or catatonia.

It behooves clinicians then to be vigilant and mindful of these caveats when managing these patients. Some authorities have advised flu vaccinations, vitamin D supplementation, and reducing total clozapine dose in the setting of COVID-19 infection.[5]

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Lessons from psychiatry for treating post-acute Covid-19 fatigue

The current SARS-CoV-2 pandemic and associated Covid-19 disease continue to cause major problems. In recent months, it has become apparent that many with the disease (early evidence suggests at least 10%) will not make a complete recovery but suffer from post-acute COVID-19 (so-called 'long Covid').[1] One of the features of long Covid is persistent, moderate to chronic fatigue. Not a great deal is known about how to best manage this.[2] It is possible that existing methods of managing post-viral fatigue, as well as approaches used in myalgic encephalomyelitis, will be applicable to long Covid. It may also be the case that approaches from psychiatry can be successfully applied to target fatigue.

Fatigue is a well-documented feature in many psychiatric illnesses. The biological basis of fatigue may differ between diseases; the often-debilitating effects remain fairly consistent. While unproven yet, it is conceivable that psychostimulant drugs could be of use to individuals suffering from chronic fatigue as a result of long Covid. Targeting the symptom of fatigue through temporary use of lisdexamfetamine or methylphenidate could offer some respite for long Covid patients and lead to higher quality of life, until more efficacious treatment options are available. The Rochester Center for Behavioral Medicine has had success with a small open label trial of lisdexamfetamine in 30 patients with Long covid.

Recent contributions[2] argue that 'priority' should be given to understanding post-acute Covid-19 fatigue and emphasise the need to 'explore pragmatic relatively low-cost techniques to treat post-viral fatigue'. It is also very possible that the wakefulness agent modafinil could serve as a safe and effective intervention. In post-stroke fatigue, modafinil use leads to a decrease in fatigue and improved quality of life compared with placebo.[3]

While there are of course risks with this class of drug, on balance it may be a risk worth taking (or at least investigating further). These drugs should form part of a broader, multisystem rehabilitation model and recovery framework, which also gives due consideration to patient pathology.

Beyond pharmacological approaches, there may also be other takeaways from psychiatry. Psychotherapies such as cognitive behavioural therapy can play a role in helping patients cope with the fatigue feature of mood disorders.

Given its variability in presentation, a patient-centric and symptom-specific approach should be taken in managing post-acute Covid-19. As such, we must be constantly looking across all areas of medicine for treatment options.

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Doggone it! Canine therapy doesn't tame the Black Dog

Dear Sir,

> *I am fond of pigs. Dogs look up to us. Cats look down on us. Pigs treat us as equals. – Winston Churchill*

The companionship of animals, especially dogs and horses, to improve the mental well-being of humans dates back to antiquity, including Hippocrates' recommendation of horse riding to treat insomnia. However, scientific research into pet psychotherapy began in the mid-1960s, with the use of pet therapy to manage behavioural disorders in children.[1] Canine therapy is intuitively appealing and receives much public and media attention (https://www.pawspettherapy.com).

Although it is clear that pets can provide company, affection, activity and protection for some individuals (https://www.beyondblue.org.au/personal-best/pillar/supporting-yourself/pets-and-their-impact-on-mental-health), there has been a paucity of quality research into canine-assisted therapy for clinical depression. Despite dogged investigation for evidence of improvement in depressive symptoms using canine therapy, there is little support for this modality of treatment in major depressive disorder. Charry-Sanchez et al. (2018) performed a systematic review and identified only relevant two studies.[2] The first was a randomized parallel clinical trial (Panzer-Koplow 2000) examining the response to canine-assisted therapy (15 minutes once a week for 10 weeks with a facilitator and a trained therapy dog) in 35 nursing home residents, using Beck Depression Inventory (BDI) and Geriatric Depression Scale as outcome measures.[3] There were no statistically significant differences between the control group and the canine-assisted therapy group. The second study (Le Roux and Kemp 2009) was also a randomized parallel clinical trial involving elderly residents of a long-term care facility.[4] Canine-assisted therapy involved 30-minute interactions weekly for 6 weeks and a BDI was used to assess efficacy. Although there were statistically significant differences between the two groups ($z = –2.385$, $p = .017$), there was a substantive risk for performance bias, as the volunteers had frequent contact with staff members who had knowledge of the group allocation.

Therefore, we have been hounded by doubt regarding the recommendation of canine-assisted therapy for clinical depression, although there may be contention regarding how much emphasis to place on the Le Roux and Kemp (2009) study. Some may view the findings in this small study as a case of the tail wagging the dog. Clearly, there is a need for further research for the development of better treatment paradigms in this area. Or perhaps, as Churchill opines, the boar may yet banish the Black Dog.

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Reply to Allison et al.: All-age eating disorder services

Dear Sir,

We applaud Allison and colleagues[1] for their thought-provoking article. This lays out the problems associated with a division of eating disorder (ED) services based on age and provides cogent arguments for the introduction of 'reach down' all-age ED services.

Although the authors rightly point to all-age service models in the UK as a good practice example, currently, the vast majority of UK ED services are strictly age-segregated. In England, there has been substantial government investment in resourcing existing and setting up new ED services for the under 18s, with associated national team training and access and waiting time standards. There has been no parallel investment in adult ED services, despite year on year increases in referrals. This has led to major inequalities in young people's access to ED care. For example, in our own large catchment area in South East London, young people under the age of 18 can self-refer,