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MELBOURNE

Melbourne Medical School
Department of Paediatrics

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COVID-19 KIDS RESEARCH EVIDENCE UPDATE

WHAT THE MELBOURNE
CHILDREN'S CLINICIANS,
SCIENTISTS, EPIDEMIOLOGISTS,
AND MEDICAL STUDENTS HAVE
BEEN READING THIS WEEK

Weekly Update No.16

6th August 2020

BE COVIDSAFE

CURRENT STATUS OF CONFIRMED CASES



43

CURRENT CASES
 INTENSIVE CARE UNITS (ICU)

| ACT | NSW | NT | QLD | SA | TAS | VIC | WA |
|-----|-----|----|-----|----|-----|-----|----|
| 0 | 8 | 0 | 0 | 0 | 0 | 35 | 0 |

439

CURRENT CASES
 ADMITTED TO HOSPITALS

| ACT | NSW | NT | QLD | SA | TAS | VIC | WA |
|-----|-----|----|-----|----|-----|-----|----|
| 0 | 13 | 3 | 7 | 0 | 0 | 416 | 0 |

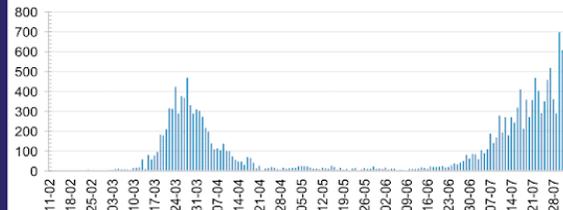
4,386,911

0.4% POSITIVE

TOTAL TESTS
 CONDUCTED

| ACT | NSW | NT | QLD |
|----------|-----------|-----------|----------|
| 53,182 | 1,526,863 | 25,351 | 569,392 |
| POSITIVE | POSITIVE | POSITIVE | POSITIVE |
| 0.2% | 0.2% | 0.1% | 0.2% |
| SA | TAS | VIC | WA |
| 250,229 | 70,359 | 1,633,953 | 257,582 |
| POSITIVE | POSITIVE | POSITIVE | POSITIVE |
| 0.2% | 0.3% | 0.7% | 0.3% |

DAILY NUMBER OF REPORTED CASES

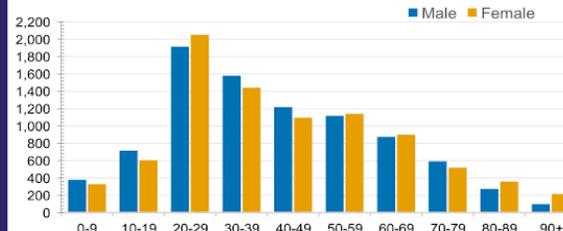


CASES IN AGED CARE SERVICES

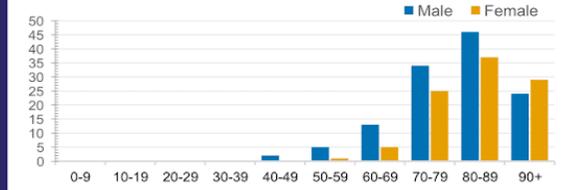
| Confirmed Cases | Australia | ACT | NSW | NT | QLD | SA | TAS | VIC | WA |
|-----------------------------|-----------|-----|---------|----|-------|-------|-------|----------|-------|
| Residential Care Recipients | 839 (45) | 0 | 61 (32) | 0 | 1 (1) | 0 | 1 (1) | 776 (13) | 0 |
| In Home Care Recipients | 54 (5) | 0 | 13 (13) | 0 | 8 (8) | 1 (1) | 5 (3) | 26 (7) | 1 (1) |

Cases in care recipients [recovered] (deaths)

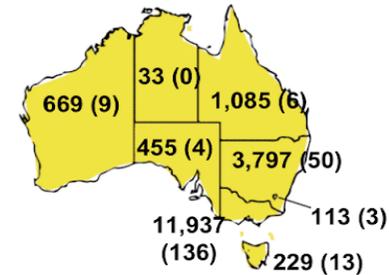
CASES BY AGE GROUP AND SEX



DEATHS BY AGE GROUP AND SEX



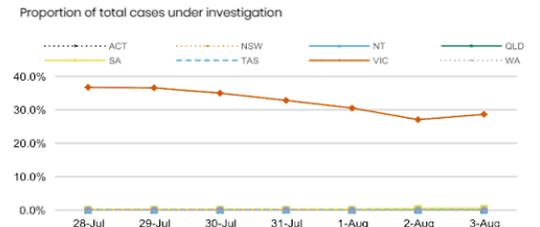
CASES (DEATHS) BY STATE AND TERRITORIES



CASES BY SOURCE OF INFECTION



PUBLIC HEALTH RESPONSE MEASURE



Last updated 3 August 2020

This infographic is updated every afternoon based on the data we receive by 3.00pm from states and territories

Source: Australian Government: Department of health [Internet]. 2020 [updated 2020 August 4; cited 2020 July 29]. Available from: <https://www.health.gov.au/news/health-alerts/novel-coronavirus-2019-ncov-health-alert/coronavirus-covid-19-current-situation-and-case-numbers#at-a-glance>

GUEST EDITORIAL

Professor Steve Graham - Murdoch Children's Research Institute,
The University of Melbourne and The Royal Children's Hospital

Welcome to the 16th edition of the weekly report and many thanks to the team who continue to provide highlights and summary reviews of recent literature, particularly relevant to aspects of epidemiology, clinical care and public health of women and children during COVID19. This edition coincides with a major escalation of public health measures in Victoria because of persistently high numbers of new and active cases in the community, and increasing numbers of COVID-related deaths, especially in our elderly population. These measures include the closure of all schools, further reinforcing the realisation that this pandemic will continue to provide huge challenges with massive consequences for a long time yet.

The highlights from this week's literature reviews are listed below. The quantity of output of published (or pre-published) COVID-19-related literature continues undiminished, while the quality or study limitations of many of the publications continue to challenge the clarity of interpretation of the findings. Conclusions often highlight possibilities or associations rather than provide a definitive message, and as for most pandemics, the relative importance of consequences and impact of potential solutions will vary between settings, populations and regions.

The uncertainty is not surprising as we are likely still in a relatively early and emerging phase of this pandemic, especially in low- and middle-income countries with large vulnerable populations of children, adolescents and mothers. This week's highlights include another projection of the largely "secondary" or indirect impact of the COVID-19 pandemic on such populations, this one providing dire predictions of the immediate and long-term devastating impact of food insecurity and childhood malnutrition. This forecasting is published as a Lancet commentary, was led by the International Food Policy Research Institute in Washington and is co-authored by Nick Scott of the Burnet Institute, Melbourne. In recent weeks within our region, we have also noted, with concern, the large and rising numbers of cases in Indonesia and the Philippines, or the recent increases after months of very few cases in Viet Nam and Papua New Guinea. The impact on adolescents of infectious disease pandemics, such as HIV or tuberculosis, has often been neglected. The GAGE (Gender and Adolescence Global Evidence) group has sought to provide a voice and perspective of COVID-19 experience from adolescents in Ethiopia, Jordan, Lebanon and Bangladesh, where GAGE has research teams based.

