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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.27

22nd October 2020



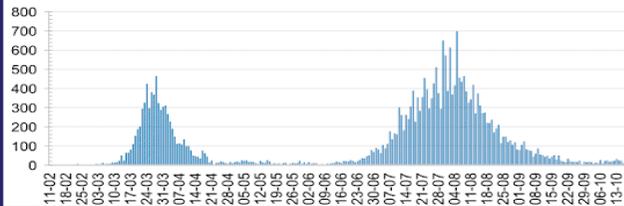
Australian Government
 Department of Health

BE COVIDSAFE

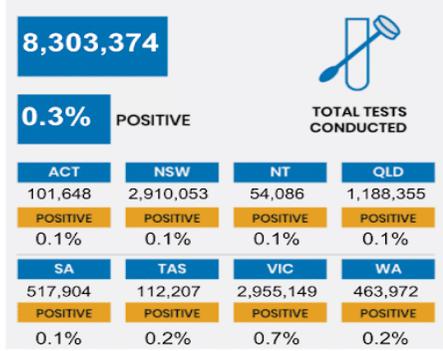
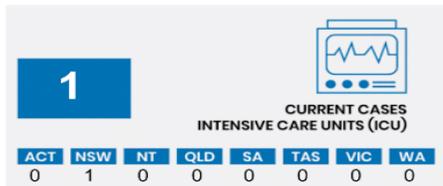
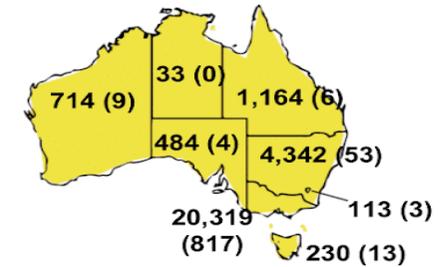
CURRENT STATUS OF CONFIRMED CASES



DAILY NUMBER OF REPORTED CASES



CASES (DEATHS) BY STATE AND TERRITORIES

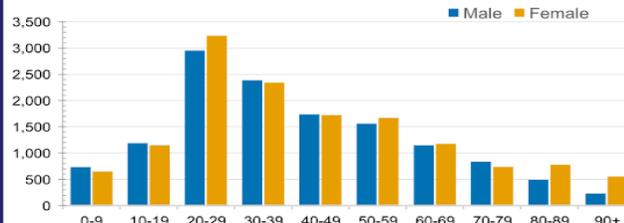


CASES IN AGED CARE SERVICES

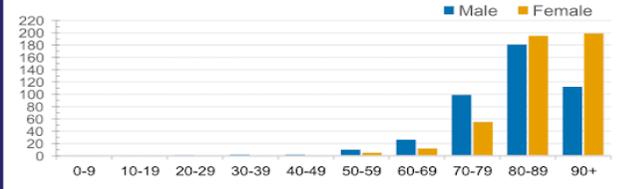
Confirmed Cases	Australia	ACT	NSW	NT	QLD	SA	TAS	VIC	WA
Residential Care Recipients	2049 [1364] (683)	0	61 [33] (28)	0	1 (1)	0	1 (1)	1986 [1331] (653)	0
In Home Care Recipients	82 [74] (8)	0	13 [13]	0	8 [8]	1 [1]	5 [3] (2)	54 [49] (5)	1 (1)

Cases in care recipients [recovered] (deaths)

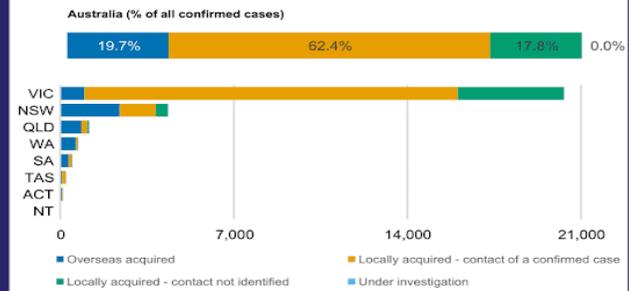
CASES BY AGE GROUP AND SEX



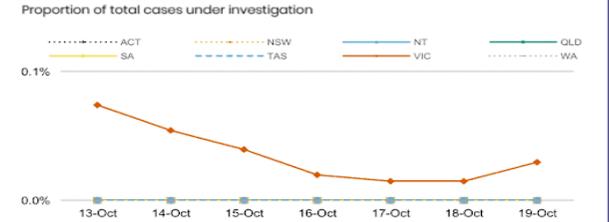
DEATHS BY AGE GROUP AND SEX



CASES BY SOURCE OF INFECTION



PUBLIC HEALTH RESPONSE MEASURE



Last updated 19 October 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 October 19; cited 2020 October 20]
 Available from: <https://www.health.gov.au/resources/collections/coronavirus-covid-19-at-a-glance-infographic-collection>

GUEST EDITORIAL

Associate Professor Nigel Crawford - General Paediatrician, The Royal Children's Hospital; Medical Head, Immunisation Services, Department of General Medicine, The Royal Children's Hospital; Director of SAEFVIC (Surveillance of Adverse Events Following Vaccination in the Community); Senior Fellow, Department of Paediatrics, University of Melbourne.

This 27th edition of the COVID-19 Kids Research Evidence Update has coincided with the easing of restrictions in Victoria. This is something that everyone in the state should be extremely proud of, including the DHHS public health teams, the healthcare workers on the front line, and all of the researchers involved in the epidemiology, virology and immunological investigations into the SARS-CoV-2 virus.

The health literacy regarding infectious diseases epidemiology has never been higher, as the mainstream media, TV and radio presenters discuss modelling, rolling 14-day averages and 'mystery COVID-19 cases'. As Melburnians start to travel more than 5kms from their home but reach the end of the road at 25 km, thoughts move to what will be our 'COVID normal'? How will it look in Australia, compared to the United States and Europe as they approach winter in the middle of an increasing second COVID-19 wave?

What is certain is that SARS-CoV-2 vaccines will need to be a part of our arsenal, as they have been for so many emerging infections over time. Ebola in Africa is now a vaccine-preventable disease, and the H1N1 2009 influenza pandemic required a vaccine to moderate the spread of that infection. Australia has a long history of being early introducers of vaccines, such as the Human Papillomavirus vaccine in 2007. With a comprehensive National Immunisation Program, we are well placed to roll-out a comprehensive SARS-CoV-2 vaccine program, as soon as a safe and effective vaccine is available. Australia is in a position to support international vaccine efforts, both within our region and beyond.

At the Melbourne Vaccine Education Centre (MVEC), based at the Murdoch Children's Research Institute, we started a podcast series called 'COVID-19 Road to a vaccine' in May 2020. [1] That road is now being travelled at pandemic speed, with 44 vaccines currently in human clinical trials and Australia has entered advanced market agreements with AstraZeneca-Oxford and CSL- University of Queensland. [2, 3] The Melbourne Children's campus has identified 'SARS-CoV-2 vaccine preparedness' as a priority area, where we can contribute across all aspects of preparations, including epidemiological, laboratory, vaccine safety, as well as confidence and communication.

But what about children, are they on the 'road to a vaccine'? Or did they miss the bus? A systematic review found that children are unlikely to be the main drivers of the pandemic [4], but we need to still consider their role in transmission, both up to primary school age (0-11 years) and secondary school (12-18 years). Those in the 15-24 years age-bracket, have in fact felt some of the most significant social impacts of the pandemic, including disruption to the late high school years 11 & 12 and higher education, with significant impact on well-being and mental health, as highlighted in an increasing number of scientific articles and previous editorials.

