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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.17**

14<sup>th</sup> August 2020



**BE COVIDSAFE**

**CURRENT STATUS OF CONFIRMED CASES**



**47**



ACT	NSW	NT	QLD	SA	TAS	VIC	WA
0	5	0	0	0	0	42	0

**275**



ACT	NSW	NT	QLD	SA	TAS	VIC	WA
0	11	1	2	0	1	260	0

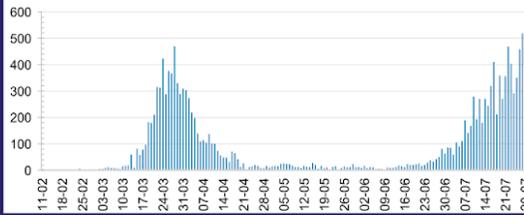
**4,032,061**



**0.4% POSITIVE**

ACT	NSW	NT	QLD
48,686	1,391,144	23,084	510,206
POSITIVE	POSITIVE	POSITIVE	POSITIVE
0.2%	0.3%	0.1%	0.2%
SA	TAS	VIC	WA
212,490	66,544	1,536,628	243,279
POSITIVE	POSITIVE	POSITIVE	POSITIVE
0.2%	0.3%	0.6%	0.3%

**DAILY NUMBER OF REPORTED CASES**

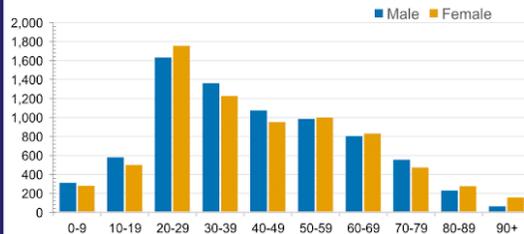


**CASES IN AGED CARE SERVICES**

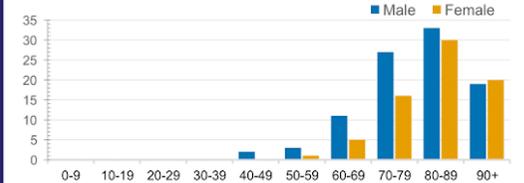
Confirmed Cases	Australia	ACT	NSW	NT	QLD	SA	TAS	VIC	WA
Residential Care Recipients	547 (41)	0	61 (32)	0	1 (1)	0	1 (1)	484 (9)	0
In Home Care Recipients	50 (30)	0	13 (13)	0	8 (8)	1 (1)	5 (3)	22 (5)	1 (1)
	(5)						(2)	(2)	

Cases in care recipients [recovered] (deaths)

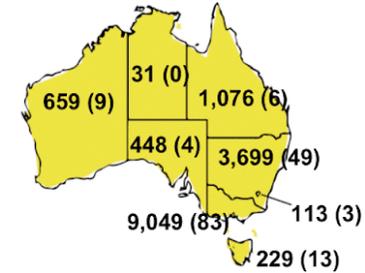
**CASES BY AGE GROUP AND SEX**



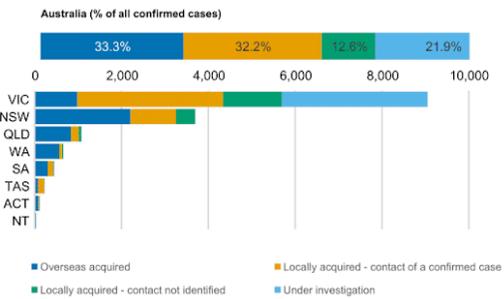
**DEATHS BY AGE GROUP AND SEX**



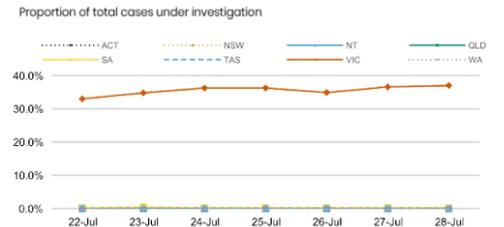
**CASES (DEATHS) BY STATE AND TERRITORIES**



**CASES BY SOURCE OF INFECTION**



**PUBLIC HEALTH RESPONSE MEASURE**



Last updated 28 July 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 11; cited 2020 August 12]. Available from: <https://www.health.gov.au/resources/collections/coronavirus-covid-19-at-a-glance-infographic-collection>

# GUEST EDITORIAL

## **Professor Dave Coghill** - Financial Markets Foundation Chair of Developmental Mental Health, The University of Melbourne

Welcome to the 17<sup>th</sup> edition of the COVID-19 Kids Evidence Update, and I want to start by giving my thanks to the team that continue to work so hard keeping us up to date with the latest COVID-19 related publications from around the world. The breadth of coverage is remarkable, including basic science, clinical medicine, public health, and my own particular area of interest, mental health.

I wanted to kick off with some of the important news about the development of potential vaccines. Still a long way off but hopefully edging closer. The report describing the results of the first in-human trial of a recombinant nanoparticle vaccine indicated that it is immunogenic and now ready to progress to the next phase of development is very welcome. Mixed news for another vaccine in the early stages of development that prevented pneumonia in macaques but not nasal shedding suggesting that it may not be effective at preventing transmission. The importance of developing safe and effective vaccines can't be underestimated - indeed here in Melbourne where we are still in a Stage 4 lockdown with an 8pm curfew. There is a fierce ongoing debate about whether we should be aiming for suppression or elimination of the virus and indeed whether elimination is even going to be possible. Even if it is, it will be necessary for us to maintain very strict border controls until there is a vaccine whilst keeping alert for new cases. Whilst this would be very challenging for us here in Australia it would, however, be technically much easier in our island that it would be for countries with multiple land borders. However, the news over the last few days of new cases and a new lockdown in New Zealand where it was thought, as reported this week in a letter to the New England Journal of Medicine, they had entered a 'post-elimination stage', is another salutatory reminder that, as predicted by the NEJM correspondent, our situation remains very fragile.

As Prof. Steve Graham pointed out in last week's editorial despite the number of COVID-19 publications remaining high most of the community studies reporting data uncontrolled cross-sectional observational studies. This is of course understandable under the circumstances, but does mean that it is often only possible to talk about correlations between variables rather than causal relationships between them. Perhaps as methods improve and sample sizes increase it will become possible to apply some of the methods pioneered by Judea Pearl and others that, with careful analysis and modelling, can allow us to draw causal inferences from observational data (see <http://bayes.cs.ucla.edu/home.htm>).

We all understand how difficult it has been to adapt and cope through the restrictions of lockdown, working from home and homeschooling. We all feel the pressures and see the impact on mental health and wellbeing in our own families, our friends and our colleagues. Although many of the papers focussing on the impact of school closures and re-opening (and closing again in the case of Victoria), including those in this edition of the Update, highlight the likely negative impacts on child and adolescent mental health we currently have few data to confidently describe the scale of these problems. I have been fortunate enough to join a WHO working group looking at the indirect effects of school closures. The early data that is becoming available does suggest a significant and meaningful impact with anxiety, depression and loneliness being common themes. There does, however, seem to be different patterns across different populations, and it is still too early to properly describe these or to make a clear prediction about long term impacts.

Several of the papers in this week's Update focus on the impact of COVID-19 on mental health in adults. A cross-sectional study looking at post-discharge symptoms in 100 adult COVID-19 positive patients in the UK found psychological distress (46.9% in the ICU group; 23.5% in the non-ICU group) to be the third most common symptoms after fatigue and breathlessness. Of the 35 participants overall reporting anxiety and depression post-COVID-19, 74% had no previously diagnosed mental health condition. An Italian study that followed 402 adults surviving COVID-19 also reported higher than expected rates of mental health problems. The most common presentations were: PTSD (28%), depression (31%), anxiety (42%), obsessive-compulsive symptoms (20%) and insomnia (40%). Overall, 56% of participants had a pathological score on at least one clinical dimension. Another UK study looked at 1329 new mothers with babies under a year. Interestingly, although many participants reported feeling down (56%), lonely (59%), irritable (62%) and worried (71%), although, 70% felt that they were able to cope with the lockdown.

As is always the case, a lot more data is needed to determine just what the impact is going to be, both at a population level and within particularly vulnerable groups. While the data available so far has been collected carefully there is a distinct lack of reliable comparison data against which these data can be judged. Some studies have within-subject comparisons, but many of these rely on retrospective accounts of pre-COVID-19 functioning and current status rather than from more robust prospective longitudinal studies. Many have also used non-standard instruments that make it difficult to compare the scores of our current samples with population norms. One potential approach will be to use standardised measures to assess the mental health impacts across different populations using the same measures.