One feature of COVID-19 which is consistently clear and again addressed by a number of publications, is the serious cardiovascular-related pathology. It is concerning to learn that the majority of a cohort of German adults without prior co-morbidities and most of whom did not require hospitalisation during the course of COVID-19, still had abnormal cardiovascular findings due to ongoing myocarditis between 2-3 months following diagnosis. Is this a manifestation of the sensitivity of modern diagnostic tests that measure cardiac function following viral illnesses or is this specific to COVID-19 with clinical impact on mortality and quality of life?

Again, it is too early to know, but what are the long-term consequences? There are further reports of multisystem inflammatory syndrome in children, commonly fulfilling criteria for Kawasaki disease, in children hospitalised with COVID-19 in Spain. The long-term cardiovascular effect in children is a focus of proposed research on Melbourne Children's Campus, as it has been for other early childhood infections.

Children, transmission and school closures – critically important to get the balance right for public health implementation of benefit v risk for so many compelling reasons, but still shrouded in uncertainty. An article from the USA where the beginning of a new school year approaches in the context of a major epidemic was published last week in the New England Journal of Medicine. The authors weigh the reasons as to why the issue is so complex - and important - and so contested, and refer to experience from other countries to make the case for the physical re-opening of primary schools (as for other "essential services") in low transmission settings with appropriate measures in place. A recent study of age-related viral load might provide a counter argument. Young children with mild to moderate COVID-19 were found to have higher amounts of SARS-CoV-2 viral RNA in their nasopharynx compared with older children and adults. However, there are more factors that determine transmission risk or likelihood than pharyngeal load.

School closure was one of the most consistently applied interventions in response to the pandemic in the USA, with all 50 states schools from kindergarten to grade 12 and childcare centres in March. An association of school closures with the incidence and mortality of COVID-19 in the USA was published last week in JAMA. School closure was associated with a significant reduction in incidence and mortality, and findings were extrapolated to provide estimates of impact – over 1 million less cases over a one-month period and 40,600 fewer deaths. However, association does not mean direct causality and there were so many other interventions around the same time which could provide a long list of potential confounders. The many limitations for interpretation are highlighted by the accompanying editorial and by our own expert reviewer. Nonetheless, the authors conclude that "it remains possible" that school closure would have such a dramatic impact. This perhaps best sums up the ongoing uncertainty of many issues at so many levels, and reinforces the importance of high quality evidence and critical review.

HIGHLIGHTS

- > Recent stage three control measures in Victoria have averted ~9,000–37,000 infections between 2nd and 30th July, but there remains significant ongoing growth, with an estimated further 14% reduction in transmission required to control the epidemic.
- > The value of masks - surgical masks are better than two-layer cloth masks which are better than one layer of cloth mask. All masks are vastly better than no mask at all. Watch this video: [thoraxjnl-2020-215748supp001.wmv](https://www.youtube.com/watch?v=thoraxjnl-2020-215748supp001.wmv).
- > Findings from a study looking at SARS-CoV-2 load and an outbreak in a school camp, suggest children can be important drivers of SARS-CoV-2 spread in the general population.
- > Scent dogs are being trained to detect SARS-CoV-2: promising findings suggest further research needed to determine their role in detecting infections in public gatherings.
- > School closures associated with reductions in mortality in the U.S., but subject to substantial confounding as other mitigation strategies employed simultaneously.
- > When to re-open schools? - An opinion piece suggests face-to-face primary school classes should be considered essential; when community transmission is low, secondary schools should re-open.
- > A recombinant vaccine, consisting of spike protein receptor-binding domain residues is immunogenic in pre-clinical trials and protects non-human primates in an infection challenge model.
- > High-throughput analysis describes 21 molecules identified as potential therapeutic options for SARS-CoV-2.
- > Some ACE2 genomic variants and TMPRSS2 polymorphisms may play important roles in susceptibilities to COVID-19.
- > A brief report raises concerns about COVID-related maternal mortality in middle and low-income countries being higher than that reported from high-income countries, but most data is from one middle-income country, Brazil. Highlights the need for better data.
- > 140 million more people will be living on < U.S. \$1.90 / day, doubling acute food insecurity to 265 million worldwide resulting in increased childhood malnutrition and an additional 130,000 deaths in young children this year.
- > Blood type may be associated with COVID-19 but there is a need for better studies.
- > Study findings indicate that the lineage giving rise to SARS-CoV-2 has been circulating undetected in bats for decades and that bats are the primary reservoir for the SARS-CoV-2 lineage.
- > Treatment for ADHD may help with controlling behaviours that make people with ADHD more likely to be able to comply with public health mitigation measures.
- > Patients who report significant idiopathic smell loss but test negative for COVID-19, should be prioritised for re-testing.

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Response to COVID-19 and any other medical condition at this time is based on science that is new, often uncertain, subject to change, and dependent on context.

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ADULT MEDICINE

Evelyn Andrews – 4th Year Medical Student,
Department of Paediatrics, The University of Melbourne

The best COVID-19 predictor is recent smell loss - a cross-sectional study (not peer reviewed)

<https://protect-au.mimecast.com/s/eyzgCGvmpxh104003tkRvrj?domain=medrxiv.org>

- > This study aimed to investigate whether olfactory loss was a reliable predictor of COVID-19 infection.
- > An online survey was completed by 15,747 adults with current or recent respiratory illness. Self-reported COVID-19 status was used to create two groups: COVID-19 positive (C19+) and negative (C19-). The survey used binary, categorical and continuous measures to quantify self-reported changes in chemosensory ability.
- > C19+ patients reported greater loss of smell (-82.5 ± 27.2 vs -59.8 ± 37.7), taste (-71.6 ± 31.8 vs -55.2 ± 37.5) and chemesthesis ability (-36.8 ± 37.1 vs -28.7 ± 37.1) compared with C19- patients. Both groups report a similar degree of nasal obstruction.
 - Change in olfactory function is the single best predictor of COVID-19 infection (AUC=0.71), followed by a change in taste ability (AUC=0.64-0.65).
 - Continuous rating of olfactory function is better at predicting COVID-19 infection compared with a binary (yes/no) assessment.
 - The Olfactory Determination Rating scale in COVID-19 (ODoR-19) is a visual analogue scale for quantifying olfactory loss. A score ≤ 2 indicates high risk of COVID-19 infection.
- > Conclusions: Chemosensory impairment is the strongest predictor of COVID-19 infection. The ODoR-19 tool is a simple and accurate measure of olfactory loss, which may be added to the repertoire of COVID-19 screening tools. Patients who test negatively for COVID-19, but who report significant idiopathic smell loss (ODoR-19 ≤ 2), should be prioritised for re-testing.
- > Limitations: There was a high proportion of COVID-19 positive participants and a high proportion of chemosensory disorders in both groups. These factors may have led to an underestimation of the positive correlation between smell loss and COVID-19. Online sampling may have disproportionately selected for patients with interest in altered chemosensation.

Reviewed by: Dr Wonie Uahwatanasakul

Renee Cocks - 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Outcomes of cardiovascular magnetic resonance imaging in patients recently recovered from coronavirus disease 2019.

