



# Managing Fever in adults with possible or confirmed COVID-19 in Primary Care

Sophie Park, Jon Brassey, Carl Heneghan and Kamal Mahtani

19th March 2020

## Verdict

the current evidence does not support routine antipyretic administration to treat fever in acute respiratory infections and COVID-19.

Many protocols and professionals advise patients to self-medicate for Covid-19 using antipyretics (e.g. paracetamol and ibuprofen). The rapid and widespread purchase of antipyretic medication over-the-counter has led to temporary shortages.

## What is a fever?

A common symptom of Covid, influenza and sometimes other viral upper respiratory tract infections (URTI) is fever. Reports of the pattern of Covid symptoms suggest that fever is most common an average 5 days after exposure. The range of 'normal' temperatures **depends on the site**

[<https://www.racgp.org.au/afp/2015/januaryfebruary/a-is-for-aphorisms/>]

Site of measurement	Normal low	Normal high	Single measure fever	Multiple measures fever
Axilla	35.5	37.0	>37.5	-
Oral	35.6	37.7	>37.8	>37.2
Rectal	34.4	37.8	>38.0	>37.5
Tympanic	35.4	37.8	>38.0	-
Any	-	-	-	>1.1 over baseline

**A review of 'normal body temperature** [https://pubmed.ncbi.nlm.nih.gov/12000664/] in adults' including studies from 1935-1999 concluded the range of normal oral temperature was 35.6 c to 38.2 c. **The American College of Critical Care Medicine and Infectious Disease Society** [https://pubmed.ncbi.nlm.nih.gov/18379262/] define fever as core body temperature greater or equal to 38.3 c. **NICE consider** [https://cks.nice.org.uk/feverish-children-management#!backgroundSub] an infant or child has a fever if their temperature is 38°C or higher.

**A systematic review** [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6456186/] of normal body temperature found that older adults (age  $\geq 60$ ) had a lower temperature than younger adults (age  $< 60$ ) by 0.23°C, on average.

### What are the benefits of a fever?

Fever is a complex, physiological and adaptive response to infection. Fever is a symptom, rather than a diagnosis. It is important to establish the cause of fever in relation to the patient's clinical condition and symptom pattern – remember, some patients may have both Covid-19 and other illness.

- **Fever is common and is a good prognostic sign** [https://pubmed.ncbi.nlm.nih.gov/17481490/] in acutely unwell patients with infection, associated with higher rates of survival.
- In a prospective observational study (n= 502) **fever inhibited microbial reproduction and viral replication**, [https://pubmed.ncbi.nlm.nih.gov/25313306/] as well as accelerated the rate of phagocytosis.
- **Heat-shock proteins** [https://pubmed.ncbi.nlm.nih.gov/23199670/] (present in fever) are also thought to prevent thermal damage to cells by inhibiting pro-inflammatory-signalling pathways.
- **An individual's ability to mount a febrile response** [https://pubmed.ncbi.nlm.nih.gov/25313306/] has been shown to be a good prognostic sign in critically unwell patients (Lee 2012, Young 2012),

### What are the indications for taking an antipyretic in Covid-19?

**First, ask 'what symptom am I aiming to treat?'** For most adults, **there is no convincing evidence that fever** [https://pubmed.ncbi.nlm.nih.gov/31116598/] is itself detrimental and does not automatically require suppression.

**Children:** A systematic review on the prolongation of febrile illness with the use of antipyretics in children who have acute infections suggested antipyretics do not slow recovery from infectious diseases. Six papers were included in the review. Three focused on children with malaria and 3 considered general viral and respiratory infections and varicella. The mean difference in time to fever clearance was 4 hours and was faster in those receiving antipyretics compared with those not (95% CI -6.35 to -1.96 hours; P = .0002).

However, based on extrapolations from studies of the use of paracetamol following vaccination, showing reduced antibody response to some antigens (Prymula 2009),

they advocate avoidance of antipyretic use early in infections. Although childhood fevers can be lowered by antipyretics (Wong 2014), several randomised clinical trials have shown no evidence that antipyretic administration reduces the incidence of seizures in susceptible children (Offringa and Newton 2013).