On the Melbourne Children's Campus, we are using a standardised approach to measure the impacts of the pandemic and subsequent restrictions on groups of children and adolescents with a range of chronic physical health problems, neurodevelopmental disorders and pre-existing mental health difficulties. All these children will have been subject to similar restrictions, including a second school closure. Our colleagues in Brisbane are using the same measure to assess impact in children there, where of course there were similar rates of infection and restrictions in the early stages of the pandemic but where the paths have diverged greatly since the second wave of infections hit Victoria. A similar measure is also being used in several of the existing Lifecourse studies at the Murdoch Children's Research Institute on our campus. These studies have the advantage of already knowing their participants very well meaning that they will be able to make meaningful before and after comparisons.

These measures were all modified from the CRISIS tool originally developed by colleagues at the National Institute for Mental Health in the USA (<https://github.com/nimh-comppsyh/CRISIS>) and are being used in its original form by multiple studies worldwide. We developed our mental health focussed version with colleagues both here in Melbourne and an international group of child and adolescent mental health researchers from Europe. It is now being administered in countries including the UK, Italy, Germany, Spain, Serbia, and Hungary, all of which have had very different experiences during the COVID-19 crisis. This may allow us to understand better which factors both COVID-specific and more general cultural, social, political and demographic, mediate and moderate the impact and resilience of children to the pandemic. We will not know the results for some time yet, but hopefully, they will help us to determine how best we can support our young people on the long road to recovery.

Thank you for choosing to pick up this week's update. I hope you enjoy reading it as much as I have, and we will now get started on preparing next week's instalment for you – so please stay tuned.

# HIGHLIGHTS

- > Editorial Bulletin from the World Health Organization evaluates the current challenges with regards to managing refugee health during the COVID-19 pandemic.
- > It is forecasted that 130 million more people will be affected by chronic hunger by the end of 2020.
- > In Nepal, institutional childbirth reduced by more than half during the lockdown, with increases in institutional stillbirth rate and neonatal mortality, and decreases in quality of care. Some behaviours improved, notably hand hygiene and keeping the baby skin-to-skin with their mother.
- > Phase 1 trial of a recombinant nanoparticle vaccine composed of trimeric full-length SARS-CoV-2 spike glycoproteins (NVX-CoV2373, Novavax Inc.) in healthy adults in Australia is immunogenic; and will progress to the next phase of development.
- > Prevention of pneumonia in pre-clinical studies with adenovirus-vectored vaccine ChAdOx1 nCoV-19 vaccine in macaques is promising, but lack of prevention of nasal shedding indicates that transmission may not be prevented.
- > Viral exanthem with COVID-19 may also be associated with mucocutaneous lesions in adults.
- > Risk-benefit of school closure in lower middle-income countries needs further attention.
- > Monitoring impact of schools re-opening is essential in returning to full-time education for all children, adolescents and young adults as soon as possible.
- > Household attack rates in children were higher than adults in Italy.
- > Successful school re-opening program in South Korea outlines school online and face-to-face learning based on cases in the local area, size of the school, and other local factors.
- > A model from the UK predicts that opening primary schools has a modest impact on R, while opening secondary schools is predicted to have a larger overall impact; a combination of re-opening both would result in a loss of epidemic control.
- > Small (5%) reductions in breastfeeding due to COVID-19 disruptions would result in 16,469 child deaths globally, with a 50% reduction resulting in an estimated additional 138,398 child deaths.
- > Travelling for work, if lockdown had a major impact on the ability to buy food and having an income less than £30 K predicted poorer maternal mental health in the UK.
- > Observations in reductions in preterm births were confined to people living in high-SES neighbourhoods in the Netherlands.
- > Inflammatory markers and clinical indicators did not predict psychopathology in COVID-19 survivors.

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# ADULT MEDICINE

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

## **Persistent self-reported changes in hearing and tinnitus in post-hospitalisation COVID-19 cases**

<https://www.tandfonline.com/doi/pdf/10.1080/14992027.2020.1798519?needAccess=true>

- > A letter to the editor regarding a review of 138 COVID-19 patients eight days post-discharge after admission to Wythenshawe Hospital in the UK due to the severity of COVID-19 symptoms, with 121 of them questioned about hearing and/or tinnitus.
- > 16 patients (13.2%) reported changes in hearing and/or tinnitus since being diagnosed with COVID-19.
  - Epidemiology: Median age - 64 years old (44-82 years old); 87.5% male; Comorbidities common.
  - Self-reported deterioration in hearing: eight cases (four had a pre-existing hearing loss).
  - Self-reported tinnitus: eight cases (three had a pre-existing hearing loss).
  - Conclusion: There is a need for further study on longstanding risks on the audiovestibular system.

Reviewed by: Dr Wonie Uahwatanasakul

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

## **Enanthem in patients with COVID-19 and skin rash (research letter)**

[Jamadermatology jimenezcauhe 2020 Id\\_200016.pdf](#)

- > A research letter (Spain) describing the incidence and characteristics of oral cavity lesions (enanthem) in adult patients with COVID-19 and skin rash (exanthem).
- > 21 adult patients with laboratory-confirmed SARS-CoV-2 who underwent dermatological review for exanthem were included.
  - Of the 21 patients with skin rash, six patients (29%) also had enanthem.
  - The enanthem was macular in one patient, petechial in two patients, and macular with petechiae in three patients. All lesions were located in the palate.
  - The mean time between the onset of COVID-19 symptoms and appearance of mucocutaneous lesions was 12.3 days (range -2 to 24 days).

- > Presence of enanthem increases the likelihood of an infectious aetiology of skin rash. Further research is needed to determine the clinical utility of dermatological manifestations of COVID-19.

Reviewed by: Dr Wonie Uahwatanasakul

Isabella Overmars - 2nd Year Master of Public Health Student,  
The University of Melbourne

**Post-discharge symptoms and rehabilitation needs in survivors of COVID-19 infection: A cross-sectional evaluation (pre-print, peer-reviewed)**  
<https://onlinelibrary.wiley.com/doi/abs/10.1002/jmv.26368>

- > This cross-sectional study evaluated 100 COVID-19 positive patients in the UK, who had been discharged following admission. They were assessed between 29 and 71 days (mean 48 days) post-discharge from the hospital, using a telephone screening tool to capture symptoms and impact on daily life.
- > Of the 100 patients, 32 were admitted to ICU at some stage of their admission. Patients predominantly had single-organ (respiratory) dysfunction requiring oxygen or non-invasive ventilation, and only one patient in this cohort was intubated. The age range in the ICU group was 34-84 years (median 58.5 years) and 20-93 years (median 70.5 years) in the non-ICU group.
- > New illness-related fatigue was the most common reported symptom by 72% participants in the ICU group and 60.3% in non-ICU group.
- > The next most common symptoms were breathlessness (65.6% in ICU group; 42.6% in non-ICU group) and psychological distress (46.9% in ICU group; 23.5% in non-ICU group). Of the 35 participants overall reporting anxiety and depression post COVID-19, 74% had no previously diagnosed mental health condition. 60% of the ICU group and 15% of the non-ICU group remained off-sick from work at the point of follow-up.
- > Patients admitted to ICU in this study had a greater prevalence of symptoms in almost all reported symptom domains, despite being younger with fewer co-morbidities.
- > It is recommended that rehabilitation services are delivered to COVID-19 patients after their discharge, to manage these symptoms appropriately and maximise the functional return to baseline.
- > There is no data yet on longcovid in children.

Reviewed by: Dr Wonie Uahwatanasakul

# CHILD DEVELOPMENT

Dan Lindholm - 4th Year Medical Student,  
Department of Paediatrics, University of Melbourne

**Re-opening schools during the COVID-19 pandemic: Governments must balance the uncertainty and risks of re-opening schools against the clear harms associated with prolonged closure**

<https://adc.bmj.com/content/early/2020/08/02/archdischild-2020-319963>

- > There are both benefits and harms of closing schools in the context of the COVID-19 pandemic. This article reviews the limited evidence that exists on both sides of this equation and offers key principles to guide school re-opening.
- > Data suggests children play a minimal role in virus transmission. In Australia, population-based contact tracing data on transmission in schools have revealed minimal transmission.
- > Conversely, closure of schools is well documented to adversely impact children in their learning, physical and mental health, social support, and exposure to violence in the home, school-delivered public health interventions, and a range of indirect impacts on families.
- > Little attention has been given to the drastically different risk-benefit equation in low and lower-middle-income countries. Here, school programs are even more essential for a range of social development and public health reasons for children, families and broader society.
- > The authors propose five key principles to guide the re-opening of schools: doing so in a staged fashion, incorporating distancing measures, infection control measures, protecting teachers and vulnerable students, as well as research and evaluation.