<https://jamanetwork.com/journals/jamacardiology/fullarticle/2768916>

- > The effects of SARS-CoV-2 infection on the cardiovascular system in unselected patients and those with no pre-existing conditions is not well understood.
- > This is a prospective observational cohort study conducted at the University Hospital Frankfurt. 100 patients who recovered from COVID-19 between April and June 2020 were followed up for blood tests and cardiovascular magnetic resonance imaging (CMR). 67 patients recovered at home, with symptoms ranging from asymptomatic to minor and moderate symptoms. One-third (33 patients) required hospitalisation, with two patients requiring mechanical ventilation.
- > Comparisons were made with age-matched and sex-matched control groups of healthy volunteers (n=50) and risk factor matched patients (n=57), matched for hypertension, diabetes, smoking, known coronary artery disease or co-morbidities (asthma and COPD).
- > Cardiovascular magnetic resonance imaging measures cardiac inflammation through measuring abnormal native T1 (fibrosis or oedema) and native T2 (specific for oedema).
- > 53% of the patients were male, and the median age was 49 years.
 - The median time between COVID-19 diagnosis and cardiovascular magnetic resonance imaging was 71 days.
 - At the time of CMR, high sensitivity troponin was detectable in 71% patients and significantly elevated in 5% patients.
 - 78% patients who recently recovered from COVID-19 had abnormal CMR findings- including raised myocardial native T1 (73%), raised myocardial native T2 (60%), myocardial late gadolinium enhancements and pericardial enhancement.
 - Compared with healthy controls and risk factor matched controls, patients who recently recovered from COVID-19 had lower left ventricular ejection fraction, higher left ventricular volumes, higher left ventricle mass and raised native T1 and T2.
 - There was a statistically significant difference between patients who recovered at home vs in hospital for native T1 measures, but not for native T2 or other measures.
 - Endomyocardial biopsy in patients with severe findings revealed active lymphocytic inflammation.
- > Limitations: the long term health effects of these findings cannot be determined; several patients within the cohort had new or persistent symptoms, increasing the likelihood of positive CMR findings.
- > Of this cohort of German adults recently recovered from COVID-19 infection, one-third required hospitalisation but the majority recovered at home, and so this cohort represents a range of severity.

- It is concerning that two to three months following diagnosis the majority had ongoing evidence of myocardial inflammation which was independent of pre-existing conditions and severity of the acute disease.
- Investigation of the long term cardiovascular consequences of COVID-19 will be important.

Reviewed by: Professor Steve Graham

Ha My Ngoc Nguyen – 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Lung fibrosis: an undervalued finding in COVID-19 pathological series

<https://www.thelancet.com/action/showPdf?pii=S1473-3099%2820%2930582-X>

- > Autopsy findings from eight patients who died in ICU in Italy with COVID-19 after a mean disease duration of 31 days.
- > This short research letter adds to previous autopsy findings of 38 patients who died with COVID-19 in Italy that showed that diffuse alveolar damage was the main pathological finding, along with fibrin thrombi in small arterial vessels.
- > Observed significant fibrotic lung parenchymal remodelling, characterised by fibroblast proliferation, airspace obliteration, and micro-honey combing in many available cryobiopsies from the eight patients. It remains unknown whether the fibrotic changes are due to viral infection, secondary cytokine cascade, treatment- or ventilation-related, or a combination of factors.

Reviewed by: Professor Steve Graham

CLINICAL PAEDIATRICS

Ha My Ngoc Nguyen – 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

COVID-19 in children with chronic kidney disease: findings from U.K. renal registry <https://adc.bmj.com/content/early/2020/07/24/archdischild-2020-319903>

- > The NHS England COVID-19 service evaluation has identified 220 confirmed cases of children admitted to hospital in England, of whom 44.4% of cases have a co-existing disease; two children are reported to have chronic kidney disease (CKD).
- > The U.K. Renal Registry (UKRR) and in collaboration with the British Association for Paediatric Nephrology (BAPN) have set up an ongoing weekly COVID-19 surveillance system specifically for children with CKD.
- > This helps to report cases on the population of interest and analyses data for research.
- > Between 26th March and 15th July 2020, five U.K. children with CKD testing positive for COVID-19 were reported; none have died. This includes children with Stage IV CKD and Stage V requiring dialysis or a kidney transplant. 4/5 patients were male, with a median age of 11.
- > While there is a low number of reported cases (though the number of children in the U.K. with CKD is not provided in this paper), the data supports the observation that infection in children with chronic co-existing disease is fortunately uncommon.
- > These findings have allowed relaxed shielding criteria for children with kidney disease and revised recommendations adopted by the U.K. government.

Reviewed by: Dr Martin Wright

Samar Hikmat – 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Multi-inflammatory Syndrome in Children related to SARS-CoV-2 in Spain <https://academic.oup.com/cid/article/doi/10.1093/cid/ciaa1042/5876334>

- > Multisystem inflammatory syndrome (MIS-C) is a potentially severe infection that occurs in some children following SARS-CoV-2 infection. It shares features of Kawasaki disease, toxic shock syndrome and macrophage activation syndrome.
- > This article presents a case series of children (<18 years) with MIS-C from 49 hospitals in Spain, auspiced by the Spanish Society of Paediatrics, to describe the epidemiological and clinical features of the syndrome.
- > Of 252 hospitalised children with SARS-CoV-2 infection from 1st March to 1st June 2020; 31 (12%) were diagnosed with MIS-C and/or Kawasaki disease.
 - The median age was 7.6 years, 58% male.

The peak of MIS-C cases was one month after the peak of admissions for other COVID-19 related reasons and decreased afterwards.

- 30/31 (97%) had microbiological or serological evidence of SARS-CoV-2 infection. The remaining one patient had household contact with a COVID-19 patient.
- All patients with the exception of one met the WHO case definition for MIS-C characterised by:
 - Fever for ≥ 3 days.
 - Plus two of the following:
 - Rash or bilateral non-purulent conjunctivitis, or mucocutaneous signs (occurred in 21/31; 67%).
 - Hypotension or shock (occurred in 15/31; 48%).
 - Features of myocardial dysfunction: pericarditis, valvulitis, arrhythmias, or coronary abnormalities (occurred in 19/31; 61%). Six (19%) had only elevation of NT-proBNP (marker of heart dysfunction).
 - Evidence of coagulopathy (occurred in 29/30; 97%).
 - Acute G.I. symptoms: diarrhoea, vomiting, or abdominal pain (occurred in 27/31; 87%).
 - Plus elevated inflammatory markers.
 - Plus no obvious microbial cause of inflammation.
 - The patient who did not meet the WHO criteria didn't have elevated inflammatory markers which were attributed to her chronic immunosuppressive steroid therapy for the pulmonary interstitial disease.
- 13/31 (45%) fulfilled the criteria of complete or incomplete Kawasaki disease.
- 20/31 (65%) were admitted to the ICU, 6/31 (19%) required invasive mechanical ventilation.
- Treatment included: remdesivir (6%), lopinavir/ritonavir (23%), corticosteroids (68%), intravenous immunoglobulin (65%), broad-spectrum antibiotics (90%).
- One patient developed coronary aneurysm, and one patient with acute leukemia and bone marrow transplant died. The rest recovered without further complications.
- > Limitations include exclusion of cases without the microbiological, serological or epidemiological link to COVID-19.

