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.

high-cost polysomnography is reserved when the diagnosis of other sleep disorders is suspected.

Access to continuous positive airway pressure (CPAP) machines for the treatment of sleep disordered breathing is scarce in Africa and probably contributes to suboptimal NCD outcomes. Therefore, innovative ways to make CPAP machines available and affordable must be explored. Access to low-cost machines through government health-insurance schemes is a useful strategy where such programmes exist. Machine rental services are also an approach that could increase access with reduced out-of-pocket costs.

In summary, Wachinou and colleagues[7] have reported a high prevalence of sleep disordered breathing in a large African population that is similar to those reported from high-income countries. This finding underscores the need to intensify preventive measures to reduce obesity in Africa and for further research to substantiate these findings. These measures are needed to inform policy that will drive training on sleep disordered breathing and also enhance access to diagnosis and treatment of this condition in Africa.

We declare no competing interests.

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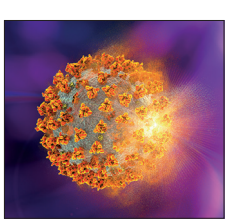
Improving COVID-19 vaccine immunogenicity by interrupting methotrexate treatment

People with immune-mediated inflammatory diseases are at increased risk for COVID-19 infection and poor outcomes.[1] This risk might be partly due to immunosuppression from drugs such as methotrexate, commonly used to treat many immune-mediated inflammatory diseases.[2] Although COVID-19 vaccination has proven to be safe and effective, even for people with immune-mediated inflammatory diseases,[3,4] specific immunosuppressive medications, including methotrexate, have been associated with impaired immunogenicity.[5] Due to the public health crisis and this at-risk population, the American College of Rheumatology recommends that conventional synthetic disease-modifying anti-rheumatic drugs such as methotrexate should be withheld "for 1–2 weeks (as disease activity allows) after each COVID-19 vaccine dose".[6] The only previous clinical trial to support this statement at that time was of methotrexate interruption after seasonal influenza vaccination in patients with rheumatoid arthritis.[7] Thus, the possible effect on immunogenicity of pausing methotrexate after COVID-19 vaccination among people with other immune-mediated inflammatory diseases was unclear.

In *The Lancet Respiratory Medicine*, Abhishek Abhishek and colleagues did a randomised controlled trial in patients with immune-mediated inflammatory diseases investigating a 2-week interruption versus no interruption of methotrexate after a COVID-19 booster vaccine.[8] 127 participants were randomly assigned to the suspend methotrexate group and 127 to the continue methotrexate group of the Vaccine Response On/Off Methotrexate (VROOM) study.[8] About half of the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participants had rheumatoid arthritis; other immune-mediated inflammatory diseases included psoriatic disease, spondyloarthritis, and polymyalgia rheumatica. 82% received the BNT162b2 vaccine (Pfizer–BioNTech) as their booster dose. The primary outcome was the geometric mean ratio (GMR) of the anti-spike-1 receptor-binding domain antibody (anti-S1-RBD) 4 weeks after receiving the vaccine, comparing the suspend and continue methotrexate groups. The suspend group had higher anti-S1-RBD concentrations than the continue group (GMR 2·19 [95% CI 1·57–3·04], p<0·0001) at week 4. This difference was present across many subgroups. At week 12, the suspend group also had higher anti-S1-RBD concentrations than the continue group. However, the suspend group was significantly more likely to report disease flare-ups at week 4 (56% *vs* 31%) and week 12 (71% *vs* 45%). Most flare-ups were mild, but systemic glucocorticoid use for flare-ups was numerically higher in the interruption group (18% *vs* 12%).

These results extend previous findings showing that interruption of methotrexate improves vaccine immunogenicity. Another recent trial among people with rheumatoid arthritis showed that a 2-week interruption of methotrexate after the CoronaVac COVID-19 vaccine (Sinovac) resulted in improved immunogenicity compared with no interruption.[9] The VROOM study is the first to show that improved vaccine immunogenicity after methotrexate interruption occurs in people with immune-mediated inflammatory diseases other than rheumatoid arthritis. Considering this and the previous trials,[7-9] the improvement in vaccine immunogenicity after methotrexate interruption might be broadly applicable across different vaccine types. However, the precise threshold of humoral response necessary for protection against COVID-19 is unclear. An observational study showed that there was an increased risk of COVID-19 breakthrough infection in patients with rheumatoid arthritis who had an absent humoral vaccine response compared with those with a good humoral vaccine response.[10] Thus, although immunogenicity is clearly improved after methotrexate interruption, the clinical benefits to optimise clinical protection are still somewhat theoretical. Future work should investigate cellular responses and possible improved immunogenicity after interruption of other immunosuppressive medications, different vaccines, and other immune-mediated inflammatory diseases.