Reviewed by: Dr Wonie Uahwatanasakul

**Finding a path to re-open schools during the COVID-19 pandemic**

<https://www.sciencedirect.com/science/article/pii/S2352464220302492?via%3Dihub>

- > Commentary on the studies which inform a similar cost-benefit analysis of closing schools in the COVID-19 pandemic.
- > While children are well documented to be excellent transmitters of disease in other pandemics, this has not been true in the COVID-19 context.
- > The author highlights New South Wales based research which found that open schools with robust infection control measures in place in the early phase of the pandemic were rarely the sources of COVID-19 transmission, but this was in the context of low community transmission and schools being closed. Conversely, some cases from France and Korea highlight that adolescents attending school may still pose an unacceptable risk of transmission.

- > A modelling study based on UK data was also reviewed and suggested that even partially re-opening schools could lead to the second wave of COVID-19 infections. However, it was unclear whether this stemmed from increased adult interaction who were then able to return to some normal activities, or due to increased contact between children at school.
- > The comment emphasises the need for large-scale research which monitors the impact of schools re-opening, as returning to full-time education for all children, adolescents and young adults must occur as soon as possible.

Reviewed by: Dr Wonie Uahwatanasakul

# DIAGNOSTICS & SAMPLING

Dr Lien Anh Ha Do - Virologist, New Vaccines, Infection & Immunity Theme, MCRI and Honorary Fellow, Department of Paediatrics, The University of Melbourne

**SalivaDirect: Simple and sensitive molecular diagnostic test for SARS-CoV-2 surveillance (not peer reviewed)**

<https://www.medrxiv.org/content/10.1101/2020.08.03.20167791v1.full.pdf+html>

- > Saliva has been demonstrated to be a suitable sample for SARS-CoV-2 screening with less infection risk to health care workers and easily collected. This study published a validated protocol named as SalivaDirect that (1) does not require nucleic acid preservatives at sample collection, (2) replaces nucleic acid extraction with a simple proteinase K and heat treatment step, and (3) tests saliva samples with a dualplex quantitative reverse transcription PCR (RT-qPCR) assay adapted from US CDC protocol.
- > SARS-CoV-2 RNA in saliva was demonstrated to be stable for at least seven days at 4°C, room temperature (RT, ~19°C), and 30°C without the addition of stabilising buffers.
- > The simplified nucleic acid extraction by simply mixing the specimen with proteinase K followed by heat inactivation showed an increased Ct-value by 1.8 (p<0.01).
- > Dualplex qRT-PCR adapted from US CDC protocol with two targets N1, and human Rnase P genes showed highly sensitive with a limit of detection of 6-12 SARS-CoV-2 copies/μL.
- > The SalivaDirect protocol produced consistent results across a number of commercial reagents and thermocycler platforms.
- > The reagent cost of SalivaDirect protocol is ranged from \$1.29-\$4.27/ sample.
- > Significance: SalivaDirect protocol provides a cheap, viable and accessible option to help alleviate SARS-CoV-2 testing demands.
- > Limitations: Was validated for the clear and liquid saliva that naturally pools in the mouth. The protocol is not intended for the use of hospitalised COVID-19 patients.
- > Large-scale testing of uninfected populations, asymptomatic and pre-symptomatic cases is required to evaluate whether automation and/or pooling is cost-effective.

**Simply saliva: stability of SARS-CoV-2 detection negates the need for expensive collection devices (not peer reviewed)**

<https://www.medrxiv.org/content/10.1101/2020.08.03.20165233v1.full.pdf+html>

- > It was not clear how the stability of SARS-CoV-2 RNA and infectious virus in saliva samples without supplementations. This information is important for saliva use as a simple specimen collection for massively expanding SARS-CoV-2 testing. This study characterised SARS-CoV-2 RNA stability and virus infectivity from saliva specimens stored in widely available, sterile, nuclease-free laboratory plastic (polypropylene) tubes, over extended periods (2-25 days) and at different temperatures (-80°C, 4°C, room temperature -recorded as ~19°C and 30°C). These temperatures represent laboratory storage condition as well as at-home storage and elevated temperatures when cold chain transport may be unavailable.
- > Based on qPCR results using US CDC protocol targeting N1 gene, no significantly different in RT-qPCR tested cycle threshold (Ct) values between samples tested on the day of collection or after storage at -80°C freeze/thaw, room temperature (five days), and 30°C (three days).
- > SARS-CoV-2 RNA in saliva was also demonstrated to be stable up to 25 days at room temperature (~19°C; Ct-value increase of 0.027, 95% CI: -0.019, 0.071).
- > Human RNase P (RP) at higher temperatures was degraded with increased Ct-value at room temperature as well as at 30°C.
- > At 72 hours post-inoculation of a saliva sample to Vero-E6 cells, five of the 43 (11.6%) saliva samples exhibited a reduction in Ct values when tested by RT-qPCR (-4.41, -4.3, -3.86, -3.49 and -2.66) however, the cellular lysates from the inoculation of these samples did not show any plaque-forming units after 48 hours post-infection in plaque assays.
- > Significance: The study provided supporting data for the use of saliva samples as a simpler and stable specimen in expanding SARS-CoV-2 testing.
- > The saliva samples in this study were from COVID-19 patients, reflecting a real clinical condition.
- > Limitations: The study did not have enough passages to check the presence of infectious viruses in saliva. A clinical specimen can require three to five passages in order to have a successful viral culture. This information is important to understand the infectious status of patients and the value of saliva samples for not only clinical diagnostics but also for in-depth virological research questions.

# EPIDEMIOLOGY & PUBLIC HEALTH

Dan Lindholm - 4th Year Medical Student,  
Department of Paediatrics, University of Melbourne

**Child maltreatment prevention in the era of coronavirus disease 2019 (editorial)**  
<https://jamanetwork.com/journals/jamapediatrics/fullarticle/2769069>

- > This article emphasises the existential threat that COVID-19 presents to disadvantaged communities, as well as the inequalities which COVID-19 has highlighted, with potential for a greater risk of violence to vulnerable children and or parents.
- > The author notes the growth of predictive risk modelling in child welfare, as well as how such modelling may be coded to reflect similar inequity to that which has been highlighted by COVID-19.
- > The public health approach to child maltreatment is discussed, emphasising the need to focus on prevention throughout childhood, and for all families that experience inequalities.
- > The author contends that now is the time to eliminate systematic injustices which exist in communities and have been highlighted by COVID-19. They argue that policy work and resources must be devoted to these issues before the next global crisis, such that children and others can be protected from the varied ramifications of such inequity.

Reviewed by: Dr Wonie Uahwatanasakul

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

**COVID-19 in children and the dynamics of infection in families**  
<https://pediatrics.aappublications.org/content/146/2/e20201576>

This study explored the characteristics and dynamics of family clusters of children < 16 years of age with COVID-19 presenting from 10<sup>th</sup> March - 10<sup>th</sup> April 2020 in Geneva, Switzerland. A total of 39 patients were included.

- > Clinical characteristics
  - Most children (29/39; 74%) were previously healthy. Top associated co-morbidities were asthma (10%), diabetes (8%), obesity (5%), premature birth (5%), and hypertension (3%).

- Most common symptoms were cough (32/39; 82%), fever (26/39; 67%), nasal discharge (25/39; 64%), headache (22/39; 56%), sore throat (14/39; 36%), shortness of breath (13/39; 33%), myalgia (13/39; 33%), and abdominal pain (11/39; 28%).
  - 7/39 (18%) were hospitalised. None required ICU admission or SARS-CoV-2 specific therapies. All patients recovered within seven days of diagnosis.
- > Familial clusters
- A total of 111 household contacts (HHCs) were identified for the study children (23 of these were themselves children). In the majority of cases (31/39; 79%), adult HHCs had suspected or confirmed COVID-19 before the study child. In only 3/39 (8%), the study child developed symptoms before any HHC.
  - 75/88 (85%) of adult HHCs developed symptoms compared to 10/23 (43%) of paediatric HCCs.
  - 36/39 (92%) of mothers developed symptoms compared to 24/32 (75%) of fathers.
- > Limitations
- Case ascertainment was through a hospital surveillance unit. The population characteristics of this sample are not evident.
  - Not all HHCs were tested (50/88 adult and only 4/23 paediatric)
- > This study in Switzerland early in the pandemic highlights that children in a household are less likely than adults to be the primary source of infection and children are also less likely to develop symptoms than adults once COVID-19 is introduced to the household - more complete data on HH transmission dynamics are needed from larger samples.