So, there is now a call in the vaccinology sphere to ‘pivot’ and not just continue with a model of SARS-CoV-2 trials that only focus on protection from disease, but expand by including COVID-19 transmission. As noted by Adam Finn & Richard Malley in the New York Times. [5] *“The best vaccines don’t just protect the inoculated from getting sick from the disease. They also protect everyone else from even contracting the pathogen that causes that disease. Preventing the very transmission of SARS-CoV-2, no less than stopping it from turning into Covid-19, should be the main priority of current efforts to develop the vaccines to end this pandemic.”*

This position has been formally represented by the American Academy of Pediatrics, who in an open letter to the US Department of Health and Human Services and the FDA, highlight the need to include children in the SARS-CoV-2 vaccine trials, as they are currently limited to healthy adults aged 18 years and above. [6] *“As paediatricians, we must also stress how crucial it is for children to be included in vaccine trials of SARS-CoV-2 vaccines. While some studies have shown that children under the age of 10 may be less likely to become infected and less likely to spread the virus to others, more recent data suggest children older than ten years may spread SARS-CoV-2 as efficiently as adults. While the likelihood of spreading the disease may vary among different aged children, we know that children can and do spread the virus to household members, grandparents, teachers, and other children. In fact, in the United States alone, more than 587,000 COVID-19 cases have been reported in children, representing approximately ten per cent of all cases. Among the children who have acquired COVID-19, 109 have died from the virus, with more than two-thirds being Black and Latino children.”*

The Melbourne Children’s campus has an opportunity to contribute to COVID-19 vaccine preparedness on many levels. Examples include immunisation education for our adult healthcare worker colleagues, including those caring for the most vulnerable in the community, such as residents of aged care facilities. We can all contribute to the messaging around the safety profile of the vaccines as they emerge from the pipeline and contribute as local immunisation champions and/or spokespeople.

As a final comment, coming back to the MVEC ‘COVID-19 Road to a vaccine’ podcasts series, at the end of each episode we have started to ask the interviewee to tell us something ‘positive’ that has happened to them personally or professionally during the pandemic. These positive reflections can help us remember the collaborative nature of clinical care and research. All of these activities have helped bring COVID-19 under control here in Victoria. We are all in this together.

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3. Flanagan KL, Best E, Crawford NW, Giles M, Koirala A, Macartney K, Russell F, Teh BW, Wen SC. [Progress and Pitfalls in the Quest for Effective SARS-CoV-2 \(COVID-19\) Vaccines. *Frontiers in Immunology*. 2020 2nd October;11:2410.](#)
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5. Finn A, & Malley R. Opinion | A Vaccine That Stops Covid-19 Won't Be Enough [Internet]. New York Times. 2020 [24 August 2020; cited 21 October 2020]. Available from: <https://www.nytimes.com/2020/08/24/opinion/coronavirus-vaccine-prevention.html>
6. American Academy of Paediatrics, open letter, [Internet] 2020 {2020 September 29; cited 2020 October 21] Available from: <https://downloads.aap.org/DOFA/AAPLettertoHHSandFDACHildreninCOVID19VaccineTrials.pdf>

HIGHLIGHTS

- > A study from the UK found a high prevalence of acute kidney injury in children with paediatric inflammatory, multisystem syndrome (PIMS-TS) temporally associated with SARS-CoV-2.
- > In asymptomatic and symptomatic children with COVID-19 infection, ventricular repolarisation was impaired; therefore it is recommended to do a baseline ECG on all children presenting with COVID-19.
- > In regions of high COVID-19 transmission (hotspots), percent positivity tends to increase earlier in persons aged ≤ 24 years; percent positivity increases more gradually over a period of several weeks for those aged ≥ 25 years.
- > Interviews with young people infected with SARS-CoV-2 in the US identified several themes, including social/peer pressure to not wear a mask, decreased perceived severity of disease outcomes, perceived responsibility to vulnerable loved ones and others, attitudes regarding public health guidance, misinformation, conflicting and opposing messages, and workplace mitigation measures.
- > A systematic review found the secondary attack rates to be lower in asymptomatic cases versus symptomatic cases.
- > Frequent testing of household contacts may increase the yield of detecting secondary cases, thus mitigating the likely underestimation of transmission by single follow-up tests.
- > Phylogenetic data of SARS-CoV-2 combined with in-depth interviews suggest asymptomatic transmission contributes to ongoing infection, as highlighted in a super spreading event from a bar in Vietnam.
- > It is important to identify super spreading events (SSEs) during the early stages of an outbreak due to benefits from tailored preventative and public health policies.
- > A survey found that exposure to centre-based childcare settings in the US was not associated with an increased odds of COVID-19; however, home-based child care settings were.
- > A cluster of SARS-CoV-2 was described in a nursery in Poland.
- > The Australian Government's COVIDSafe app had a 37% uptake in May 2020 with privacy concerns being the most common reason for not downloading the app.
- > With many countries facing epidemic resurgence, evaluating the impact of different strategies New Zealand implemented in the early phases of the pandemic is crucial for developing an effective long-term response.
- > Air purifiers equipped with HEPA filters can efficiently, quickly and homogeneously reduce the aerosol load in a closed room.

- > In-utero vertical transmission of SARS-CoV-2 is possible but rare. SARS-CoV-2 genome can be detected in umbilical cord blood, at-term placenta, vaginal mucosa and breast milk.
- > There is potential for maternally derived antibodies to be protective for neonates against SARS-CoV-2 infections, demonstrated by efficient SARS-CoV-2 IgG maternal-foetal transfer.
- > The infant formula industry has been actively exploiting concerns about COVID-19 to increase sales, in violation of the WHO International Code of Marketing of Breast-milk Substitutes.
- > A population study of preterm birth rates in the Netherlands demonstrates reductions in preterm birth linked with nation-wide COVID-19 mitigation policies.

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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.

Always seek the advice of your physician or another qualified health provider properly licensed to practice medicine or general healthcare in your jurisdiction concerning any questions you may have regarding any information obtained from this publication.

Never disregard professional medical advice or delay in seeking it because of something you have read in this publication. Information obtained in this publication is not exhaustive and does not cover all possible manifestations of COVID-19 nor its interaction with other conditions, diseases, ailments, or their treatment.

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CLINICAL PAEDIATRICS

Chelsea Haliburton – 3rd Year Medical Student, University of Ottawa

Assessment of cardiac arrhythmic risk in children with COVID-19 infection cardiac arrhythmic risk in children with COVID-19 Infection

<https://link.springer.com/article/10.1007/s00246-020-02474-0>

- > Major cardiac complications – including acute myocardial damage, arrhythmia and cardiogenic shock – are being reported in adults due to COVID-19; however, the mechanism of cardiac injury and arrhythmia is unclear. Also, several drugs being used to treat COVID-19 infection have cardiovascular side-effects such as inducing arrhythmias.
- > Aim of this case-control study was to investigate the effects of COVID-19 infection on trans-myocardial repolarisation parameters in children with asymptomatic or mild symptoms.
 - 105 children with asymptomatic or mild COVID-19 presenting to a hospital-based paediatric cardiology clinic in Turkey were compared with 40 age and sex-matched healthy children with an innocent murmur.
 - 12-lead electrocardiogram recordings were completed at the time of diagnosis of COVID-19 infection.
 - QT interval, corrected QT (QTc), QT dispersion (QTd), QTc dispersion (QTcd), Tpeak-end (Tp-e), Tpe-dispersion, Tp-e/QT ratio, and Tp-e/QTc ratio were compared.
- > Mean age of 11.2 ± 0.3 years in the patient group and 10.8 ± 2.1 years in the control group.
 - Cardiac troponin I, creatinine kinase-myocardial band (CK-MB) and D-dimer values were in normal ranges for the children with COVID-19.
 - Heart rate was higher in the COVID-19 group (89.7 ± 23.7 versus 82.1 ± 13.2).
 - In the COVID-19 group, QTd, QTcd, Tp-e, Tp-e dispersion, Tp-e/QT ratio and Tp-e/QTc ratio were statistically significantly higher than the control group.
- > Implication: Ventricular repolarisation was impaired in asymptomatic and symptomatic children with COVID-19 infection.
 - The mechanism of cardiac injury is unclear.
 - Baseline ECG should be performed in all COVID-19 positive children planned to receive QT prolonging medication.
- > Limitations: Sharp limits for QTc and QTc interval dispersion in children are not seen in the literature.
- > The results suggest the need for further assessment of the long-term risk of prolonged QT dispersion in the setting of COVID-19 infection.