Because methotrexate is the anchor drug for control of immune-mediated inflammatory diseases, flare-up and increased disease activity are the risks patients take when interrupting this medication. Indeed, the VROOM study and other trials show short-term increased disease activity.[7-9] Given that VROOM included many immune-mediated inflammatory diseases, a single validated measure of disease activity could not be obtained. The investigators were dependent on patient or provider reports, which might have been influenced by the open-label and unblinded nature of the study. Participants were required to have low disease activity at screening, so results might not generalise to patients with high disease activity. Trials investigating a 2-week versus 1-week interruption would establish whether a similar humoral response is achieved while conferring a lower flare-up risk. An observational study of patients with rheumatoid arthritis showed no difference in disease activity measured weekly pre-vaccination versus post-vaccination in those who interrupted versus continued methotrexate or other immunosuppressants.[4] However, in routine clinical practice outside of a trial setting, it is difficult to discern whether increased disease activity after vaccination is due to methotrexate interruption, immune activation from the vaccine itself, or idiosyncrasies in these diseases that have a background flare rate. Thus, the VROOM study shows both possible benefit in optimising humoral vaccine response and the possible risk in underlying disease flares.

In summary, this important study shows that a 2-week interruption of methotrexate after booster COVID-19 vaccination results in increased immunogenicity compared with no interruption among patients with several immune-mediated inflammatory diseases. Although this finding adds to the evidence base to support interruption of methotrexate after vaccination, a shared decision process is needed to weigh the possible benefit of optimising protection from COVID-19 and the possible risk of underlying disease flare.

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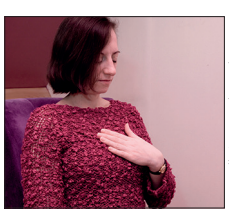
Treating COVID-19-related breathlessness with novel interventions

COVID-19 was announced as a global pandemic in March, 2020, by WHO, and shortly afterwards it was noted that people infected with SARS-CoV-2 might have ongoing symptoms, commonly breathlessness, fatigue, joint pain, and changes in cognition and health-related quality of life.[1] The number of people with lasting symptoms of COVID-19 continues to rise and it is estimated that 1·5 million people have lasting symptoms of COVID-19 in the UK alone.[2] Up to 25% of individuals admitted to hospital with COVID-19 felt they needed rehabilitation, although the proportion of non-hospitalised patients requiring support for symptoms is intangible.[3,4] The need for rehabilitation causes a huge demand on current and emerging services in the context of the ongoing impacts of COVID-19 on service provisions. Considering this, there is a huge need for a variety of flexible interventions to improve the lasting symptoms of COVID-19.

In *The Lancet Respiratory Medicine,* Keir Philip and colleagues[5] report their findings from a randomised controlled trial of an online wellbeing and breathing programme (English National Opera [ENO] Breathe), developed by the ENO learning and participation team alongside clinicians. This programme focuses on breathing retraining using singing techniques, and is delivered via an online platform. This is the first study to explore a singing-based intervention for individuals with lasting symptoms of COVID-19. The provision and implementation of singing techniques for breathlessness vary but are largely provided by charities and support groups and not as part of routine health care. Singing techniques have demonstrated improvements in conditions such as chronic obstructive pulmonary disease (COPD) for health-related quality of life and exercise capacity, and the evidence for this is increasing.[6,7] Philip and colleagues[5] found improvements in elements of breathlessness and mental wellbeing for individuals with breathlessness following SARS-CoV-2 infection and, as a result, suggest that ENO Breathe provides a flexible and suitable strategy for managing some of the lasting symptoms of COVID-19. Access to this intervention can provide health-care professionals with a useful tool to aid recovery and can supplement routine care.

This randomised controlled trial was delivered pragmatically and, as a result, it is difficult to determine uptake. Encouraging uptake of therapeutic interventions is often challenging, and the participants in Philip and colleagues' study will undoubtedly be self-selecting; however, generally one size doesn't fit all in therapeutic interventions and, therefore, ENO Breathe might be a useful addition to treatment for those who wish to participate. Participants in this study had received routine care before receiving the intervention and, therefore, its benefits and safety in individuals without



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