Reviewed by: A/Prof Margie Danchin

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

**Contact tracing during Phase I of the COVID-19 pandemic in the Province of Trento, Italy: Key findings and recommendations (not peer reviewed)**

<https://www.medrxiv.org/content/10.1101/2020.07.16.20127357v1?rss=1>

- > Trento in Northern Italy implemented contact tracing at the end of February after the first cases were identified in the province.
- > A contact tracing website was developed, which collated information on the contacts of confirmed and probable cases from telephone interviews following a standard questionnaire. The information included personal data, nature of the contact and preferred to follow up and monitoring, including the development of symptoms.
- A contact was defined as any person who has had contact with a COVID-19 case within a timeframe of 48 hours before the onset of symptoms to 14 days after onset, and two or more related cases constituted an outbreak.
- Visual mapping of relationships between cases was useful in the identification of possible outbreaks to be investigated.

- > 7791 people were identified as contacts and placed in self-isolation during March and April 2020. 1101 of these were linked to institutional settings and excluded from analysis.
  - The remaining 6690 contacts linked to 2812 cases, with a mean 2.3 contacts per case (range 1-42). 30% of cases had no identified contacts.
  - 56% of contacts were living in the same household as cases, 27.2% were non-cohabitating family or friends, 8% workplace contacts and 8.8% other. Before the lockdown on 10<sup>th</sup> March non-cohabitating family and friends were the largest group of contacts. The mean number of contacts per case dropped following the lockdown from 4.1 contacts per case in the week of 8<sup>th</sup> March to 2.1 during the week of 26<sup>th</sup> April.
  - The secondary attack rate was 13.3%. The risk of developing symptoms increased with the age of the contact (8.4% in 0-14 year olds, 18.9% in over 75 year olds). The highest risk exposure was in the workplace.
  - Contagiousness (contacts who became cases and infected others) was examined for 1489 cases with the highest rate in 0-14 year olds (11 of 49 contacts became cases, 22.4%). The lowest rate was in 30-49 year olds (10.6%). Notably, schools were closed during this study period, so these contacts were most likely in the household. The age breakdown of the tertiary cases was not presented.
- > The higher contagiousness in children may be due to the different nature of interactions between children and adults and the challenges of truly isolating a child. This has implications for the opening of primary schools, with the authors suggesting maximum caution.
  - The high risk of infection associated with workplaces can be mitigated by the lockdown but is of fundamental importance in Phase-2 of re-opening.
  - Ongoing spread despite follow up of contacts may be due to asymptomatic cases, lack of unified approach to contact tracing, issues in case investigation during the peak of the epidemic, and delays in initiating contact tracing.
- > Limitations: contacts were not routinely tested and determining if they had become a case was based on symptoms plus an epidemiological link, the number of cases and contacts among children in the study of contagiousness was relatively small as schools were closed.

Reviewed by: Professor Fiona Russell

Daniel Lamanna - 3rd Year Medical Student,  
Department of Paediatrics, The University of Melbourne

**Successful elimination of COVID-19 transmission in New Zealand (correspondence)**  
[https://www.nejm.org/doi/full/10.1056/NEJMc2025203?query=featured\\_home](https://www.nejm.org/doi/full/10.1056/NEJMc2025203?query=featured_home)

- > The first reported case of COVID-19 in New Zealand was diagnosed on 26<sup>th</sup> February 2020 - it was during that same week that the WHO-China Joint Mission's report on COVID-19 demonstrated that the SARS-CoV-2 virus behaved with more similarity to severe acute respiratory syndrome than influenza, which suggested containment was possible.
- > By the middle of March 2020, it was clear that community transmission was occurring in New Zealand, and that the country lacked the capacity to test and contact trace the virus adequately. During this time, country leaders decisively switched from a mitigation strategy to an elimination strategy with a stringent lockdown (Alert Level 4) implemented on 26<sup>th</sup> March 2020.
  - Five weeks of lockdown resulted in a rapid decline in the number of new cases.
  - Two additional weeks of less stringent lockdown measures (Alert Level 3) were then implemented, resulting in a total of seven weeks of a national stay at home order.
- > The last known case of COVID-19 was identified in early May 2020.
- > On 8<sup>th</sup> June 2020, the government announced an easing of restrictions (Alert Level 1), effectively marking the end of identified community spread (103 days after the first identified case).
- > New Zealand is now in the post-elimination stage, which has its own challenges. It remains vulnerable to future outbreaks.
- > The total case count (1569) and deaths (22) have remained low, and the COVID-19-related mortality (4 per 1 million) is the lowest among the 37 Organization for Economic Cooperation and Development countries - public life has returned to near normal.
- > The lockdown resulted in adverse economic effects - the government has instituted programs to address these effects.
- > Interventions at multiple levels (border-control measures, community based-transmission measures, case-based control measures) proved effective in the pandemic response.
- > This week, however, there has been an outbreak in Auckland which has triggered lockdown.

Reviewed by: Dr Claire von Mollendorf

# GLOBAL 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

**Effect of the COVID-19 pandemic response on intrapartum care, stillbirth, and neonatal mortality outcomes in Nepal: A prospective observational study**  
[https://www.thelancet.com/journals/langlo/article/PIIS2214-109X\(20\)30345-4/fulltext](https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(20)30345-4/fulltext)

- > In this prospective observational study, participant-level data for pregnant women enrolled in the SUSTAIN and REFINE studies between 1<sup>st</sup> January and 30<sup>th</sup> May 2020, from nine hospitals in Nepal was collected.
- > Included 12.5 weeks before the national lockdown and 9.5 weeks during the lockdown.
- > Women were eligible for inclusion if they had a gestational age of 22 weeks or more, a foetal heart sound at the time of admission, and consented to inclusion. Women who had multiple births and their babies were excluded.
- > Of 22,907 eligible women, 21,763 women were enrolled, and 20,354 gave birth, and health worker performance was recorded for 10,543 births.
- > From the beginning to the end of the study period, the mean weekly number of births decreased by 52.4%.
- > The institutional stillbirth rate increased from 14 per 1000 total births before lockdown to 21 per 1000 total births during lockdown ( $p=0.0002$ ), and institutional neonatal mortality increased from 13 per 1000 live births to 40 per 1000 live births.
- > In terms of quality of care, intrapartum fetal heart rate monitoring decreased by 13.4%, and breastfeeding within one hour of birth decreased by 3.5%. The immediate newborn care practice of placing the baby skin-to-skin with their mother increased by 13.2%, and health workers' hand hygiene practices during childbirth increased by 12.9% during the lockdown.
- > Institutional childbirth reduced by more than half during the lockdown, with increases in institutional stillbirth rate and neonatal mortality, and decreases in quality of care. Some behaviours improved, notably hand hygiene and keeping the baby skin-to-skin with their mother.
- > An urgent need exists to protect access to high-quality intrapartum care and prevent excess deaths for the most vulnerable health system users during this pandemic period.

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

**WHO: Public health round-up**

<https://www.who.int/bulletin/volumes/98/8/20-010820.pdf>

- > Disruption in immunisation programs:
  - 85% of countries indicated a decreased level of vaccination coverage in May compared to January-February 2020.
  - 1.4 million fewer doses of diphtheria-tetanus-pertussis vaccine in January - April 2020 compared to the same period in 2019.
- > Access to COVID-19 Tools (ACT) accelerator requires an addition US\$13.7 billion in funding to support the development and equitable distribution of COVID-19 related tests, treatments, and vaccines.
- > 75 countries interested in COVAX facility to assist up to 90 lower-income countries access a vaccine.
- > WHO accepted the Solidarity Trial's International Steering Committee's recommendation to discontinue the hydroxychloroquine and lopinavir/ritonavir arms.
- > The Independent Panel for Pandemic Preparedness and Response (IPPR) has been formed to evaluate the lessons learnt from the world's health response to the COVID-19 pandemic.
- > 73 countries have reported they are at risk of stock-outs of antiretrovirals for HIV treatment, with 24 countries having critically low stocks or disrupted supply.
- > Forecasted 130 million more people affected by chronic hunger by the end of 2020.

Reviewed by: A/Prof Margie Danchin

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

**Refugees and COVID-19: achieving a comprehensive public health response**

<https://www.who.int/bulletin/volumes/98/8/20-271080.pdf>

- > Editorial Bulletin from the World Health Organization evaluating the current challenges with regards to managing refugee health during the COVID-19 pandemic.
- > Current and foreseeable vulnerabilities of refugees during the COVID-19 pandemic.
  - Living conditions of refugee camps increase the risk of contagion.
  - Co-existing infectious diseases (such as tuberculosis) is likely to cause a worse prognosis – and these diseases are common in refugee camps.
  - Language barriers between refugees and host communities make information dissemination difficult.
  - This may also compound public fear of refugees.
  - Economic strain diverts or reduces funding received by humanitarian organisations.