Reviewed by: Dr Martin Wright

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

Anti-NMDA-receptor encephalitis associated with COVID-19 infection in a toddler
[https://www.pedneur.com/article/S0887-8994\(20\)30329-5/fulltext](https://www.pedneur.com/article/S0887-8994(20)30329-5/fulltext)

- > A first case report of a 23-month-old female with anti-NMDA-receptor encephalitis thought to be secondary to SARS-CoV-2 infection (2 case reports of adults have been published).
- > Anti-NMDA-receptor encephalitis develops secondary to an autoimmune and/or paraneoplastic process and occurs most commonly in young adults.
- > Triggers thought to be associated with the disease include ovarian teratoma, HSV infection and Japanese encephalitis.
- > Case report
 - D1: onset of symptoms - fever, decreased oral intake, poor sleep, constipation and fussiness.
 - D7: the patient presented to the ED with a fever and dehydration. She was not interacting/talking with caregivers and had constant kicking and thrashing movements of extremities. SARS-CoV-2 PCR testing was positive. Extensive testing of the CSF for other infectious causes revealed no abnormalities.
 - D9: the patient had several seizures.
 - D14: fever resolved, but neurological symptoms worsened, with worsening encephalopathy and hyperkinetic movements. Further testing revealed the presence of NMDAR-IgG autoantibodies in the serum and CSF. Anti-SARS-CoV-2 IgG was also detected in the serum. The patient was treated with a five-day course of IV methylprednisolone.
 - Symptoms still persisted, and then treatment with IVIG was commenced. The symptoms resolved over the next week, and the patient returned to baseline approximately two weeks after being discharged.
- > Increased autoantibody production in children with MIS-C (a multisystem inflammatory syndrome in children) has been noted.
- > With the lack of known precipitants and negative testing for a wide range of other pathogens, SARS-CoV-2 infection may be a risk factor for developing anti-NMDA-receptor encephalitis.

Reviewed by: Dr Martin Wright

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

Acute kidney injury in Pediatric Inflammatory Multisystem Syndrome temporally associated with severe acute respiratory syndrome coronavirus-2 pandemic: experience from PICUs across United Kingdom

https://journals.lww.com/ccmjournal/Abstract/9000/Acute_Kidney_Injury_in_Pediatric_Inflammatory.95467.aspx

- > Paediatric inflammatory, multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS), also known as a multisystem inflammatory syndrome in children (MIS-C), is an inflammatory condition that occurs in some children following acute SARS-CoV-2 infection. It is characterised by fever and multi-organ involvement (mainly cardiac dysfunction and shock).
- > The aim of this observational multicentre cohort study from the United Kingdom was to determine the prevalence, risk factors, and outcomes associated with acute kidney injury (AKI) in children < 18 years admitted to 15 PICUs with PIMS-TS between 14th March and 20th May 20, 2020.
- > A total of 116 patients were included. Children with known renal disease and those on dialysis were excluded.
 - Median age: 11 (IQR 7-14) years.
 - Children were diagnosed and staged for AKI based on the rise of serum creatinine levels above the age-specific upper limit of reference interval (ULRI), with AKI stage 1: 1.5-2x ULRI; stage 2: 2-3x ULRI; stage 3: >3xULRI. Stages 2-3 were classified as severe AKI.
- > Prevalence of AKI
 - 48/116 patients (41.4%) had AKI of any stage, and 32/116 (27.6%) had severe AKI. The majority of these patients either had AKI at admission or developed it within 48 hours of admission.
- Factors associated with AKI
 - In univariate analyses, high BMI, hyperferritinemia, high CRP, high Paediatric Index of Mortality 3 score, vasoactive medication and invasive mechanical ventilation were associated with severe AKI.
 - In multivariable analyses, hyperferritinemia was the only factor that was significantly associated with severe compared with non-severe AKI (adjusted OR 1.04; 95% CI: 1.01-1.08; P=0.04).
- Impact of AKI on outcomes
 - Overall, renal function improved over time. All, apart from three patients, had resolved AKI at the time of discharge. Three patients received continuous renal replacement therapy (CRRT), and three patients received extracorporeal membrane oxygenation (ECMO). Two patients died, both of whom had stage three AKI at/during admission.

- Severe AKI was associated with longer PICU stay compared with non-severe/no AKI (median 5 [IQR 4-7] days vs 3 [IQR 1.5-5] days; $P<0.001$) and increased duration of invasive mechanical ventilation (median 4 [IQR 2-6] days vs 2 [IQR 1-3] days; $P=0.04$).
- > Conclusions: There was a high prevalence of AKI in children with PIMS-TS, and it appears to have good short-term outcomes. Long-term outcomes are, however unknown, and further studies are needed to determine this.
- > Limitations: complete follow-up of patients was not available, markers of kidney involvement (proteinuria and haematuria) which could further inform the degree of renal damage were not performed in every patient, and baseline serum creatinine levels were not available for every patient for comparison.

Reviewed by: Dr Martin Wright

EPIDEMIOLOGY & PUBLIC HEALTH

Rebecca Seliga - 3rd Year Medical Student, University of Ottawa

Factors influencing risk for COVID-19 exposure among young adults aged 18 - 23 years - Winnebago County, Wisconsin, March - July 2020

<https://protect-au.mimecast.com/s/chZOCXLKNwFXkQEL8iMOBlc?domain=cdc.gov>

- > This study aimed to identify factors that influence young adults' behaviour and risk for exposure to COVID-19 in Winnebago County, Wisconsin.
- > Characteristics of young adults who tested COVID-19 positive from 1st March-18th July 2020 were retrieved from Wisconsin's Electronic Disease Surveillance System.
- > Thirty key informant interviews were summarised to assess factors that contributed to exposure.
 - Of these 30 interviews, 13 were young adults, nine were business owners of establishments frequented by young adults, and eight were community leaders.
 - Interviewees were recruited by snowball sampling (enrolled participants referring to other potential participants).
- > During the study period, young adults accounted for 240 (32%) of 757 cumulative COVID-19 cases in Winnebago County.
 - During their exposure period (defined as 14 days preceding symptom onset) 83% reported working outside of the home (with 58% working within two days of symptom onset), 38% attended a social gathering, and 84% experienced clinical symptoms.
 - During the interviews with young people, themes included social/peer pressure to not wear a mask, decreased perceived severity of disease outcomes, perceived responsibility to vulnerable loved ones and others, attitudes regarding public health guidance, misinformation, conflicting and opposing messages, and workplace mitigation measures.
 - Of those with negative attitudes towards masks and social distancing, the need for a personal agency (i.e. the right to make one's own decisions and choices) was a key factor.
 - Business owners expressed that the absence of a country-wide mask guideline was a major barrier to requiring their patrons to wear masks.

- > Limitations: Limited study population. The sample size was very small and limited to Winnebago County, therefore not generalisable. Also, participants were gathered through snowball sampling and may all have similar views and characteristics, limiting this report's diversity of responses. Self-reports gathered from Wisconsin's Electronic Disease Surveillance System and interviews are subject to social desirability bias. There was some missing information in text fields that could result in underestimation of some characteristics.
- > Recommendations: Messages that amplify personal responsibility to protect others, or that address the social pressure to not wear a mask may be useful. Clear and consistent public health information about masks, while limiting misinformation and conflicting information is important. A universal masking guideline would help to prevent SARS-CoV-2 transmission.

Reviewed by: Dr Claire von Mollendorf

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

Stringent containment measures without complete city lockdown to achieve low incidence and mortality across two waves of COVID-19 in Hong Kong <https://gh.bmj.com/content/5/10/e003573>

- > This study compared the epidemiological features of patients with COVID-19 in the context of containment policies between the first and second waves in Hong Kong.
- > There were significant differences in containment measures between the first and second waves.
- > Researchers retrieved information on the first 1038 cases detected in Hong Kong (23rd January to 25th April 2020) to analyse epidemiological characteristics.
- > The overall cumulative incidence and mortality rates were 135.5 and 0.5 per 1,000,000 population (amongst the lowest in the world).
- > Aggressive escalation of border control correlated with reductions in R_t from 1.35 to 0.57 and 0.92 to 0.18, and averted 450 and 1,650 local infections during the first and second waves, respectively.
- > Implementing COVID-19 tests for overseas returners correlated with an upsurge of asymptomatic case detection, and shortened containment delay in the second wave.
- > Medium-sized cluster events in the first wave were family gatherings, whereas those in the second wave were leisure activities among youngsters.
- > Factors associated with containment delay were evaluated by multiple linear regression analysis and included age, gender, epidemic wave and infection source as covariates. A time series of 5-day moving average was plotted to examine the changes across the two epidemic waves.
- > Containment delay was associated with older age, male gender and local cases, and with significant improvement in the second wave compared with the first wave.
- > A higher incidence rate was observed for males, raising the possibility of gender predilection in susceptibility of developing symptoms.
- > Prompt and stringent containment strategies translated into successful measures in pandemic control.

