

Largest study to date confirms non-steroidal anti-inflammatory medications do not result in worse COVID-19 outcomes

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Transmission electron micrograph of SARS-CoV-2 virus particles isolated from a patient. Credit: NIAID

The use of non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen, does not lead to higher rates of death or severe disease in patients who are hospitalised with COVID-19, according to a new observational study of more than 72,000 people in the UK published in The Lancet Rheumatology journal.

NSAIDs are common treatments for acute pain and rheumatological diseases such as rheumatoid arthritis and osteoarthrosis. Early in the pandemic, there was debate on whether the use of such drugs increased the severity of COVID-19, which led to urgent calls for investigations between NSAIDs and COVID-19.

The ISARIC CCP-UK (International Severe Acute Respiratory and emerging Infection Consortium Clinical Characterisation Protocol United Kingdom) study, which is the largest of its kind, provides clear evidence that the continued use of NSAIDs in or non-invasive ventilation, use of supplemental patients with COVID-19 is safe.

In the study, around a third of patients (30.4%. 1,279 out of 4,211) who had taken NSAIDs prior to hospital admission for COVID-19 died, a rate which was similar (31.3%. 21,256 out of 67,968) in patients who had not taken NSAIDs. In patients with rheumatological disease, the use of NSAIDs did not increase mortality.

Prof Ewen Harrison, of the University of Edinburgh and lead author of the study, said: "NSAIDs are commonly used to treat people all over the world for a range of conditions, from minor aches and pains to chronic conditions such as arthritis and cardiovascular disease. Many people rely on them to be able to carry out their day-to-day activities. When the pandemic began over a year ago, we needed to be sure that these common medications would not lead to worse outcomes in people with COVID-19. We now have clear evidence that NSAIDs are safe to use in patients with COVID-19, which should provide reassurance to both clinicians and patients that they can continue to be used in the same way as before the pandemic began."

The study collected data on the medication patients had been prescribed, were currently taking, or had taken within 14 days prior to being admitted to hospital, as well as demographic information, and medical history. The study cohort included patients with confirmed or highly suspected COVID-19 infection admitted to 255 healthcare facilities in England, Scotland, and Wales, between January and August 2020. Of the 72,179 patients eligible for the study, 5.8% (4,211) had taken NSAIDs prior to admission

Modelling analyses were used to estimate the effects of NSAIDs taken prior to hospitalisation on mortality rates in hospital, disease severity, admission to critical care, requirement for invasive



oxygen, or development of acute kidney injury, which were then compared to patients who had not taken NSAIDs. Those who took NSAIDs were no more likely to be admitted to <u>critical care</u>, need invasive or non-invasive ventilation, or require oxygen.

The authors noted some limitations to the study. Despite being the largest ongoing prospective study of patients admitted to hospital, it only represents 60% of hospitalised patients in the UK over the time of the study and it did not include patients with severe COVID-19 who were not hospitalised. However, it would be expected that most patients who had severe COVID-19 would have been admitted to hospital and therefore included in the study, the authors said. The study did not determine whether patients continued to be given NSAIDs while they were in <u>hospital</u>, so the authors cannot make any recommendations on this.

Additionally, the study could not capture how long patients were taking NSAIDs prior to hospital admission and whether they were being taken for long-term conditions or short-term symptom relief. In the UK, ibuprofen is the most commonly used NSAID, so it is unclear whether the results of this study are generalisable to other countries where other NSAIDs are more frequently used. Further analyses performed suggested other non-ibuprofen NSAIDs had a similar safety profile to ibuprofen. Further research and clinical trials may help definitively establish whether NSAIDs are safe in different populations and whether their antiinflammatory effects have any impact on patients with COVID-19.

More information: Thomas M Drake et al, Nonsteroidal anti-inflammatory drug use and outcomes of COVID-19 in the ISARIC Clinical Characterisation Protocol UK cohort: a matched, prospective cohort study, *The Lancet Rheumatology* (2021). DOI: <u>10.1016/S2665-9913(21)00104-1</u>

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