Reviewed by: Dr Martin Wright

Natalie Commins - 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Diagnosing SARS-CoV-2 related multisystem inflammatory syndrome in children (MIS-C): focus on the gastrointestinal tract and the myocardium
<https://academic.oup.com/cid/article/doi/10.1093/cid/ciaa1080/5876871>

- > This is a commentary on the relationship between Kawasaki Disease (K.D.), MIS-C, and COVID-19, in conjunction with the paper from the Spanish Society of Paediatrics, reported above.
- > The older age group (median 7.6 years) and a high proportion of gastrointestinal symptoms (87%) are some features suggesting a difference between MIS-C and K.D.
- > Many of the features of K.D. and MIS-C are non-specific to any virus infections, but unique features of MIS-C appear to be related to the gastrointestinal tract and myocardium.
- > The aetiology of MIS-C is uncertain. Possible theories include a cytokine storm from GIT SARS-CoV-2 infection or a post-infectious phenomenon.
- > The author queries whether MIS-C and K.D. are in fact, different diseases.
 - Virus-like inclusion bodies present in tissues affected by K.D. are the target for antibodies a patient produces after the disease, and so represent strong evidence for a single viral agent as the cause.
 - However, the epidemiology of K.D. has remained unchanged for 50 years and is seen in younger children compared to the children who tend to develop MIS-C.
 - Whilst acute myocardial complications are part of MIS-C, so far, there is no evidence of persisting coronary artery aneurysms.
 - As the prevalence of COVID-19 increases, there is an increasing chance children with K.D. will have co-existing positivity for SARS-CoV-2 infection.
- > MIS-C is not common, and children generally show improvement with IV gammaglobulin and/or corticosteroids.
- > More research is required in order to further define MIS-C as a clinical entity and to distinguish it from other clinical syndromes such as K.D.

Reviewed by: Dr Martin Wright

CRITICAL CARE

Benjamin Watson – 4th Year Medical Student,
Department of Paediatrics, The University of Melbourne

Ventilator allocation for pediatrics during COVID-19 - how we avoided drawing lots for tots

<https://www.tandfonline.com/doi/pdf/10.1080/15265161.2020.1779856?needAccess=true>

- > This was an open peer commentary led by Massachusetts General Hospital discussing the difficulties of allocating ventilatory support to paediatric patients during the COVID-19 pandemic.
- > The public understands that, in a crisis, there is no willing neglect – but the enactment of difficult decisions that must and will be made.
- > However, there is the concern of discriminatory allocation and some considerations (such as the determining ventilatory eligibility by age, is unethical).
- > Additionally highlighted is the moral distress amongst providers forced to choose who gets a ventilator.
- > This hospital developed a formal ventilator allocation policy utilising a complex score and colour code based on organ dysfunction, benefits of medical intervention, and short-term mortality.
- > Given that this hospital was a mixed adult/paediatric hospital, one outstanding fact was the reality of prolonged neonatal ventilation for infants and children – a process which would preclude the availability of resources for adult COVID-19 patients.
- > Thus the hospital incident command made two decisions:
 - Closure of paediatric admissions and transition of staff to providing adult ICU care.
 - Two neonatal options were permitted: immediate transfer post-delivery to children's hospital, or short term ventilation with early extubating by 48 hours post-birth.
- > Considerations: This hospital had the highest volume of COVID-19 positive patients in the state, and there is a children's hospital within ten miles.
- > This solution avoided staff having to make difficult decisions or to incur moral distress.
- > Additionally, the decision was transparent and based on evidence of need and available resources.

Reviewed by: Dr Wonie Uahwatanaskul

DIAGNOSTICS & SAMPLING

Rose Noble Kizhakekara – 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Scent dog identification of samples from COVID-19 patients - a pilot study

<https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-020-05281-3>

- > Eight detection dogs were trained for one week to detect saliva or tracheobronchial secretions of SARS-CoV-2 infected patients in a double-blinded randomised controlled study.
- > Average diagnostic sensitivity was 82.6% and diagnostic specificity was high at 96.4%. All dogs had high diagnostic specificity, but there was a varied range of sensitivity for an individual dog and between dogs. There was no difference in saliva and tracheobronchial sample detection rates.
- > Within 1012 sample presentations, dogs achieved an average detection rate of 94% with 157 correct indications of positive, 792 correct rejections of negative, 33 false-positive and 30 false-negative indications.
- > Fast and reliable testing is important for effective infection control. This method could potentially be employed in public areas such as airports and sports events.
- > These are preliminary results, and further research must be conducted before this method is employed, including research into analytical sensitivity (e.g., differing dilutions and stages of disease) and analytical specificity (e.g., differentiation to other lung diseases including other respiratory infections).
- > This study used inactivated virus samples. In a real-world setting, the risk of detection dogs also needs to be considered.

Reviewed by: Dr Celeste Donato

EPIDEMIOLOGY & PUBLIC HEALTH

Professor Fiona Russell - Director of Child and Adolescent PhD Program, Department of Paediatrics, the University of Melbourne; Group Leader Asia-Pacific Health Research, MCRI

Victoria's response to a resurgence of COVID-19 has averted 9,000-37,000 cases in July 2020

https://www.mja.com.au/journal/2020/victorias-response-resurgence-covid-19-has-averted-9000-37000-cases-july-2020?utm_source=carousel&utm_medium=web&utm_campaign=homepage

- > The resurgence of COVID-19 in Victoria led to multiple control measures being introduced in early July; however, the ongoing high number of daily cases has led to concern about the impact of the measures on COVID-19 transmission.
- > Daily diagnosed COVID-19 cases in Victoria were analysed, examining the effectiveness of control measures to date.
- > Control measures were estimated to have reduced the reproduction number from 1.75 to 1.16 and averted 9,000–37,000 infections between 2nd and 30th July.
- > Despite this reduction, there remains significant ongoing growth, with an estimated further 14% reduction in transmission required to control the epidemic.

Re-opening primary schools during the pandemic

<https://www.nejm.org/doi/full/10.1056/NEJMms2024920>

- > School closures mean kids lose out on essential educational, social, and developmental benefits; but the economy nor the health care system will be able to return to full strength given parents' caretaking responsibilities.
- > Highlights inequities in the U.S. regarding class size, overcrowding etc.
- > What is the role of children in transmission? Findings from a few contact-tracing studies suggest that children may be less infectious than adults, but the strength of the evidence is weak. May be age-related.
- > School outbreaks:
 - COVID-19 outbreaks in high schools in France, Israel, and New Zealand did not extend to nearby elementary schools, which suggests that susceptibility, infectiousness, or both are lower among younger children.
 - When schools in the Netherlands opened in April with low community transmission, they cut class sizes in half but did not enforce distancing among students younger than 12. Case rates have remained flat.

- > When to re-open schools?
 - Schools in low-transmission settings could probably provide pedagogically sound and socio-emotionally appropriate instruction to all students, in person, in ways that do not put educators or families at undue risk.
 - Adults would need to maintain social distance from each other and engage in other measures to reduce adult-to-adult transmission: e.g., wearing PPE, closing school buildings to all non-staff adults, and holding digital staff meetings.
 - Authors argue that primary schools are essential - outlines measures to take to protect staff.