Reviewed by: Dr Claire von Mollendorf

Emma Tovey Crutchfield - 3rd Year Medical Student,
Department of Paediatrics, University of Melbourne

The household secondary attack rate of SARS-CoV-2: a rapid review

<https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1558/5921151>

- > A systematic review that aims to estimate the household secondary attack rate (SAR) of SARS-CoV-2 and what influences this estimate. Data from 20 published and two pre-published international studies consider a total of 20,291 household contacts, 3,151 of whom tested positive.
- > Household transmission is a means of spread given members within a house have prolonged close contact and are thus high risk.
- > Household SAR estimated to be 17.1%.
 - Estimates of the household SAR were lower in studies with less frequent testing of contacts. This suggests that more frequent testing of contacts may allow more secondary cases to be detected;
 - SARs were higher amongst adults and older children than young children, female contacts and contacts of symptomatic cases;
 - Spouses of the index case were more likely to test positive than non-spouse household members;
- > Limitations of this study include; heterogeneity of the data and design of the included studies and thus limited external validity.

Reviewed by: Professor Fiona Russell

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

Concerns and misconceptions about the Australian Government's COVIDSafe App: a cross-sectional online survey

<https://s3.ca-central-1.amazonaws.com/assets.jmir.org/assets/preprints/preprint-23081-accepted.pdf>

- > An online national survey in May 2020 to determine the proportion of people who had downloaded the COVIDSafe app or why not.
- > Healthcare professionals and those who had been tested for COVID-19 were excluded.
- > App uptake:
 - 37% downloaded the app, 19% intended to, 28% refused to, and 16% were undecided.
 - Little difference between age groups regarding those that have downloaded or intended to download the app.
 - 65-74 and 75+ age groups had the highest proportion of downloads.
 - 25% did not download the app due to privacy concerns, 24% due to technical concerns, 16% due to believing that app was unnecessary with social distancing, 11% due to distrust in the Government, and 11% due to apathy with little difference between age groups.

- > App understanding:
 - 75% agreed it would enable faster and easier contact tracing.
 - 73% agreed may find more exposed people.
 - 60% correctly understood that the app does not inform if the user has COVID-19.
 - 45% correctly understood that the app does not inform if it is safe to leave the house.
 - 39% correctly understood that personal information would not be shared after the COVID-19 pandemic is under control, whilst 30% incorrectly believed it would.
 - 18% correctly understood the app does not detect COVID-19 positive people near them.
- > Public health measures must address concerns of the general public to improve the uptake of any public health measure.

Reviewed by: Associate Professor Margje Danchin

Celina DeBiasio - 3rd Year Medical Student, University of Ottawa

Lessons from New Zealand's COVID-19 outbreak response

<https://linkinghub.elsevier.com/retrieve/pii/S2468266720302371>

- > With the threat of an epidemic resurgence in many countries looming, it is important to evaluate the impact of different strategies used in the early phases of the pandemic.
- > New Zealand used a set of non-pharmaceutical interventions aiming to bring COVID-19 incidence to zero.
- > Transmission chains in New Zealand were prevented from reaching vulnerable populations due in part to rapid improvements in testing capacity and case management.
- > This, in turn, led to cases and their contacts being isolated/quarantined from the community promptly, reducing the risk of onwards local transmission.
- > The lockdown implemented in New Zealand was remarkable for its rigour and its brevity.
- > New Zealand highlights that successful non-pharmaceutical interventions rely on early decisive reactions from health authorities, performant surveillance systems, and targeted testing strategies as much as a stringency.

Reviewed by: Dr Wonie Uahwatanasakul

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

Modelling the potential impact of mask use in schools and society on COVID-19 control in the UK (not peer reviewed)

<https://www.medrxiv.org/content/10.1101/2020.09.28.20202937v2>

- > Recent findings suggest that an adequate test-trace-isolate (TTI) strategy is needed to prevent a secondary COVID-19 wave with the reopening of society in the UK.
- > This study assessed the potential importance of mandatory masks in the parts of the community and secondary schools.

- > This study demonstrates that adoption of masks in secondary schools in addition to community settings can reduce the size of a second wave, but will not prevent it; more testing of symptomatic people, tracing and isolating of their contacts is also needed.
- > To avoid a second wave, with masks mandatory in secondary schools and certain community settings, under current tracing levels, 68% or 46% of those with symptomatic infection would need to be tested if masks' effective coverage were 15% or 30% respectively, compared with 76% and 57% if masks are mandated in community settings but not secondary schools.

Reviewed by: Professor Fiona Russell

Angela Zhu – 3rd Year Medical Student, Department of Paediatrics, The University of Melbourne

Inference of person-to-person transmission of COVID-19 reveals hidden super spreading events (SSEs) during the early outbreak phase

<https://www.nature.com/articles/s41467-020-18836-4>

- > This study modelled the transmissions of COVID-19 based on 208 genome sequences of SARS-CoV-2 identified during the early stages of the outbreak.
- > The transmission tree that was constructed using epidemiological modelling methods such as SARS-CoV-2 phylogenetics and Bayesian inference proved the presence of SSEs during the early outbreak.
 - Person-to-person transmission was inferred from the model; however, only 18 pairs of direct transmissions were identified.
 - There were significant uncertainties regarding the directionality of transmission in paired infections.
 - Offspring distribution: each infected individual resulted in an average of 1.23 secondary infections (95% CI: 1.09-1.39), with a variance of 8.1.
 - SSEs likely took place during the first month of the outbreak, before movement restrictions were implemented by the Chinese Government on 23rd January 2020.
- > It is important to identify SSEs during early stages of an outbreak due to benefits from tailored preventative and public health policies.
 - Understand the direct of transmission is important to inform public health strategies.
 - Patient recall biases and the unique features of SARS-CoV-2, including the long incubation period (5.2 days) and the possibility for asymptomatic transmissions, are barriers to creating a reliable contact tracing database.

Reviewed by: Associate Professor Margie Danchin

GLOBAL HEALTH

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

2.5 million more child marriage due to COVID-19 pandemic

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)32112-7/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32112-7/fulltext)

- > Save the Children Fund report that up to 2.5 million additional girls are at risk of child marriage in the next five years due to the pandemic, reversing years of progress aimed at reducing child marriage globally.
- > 2020 was defined as the year of “irreversible setbacks and lost progress” for girls.
- > School closures and economic factors have been identified as major contributors.
- > In 2020 alone, it is estimated that ~200,000 extra girls are to be entered into child marriage in South Asia.
- > India has high rates of child marriage but had been on track to reducing these numbers with increased awareness and education. However, now this progress is expected to be halted due to the impact of the pandemic, forcing many further into poverty.
- > It is estimated that globally ~1 million adolescents will become pregnant this year. Childbirth is already the leading cause of death among girls aged 15-19 years old with the risk of pregnancy increased due to closure of healthcare and reproductive facilities during the pandemic.
- > An estimated ten million children, many of them girls, are not expected to return to school, contributing to further educational disadvantage.
- > A number of interventions for preventing child marriage have been suggested, including home visits, education, increasing financial support and economic opportunities.
- > Existing goals set for ending child marriage may need to be adjusted in light of the global impact of the COVID-19 pandemic.

Reviewed by: Professor Julie Bines

Celina DeBiasio - 3rd Year Medical Student, University of Ottawa

Marketing of breastmilk substitutes during the COVID-19 pandemic

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)32119-X/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32119-X/fulltext)

- > The infant formula industry has been actively exploiting concerns about COVID-19 to increase sales, in violation of the WHO International Code of Marketing of Breast-milk Substitutes.
- > With decreased household incomes due to lockdown and the estimated rise in food insecurity predicted by the UN World Food Programme, breastfeeding has become even more critical.

- > WHO and the Royal College of Paediatrics and Child Health, has stated that no evidence exists to suggest breastfeeding increases the risk of infants contracting COVID-19, and that skin-to-skin contact remains essential for newborn health and maternal health.
- > Breastmilk substitute manufacturers have suggested various unnecessary hygiene measures, the use of expressed breastmilk, and the separation of mothers from their babies, which undermine breastfeeding and increase the risk of infant death.
- > Improved implementation and enforcement of the WHO Code in every country is urgently required, with severe sanctions for any violations.

