

# COVID-19 and NCDs: The use of Non-steroidal anti-inflammatory drugs (NSAID) in patients with COVID-19

Scientific brief  
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## Introduction

Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most commonly used drugs, and have a wide range of uses. NSAIDs include unselective cyclooxygenase (COX) inhibitors (such as ibuprofen, aspirin (acetylsalicylate), diclofenac and naproxen) as well as selective COX 2 inhibitors (such as Celecoxib, Rofecoxib, Etoricoxib, Lumiracoxib, and Valecoxib).

Concerns have been raised that non-steroidal anti-inflammatory drugs (NSAIDs) may be associated with an increased risk for adverse effects when used in patients with acute viral respiratory infections, including COVID-19.<sup>1,2</sup> This review aimed to assess the effects of prior and current use of NSAIDs in patients with acute viral respiratory infections on acute severe adverse events (including mortality, acute respiratory distress syndrome (ARDS), acute organ failure and opportunistic infections), on acute healthcare utilization (including hospitalization, intensive care unit (ICU) admission, supplemental oxygen therapy and mechanical ventilation) as well as on quality of life and long-term survival.

## Methods

A rapid systematic review was carried out on 20 March 2020 on NSAIDs and viral respiratory infections from available studies in MEDLINE, EMBASE and WHO Global Database. Review included studies conducted in humans of any age with viral respiratory infections exposed to systemic NSAIDs of any kind. Studies on COVID-19, Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS) were all included irrespective of their sample size.

## Review of the evidence

In total 73 studies were included (28 studies in adults, 46 studies in children and one study included both adults and children. All studies were concerned with acute viral respiratory infections or conditions commonly caused by respiratory viruses, but none specifically addressed COVID-19, SARS or MERS. Review showed very low certainty evidence on mortality among adults and children.<sup>3</sup> Effects of NSAIDs on the risk for ischemic and hemorrhagic stroke and myocardial infarction in adults with acute respiratory infections are unclear.<sup>4,5</sup> Moderate to high certainty evidence showing little or no difference between ibuprofen and acetaminophen (paracetamol) among children with fever with regard to effects on death from all causes, hospitalization for any cause, acute renal failure and acute gastro-intestinal bleeding.<sup>6,7,8,9</sup> Most studies report that no severe adverse events occurred, or that only mild or moderate adverse events were observed. There was no evidence regarding the effects of NSAID use on acute healthcare utilization, explicit quality of life measures or long-term survival.

## Limitations

No direct evidence from patients with COVID-19, SARS or MERS was available. Therefore, all evidence included should be considered indirect evidence in relation to the use of NSAIDs prior to or during the management of COVID-19. Only one RCT included a sufficiently large number of participants to identify rare severe adverse events. The remaining evidence derives from smaller RCTs, which are likely to be underpowered for detecting rare severe adverse events, and from case control and cohort studies with methodological limitations. Studies included not only patients with confirmed viral respiratory infections and known pathogens, but also those with conditions commonly caused by respiratory viruses, such as upper respiratory tract infections and fever in children. It is likely that not all participants of these studies had viral respiratory infections. NSAIDs are a diverse set of drugs with diverging risk profiles for different populations and conditions. Not all studies distinguished between different types of NSAIDs. Some of the older studies are likely to have included patients taking specific NSAIDs that are no longer available on the market due to their known side effects

## Conclusions

At present there is no conclusive evidence of severe adverse events, acute healthcare utilization, long-term survival or quality of life in patients with COVID-19, SARS or MERS due to NSAIDs in children or in adults, but this absence of evidence should not be interpreted as evidence for the absence of such effects.

## References

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