SARS-CoV-2 transmission and infection among attendees of an overnight camp – Georgia, June 2020

<https://www.cdc.gov/mmwr/volumes/69/wr/mm6931e1.htm>

An outbreak in 597 attendees in a school summer camp is reported.

- > The median age was 12 years (range = 6 - 19 years).
- > The median age of staff members and trainees was 17 years (range = 14 - 59 years).
- > Test results were available for 344 (58%) attendees; among these, 260 (76%) were positive.
- > The overall attack rate was 44%.
 - 51% among those aged 6 - 10 years.
 - 44% among those aged 11 - 17 years.
 - 33% among those aged 18 - 21 years.
- > Asymptomatic infection was common and potentially contributed to undetected transmission.
- > Limitations: attack rates presented are likely an underestimate because cases might have been missed among persons not tested or whose test results were not reported; some cases might have resulted from transmission occurring before or after camp attendance; it was not possible to assess individual adherence to COVID-19 prevention measures.
- > These findings demonstrate that children are susceptible to SARS-CoV-2 infection and that they efficiently spread SARS-CoV-2 when living in close contact.
- > This demonstrates that physical distancing and consistent and correct use of cloth masks should be emphasised as important strategies for mitigating transmission in congregate settings, including schools, boarding schools, and residential colleges.

Samar Hikmat – 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Association between statewide school closure and COVID-19 incidence and mortality in the U.S.

<https://jamanetwork.com/journals/jama/fullarticle/2769034>

- > School closures were introduced as one of the public health interventions in all U.S. states in an attempt to reduce the spread of SARS-CoV-2 despite a lack of evidence regarding the effectiveness of this strategy.
- > This article describes a population-based interrupted time series analysis of all 50 U.S. states, conducted between 9th March to 7th May 2020. The study aimed to determine if there was a temporal association between the timing of primary and secondary school closures and subsequent COVID-19 incidence and mortality. Other public health interventions were included as covariates.
- > School closure was associated with a decline in COVID-19 incidence (–62% adjusted relative change in incidence per week) and decline in COVID-19 mortality (–58% adjusted relative change in mortality per week). This translates into an estimated absolute difference in the incidence of 423.9 cases per 100,000 and the absolute difference in mortality of 12.6 deaths per 100,000.
 - States that closed schools earlier, when the cumulative COVID-19 incidence was low, had a larger relative change in both COVID-19 incidence (–72%) and mortality (–64%).
 - States that closed schools later when COVID-19 cumulative incidence was high, showed smaller relative declines in incidence (–49%) and mortality (–53%).
- > Limitations: School closures were introduced around the same time (IQR 2-14 days) as other public health interventions (including non-essential business closures, restaurant and bar closure, prohibiting large gatherings, recommendations for increased handwashing). It is difficult to distinguish the relative contribution of each of these interventions, and some of the reported reductions in incidence and mortality may not be due to school closures.
 - Inadequate testing rates may have underestimated the incidence of COVID-19.
 - The database from which the incidence and mortality of COVID-19 were estimated may have been incomplete.
 - The study design and analysis are consistent with the association and not causation.
 - The study does not describe mechanisms through which school closures might affect viral transmission.
- > Timing of school closure plays a role in the magnitude of changes associated with school closures.
 - Some of the reported reductions may have been related to other concurrent interventions.
 - There may be a role for school closures in virus mitigation, however, this must be balanced against academic, health, and economic consequences.

Reviewed by: Dr Claire von Mollendorf

GLOBAL HEALTH

Alastair Weng – 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Impacts of COVID-19 on childhood malnutrition and nutrition-related mortality
[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)31647-0/fulltext?utm_campaign=tlcoronavirus20&utm_source=twitter&utm_medium=social](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31647-0/fulltext?utm_campaign=tlcoronavirus20&utm_source=twitter&utm_medium=social)

- > The authors examine the additional challenges posted by the COVID-19 pandemic.
- > COVID-19 has disrupted economic, food, and health security and exacerbates the nutritional inequities faced by children in lower-middle income countries.
- > 140 million more people will be classified as living in "extreme poverty" (< US\$1.90/day), doubling acute food insecurity to 265 million worldwide.
- > Coupled with economic forecasts, this correlates with increased childhood wasting and an additional estimated 130,000 deaths in children under five years in 2020.
- > Malnutrition and food insecurity will have intergenerational effects, and the burden will be shouldered by lower-middle income countries.

Reviewed by: Professor Fiona Russell

WHO situation report 196

https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200803-covid-19-sitrep-196-cleared.pdf?sfvrsn=8a8a3ca4_4

Burnet COVID-19 Global Trends & Analyses: July update 2

https://burnet.edu.au/system/asset/file/4136/7.2_Know_C-19_Hub_Global_Analysis_July-24.pdf

Adolescent experiences of COVID-19

<https://www.gage.odi.org/adolescent-experiences-of-covid-19/>

INFECTION CONTROL

Julian Loo Yong Kee - 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Face coverings and mask to minimise droplet dispersion and aerosolisation: a video case study

<https://thorax.bmj.com/content/early/2020/07/24/thoraxjnl-2020-215748>

- > Efficacy of three levels of face coverings visually assessed using a LED lighting system and high-speed camera to capture the light scattered by droplets and aerosols expelled during speaking, coughing and sneezing.
 - Face coverings assessed: single-layer cloth mask ('quick cut T-shirt face covering (no-sew method)', double-layer cloth mask, three-ply surgical mask.
- > Droplet reduction whilst speaking: surgical mask > double-layer cloth mask > single-layer cloth mask > no mask.
- > Droplet reduction whilst coughing and sneezing: surgical mask > double-layer cloth mask.
- > Conclusions: a single-layer face covering is better than no face covering; however, a double-layer cloth face covering is better at reducing droplet spread from coughing or sneezing.
- > Discussion: Factors affecting the efficacy of cloth face coverings: type of material; the number of layers; the arrangement of different layers; frequency of washing.
 - Guidelines should stipulate multiple layers (≥ 3) for home-made cloth masks.
 - More evidence required to inform safer cloth mask design.

Reviewed by: Dr Samantha Bannister

Julian Loo Yong Kee - 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Systematic SARS-CoV-2 screening at hospital admission in children: A French prospective multicentre study

<https://academic.oup.com/cid/article/doi/10.1093/cid/ciaa1044/5876373>

- > Aim: To assess the proportion of children with confirmed SARS-CoV-2 infection that would not have been detected by screening strategy based on clinical presentation alone.
- > Methods: Prospective multicentre study of 438 consecutive hospitalised children in four tertiary paediatric hospitals in Paris, France from 15th to 30th April 2020.
 - Nasopharyngeal specific SARS-CoV-2 rRT-PCR using Xpert Xpress SARS-CoV-2 (Cepheid).