- This may also prolong or exacerbate mental trauma.
- > Recommendations as per the Lancet's guiding principles of health networks:
  - Leave no one behind during this pandemic.
  - The timely deployment of outbreak response teams within refugee camps to promote health education sensitively and ensuring healthcare access.
  - Priority should be given to screening vulnerable subgroups to manage their conditions more effectively and encourage the reduction of high-risk behaviour.
  - The impacts of psychological trauma should not be ignored.

Reviewed by: Professor Fiona Russell

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

### Impact of COVID-19 on maternal and child health (correspondence)

[https://www.thelancet.com/journals/langlo/article/PIIS2214-109X\(20\)30327-2/fulltext](https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(20)30327-2/fulltext)

- > A recent study modelled the indirect effects of COVID-19 on maternal and child mortality in low-income and middle-income countries (LMICs). However, the authors of this letter to the researchers point out it did not model breastfeeding reductions.
- > Yet the COVID-19 pandemic could cause reductions in breastfeeding, both in early initiation, and exclusive and continued breastfeeding
- > This may be due to limited provision and use of health services including antenatal care, postnatal care and community-based lactation support and counselling. Anecdotal evidence suggests that there may be unfounded fears of COVID-19 transmission through breast milk. Moreover, the enabling household environment of breastfeeding may be disrupted due to the increased demand of caring for other children during lockdown periods.
- > Using the Alive & Thrive cost of not breastfeeding:
  - Hypothetical effect of small (5%) reductions in the prevalence of breastfeeding due to COVID-19 disruptions would result in 16,469 child deaths across 129 LMICs over a one year period, plus additional morbidity.
  - Moderate (10%) reduction – 32,139 child deaths
  - Medium (25%) reduction – 75,455 child deaths.
  - Severe (50%) reduction – 138,398 child deaths.
- > The authors highlight in this correspondence that governments should continually support and promote breastfeeding in line with the Global Breastfeeding Collective's call to action during COVID-19 and that future research into indirect impacts of COVID-19 should also consider disruptions to breastfeeding.

Reviewed by: Prof Suzanne M Garland

**WHO situation report 203**

<https://reliefweb.int/sites/reliefweb.int/files/resources/20200810-covid-19-sitrep-203.pdf>

**Burnet COVID-19 Global Trends & Analyses: August update 1**

[https://burnet.edu.au/system/asset/file/4155/8.1\\_Know\\_C-19\\_Hub\\_Global\\_Analysis\\_August\\_7.pdf](https://burnet.edu.au/system/asset/file/4155/8.1_Know_C-19_Hub_Global_Analysis_August_7.pdf)

**Adolescent experiences of COVID-19**

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

# IMAGING

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

## **Automated assessment of CO-RADS and chest CT severity scores in patients with suspected COVID-19 using artificial intelligence**

<https://pubs.rsna.org/doi/10.1148/radiol.2020202439>

- > The artificial intelligence (AI) system was developed to predict the likelihood of COVID-19 on unenhanced chest CT scans.
- > The AI system scores via the CO-RADS system, which assesses COVID-19 lung pathology in unenhanced CT and is used to predict COVID-19 in patients with moderate to severe symptoms.
- > CT severity score assigned for a degree of parenchymal involvement per lobe.
- > The training set of 520 scans of 476 patients, scans scored and rescored independently by chest radiologist blinded to clinical data and prior reports.
- > When tested (105 patients in the internal test set and 262 in the external set), the system had high diagnostic performance, discriminating between COVID-19 positive and negative patients (ROC 0.95 and 0.88), with similar sensitivity and specificity compared to the eight radiologist observers.
- > Median runtime of the algorithm was 212 seconds versus median reading time by radiologists of 82 seconds.
- > Average Dice scores of automatic lobe segmentations between 92.2% and 95.2% (lowest RML).
- > Significantly better sensitivity of observer for only 3 of 36 tested operating points for identification of COVID-19.
- > Moderate agreement between AI-predicted severity scores vs observers, internal test set mean kappa 0.54+/-0.01 for AI and 0.77+/- 0.03 for left-out observer (p<0.001 for all observers).
- > Summary:
  - This system showed high diagnostic performance with AUC of 0.95 on the internal test set and 0.88 on the external test set. Interobserver agreement much higher than AI 0.79 vs 0.6 .
  - AI not able to differentiate motion artefacts or other diagnoses so should be verified by humans.
  - This system adheres to a standardised reporting scheme, previous publications unstandardized / uncalibrated.

- Limitations: the AI system was trained using data from a single centre. Patients receiving CT scans had a high suspicion of COVID-19. Inclusion took place after the influenza season. Limited inclusion of patients with pre-existing lung disease in the training set.
- The AI system may be used to support radiologists during busy periods only if the algorithm is trained to adhere to CO-RADS categories, interpretable by radiologists and if trained with a larger dataset to differentiate overlapping abnormalities.

Reviewed by: A/Prof Simone Mandelstam

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

**Thoracic imaging findings of Multisystem Inflammatory Syndrome in Children (MIS-C) associated with COVID-19: What radiologists need to know now**

<https://pubs.rsna.org/doi/10.1148/ryct.2020200346>

- > A study reviewing key intra- and extra- thoracic imaging findings of all published cases of multisystem inflammatory syndrome in children (MIS-C).
- > MIS-C is a severe inflammatory illness that clinically manifests approximately one or more months after the peak of COVID-19 cases in a geographic region.
- > Clinical course, treatment and outcomes are described.
- > Thoracic CT imaging findings for MIS-C differ from those seen in acute SARS-CoV-2 infection.
- > Intrathoracic manifestations:
  - Three main pathologies identified on imaging as a result of MIS-C are heart failure, ARDS and pulmonary embolism.
  - Heart failure: the majority of patients with MIS-C present with cardiogenic shock.
    - Often findings of acute heart failure/myocarditis.
    - CXR shows typical left heart failure findings.
    - Echo: left ventricular systolic dysfunction with depressed ejection fraction, pericardial effusion (9-40% of patients), coronary artery dilation (17-24%).
    - Cardiac MR: diffuse left ventricular myocardial T2 hyperintensity, suggestive of myocardial oedema and hyperaemia. There is a lack of late contrast enhancement that would typically be seen in myocardial necrosis and fibrosis, which suggests that the myocardial damage seen in MIS-C is more likely to be from a post-viral rather than direct viral myocarditis as seen in adults.
    - Imaging findings may be transient.
  - ARDS: children can present with signs of ARDS.
    - Bilateral multifocal ground-glass and consolidative airspace opacities.
    - Airspace opacities may be asymmetric.

- Pulmonary embolism.
  - Adults with severe COVID-19 infection are prothrombotic. The cause is thought to be related to cytokine storm with increased inflammatory markers.
  - Children with MIS-C have similar inflammatory markers and are likely to have the same prothrombotic coagulopathy.
  - Small segmental PEs were noted on CTA as expansile filling defects in the PA. Clinical significance unclear as no significant difference in ICU admission and course in adults.
- Extra thoracic manifestations are rare in acute COVID-19 but common in MIS-C.
  - Abdominopelvic lymphadenopathy (most prominent in RLQ and looks similar to mesenteric adenitis) is commonly seen.
  - Echogenic kidneys on USS.
  - Ascites and hepatomegaly.
  - Gallbladder wall thickening.
- > In summary, imaging features of MIS-C are different from COVID-19 as it is a multi-organ system disease.

Reviewed by: A/Prof Simone Mandelstam

# MENTAL HEALTH

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

**How has COVID-19 impacted maternal mental health and coping? (not peer reviewed)**

<https://www.medrxiv.org/content/10.1101/2020.08.04.20168039v1?%253fcol=lection=>

- > 1329 new mothers participating in the anonymous online COVID-19 New Mum Study in the United Kingdom responded to questions regarding perceptions of lockdown, activities undertaken, support received, and consequences of lockdown. Mothers were  $\geq 18$  years of age and had given birth  $\leq 12$  months ago.
- > To some or high extent since lockdown began participants reported feeling down (56%), lonely (59%), irritable (62%) and worried (71%), although, 70% of respondents felt that they were able to cope with the lockdown.
- > Support with her health, contact with maternal support groups and a higher infant gestational age predicted better maternal mental health.
- > Travelling for work, if lockdown had a significant impact on the ability to buy food and having an income less than £30k predicted poorer mental health.
- > Greater equality in the division of household chores was associated with better maternal coping, but not maternal mental health.
- > Limitations: As this is an anonymous survey, participants could not be followed up and formally assessed for anxiety and depression using validated tools.
  - A majority of participants self-identified as white, and were married and living with a partner, limiting the generalisability of the findings.