Reviewed by: Dr Wonie Uahwatanasakul

INFECTION CONTROL

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

Efficacy of face masks, neck gaiters and face shields for reducing the expulsion of simulated cough-generated aerosols (not peer reviewed)

<https://www.medrxiv.org/content/10.1101/2020.10.05.20207241v1.full.pdf>

- > SARS-CoV-2 can be transmitted by large respiratory aerosols (>10 µm in diameter) produced while talking, singing, coughing, breathing or sneezing. Smaller aerosols are also produced during these activities, raising the possibility of short-range airborne transmission.
- > The Centers for Disease Control (CDC) and the World Health Organization (WHO) have recommended the use of face coverings by the general public as a form of source control to reduce the expulsion of aerosols from people who are speaking, coughing, and or breathing.
- > A cough aerosol simulator with a headform was used to propel small aerosol particles (0-7 µm) into a collection chamber.
- > The amount of aerosol in the collection chamber was measured in each of six size fractions and the collection efficiency of each face covering was determined by comparing the amount of aerosol collected from the chamber with and without the face covering.
- > Percentage of total test aerosol blocked from being released into the environment:
 - The N95 respirator (3M model 1860): 99%.
 - Medical procedure mask (Kimberly-Clark model 47107): 59%.
 - Commercially available 3-ply cloth face mask (Hanes Defender): 51%.
 - Single-layer neck gaiter (KFGIONG Sun IV Protection Neck Gaiter, 95% polyester): 47%.
 - Double layer neck gaiter (above gaiter folded over): 60%.
 - Face shield (Fisher Scientific # 19-181-600A): 2%.
- > All face coverings significantly reduced the aerosol emitted into the environment compared with no device, except the face shield.
- > The collection efficiencies of all devices tested increased as the aerosol particle size increased.
- > Limitations: This study utilised a single cough volume, airflow profile and aerosol size distribution. These parameters can vary greatly from person to person and in different activities such as breathing or speaking. The fit of a particular mask on the individual wearer and compliance impact how the mask performs as a source control device. The amount and sizes of aerosol particles containing SARS-CoV-2 that are expelled by people who are infected are not yet known.
- > Face masks and neck gaiters can significantly reduce the expulsion of smaller respiratory aerosols during coughing and are more effective than face shields as source control devices.

MENTAL HEALTH

Professor Sharon Goldfeld – Paediatrician, public health physician, Co-Group Leader of Policy and Equity at the MCRI, Director of the Centre for Community Child Health at The Royal Children's Hospital Melbourne and Professor, Department of Paediatrics, University of Melbourne

Psychosocial stress contagion in children and families during the COVID-19 pandemic

<https://journals.sagepub.com/doi/full/10.1177/0009922820927044>

- > The COVID-19 pandemic is a chronic stressor, with the potential to result in long-term negative health consequences.
- > For children and families, stress contagion may occur, where pandemic-related stress is exacerbated and proliferated among family members.
- > Families from disadvantaged backgrounds may have limited resources to cope with the stressors of the pandemic, and existing health disparities may widen.
- > Psychosocial stress due to COVID-19 affects the relationships between family members and impacts children's sense of security and safety.
- > The authors list some principles for paediatric health providers to consider when working with families during the pandemic:
 - Encourage family members to make plans for the future and goals to accomplish, for a sense of hope, as well as encouraging parents to have empathy for their children's negative feelings and behaviours.
 - Encourage children and their families to maintain social contact with friends and family, in a way that is appropriate for that particular family.
 - Encourage ways to reduce and manage stress within the family; this may include limiting news exposure or mindfulness-based or physical exercise.
- > Paediatric health providers can offer behavioural health guidance during the COVID-19 pandemic to encourage and promote healthy family relationships.

How a pandemic could advance the science of early adversity

<https://jamanetwork.com/journals/jamapediatrics/fullarticle/2768833>

- > The psychosocial consequences of COVID-19 may be magnified for vulnerable families.
- > Vulnerable families may have limited resources to cope with the indirect effects of COVID-19.
- > The authors provide a series of recommendations for child development researchers to consider:

- Measure the extent of exposure to COVID-19 news coverage, for both parents and children; as well as losses and strains experienced due to the pandemic (e.g., domestic violence).
- Conduct research that is longitudinal, with repeated assessments following the acute phase of the pandemic.
- In addition to measures of negative consequences, including measures of positive adjustment or protective factors (e.g., emotion regulation skills).
- Measure biological markers of adverse childhood experiences.
- Utilise complex modelling of mediating or moderating factors, given the complexity of the effects of the pandemic.
- Measure the mental health of the caregivers when evaluating children’s response to the COVID-19 pandemic.
- Examine the disparities in the social determinants of health across vulnerable populations.
- Evaluate ongoing and new prevention and treatment programs, ideally with a comparison group.
- Encourage collaboration and harmonised data collection across the research community.
- Consider data collection methods that enhance the representation of the most vulnerable groups.

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

Children and families behavioural and mental health during COVID-19 (Editorial)

<https://www.healio.com/pediatrics/journals/pedann/2020-10-49-10/%7Bd84bc6ae-8dd6-4a3f-8830-f3a2c8905e0b%7D/childrens-and-families-behavioral-and-mental-health-during-covid-19>

- > In this editorial, the author addresses the stressors associated with the disruption of daily life as a result of the pandemic and outlines the role of paediatricians in addressing children’s and families’ behavioural needs.
- > The pandemic has resulted in massive disruptions to everyone’s daily routines, including children, adolescents and young adults. Pertinent disruptions include the ability to attend in-person schooling, physical exercise, social interactions, nutrition, screen time, family mealtime, bedtime routine and quality of sleep.
- > The relative distress associated with these disruptions is dependent on the child’s developmental stage, as well as socioeconomic status, family situation, and the ability to utilise technology for remote education and social interaction.
- > The mental health implications of these stressors include high rates of depression, anxiety and post-traumatic stress among children.
- > Stressors have a disproportionate effect on children from underprivileged and under-resourced families, as well as children with chronic illness, development disorders and psychological/psychiatric illness.

- > To ensure the health and well-being of children and young people, paediatricians can continue to provide vaccinations, well-child and sick care, and provide trauma-informed care via telehealth.
- > The strategy of social prescribing may be an option, where general practitioners refer patients to community-based fitness groups such as yoga and exercise classes.

Reviewed by: Professor David Coghill

PERINATAL HEALTH

Julia Sweet – 3rd Year Medical Student, University of Ottawa

Maternal transmission of SARS-COV-2 to the neonate, and possible routes for such transmission: a systematic review and critical analysis

<https://obgyn.onlinelibrary.wiley.com/doi/10.1111/1471-0528.16362>

- > Early in the pandemic, with the many unknowns surrounding the maternal transmission of COVID-19, strict rules were implemented regarding neonates born to COVID-19 positive mothers, including caesarean section birth, formula feeding, and isolation.
- > This systematic review examined rates of neonatal infection with COVID-19 by delivery route, infant feeding, and interaction. Studies included 49 studies from China, USA, Europe, Honduras, Korea, Australia, Peru, Canada, UK and Iran.
- > 666 neonates of which 28 were confirmed positive, were included.
- > 2.7% (8/292) of vaginally delivered neonates were COVID-19 positive, while 5.3% (20/374) of neonates delivered by C-section tested positive.
 - Of the 28 COVID-19 positive neonates, feeding methods varied: breastmilk (7), formula (3), expressed breast milk (1) and method of feeding was not reported for the rest.
 - Of the 28 COVID-19 positive neonates, seven were isolated from their mother, while five were cared for in the same room. Isolation status was not recorded for others.
- > Discussion: newborn contraction of COVID-19 is uncommon, and rarely severe. Therefore, likely that the benefits of contact with the mother and breastfeeding outweigh the potential separation benefits.
- > Limitations: Potential bias of case reports reporting interesting cases, i.e. Differentially report on infected or uninfected babies. No proven cases of vertical transmission. High rates of missing information regarding the outcome and care types. Variety of test types used, such as serology and RT-PCR, with differing sensitivity and specificity rates.

