

**MARCH 16, 2020**

**expert reaction to reports that the French Health Minister recommended use of paracetamol for fever from COVID-19 rather than ibuprofen or cortisone**

The French Health Minister has recommended the use of paracetamol for fever from COVID-19 rather than ibuprofen or cortisone.

**Prof Paul Little, Professor of Primary Care Research, University of Southampton, said:**

“There is now a sizeable literature from case control studies in several countries that prolonged illness or the complications of respiratory infections may be more common when NSAIDs are used – both respiratory or septic complications (1-10) and cardiovascular complications (11, 12). The observational evidence is always difficult to interpret due to so called protopathic bias/confounding by indication (i.e. were the NSAIDs prescribed at an early stage of the complications developing and so the NSAID use reflects the complications or a more severe illness rather than causing it), but where this has been controlled for the associations still persists(2). The finding in two randomised trials that advice to use ibuprofen results in more severe illness or complications (13, 14) helps confirm that the association seen in the observational studies is indeed likely to be causal. Advice to use paracetamol is also less likely to result in complications(13).”

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**Prof Ian Jones, Virologist at the University of Reading, said:**

“The advice relates to Ibuprofen’s anti-inflammatory properties, that is, it dampens down the immune system, which may slow the recovery process. In addition, it is likely, based on the substantial literature around SARS I and the similarities this new virus (SARS-CoV-2) has to SARS I, that the virus reduces a key enzyme which part-regulates the water and salt concentration in the blood and could be part of the pneumonia seen in extreme cases. Ibuprofen aggravates this while paracetamol

does not. It is recommended that people use paracetamol to reduce temperature if you are feverish.”

**Dr Tom Wingfield, Senior Clinical Lecturer and Honorary Consultant Physician, Liverpool School of Tropical Medicine, said:**

“In the UK, paracetamol would generally be preferred over non-steroidal anti-inflammatory drugs (“NSAIDs”) such as ibuprofen to relieve symptoms caused by infection such as fever. This is because, when taken according to the manufacturer’s and/or a health professional’s instructions in terms of timing and maximum dosage, it is less likely to cause side effects. Side effects associated with NSAIDs such as ibuprofen, especially if taken regularly for a prolonged period, are stomach irritation and stress on the kidneys, which can be more severe in people who already have stomach or kidney issues. It is not clear from the French Minister’s comments whether the advice given is generic “good practice” guidance or specifically related to data emerging from cases of Covid-19 but this might become clear in due course. It should also be noted that, in the UK, we would not commonly use cortisone to relieve infection-related symptoms such as fever.”

**Dr Rupert Beale, Group Leader in Cell Biology of Infection at The Francis Crick Institute**

“There is a good reason to avoid ibuprofen as it may exacerbate acute kidney injury brought on by any severe illness, including severe COVID-19 disease. There isn’t yet any widely accepted additional reason to avoid it for COVID-19. Patients taking cortisone or other steroids should not stop them except on advice from their doctor. The Society for Endocrinology has issued advice for patients who are taking hydrocortisone or other steroids for pituitary or adrenal deficiency. <https://www.endocrinology.org/news/item/14050/Coronavirus-advice-statement-for-patients-with-adrenal%2fpituitary-insufficiency>.”

**Dr Charlotte Warren-Gash, Associate Professor of Epidemiology, London School of Hygiene and Tropical Medicine, said:**

“Most deaths from COVID-19 have been among older people and those with underlying health conditions such as cardiovascular disease. We already know that non-steroidal anti-inflammatory drugs (NSAIDs) should be prescribed with caution for people who have underlying health conditions. In England, NICE recommends prescribing the lowest dose for the shortest duration to prevent adverse effects such as gastrointestinal bleeding and cardiovascular or kidney problems<sup>1</sup>. In the context of respiratory infections, a study in Taiwan published in 2017 showed that there was a higher risk of having a heart attack during a respiratory infection when patients were treated with NSAIDs compared to those with respiratory infection alone, or on NSAID treatment alone – there seemed to be some interaction between the respiratory

infection and anti-inflammatory drugs<sup>2</sup>. That study looked at a range of NSAIDs, but unfortunately no data were available on naproxen or low dose ibuprofen<sup>3</sup>, which are the two NSAIDs considered safest for older people and those with cardiovascular disease. For COVID-19, research is needed into the effects of specific NSAIDs among people with different underlying health conditions, which takes into account the severity of infection. In the meantime, for treating symptoms such as fever and sore throat, it seems sensible to stick to paracetamol as first choice.”

1. <https://cks.nice.org.uk/nsaids-prescribing-issues#!scenarioRecommendation:2>

2. Wen YC et al. Acute Respiratory Infection and Use of Nonsteroidal Anti-Inflammatory Drugs on Risk of Acute Myocardial Infarction: A Nationwide Case-Crossover Study. J Infect Dis. 2017; 215(4):503-509.]

3. Warren-Gash C, Udell J. Respiratory Tract Infections, Nonsteroidal Anti-inflammatory Drugs and Acute Myocardial Infarction: Is Understanding Interaction Between Risk Factors the Key to Personalizing Prevention? J Infect Dis 2017;215(4):497-499.