Reviewed by: Prof David Coghill

**Anxiety and depression in COVID-19 survivors: role of inflammatory and clinical predictors (in press)**

<https://www.sciencedirect.com/science/article/pii/S0889159120316068>

- > 402 patients who survived COVID-19, median age 58, were screened on follow-up for post-traumatic stress disorder (PTSD), depression, anxiety, obsessive-compulsive symptoms and insomnia.
- > Baseline inflammatory markers C-reactive protein (CRP), neutrophil lymphocyte ratio (NLR), monocyte lymphocyte ratio (MLR) and systemic immune-inflammatory index (SII) taken on initial ED presentation were used to assess a potential relationship between the inflammatory response to SARS-CoV-2 and psychiatric sequelae.
- > For PTSD (28%), depression (31%), anxiety (42%), obsessive compulsive symptoms (20%) and insomnia (40%) participants' self-rated symptoms in a pathological range. 56% of participants had a pathological score in at least one clinical dimension.

- > Males had higher baseline inflammatory markers. However, females scored higher for anxiety and depression.
- > In participants with a previous psychiatric diagnosis, there was no difference in baseline inflammatory markers, but higher scores in all psychological dimensions were observed.
- > Participants managed at home had lower baseline inflammatory markers but scored higher in PTSD, anxiety and insomnia.
- > For inpatients, length of hospital stays inversely correlated with PTSD, depression, anxiety and obsessive-compulsive symptoms.
- > Baseline inflammatory markers as well as follow up oxygen saturation, did not correlate with psychopathological scores, except SII, which positively correlated with scores of depression and anxiety.
- > Limitations: As this study implemented a cross-sectional design causality cannot be inferred.

Reviewed by: Prof David Coghill

# PERINATAL HEALTH

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

## **PrEP retention and prescriptions for pregnant women during COVID-19 lockdown in South Africa (correspondence)**

[https://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018\(20\)30226-5/fulltext](https://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018(20)30226-5/fulltext)

- > HIV is highly prevalent in sub-Saharan Africa, and transmission risk is high during pregnancy and the puerperium including breastfeeding.
- > Pre-exposure prophylaxis is an effective prevention intervention during pregnancy and in the post-partum period.
- > A primary care clinic which has remained open during the lockdown in a community with high antenatal HIV prevalence in Cape Town, South Africa has a cohort study entitled PrEP in Pregnant and Post-partum Women who are HIV negative and pregnant or in the post-partum period. Women are screened for eligibility at the first antenatal visit to the primary care clinic and complete an interviewer-delivered survey, choosing to then take PrEP at each study visit up until 12 months post-partum.
- > The study team evaluated the national COVID-19 lockdown in South Africa on study visits and PrEP prescriptions among pregnant women in antenatal care.
- > Missed study visits and PrEP prescription refill visits at the one month and three months follow up visits were compared before and during the lockdown.
- > Population: 455 HIV-uninfected pregnant women aged >16 years at their first antenatal visit, median gestation 21 weeks [IQR 14-28]; median age 25 years [IQR 22-31].
- > Sexual activity was similar before versus during lockdown (94% reporting sex in the past 30 days).
  - 414 (91%) of 455 women opted to start PrEP at their first antenatal visit. Common reasons cited included preventing infant HIV (90%), and unknown or positive partner serostatus (10%) were the most common reasons given.
  - Before lockdown, 29% of participants on PrEP missed their one-month visit, and 41% missed their three-month visit.
  - During the nationwide lockdown, missed PrEP visits increased significantly to 63% at the one-month visit and 55% at the three-month visit.
  - 34% of women missed visits before lockdown, and 57% missed visits during the lockdown.
  - The relative risk of missing a study visit increased during lockdown compared with before lockdown (odds ratio 2.36, 95% CI (1.73-3.16)).

- > These data indicate a potential for the COVID-19 pandemic to impact on HIV prevention efforts in the antenatal care setting, and missed visits have implications for maternal and infant health.
- > The study authors recommend community-based PrEP delivery and telephone interviews are needed to address barriers to attending facility-based PrEP prescription and study visits.

Reviewed by: Prof Suzanne M Garland

## Chan Ying Zhen Charissa - 3rd Year Medical Student, Department of Paediatrics, The University of Melbourne

### **Impact of COVID-19 mitigation measures on the incidence of preterm birth: a national quasi-experimental study (not peer reviewed)**

<https://www.medrxiv.org/content/10.1101/2020.08.01.20160077v1?%253fcol=lection=>

- > Previously Ireland [n=1381] and Denmark [n=5162] had independently reported a reduction in preterm birth [very low birth weight and low birth weight infants during COVID-19 mitigation measures. Speculation was this might be due to a reduction in air pollution, reduction in maternal anxiety & infections.
- > To examine this further, a National quasi-experimental difference-in-regression-discontinuity approach to study the impact of the COVID-19 mitigation measures implemented in the Netherlands in a stepwise fashion on 9<sup>th</sup>, 15<sup>th</sup> and 23<sup>rd</sup> March 2020 on the incidence of preterm birth in a much larger study population and over ten year period.
- > Data on 1,599,549 singleton newborns were available.
- > The study period was from between 9<sup>th</sup> October 2010 to 16<sup>th</sup> July 2020, the latter date representing the most recent data available at the time of extraction. The study period was set to include ten years pre-implementation of the first national COVID-19 mitigation measures (9<sup>th</sup> March 2020). There is a national database containing data from all babies having undergone neonatal blood spot screening whereby newborns are screened for a range of diseases after 72 hours of life. The proportion of Dutch babies undergoing neonatal blood spot screening is consistently >99%, so highly representative of the entire population. The study group included 56,720 post-implementation births. They assessed four time-windows before and after the intervention in separate analyses: one, two, three, and four months pre- and post-implementation to measure the incidence of preterm birth in the period directly preceding implementation of the mitigation measures versus the period directly following implementation. By nature of the dataset, stillborn babies were not included.
- > Consistent reductions in preterm birth were seen across various time windows surrounding the implementation of the 9<sup>th</sup> March COVID-19 mitigation measures. The effect was also across various degrees of prematurity.
- > Although not statistically significant – there was a suggestion that the reductions in preterm births were confined to people living in high-SES neighbourhoods which is of considerable concern and requiring further study.

Reviewed by: Prof Suzanne M Garland

# SCHOOLS

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

**Stepwise school opening online and offline and an impact on the epidemiology of COVID-19 in the paediatric population (not peer reviewed)**

<https://www.medrxiv.org/content/10.1101/2020.08.03.20165589v1>

- > School openings in South Korea were delayed three times in March 2020.
- > Online classes started from 9<sup>th</sup> April, and offline (face-to-face) classes started from 20<sup>th</sup> May to 8<sup>th</sup> June at four steps in different grades of students.
- > Physical distancing measures were implemented including limiting classroom size, physical distancing, hygiene, masks (inside only), plastic barriers, singing, and music classes were online-only etc.
- > The specific method of teaching was determined by each school:
  - Year 12 students attended the school for offline classes daily.
  - For all others, the number of students who attended offline classes was determined by the number of confirmed COVID-19 patients in the local area where the school was located and the characteristics of each school.
    - In cities or provinces where there were no recent cases recently, students of small schools (a total number of students of 60 or less) could attend school daily.
    - The rest of the schools (> 500-1,000 students) were recommended that the number of students attending school at the same time should not exceed two-thirds of the total students.
    - In areas where the confirmed cases were increasing, it was recommended that less than one-third of the total students attend the school at the same time.
    - When a confirmed case was identified at a school, the school would stop offline classes and proceed to online classes during the investigation.
- > Data on paediatric cases with COVID-19 were collected.
- > There was no sudden increase in paediatric cases after the school opening, and the proportion of paediatric cases remained around 7%.
- > As of 11<sup>th</sup> July, 45 children from 40 schools and kindergartens tested positive after offline classes started.

- > >11,000 students and staff were tested; only one additional student was found to be infected in the same classroom. Among those 45, 32 patients (71.1%) had available information for the source of infection.
  - 25/45 (55.6%) were infected by the family members.
  - The proportion of paediatric cases without information on infection source were higher in the older age group (middle and high school students) than in younger age group (kindergarten and elementary school students) (47.6% vs 12.5%).
  - In the younger age group, 79.1% of children were infected by family members, while only 28.6% of adolescents in the older age group were infected by family members ( $p < 0.001$ ).
- > South Korea had a successful transition from school closure to re-opening with online and offline classes.