Reviewed by: Professor Suzanne M. Garland

Maria Gladkikh – 3rd Year Medical Student, University of Ottawa

Analysis of SARS-CoV-2 vertical transmission during pregnancy

<https://www.nature.com/articles/s41467-020-18933-4>

- > A prospective multicentre study that included 31 pregnant women who tested positive for SARS-CoV-2 in Italy.
- > NP swabs were collected at admission, delivery and post-partum in pregnant women and in neonates at delivery. Full-thickness placental and umbilical cord biopsies, venous umbilical cord blood, maternal blood sample and vaginal swabs were collected at delivery. Breast milk samples were collected five days post-birth in lactating mothers (n=11).

- > In-utero vertical transmission was found in two of 31 (6%) of SARS-CoV-2 positive women: one case had a severe clinical outcome (premature delivery at 34 weeks, ICU admission and corticosteroid prophylaxis) and the other case was mild.
 - In the severe case, SARS-CoV-2 RNA was found in the placenta, vagina, maternal plasma, and umbilical cord.
 - In the mild case, SARS-CoV-2 RNA was negative in maternal plasma, vagina, and umbilical cord plasma, but not in the placenta. However, the newborn had a positive swab, and SARS-CoV-2 specific IgM and IgG were detected in umbilical cord plasma.
 - SARS-CoV-2 genome is found in umbilical cord blood (n=1).
 - Anti-SARS-CoV-2 IgM and IgG antibodies were found in the umbilical cord in 12 of 31 women, and in milk specimens of 1 of 11 women.
 - Consistent with existing literature, the SARS-CoV-2 genome can be found in the vaginal mucosa of pregnant women (n=1) and at-term placentas (n=19).
- > Conclusion: in-utero vertical transmission of SARS-CoV-2 is possible but rare.
- > Limitation; authors collected umbilical cord blood rather than baby blood, the former which can be contaminated with maternal blood.

Reviewed by: Professor Suzanne M. Garland

Chelsea Haliburton – 3rd Year Medical Student, University of Ottawa

Transplacental transfer of SARS-CoV-2 antibodies (not peer reviewed)

<https://www.medrxiv.org/content/10.1101/2020.10.07.20207480v1>

- > Newborn protection from infection is primarily dependent on neonatal innate immune responses and maternally derived, transplacentally-acquired antibodies.
- > Determining the extent of maternal SARS-CoV-2 antibodies that cross the placenta is important for understanding neonatal protection and for developing maternal vaccination strategies.
- > Collected maternal and neonatal blood samples, measuring SARS-CoV-2 IgG and IgM.
 - Pregnant women were routinely screened throughout study duration for SARS-CoV-2 by nasopharyngeal PCR when admitted for delivery if exposed or having COVID-19 symptoms.
 - Utilised sera and paired cord blood collected from women presenting for delivery from 9th April 2020 to 8th August 2020 at Pennsylvania Hospital in Philadelphia, Pennsylvania.
- > Matched maternal-cord blood sera was available for 1,471 mother/newborn dyads.
 - 83 women (5.6%) were SARS-CoV-2 IgG seropositive.
 - 72 infants (87%) of the seropositive mothers were SARS-CoV-2 IgG seropositive.
 - 11 (13%) were seronegative.
 - 1,388 (84.4%) women were SARS-CoV-2 seronegative.
 - All infants born to seronegative mothers were seronegative.

- All seropositive women were NP-PCR tested (except one who declined screening).
 - 44/82 (54%) were PCR-positive at some point during pregnancy.
 - 50/82 seropositive women were asymptomatic.
 - 20/83 newborns were tested for SARS-CoV-2 by NP-PCR between 24-48 hours after birth if the mother was NP-PCR positive and met clinical criteria for being contagious at the time of delivery.
 - All infants were PCR negative.
- There was a positive correlation between SARS-CoV-2 IgG levels in the cord and maternal sera.
- SARS-CoV-2 IgM antibodies were not detectable in any of the 72 seropositive infants.
- Women with moderate or critical illness trended to higher IgG and IgM levels and infants born to these women trended to higher cord IgG levels, but the differences were not statistically significant.
- A positive correlation between transfer ratio and increasing time between NP-PCR testing and delivery.
- > Placental and neonatal SARS-CoV-2 transmission has been reported; however current evidence suggests this is not common.
 - This study did not detect IgM antibodies in any blood cord sera samples even in cases of critical maternal illness or preterm delivery, supporting that maternal-foetal SARS-CoV-2 transmission is rare.
 - The longer duration between onset of maternal infection and time of delivery led to higher maternal antibodies levels and higher transfer ratios.
 - This study showed there is efficient SARS-CoV-2 IgG maternal-foetal transfer, which demonstrates the potential for maternally derived antibodies to be protective for neonates against SARS-CoV-2 infection.
- > Strengths: Large cohort. Access to available discarded specimen allowed all women presenting for delivery to be eligible.
- > Limitations: Small number of samples from preterm births. Use of discarded specimens with retrospective data collection that does not provide information on post-discharge outcomes.

Reviewed by: Professor Suzanne M. Garland

Alastair Weng – 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

[https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667\(20\)30223-1/fulltext](https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(20)30223-1/fulltext)

- > The authors use a difference-in-regression-discontinuity analysis to characterise the association between preterm births and national COVID-19 prevention policies in the Netherlands.
- > Approximately 10% of global births are preterm, with few identified risk factors and robust prevention strategies.
- > Previous population data in Denmark and Ireland reported that the rate of extremely preterm and very low birth weight births had decreased during COVID-19, possibly due to improved air quality, lower maternal stress, and fewer maternal infections, but were based on relatively small numbers.
- > This quasi-experimental study was conducted in the Netherlands, where national public health measures were announced between 9th and 23rd March 2020. Singleton birth records from 2010 to 2020 were used, including 1,599,547 total births and 56,620 following COVID-19 measures announced on 9th March. It can be repeated at varying times and allows a more significant database.
- > The first mitigation strategies announced in the Netherlands occurred on 9th March (hand hygiene, stay home when sick) resulted in a decrease in preterm births, with discontinuous regression lines in the 2-, 3-, and 4-month windows before and after the implementations. This was apparent for all degrees of prematurity, but only statistically significant for the 32+0 to 36+6 group.
- > Most reductions in preterm birth occurred in high socioeconomic status neighbourhoods.
- > Further policy measures on 15th March (closing of schools and hospitality, 1.5 m distancing) and 23rd March no gatherings >3 people in public) had no demonstrable effect using this analysis.
- > There was a slight increase in the stillbirth rate from 4.6-5.7/1000 to 6/1000. Little explanatory data is available for this finding.
- > The authors conclude that this larger study provides further evidence for lower preterm birth rates due to COVID-19 mitigation measures, hand hygiene and improved air quality, but Identification of the underlying mechanisms is an essential next step.

Reviewed by: Professor Suzanne M. Garland

SCHOOLS

Chelsea Haliburton – 3rd Year Medical Student, University of Ottawa

Under the right conditions, center- based care is an unlikely COVID-19 threat to staff

<https://pediatrics.aappublications.org/content/pediatrics/early/2020/10/13/peds.2020-034405.full.pdf>

- > This is a multistate survey of over 57,000 childcare providers collecting data on exposure to childcare during the pandemic and COVID-19 infection based on a positive test or hospitalisation.
 - Respondents reported infection prevention strategies, including class size reduction, masking, and disinfection practices.
 - Calculations accounted for community infection indicators.
- > Exposure to centre-based childcare setting was not associated with an increased odds of COVID-19 infection.
 - Home-based childcare settings were associated with COVID-19 infection.
- > Strengths: Large sample size with respondents from multiple states with a high response rate for online survey. Multiple modal strategies. Use of propensity score analysis to adjust for confounding. Compared infection likelihood of in-person providers to a control group of providers who were not exposed.
- > Limitations: Self-reported data. COVID-19 infection was limited to confirmed cases by testing and/or hospitalisation at a time when national testing capacity was limited; presumed COVID-19 cases were not included, therefore likely underestimating the true infection burden. The dose of exposure to childcare was not measured. The study was conducted in March-May when infection rates in children were low, limiting the generalisability to periods when infection rates are higher.
- > The findings are consistent with many studies showing that households are a key source of infection.