- > 22/438 (5%) children were SARS-CoV-2 positive.
 - 182/428 (41.6%) presented with symptoms consistent with COVID-19.
 - Symptoms-based SARS-CoV-2 testing failed to identify 45% (95% CI: 24-68) of SARS-CoV-2 positive children.
 - Symptoms associated with an increased likelihood of positive SARS-CoV-2 PCR: dyspnoea, skin involvement, upper respiratory tract symptoms, diarrhoea, or vomiting.
 - Kawasaki disease and myocarditis strongly associated with COVID-19.
 - Children with underlying conditions or chronic immunosuppressive treatment were not more frequently infected with SARS-CoV-2.
- > Conclusion: systematic screening of all children admitted to the hospital should be considered to limit intra-hospital transmission.
- > Limitations: Lockdown may have decreased circulation of other common viruses associated with similar symptoms resulting in an overestimation of likelihood ratios of respiratory and gastrointestinal symptoms; PCR of nasopharyngeal swab may be associated with a substantial proportion of false negatives.

Reviewed by: Dr Samantha Bannister

MENTAL HEALTH

Thomas Hill – 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Is ADHD a risk factor for contracting COVID-19?

<https://www.ncbi.nlm.nih.gov/research/coronavirus/publication/32697120>

- > Medical records of 14,022 patients who had been tested for COVID-19 at least once between 1st February to 30th April were examined retrospectively to assess if a previous diagnosis of attention deficit hyperactivity disorder (ADHD) made contracting COVID-19 more likely and if pharmacological treatment of ADHD mitigated the risk of contracting the virus.
- > ADHD was deemed treated if individuals had purchased at least three ADHD medication prescriptions (92% of medication were stimulants) in the last twelve months.
- > Overall, a previous diagnosis of ADHD made contracting COVID-19 more likely (adjusted OR 1.58 (95% CI 1.27-1.96, $p < .001$)).
- > Individuals with untreated ADHD were more likely to contract COVID-19 (adjusted OR 1.68 (95% CI 1.37-2.10, $p < .001$)) compared to non-ADHD individuals.
- > Contracting COVID-19 was not more likely in individuals who were treated for ADHD (adjusted OR 0.85 (95% CI 0.54-1.34, $p < .001$)) compared to non-ADHD individuals.
- > Other mental health conditions including depression/anxiety (adjusted OR 1.09 (95% CI 0.84-1.40, $p = .528$)), schizophrenia (adjusted OR 1.21 (95% CI 0.75-1.96, $p = .439$)) and autism spectrum disorder (adjusted OR 1.39 (95% CI 0.40-4.85, $p = .603$)) did not make contracting COVID-19 more likely.
- > Findings suggest that treatment for ADHD may help with controlling behaviours that make people with ADHD less likely to be able to comply with public health mitigation measures.
- > Limitations: retrospective database design; severity of ADHD and associated behaviours could not be determined from medical records.

Reviewed by: Professor Dave Coghill

PERINATAL HEALTH

Grace Newman – 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Worldwide maternal deaths due to COVID-19: a brief review

<https://obgyn.onlinelibrary.wiley.com/doi/epdf/10.1002/ijgo.13328>

- > Recent investigations in Sweden and U.S. indicated pregnant and postpartum women are at an increased risk of severe complications of COVID-19 (require more hospitalisation, admission to ICU and require mechanical ventilation than non-pregnant infected women).
- > Method - literature search for documented COVID-19 related maternal deaths from December 2019 until 1st July 2020.
- > Six countries reported maternal deaths due to COVID-19 – three high income (France, UK, U.S.) and three middle income (Brazil, Iran, Mexico).
 - 160 total maternal deaths due to COVID-19: 22 in high-income countries, 138 in middle-income countries, with 124 of the latter from Brazil.
 - Incidence of maternal mortality in middle income countries at least six times higher than reported in high income.
 - They did not identify published cases from low-income countries, which may reflect under-reporting, rather than the absence of cases.
 - Moreover, worldwide figures of maternal deaths due to COVID-19 are likely to be even higher.
 - There were significant barriers to accessing critical care in Brazil and Mexico: ICU support occurred in 72% of the Brazilian fatalities with 15% given no ventilatory support. In Mexico, only two out of seven women who died were admitted to ICU and received invasive respiratory support.
 - In high-income countries such as the U.K. and U.S., black women and women from ethnic minorities were disproportionately affected by severe complications.
- > Limitations: Lack of reports from low income countries may indicate lack of reporting rather than the absence of cases; The time gap between events and their reporting in peer-reviewed publications; and comparability impaired due to methodological differences in studies.

Reviewed by: Professor Suzanne M Garland

THERAPEUTICS

Nicholas Baxter – 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Discovery of SARS-CoV-2 antiviral drugs through large-scale compound repurposing

<https://www.nature.com/articles/s41586-020-2577-1>

- > This study describes a high-throughput analysis of potential therapeutic options for SARS-CoV-2. The manuscript describes the process through which a library of 12,000 clinical-stage or FDA-approved small molecules were narrowed down to 21 molecules confirmed to possess dose/activity relationships against SARS-CoV-2.
- > The study outlined seven steps through which drug molecules were evaluated:
 - Optimisation of a HighThroughput Screening Model to enable large-scale screening of known drugs using Vero E6 cells coupled with an assessment of viral replication through measurement of cytopathic.
 - Repositioning analyses of the ReFRAME Drug Repurposing Library: 11,987 compounds were screened for potential antiviral activity against SARS-CoV-2 in Vero E6 cells.
 - Orthogonal validation of selected anti-SARS-CoV-2 compounds: Approximately 300 compounds were identified for validation studies, and assessed for activity at 2.5 and 1 μ M, of which 100 compounds were found to reduce viral replication by at least 40%.
 - Dose-response synergy analysis: A dose response analysis was conducted to determine the relationship between compound concentration and antiviral activity. Twenty compounds plus remdesivir demonstrated discernible dose-dependent antiviral activities. Some synergies were described in vivo for drugs administered in tandem with remdesivir which require further investigation.
 - Validation across human cell lines: These compound efficacies were evaluated on two additional human cell lines that support SARS-CoV-2 replication. Dose titration analysis found that 19/21 of the evaluated compounds inhibited viral replication in one or both of these cell lines at potencies equivalent to or greater than those observed in Vero E6 cells.
 - Impact of antivirals on the SARS-CoV-2 life cycle: Five of the most potent compounds identified - apilimod, VBY-825, ONO 5334, Z LVG CN2, and MDL 28170, act on entry or post-entry steps of the viral life cycle.

- Evaluation in primary human cell models: ONO 5334, MDL 28170, and apilimod were further evaluated for antiviral activity in human pluripotent stem cell (iPSC)-derived pneumocyte-like cells. Treatment with antivirals resulted in a decreased viral replication in these primary cell types. ONO 5334 reduced the number of infected cells by 72%, MDL 28170 by 65%, while apilimod blocked SARS-CoV-2 challenge by 85%. Antiviral activity of apilimod in an ex vivo lung culture system was evaluated with donor lung tissue showing that apilimod potently antagonises viral replication in tissues that reflect the primary site of SARS-CoV-2 replication.