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

#### **Using social contact data to predict and compare the impact of social distancing policies with implications for school re-opening (not peer reviewed)**

<https://www.medrxiv.org/content/10.1101/2020.07.25.20156471v1>

- > This study from the UK used social contact data to predict the impact of social distancing policies on Reproductive number (R), with a focus on re-opening schools. The prediction tool was calibrated to the COVID-19 pandemic in the UK using publicly available death data and Google community mobility reports. The tool was then focused on the impact of re-opening schools against a back-drop of wider easing of social distancing and adequate contact tracing.
- > Estimates were generated under the assumption that children are half as infectious as adults, and there is no immunity in the population.
- > The estimated R number in a pre-control setting (before lockdown measures in the UK) was  $R=2.7$ .
  - The estimated minimum R number that can be achieved in the UK without limiting household contacts is 0.45.
  - Preventing leisure contacts alone gave  $R=2.0$  and preventing work contacts alone reduced the R number to 1.5.
  - Opening primary schools had a small impact on the R number, taking it to  $R=0.83$ , but high adherence to other mitigation measures was needed.
  - Opening secondary schools as well resulted in  $R=0.95$ , however effective contact tracing was thought to still control transmission.
  - In general, higher adherence to other social distancing measures is required as more children return to school.

- Where 20% of contacts are effectively traced and isolated, a larger proportion of pupils could return to school while still limiting transmission. If 60% of contacts of symptomatic cases were traced and isolated it was estimated that schools could fully re-open while maintaining control of transmission, as long as 50% of other contacts were prevented.
- The most pessimistic scenario, where children are as infectious as adults, corresponds to the scenarios considered. If children are less infectious than adults, then re-opening primary and secondary schools has a smaller impact on the R number, but the impact of increasing other contacts outside the home and school settings remains the same.
- > Limitations: High levels of compliance with social distancing outside school settings and highly effective contact tracing would be required to make this model reliable.
  - The analysis used pre-existing detailed social contact data from 5,861 individuals in 2010. Up to date, social contact surveys would help gain a greater understanding of current contact patterns.
  - This is a mathematical model, and further studies would aid in understanding if this was truly representative for the UK.
  - Application to Australia would need further investigation as classroom sizes, household characteristics and public transport use may differ (i.e. contact patterns).
- > Conclusions: High adherence to social distancing outside school settings is needed to maintain epidemic control. Opening primary schools has a modest impact on R while opening secondary schools is predicted to have a more significant overall impact; a combination of re-opening both would result in a loss of epidemic control.

Reviewed by: Prof Fiona Russell

**Daniel Lamanna** - 3rd Year Medical Student,  
Department of Paediatrics, The University of Melbourne

**Assessment of SARS-CoV-2 screening strategies to permit the safe re-opening of college campuses in the United States**

<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2768923>

Universities across the United States of America are struggling with the question of whether or not to open university campuses for the fall 2020 semester

- > This analytic modelling study included a hypothetical cohort of 4,990 students without SARS-CoV-2 infection, and ten students with undetected, asymptomatic infection at the beginning of the semester. Three epidemic severity scenarios were defined during an 80-day semester period.
- > Simple compartmental epidemic modelling was used to capture the critical features of SARS-CoV-2 in this setting: a natural history of illness, regular mass screening to detect, isolate and contain the virus in residential college environments.
- > Spreadsheet implementation of the model allowed for variation in critical parameters and examination of how different test performance attributes (frequency, sensitivity, specificity, cost) changed outcomes.

- > Compartmental Model – defined three epidemic severity scenarios:
  - Best case: reproduction number ( $R_0$ ) of 1.5, test specificity of 99.7% and five exogenous, undetected infections/week.
  - Base case: reproduction number ( $R_0$ ) of 2.5, test specificity of 98%, and ten exogenous, undetected infections/week.
  - Worst case: reproduction number ( $R_0$ ) of 3.5, test specificity of 98% and 25 exogenous, undetected infections/week.
- > Isolation: assumed that after an eight-hour lag those with a positive test (true or false) and those demonstrating symptoms would be moved into an isolation dormitory where no further transmissions would occur.
- > Screening: a range of SARS-CoV-2 detection methods were considered with a range of sensitivities (70 - 99%), specificities (98 - 99.7%), and per test costs (\$10 - \$50).
  - For each combination of test characteristics, both symptom-based and routine testing every 1, 2, 3, and 7 days were considered.
- > Cost-effectiveness: estimated incremental cost-effectiveness ratios.
- > Results: Base case scenario: screening every 1, 2, 3, or 7 days with a 70% sensitive, 98% specific test resulted in 162, 243, 379, and 1,840 cumulative infections, respectively. Symptom-based screening yielded 4,970 infections. Increasing test sensitivity reduced total infections.
- > Weekly and symptom-based screening were associated with large increases in the infected occupancy of the isolation dormitory.
- > The number of students with false-positive results and the isolation capacity required to accommodate them were reduced in the presence of a more specific test.
- > Discussion: A highly specific screening test that can be easily administered to each student every one to seven days and that also reports results quickly enough to allow newly detected cases to be isolated within hours would be required to blunt infectious transmission and control campus outbreaks at a reasonable cost.
- > Stringent implementation and enforcement of handwashing etiquette, indoor masking, elimination of buffet dining, reduced washroom sharing with frequent cleaning, and reduced density of campus and classrooms would minimise  $R_0$  - any relaxation of such measures would shift  $R_t$  towards the worst-case scenario which would require daily screening.

Reviewed by: Dr Claire von Mollendorf

# TRANSMISSION

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

**SARS-CoV-2 viral load dynamics, duration of viral shedding and infectiousness:  
a living systematic review and meta-analysis (not peer reviewed)**

<https://www.medrxiv.org/content/10.1101/2020.07.25.20162107v1.full.pdf>

- > A systematic review was done to compare the viral dynamics of SARS-CoV-1 and MERS-CoV.
- > SARS-CoV-2 RNA shedding:
  - Mean duration:
    - Upper respiratory tract (URT): 17 days.
    - Lower respiratory tract (LRT): 14.6 days.
    - Stool: 17.2 days.
    - Serum: 16.6 days.
  - Most studies show the increased duration of shedding in severe illness.
  - Mean duration of shedding in URT and stool positively associated with age.
- > Viral load:
  - Peak viral loads in URT in the first week of illness: at or soon after symptoms onset or day three to five of illness (earlier than SARS-CoV-1 and MERS-CoV which peak in the second week of illness).
  - The median time to live virus clearance: URT – 3.5 days; LRT – 6 days.
  - No study has detected live virus beyond day nine of illness.
- > SARS-CoV-2 RNA shedding can be prolonged in respiratory and stool samples, but the duration of the viable virus is short-lived.
  - The peak of viral load is in the first week of illness.
  - Detection of viral RNA cannot be used to infer infectiousness.
  - Early case finding and isolation and public education on the spectrum of disease is important.
- > Limitations: Some study patients received a range of treatments; most studies are case series vulnerable to selection bias; meta-analysis identified substantial study heterogeneity.

Reviewed by: Dr Samantha Bannister

# VACCINES

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

**ChAdOx1 nCoV-19 vaccine prevents SARS-CoV-2 pneumonia in rhesus macaques**  
<https://www.nature.com/articles/s41586-020-2608-y>

- > In these pre-clinical studies, adenovirus-vectored vaccine ChAdOx1 nCoV-19, encoding the spike protein of SARS-CoV-2, was immunogenic in mice, eliciting robust humoral and cell-mediated responses.
- > This response was predominantly Th1, as demonstrated by IgG subclass and cytokine expression profiling.
- > In six non-human primates (rhesus macaques), vaccination with ChAdOx1 nCoV-19 (prime-only and prime-boost regimen) induced a balanced Th1/Th2 humoral and cellular immune response .
- > Compared to six non-vaccinated macaques, there was a significantly reduced viral load in bronchoalveolar lavage fluid and lower respiratory tract tissue of vaccinated rhesus macaques challenged with SARS-CoV-2 compared with control animals, and no pneumonia was observed in vaccinated animals.
- > However, there was no difference in nasal shedding between vaccinated and control animals.
- > There was no evidence of immune-enhanced disease following viral challenge in vaccinated animals.
- > Safety, immunogenicity and efficacy of ChAdOx1 nCoV-19 against symptomatic PCR-positive COVID-19 disease will now be assessed in randomised controlled human clinical trials.
- > Implications: prevention of disease in pre-clinical studies is promising, but lack of prevention of nasal shedding indicates possible lack of effectiveness in preventing transmission - more extensive clinical trials and studies will determine this.