Reviewed by: Professor Fiona Russell

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

COVID-19 transmission in US child care programs

<https://pediatrics.aappublications.org/content/early/2020/10/12/peds.2020-031971>

- > This case-control study compared self-reported positive rates of COVID-19 in child care providers who did or did not continue to provide in-person child care during the first three months of the US COVID-19 pandemic (n=57,335 child care providers, n=427 positive cases, 1:50 case-control ratio).
- > The survey was sent between 22nd May and 8th June 2020 with an eight week recall period. Controls were matched to cases based on age, race, ethnicity, gender, director status, county-level COVID-19 death rate, county-level median household income, personal COVID-19 health precaution measures (three continuous variables), and indicator variables for the state where the child care program was located.
- > No association was found between exposure to child care and COVID-19 in both unmatched (odds ratio 1.06; 95% confidence interval 0.82 to 1.38) and matched (odds ratio 0.94; 95% CI, 0.73 to 1.21) analyses.
- > Limitations: The sample is not representative, as while variations in state contexts and policies were controlled statistically, important policy-level variables may not have been adequately controlled. The study also relied on known symptomatic infections, and so cannot estimate asymptomatic cases. The results must be interpreted within the context of background transmission rates and the mitigation efforts implemented in child care programs; including small group sizes (eight children), high rates of handwashing, daily disinfection of surfaces and fixtures, symptom screening, cohorting (grouping students) and social distancing.

Reviewed by: Professor Fiona Russell

Victoria Ivankovic - 3rd Year Medical student, University of Ottawa

SARS-CoV-2 cluster in the nursery, Poland

https://wwwnc.cdc.gov/eid/article/27/1/20-3849_article

- > This study described the characteristics of a cluster of COVID-19 cases from a single nursery in Poland within two weeks of its reopening.
- > The index case was identified as a nursery worker with family contact with someone who had symptomatic COVID-19.
- > Subsequent PCR testing of nursery staff, children, and family members revealed positive results in an additional four employees, three children of the employees, eight children attending the nursery, three siblings of those children, eight parents, and one grandparent (a total of 29 cases).
 - One child with a negative result had two parents with positive results.
- > Overall positivity rate in this cluster was 27%.
- > A limitation of the nature of this study is that it was impossible to certainly confirm whether the children transmitted the virus to their parents or employees.

- > Several previous reports imply little to no SARS-CoV-2 transmission among children and from children to adults - however, these estimates are open to bias because most data was collected during lockdown where children had limited social contacts.
- > The high infection observed in this cluster could be explained by prolonged close contact of very young children who are less able to adjust to control measures.
- > The airborne transmission route in nursery rooms' confined environment could have played an important role.
- > Limitations of this study include the inability to confirm the index case with certainty because one child's parent had previously tested positive within two weeks, and this child could have been the index case. Moreover, information about the facility's prevention methods was not available.
- > Highlights that children transmit the virus, their role in onward transmission needs to be ascertained, and mitigation measures are key.

Reviewed by: Professor Fiona Russell

TRANSMISSION

Rebecca Seliga – 3rd Year Medical Student, University of Ottawa

Transmission dynamics by age group in COVID-19 hotspot countries - United States, April-September 2020

https://www.cdc.gov/mmwr/volumes/69/wr/mm6941e1.htm?s_cid=mm6941e1_w

- > This report from the CDC analyses temporal trends in percent positivity stratified by age cohort in COVID-19 hotspot counties.
- > Percent positivity was calculated for the 45 days before the county being identified as a hotspot and continued until 45 days after. Data were presented in a seven day moving average.
- > 767 hotspot counties were identified between June and July 2020. This represents 24% of all US counties and 63% of the US population.
- > The youngest age cohorts (those aged ≤ 24 years) were found to have the earliest increases in percent positivity (average 31 days before hotspot identification).
 - At the time of hotspot identification, people aged 18-24 had the highest percent positivity (14%).
 - Increases in percent positivity for older age cohorts (≥ 25 years) started later and continued for several weeks (average 28 days for ages 25-44, 23 days for ages 45-64, and 20 days for ages ≥ 65 before hotspot identification).
 - Percent positivity in people aged ≥ 25 eventually peaked at 10-14%, but this peak occurred 21-33 days after hotspot identification.
 - The decline in percent positivity was slower for those aged ≥ 25 .
 - There was some regional variation in these trends.
- > These results agree with regional patterns that have been seen in the southern United States.
- > These results emphasise the importance of reducing transmission early on among young people.

Reviewed by: Professor Fiona Russell

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

Estimating the extent of asymptomatic COVID-19 and its potential for community transmission: systematic review and meta-analysis

<https://jammi.utpjournals.press/doi/abs/10.3138/jammi-2020-0030>

- > The authors synthesised existing literature on the prevalence of asymptomatic cases and reported their findings from a meta-analysis.
- > Asymptomatic cases and transmission of COVID-19 have made controlling viral spread through public health measures one of the significant challenges in 2020.
- > A thorough search strategy through to 20th July 2020 found 13 studies with low risk of bias reporting primary data on the proportion of asymptomatic cases with seven day follow-up out of all those who tested positive +/- further asymptomatic transmission.
- > 17% of cases (111/663) in the included studies were asymptomatic with a slightly higher 20% (30/154) in the aged care facility subgroup.
- > The asymptomatic transmission rate ranged from 0 to 2.2% across five studies, compared with symptomatic transmission at 0.8-15.4%, resulting in relative risk of 0.58.
- > This study did not discriminate asymptomatic status by age, sex, or underlying co-morbidities. The authors also suggest that the definition of “asymptomatic” should be better defined for future studies.
- > This data is crucial for future modelling studies in informing public health policy.

Reviewed by: Professor Fiona Russell

Julia Sweet – 3rd Year Medical Student, University of Ottawa

An adolescent with COVID-19 as the source of an outbreak at a 3-week family gathering – four states, June-July 2020

https://www.cdc.gov/mmwr/volumes/69/wr/mm6940e2.htm?s_cid=mm6940e2_w

- > This short case report examines transmission through a young adult who was exposed to COVID-19 prior to attending a family reunion gathering and subsequently infected 11 of 14 people she was sharing a house with.
- > The index patient (13 years old) was exposed during a COVID-19 outbreak and tested using a rapid antigen test four days after this exposure, before the gathering. Her test result was negative, and she was asymptomatic.
- > Two days later, she developed nasal congestion but attended the planned gathering with 20 relatives; 14 staying in a house together and six visiting in the daytime and practising social distancing while there by staying two meters apart but without the use of masks.
- > Of the 14 who stayed together, 11 subsequently tested positive. Of the six who only visited, none tested positive.
- > Key takeaways:
 - Children and adolescents may have few or no symptoms but can still serve as a source for familial COVID-19 outbreaks.
 - Mitigation is important- physical distancing may be a mitigation strategy if masks cannot or will not be worn.

- Rapid antigen tests have lower sensitivity compared with RT-PCR, and caution should be taken when interpreting rapid antigen tests if there is a strong pre-test probability of a positive result.
- Despite a negative result, best practice should be to self-isolate for 14-days following a known exposure.

Reviewed by: Dr Celeste Donato

Maria Gladkikh – 3rd Year Medical Student, University of Ottawa

Testing mobile air purifiers in a school classroom: reducing the airborne transmission risk for SARS-CoV-2 (not peer reviewed)

<https://www.medrxiv.org/content/10.1101/2020.10.02.20205633v2>

- > This paper studied the role of air purifiers for the aerosol transmission pathway of SARS-CoV-2 in school settings.
- > Speaking loudly and frequently (which occurs in large amounts in schools and universities) emits large quantities of aerosols and droplets, which could potentially contain the SARS-CoV-2 virus. The amount of emitted aerosol particles increases with loudness.
- > When relative humidity is below 100%, emitted droplets rapidly lose a large fraction of their water content; the remaining small core can remain airborne for minutes/hours and be transported throughout the room by air movements.
- > The study monitored the aerosol number concentration for particles size ranging 10 nm to 10 μm , PM10 and CO₂ concentration in a closed room with and without air purifiers at different volume flows and over different time ranges. The uptake of potential virus-containing aerosol via inhalation was estimated as a function of time. The effectiveness of air purifiers was estimated on the reduction of the aerosol load as well as other factors from operating the air purifier machine such as noise level, cleaning and maintenance.
- > Commercially available mobile air purifier - Philips Model 2887/10 equipped with a HEPA filter removing >99.95% of particles (0.1 to 0.3 μm) - was used in the study. Four purifiers were operated simultaneously at the highest speed in a classroom with closed doors and windows. The noise level was determined using a simple mobile phone application.
- > Results:
 - The aerosol concentration (particles size 0.3 to 10 μm) decreased by > 95% within 37 minutes following an exponential decay rate when running the air purifiers while the total mass stayed fairly constant in the room without air purifiers. The reduction of aerosol concentration was homogenous and for all particle sizes throughout the room having air purifiers.
 - The total number concentration in the room without air purifiers decreased slowly over time and was reduced by about 30% when a window was opened, and additional particles entered the room from outside.
 - After two hours, steady-state concentrations of about 0.01 particles per litre and 0.11 particles per litre were quickly reached when air purifiers were on and when air purifiers were off.
 - After two hours, the inhaled dose of virus RNA units was 68 in the room without air purifiers compared with 11 units in the room with air purifiers.