Reviewed by: Dr Amanda Gwee

TRANSMISSION

Grace Newman – 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Age-related differences in nasopharyngeal severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) levels in patients with mild to moderate coronavirus disease 2019 (COVID-19)

<https://jamanetwork.com/journals/jamapediatrics/fullarticle/2768952>

- > Children are susceptible to infection with SARS-CoV-2 but generally present with mild symptoms compared with adults.
- > SARS-CoV-2 RT-PCR on nasopharyngeal swabs collected at inpatient, outpatient, E.D. and drive through testing centres at a paediatric tertiary medical centre in Chicago, Illinois between 23rd March and 27th April.
- > Cohort: all symptomatic individuals with mild-moderate illness, aged <1 month to 65 years who tested positive for SARS-CoV-2 within one week of symptom onset. Children who required oxygen support, patients with an unknown duration of symptoms and those whose symptoms had started more than one week prior to testing, were excluded.
- > 145 patients: younger children <5 years (n=46); older children 5-17 years (n=51); adults 18-65 years (n=48).
 - Median (interquartile range) PCR amplification cycle thresholds (CT): younger children 6.5 (4.8-12.0); older children 11.1 (6.3-15.7); adults 11.0 (6.9-17.5).
 - Lower CT values mean that younger children have equivalent or more viral nucleic acid in their upper respiratory tract compared with older children and adults.
 - Observed differences in C.T. values approximate a ten-fold to 100-fold greater amount of SARS-CoV-2 in the upper respiratory tract of young children.
 - Weak correlation between symptom duration and C.T. values in the overall cohort.
- > Children younger than five years with mild to moderate COVID-19 have higher amounts of SARS-CoV-2 viral RNA in their nasopharynx compared with older children and adults.
- > Limitation: The study is limited to the detection of viral nucleic acid, rather than an infectious virus, although other SARS-CoV-2 paediatric studies reported a correlation between higher nucleic acid levels and the ability to culture infectious virus.
- > Thus, young children can potentially be important drivers of SARS-CoV-2 spread in the general population.

Reviewed by: Dr Samantha Bannister and Professor Fiona Russell

VACCINES

Jenny Pham - 4th Year Medical Student,
Department of Paediatrics, The University of Melbourne

A vaccine targeting the RBD of the S protein of SARS-CoV-2 induces protective immunity

<https://www.nature.com/articles/s41586-020-2599-8>

- > To enter the host cell, SARS-CoV-2 virus uses its spike protein receptor-binding domain (S-RBD) to interact with the host cell receptor angiotensin-converting enzyme 2 (ACE2).
- > There has been some uncertainty whether a vaccine based only on the RBD is sufficient to induce protective antibodies, or whether the full spike protein is required.
- > A recombinant vaccine, consisting of S-RBD residues, demonstrated an antibody response (IgG and IgM) in mice, rabbits and non-human primates 7-14 days after a single dose injection.
- > Protection was demonstrated in vitro and in vivo. The vaccine can protect non-human primates from a live SARS-CoV-2 challenge.
- > Antibodies targeting RBD are elevated in the sera from patients infected with SARS-CoV-2.
- > Toxicology studies in non-human primates have demonstrated that this vaccine is safe in pre-clinical models.
- > The recombinant nature of the vaccine presents the feasibility for it to be manufactured on a global scale.
- > Further work is required to examine immunogenicity in humans, as well as safety and efficacy.

Reviewed by: Professor Allen Cheng

VIROLOGY

Dr Celeste Donato - Senior Research Officer, Enteric Diseases, Infection & Immunity Theme, MCRI and Honorary Fellow, Department of Paediatrics, The University of Melbourne

Evolutionary origins of the SARS-CoV-2 sarbecovirus lineage responsible for the COVID-19 pandemic

<https://www.nature.com/articles/s41564-020-0771-4>

- > The recent emergence of the human coronavirus SARS-CoV-2 has raised many evolutionary questions such as the role of reservoir species, the role of recombination and the time of divergence from animal viruses.
- > SARS-CoV-2 and SARS-CoV belong to the Sarbecovirus subgenus of Coronaviridae. Sarbecoviruses undergo frequent recombination events, and as a result, small genomic subregions can have independent origins.
- > A bat sarbecovirus (RaTG13), sampled from a *Rhinolophus affinis* horseshoe bat in 2013 in Yunnan Province, shares approximately 96% genome sequence identity with SARS-CoV-2, leading to the suggestion that bats were a reservoir for SARS-CoV-2. Pangolins were also suggested as a potential intermediate species and reservoir for SARS-CoV-2.
- > The results of this study indicate that SARS-CoV-2 is not derived from recombination between known sarbecoviruses and that SARS-CoV-2 represents a single lineage circulating in bats. The receptor-binding motif that facilitates binding to the human ACE-2 receptor appears to be an ancestral trait shared with other bat viruses and was not acquired recently via recombination.
- > Three different methods were employed to estimate the length of time this lineage has circulated in bats.
 - Using the most conservative approach, the divergence time estimate for SARS-CoV-2 and RaTG13 was 1969 (95% highest posterior density (HPD): 1930–2000).
 - The estimated divergence times for the pangolin virus most closely related to the SARS-CoV-2/RaTG13 lineage range from 1851 (1730–1958) to 1877 (1746–1986), indicating that these pangolin lineages were acquired from bat viruses divergent to those that gave rise to SARS-CoV-2.
- > Overall, this study indicates that the lineage giving rise to SARS-CoV-2 has been circulating undetected in bats for decades and that bats are the primary reservoir for the SARS-CoV-2 lineage.

Jun Hua Bowen Lim - 3rd Year Medical student,
Department of Paediatrics, The University of Melbourne

New insights into genetic susceptibility of COVID-19: an ACE2 and TMPRSS2 polymorphism analysis

<https://doi.org/10.1186/s12916-020-01673-z>

- > The authors seek to understand how much of the variation in COVID-19 disease severity can be explained by genetic susceptibility, with a focus of polymorphisms in the ACE2 and TMPRSS2 genes.
- > SARS-CoV-2 infection depends on Angiotensin-converting enzyme 2 (ACE2) for entry into cells.
- > The host transmembrane serine protease TMPRSS2 is responsible for SARS-CoV-2 spike protein priming (which promotes membrane fusion).
- > The authors investigated genetic susceptibility to COVID-19 by examining DNA polymorphisms in ACE2 and TMPRSS2 genes. They assembled 437 variants of ACE2 and TMPRSS2 from three large databases and applied Polyphen2 and CADD (Combined Annotation Dependent Depletion) scores to identify potentially deleterious variants.
 - 63 and 68 potentially deleterious variants were identified in ACE2 and in TMPRSS2, respectively.
 - Distribution of deleterious variants in ACE2 differs among nine populations (African/African-American (AFR), Non-Finnish European (EUR), Latino/Admixed American (AMR), East Asian (EAS), Finnish (FIN), South Asian (SAS), while Amish (AMI) and Ashkenazi Jewish (ASJ)).
 - Some ACE2 genomic variants may play important roles in susceptibilities to COVID-19 and its associated cardiovascular conditions by altering angiotensinogen-ACE2 interaction surface and subsequent pathway.
 - TMPRSS2 polymorphisms may potentially explain differences in genetic susceptibility to COVID-19 as well as for risk factors, including those with cancer and the high-risk group of male patients.
- > The authors highlight that understanding the ACE2 or TMPRSS2 polymorphisms has indications for personalised treatments of COVID-19.
- > A major limitation in the current analysis is that the data is derived from the general database without information about the incidences of COVID-19 exposures and infections in the nine populations. Case-control studies are needed to further investigate the genetic susceptibility to severe COVID-19.