Dr Ryan Toh – Postdoctoral researcher, New Vaccines, Infection & Immunity Theme, MCRI and Honorary Fellow, Department of Paediatrics, The University of Melbourne

**First-in-human trial of a SARS-CoV-2 recombinant spike protein nanoparticle vaccine (not peer reviewed)**

<https://www.medrxiv.org/content/10.1101/2020.08.05.20168435v1.full.pdf>

- > This randomised, observer-blinded, placebo-controlled, phase 1 trial describes the safety and immunogenicity results of a recombinant nanoparticle vaccine composed of trimeric full-length SARS-CoV-2 spike glycoproteins (NVX-CoV2373, Novavax Inc.) with or without the saponin-based Matrix-M1 adjuvant in healthy adults in Australia.
- > One or two doses (5- or 25- $\mu$ g) of NVX-CoV2373 with or without Matrix-M1 adjuvant (50- $\mu$ g dose) were given as a 2-dose schedule, 21 days apart to healthy adults aged 18-59 years old.
- > Five Groups (total N=131):
  - Placebo.
  - 25ug NVX-CoV2373, 25ug NVX-CoV2373.
  - 5ug NVX-CoV2373-50 ug Matrix M1, 5ug NVX-CoV2373-50 ug Matrix M1.
  - 25ug NVX-CoV2373-50 ug Matrix M1, 25ug NVX-CoV2373-50 ug Matrix M1.
  - 25ug NVX-CoV2373-50 ug Matrix M1.
- > Reactogenicity was generally mild, and vaccinations were well tolerated.
- > Local reactogenicity was more frequent for the NVX-CoV2373/Matrix-M1 regimens; tenderness and pain being the most common.
- > Systemic events were individually less frequent, with headache, fatigue, and myalgia being the most common.
- > The second dose of NVX-CoV2373/Matrix-M1 induced greater local and systemic reactogenicity, but the majority were of low-grade.
- > No serious adverse events or adverse events of special interest were reported.
- > NVX-CoV2373 alone induce low antibody responses.
- > A two-dose schedule of 5ug or 25ug of NVX-CoV2373/Matrix-M1 induces similar anti-spike IgG and neutralising antibody responses, by ELISA and micro neutralisation assay, respectively.
- > A single dose of NVX-CoV2373/Matrix-M1 generated a similar level of antibody responses as convalescent sera from asymptomatic COVID-19 patients.
- > A second dose of NVX-CoV2373/Matrix-M1 induces an anamnestic antibody response to a level that is similar to convalescent sera from severe COVID-19 patients (that require hospitalisation) by day 14 post-second dose.
- > A strong correlation was observed for NVX-CoV2373/Matrix-M1 neutralising antibody and anti-spike IgG.

- > Th1 cell responses (CD4+ cells expressing either IFN- $\gamma$ , IL-2, and/or TNF- $\alpha$ ) were detected in a subset of individuals vaccinated with NVX-CoV2373/Matrix-M1 regimens but were generally low.
- > Significance: A promising vaccine candidate to prevent SARS-CoV-2 infection and COVID-19.
- > Limitations: Limited duration for safety observations (seven days) and immune responses (35 days). The vaccine to progress to the next phase of development for efficacy and also in people with co-morbidities and/or older adults who are most at high risk of COVID-19.

# VIROLOGY

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

## **Evidence of exposure to SARS-CoV-2 in cats and dogs from households in Italy (not peer reviewed)**

<https://doi.org/10.1101/2020.07.21.214346>

- > SARS-CoV-2 sporadic detection and experimental infection in various animals, including cats, ferrets and dogs, have been documented.
- > In this study, 817 companion animals (cats and dogs) living in northern Italy were sampled between March to May 2020, from SARS-CoV-2 positive households or living in geographic areas that were severely affected by COVID-19.
- > A total of 540 dogs and 277 cats were sampled, mostly from the Lombardy region (476 dogs, 187 cats).
  - Oropharyngeal (306 dogs, 175 cats), nasal (185 dogs, 77 cats), and/or rectal (66 dogs, 30 cats) swabs were collected.
  - Sera was available for 188 dogs, and 63 cats with known clinical history and additional sera were collected from diagnostic laboratories for 200 dogs and 89 cats that lacked clinical histories.
- > No animals tested positive for SARS-CoV-2 by real-time RT-PCR.
- > 3.4% of dogs and 3.9% of cats had measurable SARS-CoV-2 neutralising antibody titres.
- > Neutralising antibodies were detected in 12.8% of dogs and 4.5% of cats from COVID-19 positive households.
- > It is unlikely that infected pets play an active role in SARS-CoV-2 transmission to humans.

## **Variant analysis of SARS-CoV-2 genomes**

<https://www.who.int/bulletin/volumes/98/7/20-253591.pdf>

- > 10,022 SARS-CoV-2 genomes from 68 countries were analysed.
- > Genome variants were identified via pairwise alignment to the reference genome NC\_045512.
- > 5775 distinct genome variants were identified, including 2969 missense mutations, 1965 synonymous mutations, 484 mutations in the non-coding regions, 142 non-coding deletions, 100 in-frame deletions, 66 non-coding insertions, 36 stop-gained variants, 11 frameshift deletions and two in-frame insertions.
- > The most common variants identified were:
  - Synonymous 3037C > T (6,334 samples).

- P4715L in the open reading frame 1ab (6,319 samples).
- D614G in the spike protein (6,294 samples).
- > 427 distinct non-synonymous variants were identified in the region of the genome encoding the spike protein; with many variants located within the receptor-binding domain and B-cell epitopes.
- > Phylogenetic analysis revealed six major clades and 14 subclades; with certain clades associated with geographic regions.
- > The nucleotide substitution rate was estimated at  $1.12 \times 10^{-3}$  mutations per site-year.
- > Clinical relevance needs to be determined.

# OTHER RESOURCES

Burnet Institute research findings, policy and technical reports

[https://www.burnet.edu.au/covid-19//36\\_know\\_c19\\_hub](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](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\\_z2uWV7r3FaPzAO86q9ZXBcTZ1OcCE\\_Nw/formResponse](https://docs.google.com/forms/u/0/d/e/1FAIpQLSfOxCoAuLV0aJdf_z2uWV7r3FaPzAO86q9ZXBcTZ1OcCE_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 US 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>

# EDITORIAL TEAM

<b>Leadership group:</b>	Professor Fiona Russell & Dr Wonie Uahwatanasakul
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**Journalists:** For any media inquiries, please contact The University of Melbourne media unit, via [news@media.unimelb.edu.au](mailto:news@media.unimelb.edu.au)

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# REVIEWERS

<b>Professor Fiona Russell</b>	Director of the Child and Adolescent Health PhD Program, Department of Paediatrics, The University of Melbourne; Group Leader Asia-Pacific Health Research, MCRI
<b>Dr Wonie Uahwatanasakul</b>	Paediatrician- Immunisation service RCH, MD Child and Adolescent Health Program Lead Coordinator, Department of Paediatrics, The University of Melbourne
<b>Professor Dave Coghill</b>	Financial Markets Foundation Chair of Developmental Mental Health, The University of Melbourne
<b>Dr Lien Anh Ha Do</b>	Virologist, New Vaccines, Infection & Immunity Theme, MCRI and Honorary Fellow, Department of Paediatrics, The University of Melbourne
<b>Associate Professor Margie Danchin</b>	General and Immunisation Paediatrician, Department of General Medicine, RCH, Group Leader, Vaccine Uptake, MCRI, Clinician Scientist Fellow, Department of Paediatrics and School of Population and Global Health, The University of Melbourne
<b>Dr Claire von Mollendorf</b>	Senior Research Officer, New Vaccines and Asia-Pacific Health Research Groups, MCRI and honorary Senior Fellow, Department of Paediatrics, The University of Melbourne
<b>Professor Suzanne M Garland</b>	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
<b>Associate Prof Simone Mandelstam</b>	Senior Specialist Paediatric Radiologist RCH, Departments of Paediatrics and Radiology University of Melbourne
<b>Dr Samantha Bannister</b>	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
<b>Dr Ryan Toh</b>	Post-doctoral researcher, New Vaccines, Infection & Immunity Theme, MCRI and Honorary Fellow, Department of Paediatrics, The University of Melbourne
<b>Dr Celeste Donato</b>	Senior Research Officer, Enteric Diseases, Infection & Immunity Theme, MCRI and Honorary Fellow, Department of Paediatrics, The University of Melbourne