- Students did not consider the noise level disturbing and were not disturbed by cold drafts or enhanced air circulation in the room.
- > Conclusion: air purifiers equipped with HEPA filters can efficiently, quickly and homogeneously reduce the aerosol load in a closed room.

Reviewed by: Dr Lien Anh Ha Do

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

Transmission of SARS-CoV-2 from children and adolescents (not peer reviewed) <https://www.medrxiv.org/content/10.1101/2020.10.10.20210492v2.full.pdf>

- > This was a retrospective cohort study among household contacts of primary cases defined as children and adolescents aged 7-19 years with laboratory evidence of SARS-CoV-2 infection acquired during an overnight school camp outbreak.
- > Among 526 household contacts of 224 primary cases, 48 secondary cases were identified, corresponding to a secondary attack rate of 9%.
- > 224 primary cases had a median age of 14 years. Of these, 184 (82%) were symptomatic. None of the primary cases were hospitalised.
- > 526 household contacts had a median age of 46 years, 67% were parents, 31% were siblings, 2% were extended family members, and 1% were non-familial contacts.
- > There were 48 household contacts as secondary cases, and 92% were symptomatic. None of the 7 secondary cases among contacts aged <18 years were hospitalised; 4/41 secondary cases among household contacts aged ≥18 years (aged 49–77 years) were hospitalised.
- > Findings show that children and adolescents can transmit SARS-CoV-2 to adult contacts and other children in a household setting.

Reviewed by: Professor Fiona Russell

Batsho Mandlebe - 3rd Year Medical Student, Department of Paediatrics, The University of Melbourne

Occurrence and transmission potential of asymptomatic and presymptomatic SARS-CoV-2 infections: a living systematic review <https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1003346>

- > This is a systematic review conducted on results from four database searches on 25th March, 20th April and 10th June 2020 to assess the proportion of people with true asymptomatic SARS-CoV-2 compared with presymptomatic SARS-CoV-2 and the impact that has on virus transmission.
- > Results
 - 20% (79 studies, 6616 people) remained asymptomatic the duration of their COVID-19 illness with a prediction interval of 3%-67%.
 - Up to 31% of screened people remained asymptomatic in seven studies with defined populations.

- The risk ratio for asymptomatic transmission was 0.35 compared with symptomatic transmission and 0.63 for presymptomatic to symptomatic.
- > Limitations – the risk of selection bias in included studies, risk of false-positive RT-PCR, and most included studies were not designed to estimate the proportion of asymptomatic SARS-CoV-2 infections.
- > The majority of SARS-CoV-2 infections do not remain asymptomatic and may confer a higher risk of transmission thus prevention measures such as social distancing, isolation of positive cases and enhanced hand hygiene and masking wearing are still necessary.

Reviewed by: Dr Wonie Uahwatanasakul

Victoria Ivankovic - 3rd Year Medical Student, University of Ottawa

Superspreading event of SARS-CoV-2 infection at a bar, Ho Chi Minh City, Vietnam

https://wwwnc.cdc.gov/eid/article/27/1/20-3480_article

- > This study examined a super spreading event of COVID-19 from a bar in Ho Chi Minh City, Vietnam, in March 2020.
- > For COVID-19, an R0 of 2-3, with 6-8 secondary cases has been suggested to constitute a super spreading event.
- > In the event described in this study, patient one was a 43-year-old man who sought treatment at the hospital on 18th March 2020 for fever, cough, muscle aches, fatigue, and headache - he subsequently tested positive for COVID-19.
- > Four days prior, he attended an event at a bar that had two small areas for patrons and no mechanical ventilation.
- > After the confirmed diagnosis inpatient one, the research team used contact tracing and testing to detect 18 additional PCR-confirmed cases: 12 cases were people at the same bar, and six cases were contacts of people who were at the bar (four were in close contact with patient one).
- > Through in-depth interviews exploring the epidemiological links, three possible transmission chains were identified.
 - 2-3 patients were asymptomatic but transmitted the virus to their contacts.
 - None of the 19 patients with confirmed cases reported that they had symptoms on the night of the bar or the following day. However, in addition to patient one, five others developed mild respiratory symptoms throughout day three, 12 following the night of the bar.
- > 11 whole-genome sequences were obtained from patients in this cluster; the sequences were 100% identical, or different by 1-2 nucleotides.
 - This strengthens the epidemiologic link between PCR-confirmed cases from this cluster
 - Together with contact history, this supports transmission chains involving asymptomatic carriers as the source of ongoing infection.
- > These data suggest that closed settings are facilitators of community transmission of SARS-CoV-2 to others.

- > The mechanism by which infected asymptomatic people spread SARS-CoV-2, especially in closed settings, needs to be explored (including transmission through aerosols).

Reviewed by: Dr Lien Anh Ha Do

VACCINES

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

WHO SAGE Roadmap for prioritising uses of COVID-19 vaccines in the context of limited supply

https://www.who.int/docs/default-source/immunization/sage/covid/sage-prioritization-roadmap-covid19-vaccines.pdf?Status=Temp&sfvrsn=bf227443_2&ua=1

- > To support countries in planning, this Roadmap suggests public health strategies and target priority groups for different levels of vaccine availability and epidemiologic settings.
- > The Roadmap will be updated, as necessary, to accommodate the dynamic nature of the pandemic and evolving evidence about vaccine impact

OTHER RESOURCES

All COVID-19 literature

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

A pandemic primer on excess mortality statistics and their comparability across countries

<https://ourworldindata.org/covid-excess-mortality>

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>

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>

Burnet Institute research findings, policy and technical reports

https://www.burnet.edu.au/covid-19//36_know_c19_hub

COVID-19 and the kidney, currently the recommended US resource

<http://www.nephjc.com/covid19>

Daily updates on COVID-19 literature compiled by Canadian medical students

https://docs.google.com/forms/u/0/d/e/1FAIpQLSfOxCoAuLV0aJdf_z2uWV7r3FaPzAO86q9ZXBcTZ1OcCE_Nw/formResponse

Focuses on paediatric clinical, epidemiological, transmission and neonatal aspects

<https://dontforgetthebubbles.com/evidence-summary-paediatric-covid-19-literature/>

Global summary, identifying changes in the reproduction number, rate of spread, and doubling time during the course of 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/>

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>

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

National COVID-19 clinical evidence taskforce: continually updated evidence-based clinical guidelines

<https://covid19evidence.net.au/>

Our world in data: statistics and research: Coronavirus pandemic (COVID-19)

<https://ourworldindata.org/coronavirus>

Oxford COVID-19 Evidence Service

<https://www.cebm.net/oxford-covid-19/>

Public Health England COVID-19 Rapid Reviewed - Knowledge & Library Service

<https://phelibrary.koha-ptfs.co.uk/covid19rapidreviews/>

Retracted coronavirus (COVID-19) papers

<https://retractionwatch.com/retracted-coronavirus-covid-19-papers/>

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/>

University of Birmingham COVID-19 Research Briefing

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

Victorian Department of Health and Human Services

<https://www.dhhs.vic.gov.au/coronavirus-covid-19-daily-update>

WHO Rolling updates on COVID-19

<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/events-as-they-happen>

WHO COVID-19 dashboard

<https://covid19.who.int/>

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