Reviewed by: Dr Lien Anh Ha Do

Natalie Commins - 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

ABO polymorphism and SARS-CoV-2 infection - a meta-analysis (not peer reviewed)
<https://www.medrxiv.org/content/10.1101/2020.07.17.20155986v1>

- > A previous study in 2005 found that Chinese healthcare workers with blood group O were less likely to develop SARS-CoV infection when exposed, compared to other healthcare workers.
- > Another study (2006) described a mechanism where the SARS-CoV spike protein/ACE2-dependent adhesion is inhibited by either a monoclonal anti-A antibody or natural plasma anti-A. SARS-CoV and SARS-CoV-2, both share the same ACE2 receptor and a similar structure of receptor-binding domains.
- > A meta-analysis of the available epidemiological data (seven studies and 13 subgroups of populations) was conducted to verify whether blood type influences a person's susceptibility to SARS-CoV-2 infection.
- > Results indicate that COVID-19 patients are most likely to have blood group A (pooled OR of 1.21, 95% CI: 1.08-1.37) and are less likely to have blood group O (pooled OR of 0.76, 95% CI: 0.66-0.87). Blood group AB (pooled OR of 1.08 (95% CI: 0.92 -1.26) and B (pooled OR of 1.05, 95% CI: 0.95 - 1.15) did not show any association.
- > The difference in transmission among blood types could be attributed to the prevalence and distribution of gene loci, the presence of receptor or receptor binding proteins involved in response to the infection and the presence of a particular antibody population.
- > The prevalence of certain blood groups varies between populations, and further research into this area would be useful to understand better the kinetics of the epidemic.
- > The reported data used for the meta-analysis are still preliminary data which are limited in number and present a great variability in terms of study design and population.

Reviewed by: Dr Lien Anh Ha Do

OTHER RESOURCES

Burnet Institute research findings, policy and technical reports
https://www.burnet.edu.au/covid-19//36_know_c19_hub

National COVID-19 clinical evidence taskforce: continually updated evidence-based clinical guidelines
<https://covid19evidence.net.au/>

Lancet COVID-19 papers
https://www.thelancet.com/coronavirus?utm_campaign=tlcoronavirus20&utm_content=126383502&utm_medium=social&utm_source=twitter&hss_channel=tw-27013292

Focuses on paediatric clinical, epidemiological, transmission and neonatal aspects
<https://dontforgetthebubbles.com/evidence-summary-paediatric-covid-19-literature/>

All COVID-19 literature
<https://www.ncbi.nlm.nih.gov/research/coronavirus/>

Oxford COVID-19 Evidence Service
<https://www.cebm.net/oxford-covid-19/>

Daily updates on COVID-19 literature compiled by Canadian medical students
https://docs.google.com/forms/u/0/d/e/1FAIpQLSfOxCoAuLV0aJdf_z2uWV7r3FaPzAO86q9ZXBcTZ1QcCE_Nw/formResponse

Victorian Department of Health and Human Services
<https://www.dhhs.vic.gov.au/coronavirus-covid-19-daily-update>

Australian Government
<https://www.health.gov.au/news/health-alerts/novel-coronavirus-2019-ncov-health-alert/coronavirus-covid-19-current-situation-and-case-numbers>
<https://www.health.gov.au/resources/publications/management-and-operational-plan-for-people-with-disability>

COVID-19 and the kidney, which is currently the recommended U.S. resource
<http://www.nephjc.com/covid19>

University of Birmingham COVID-19 Research Briefing
<https://www.birmingham.ac.uk/university/colleges/mds/Coronavirus/COVID-19-research-briefing.aspx>

Australian Government Department of Health Webinars on the COVID-19 response for primary care practitioners
<https://www.health.gov.au/news/health-alerts/novel-coronavirus-2019-ncov-health-alert/coronavirus-covid-19-advice-for-the-health-and-aged-care-sector/webinars-on-the-coronavirus-covid-19-response-for-primary-care-practitioners>

Global summary, identifying changes in the reproduction number, rate of spread, and doubling time during the COVID-19 outbreak whilst accounting for potential biases due to delays in case reporting both nationally and sub-nationally
<https://epiforecasts.io/covid/posts/global/>

WHO Rolling updates on COVID-19
<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/events-as-they-happen>

Scimex.org – breaking science news portal: COVID-19 stories (research and expert commentary)
<https://www.scimex.org/info/2019-20-coronavirus>
<https://www.covid19-hpc-consortium.org/>

Introduction to Coronavirus: free, online course aimed at teenagers and young adults: scientists and experts from the London School of Hygiene & Tropical Medicine explain research to understand the virus and guide the global response to Coronavirus
<https://www.open.edu/openlearncreate/course/view.php?id=5319>

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REVIEWERS

| | |
|------------------------------------|--|
| Professor Fiona Russell | Director of the Child and Adolescent Health PhD Program, Department of Paediatrics, The University of Melbourne; Group Leader Asia-Pacific Health Research, MCRI |
| Dr Wonie Uahwatanasakul | Paediatrician- Immunisation service RCH, MD Child and Adolescent Health Program Lead Coordinator, Department of Paediatrics, The University of Melbourne |
| Professor Allen Cheng | Medical Adviser, Melbourne Vaccine Education Centre, Infectious Diseases Epidemiology Director of the Infection Prevention and Healthcare Epidemiology, Alfred Health, Infectious diseases and an epidemiologist, Department of Epidemiology and Preventive Medicine at Monash |
| Professor Dave Coghill | Financial Markets Foundation Chair of Developmental Mental Health, The University of Melbourne |
| Dr Celeste Donato | Senior Research Officer, Enteric Diseases, Infection & Immunity Theme, MCRI and Honorary Fellow, Department of Paediatrics, The University of Melbourne |
| Dr Lien Anh Ha Do | Virologist, New Vaccines, Infection & Immunity Theme, MCRI and Honorary Fellow, Department of Paediatrics, The University of Melbourne |
| Professor Steve Graham | Centre for International Child Health, Department of Paediatrics, The University of Melbourne, MCRI |
| Dr Amanda Gwee | Infectious Diseases Physician, RCH; Team leader & Clinician-Scientist Fellow in the Infectious Diseases Group, MCRI: and Senior Lecturer, Department of Paediatrics, The University of Melbourne |
| Dr Claire von Mollendorf | Senior Research Officer, New Vaccines and Asia-Pacific Health Research Groups, MCRI and honorary Senior Fellow, Department of Paediatrics, The University of Melbourne |
| Professor Suzanne M Garland | Reproductive & Neonatal Infectious Diseases, Department of Obstetrics and Gynecology, University of Melbourne; Director Centre Women's Infectious Diseases Research; Honorary Research Fellow, Infection & Immunity, Murdoch Children's Research Institute |
| Dr Martin Wright | Paediatrician, Joan Kirner Women's and Children's, Sunshine Hospital and Senior Lecturer, Department of Paediatrics, The University of Melbourne |
| Dr Samantha Bannister | Paediatric Registrar, The Royal Children's Hospital, Melbourne, Graduate Research Student, Murdoch Children's Research Institute, PhD Candidate, Department of Paediatrics, The University of Melbourne |