**Pregnancy:** is not specifically covered in this document. See [here](#)

[<https://www.rcog.org.uk/coronavirus-pregnancy>]

**Elderly, or patients with comorbidities:** this group are thought to be the most susceptible to Covid-19 complications. The Elderly can have blunted febrile responses during severe infection (Hammond and Boyle 2011), which may indicate a less robust immune response. This group may also be more vulnerable to increased physiological demands during fever (Carey 2010, Launey 2011). Antipyretic medication in critically unwell patients with a limited cardiopulmonary reserve may reduce the risk of haemodynamic instability and hypoxic tissue damage (Kiekas 2013).

## Medications for fever

### Paracetamol

Most paracetamol studies report lower body temperature, however, reductions are modest.

**NICE BNF Cautions** [<https://bnf.nice.org.uk/drug/paracetamol.html>]

Before administering, check when paracetamol last administered and cumulative paracetamol dose over previous 24 hours; body-weight under 50 kg; chronic alcohol consumption; chronic dehydration; chronic malnutrition; hepatocellular insufficiency; long-term use (especially in those who are malnourished) Some patients may be at increased risk of experiencing toxicity at therapeutic doses, particularly those with a body-weight under 50 kg and those with risk factors for hepatotoxicity. Clinical judgement should be used to adjust the dose of oral and intravenous paracetamol in these patients. Co-administration of enzyme-inducing antiepileptic medications may increase toxicity; doses should be reduced.

For specific details on the management of poisoning, see Paracetamol, under **Emergency treatment of poisoning** [<https://bnf.nice.org.uk/treatment-summary/poisoning-emergency-treatment.html>].

### NSAIDs

**Ibuprofen has been shown** [<https://pubmed.ncbi.nlm.nih.gov/9070471/>] to reduce fever, tachycardia and oxygen consumption, but not prevent shock or acute respiratory distress syndrome, and it does not improve survival.

A randomized controlled trial (RCT) of intravenous ibuprofen in 455 patients who had sepsis (defined as fever, tachycardia, tachypnea, and acute failure of at least one organ system. There were reductions in temperature, heart rate, oxygen consumption, and lactic acidosis. Survival at 30 days (37% with ibuprofen compared with 40% placebo.

**In an RCT of ibuprofen,** [<https://pubmed.ncbi.nlm.nih.gov/24162940/>] paracetamol and steam with patients with ARIs in primary care showed that while children and patients with chest infections experienced some symptomatic relief with ibuprofen alone, most patients gained no benefit from advice to use ibuprofen alone; 889 patients were randomised to advice on analgesia (take paracetamol, ibuprofen, or both), dosing of analgesia (take as required v regularly), and steam inhalation (no inhalation v steam inhalation). Main results are:

- Advice on dosing or on steam inhalation did not affect outcomes.
- Compared with paracetamol, symptoms were not significantly different from ibuprofen or the combination of ibuprofen and paracetamol (0.11, -0.04 to 0.26).
- There was no evidence of benefit with ibuprofen among most subgroups (presence of otalgia; previous duration of symptoms; temperature >37.5 °C; severe symptoms),
- In the subgroup with chest infections, the equivalent of one in two symptoms was rated as slightly rather than a moderately bad problem.
- Reconsultations with new/unresolved symptoms or complications were slightly higher in those taking ibuprofen 20% vs 12% with paracetamol (adjusted risk ratio 1.67, 1.12 to 2.38),
- Mild thermal injury with steam was documented for four patients (2%)

In combination with paracetamol; or use of a regular regime. An RCT in 464 children studied the use of paracetamol, ibuprofen and combined regimes in children aged 6 to 36 months with fever. Children who received alternating ibuprofen and acetaminophen had a lower mean temperature and more rapid a reduction in fever. No regimes were associated with emergency department visits or serious long-term complications.

### See: NSAIDs in Acute Respiratory Infection for further advice

[<https://www.cebm.net/oxford-covid-19/nsaids-in-acute-respiratory-infection/>]

**Disclaimer:** the article has not been peer-reviewed; it should not replace individual clinical judgement and the sources cited should be checked. The views expressed in this commentary represent the views of the authors and not necessarily those of the host institution, the NHS, the NIHR, or the Department of Health and Social Care. The views are not a substitute for professional medical advice.