

Supporting Information

Supplementary material

This appendix was part of the submitted manuscript and has been peer reviewed. It is posted as supplied by the authors.

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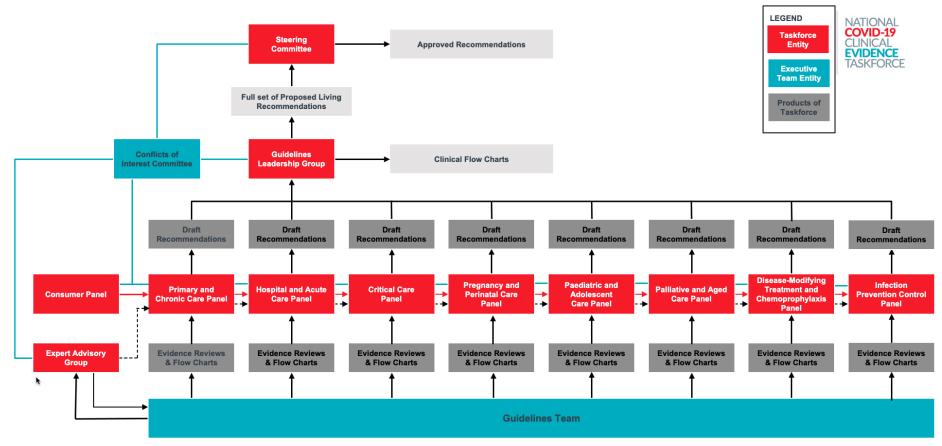


Figure 1. National COVID-19 Clinical Evidence Taskforce organisational structure. Detailed information is available at https://covid19evidence.net.au/about-the-taskforce.

Table 1. Overarching principles on caring for children and adolescents in the context of COVID-19 adopted by the Paediatric and Adolescent Care Panel

The Taskforce regards children, adolescents and family-centred care indispensable in managing the health and wellbeing of children and adolescents and urges continuity of these services, with a particular focus on equity of access. We support efforts to ensure children and adolescents are able to remain in contact with parents, carers and families despite COVID-19, recognise this may require specific attention to infection control management practices and may involve adjunctive use of technology such as video-calling. Health facilities should have plans to manage these issues for children and adolescents. We endorse the approach and goals established by the United Nations Policy Brief: the impact of COVID-19 on children.¹

Child-centred services include among others: schooling, nutrition programs, maternal and newborn care, immunisation services, sexual and reproductive health services, HIV treatment, mental health and psychosocial services, birth registration, community-based child protection programs, out-of-home care, and case management for children requiring supplementary personalised care, including those living with long-term medical conditions, disabilities and victims of abuse or family violence. Particularly relevant for the Australian context is to ensure continuity of Aboriginal and Torres Strait Islander child and adolescent services.

Table 2. Disease-modifying treatment recommendations for children and adolescents: drugs recommended only in research

Drugs recommended only in research

Do not use (any of the following list) for the treatment of COVID-19 outside of randomised controlled trials with appropriate ethical approval (GRADE: only in research recommendation):

- Anakinra
- Aprepitant
- Angiotensin II receptor agonist (C21)
- Baloxavir marboxil
- Bamlanivimab
- Bamlanivimab plus etesevimab
- Baricitinib
- Bromhexine hydrochloride
- Budesonide
- Camostat mesilate
- Chloroquine
- Combined metabolic activators
- CT-P59 monoclonal antibody
- Darunavir-cobicistat
- Dutasteride
- Enisamium
- Favipiravir
- Fluvoxamine
- Human mesenchymal stem cells
- Intravenous immunoglobulin
- Intravenous immunoglobulin plus methylprednisolone
- Interferon-β-1a (inhaled)
- Interferon-β-1b
- Interferon-γ
- Interferon-κ plus trefoil factor 2
- Ivermectin
- Ivermectin plus doxycycline
- Lenzilumab
- Nitazoxanide
- N-acetylcysteine
- Peginterferon-λ
- Recombinant human granulocyte colony-stimulating factor
- REGEN-COV
- Ruxolitinib
- Sarilumab
- Sofosbuvir-daclatasvir
- Sotrovimab
- Sulodexide
- Telmisartan
- Tofacitinib
- Triazavirin
- UmifenovirVitamin C
- Vitamin D analogues (calcifediol/cholecalciferol)
- Zinc

These treatments have typically been evaluated in one or two trials with a small number of adult participants and with no children included, resulting in low or very low certainty evidence from which no conclusions can be drawn. The Taskforce therefore recommends that these treatments should not be used outside of randomised trials, with emphasis on trials enrolling special populations including children and adolescents

Table 3. Paediatric inflammatory multisystem syndrome (PIMS-TS) definition adapted from the UK Royal College of Paediatrics and Child Health guidance statement²

A child presenting with persistent fever, inflammation (neutrophilia, elevated CRP and lymphopenia) and evidence of single or multi-organ dysfunction (shock, cardiac, respiratory, renal, gastrointestinal or neurological disorder) with additional features. This may include children fulfilling full or partial criteria for Kawasaki disease

Exclusion of any other microbial cause, including bacterial sepsis, staphylococcal or streptococcal shock syndromes, infections associated with myocarditis such as enterovirus (waiting for results of these investigations should not delay seeking expert advice)

SARS-CoV-2 PCR testing may be positive or negative. All stable children should be discussed as soon as possible with specialist services to ensure prompt treatment (paediatric infectious disease/cardiology/rheumatology). There should be a low threshold for referral to paediatric intensive care using normal pathways

Additional features include:

- clinical
 - all: persistent fever > 38.5°C
 - most: oxygen requirement, hypotension
 - some: abdominal pain, confusion, conjunctivitis, cough, diarrhoea, headache, lymphadenopathy, mucus membrane changes, neck swelling, rash, respiratory symptoms, sore throat, swollen hands and feet, syncope, vomiting
- imaging and electrocardiogram (ECG)
 - echocardiogram and ECG: myocarditis, valvulitis, pericardial effusion, coronary artery dilatation
 - b chest x-ray: patchy symmetrical infiltrates, pleural effusion
 - abdominal ultrasound scan: colitis, ileitis, lymphadenopathy, ascites, hepatosplenomegaly
 - computed tomography scan of the chest: same as for chest x-ray it may demonstrate coronary artery abnormalities if done with contrast
- laboratory
 - ▶ all: abnormal fibrinogen, absence of potential causative organisms (other than SARS-CoV-2), high CRP, high D-dimers, high ferritin, hypoalbuminaemia, lymphopaenia, neutrophilia in most (normal neutrophils in some)
 - some: acute kidney injury, anaemia, coagulopathy, high IL-10 (if available),* high IL-6 (if available),* neutrophilia, proteinuria, raised creatine kinase, raised lactic acid dehydrogenase, raised triglycerides, raised troponin, thrombocytopenia, transaminitis

CRP = C-reactive protein; CT = computed tomography; ECG = electrocardiogram; IL = interleukin; PCR = polymerase chain reaction; PIMS-TS = paediatric inflammatory multisystem syndrome; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2. * These assays are not widely available. CRP can be used as a surrogate marker for IL-6.

References

- 1. National COVID-19 Clinical Evidence Taskforce. About the taskforce. https://covid19evidence.net.au/about-the-taskforce/ (viewed May 2021).
- 2. World Health Organization. Multisystem inflammatory syndrome in children and adolescents with COVID-19: scientific brief, 15 May 2020. https://apps.who.int/iris/handle/10665/332095 (viewed May 2021).