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Department of Paediatrics

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COVID-19 KIDS RESEARCH EVIDENCE UPDATE

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

Weekly Update No.22

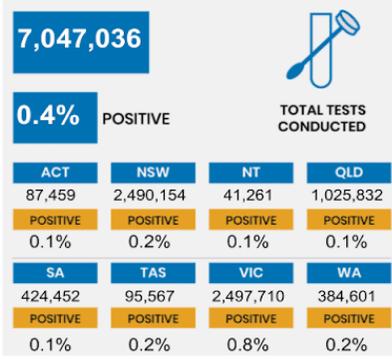
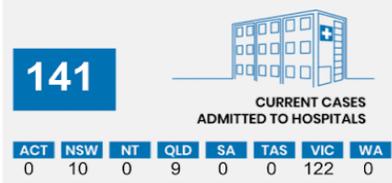
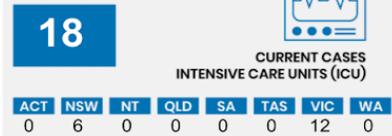
17th September 2020



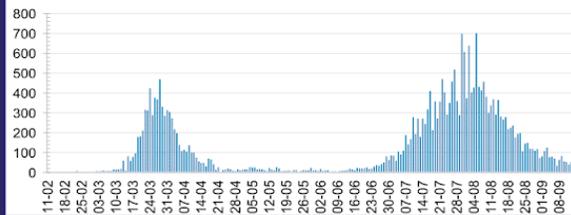
Australian Government
 Department of Health

BE COVIDSAFE

CURRENT STATUS OF CONFIRMED CASES



DAILY NUMBER OF REPORTED CASES

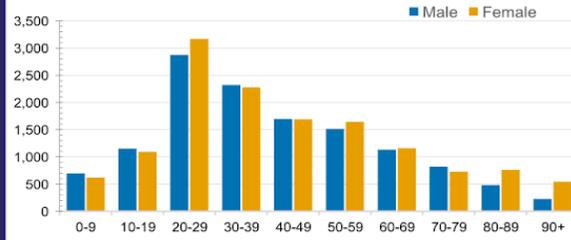


CASES IN AGED CARE SERVICES

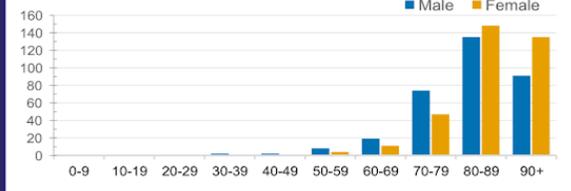
Confirmed Cases	Australia	ACT	NSW	NT	QLD	SA	TAS	VIC	WA
Residential Care Recipients	1995 (1040)	0	61 (33) (28)	0	1 (1)	0	1 (1)	1932 (1007) (574)	0
In Home Care Recipients	82 (66) (7)	0	13 (13)	0	8 (8)	1 (1)	5 (3) (2)	54 (41) (4)	1 (1)

Cases in care recipients (recovered) (deaths)

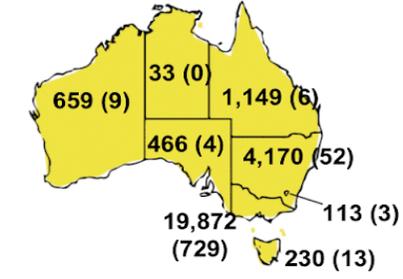
CASES BY AGE GROUP AND SEX



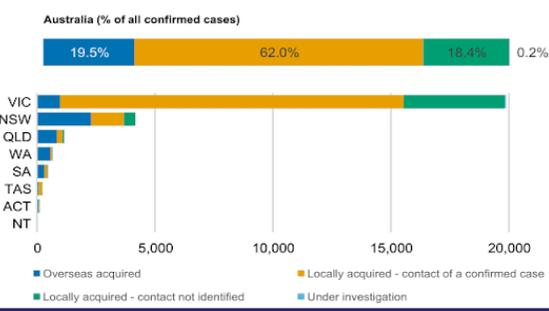
DEATHS BY AGE GROUP AND SEX



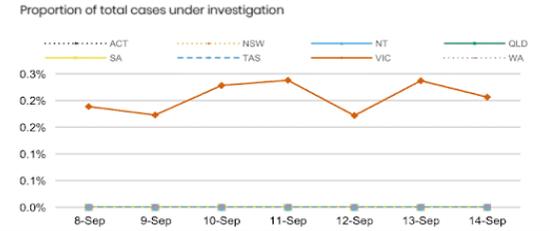
CASES (DEATHS) BY STATE AND TERRITORIES



CASES BY SOURCE OF INFECTION



PUBLIC HEALTH RESPONSE MEASURE



Last updated 14 September 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 September 14; cited 2020 September 15]. Available from: <https://www.health.gov.au/resources/collections/coronavirus-covid-19-at-a-glance-infographic-collection>

GUEST EDITORIAL

Professor Sharon Goldfeld - Director, Centre for Community Child Health, Royal Children's Hospital; Theme Director Population Health and Co-Group Leader Policy and Equity, Murdoch Children's Research Institute; Professor, Department of Paediatrics, Faculty of Medicine Dentistry and Health Sciences, University of Melbourne

This week, we entered the first days of Step Two of the Victorian roadmap out of lockdown. In some ways, there was little change for most people. However, something very significant did happen – park playgrounds opened for children. Together, with clarification of guidelines for play from the Department of Health and Human Services last week, there seems some sense of recognition of the importance of play for children's development. The unintended consequences, or indirect impact of COVID-19 on the health and development of children, is becoming increasingly clear. This is in stark contrast to the direct impact of SARS-CoV-2. The statistics provided on direct and indirect impact of SARS-CoV-2 on children makes this clear. In Australia, the number of cases of COVID-19 in children is low. Only 4.5% of cases have been in children aged from five to 17 years, with no associated deaths and few hospitalisations.

In this week's update, one paper published in the journal *Child Abuse and Neglect* (Lawson et al, *Child maltreatment during the COVID-19 pandemic: consequences of parental job loss*) signals the grim statistics that are likely to emerge over the next months to years, with regard to children. Usually, online surveys are plagued with responder bias, and of concern in this paper, is parental admission to both psychological and physical abuse of children that has seemed to worsen during the pandemic. None of this is surprising, but it is disturbing. Recent reports from the Australian Human Rights Commission and the Victorian Commission for Children and Young People signal increasing mental distress in children and young people. Similarly, the RCH National Child Health Poll suggests mental stress for parents, with 46% of parents reporting the pandemic has had an adverse impact on their mental health.

At the Centre for Community Child Health we have been tracking papers that focus on the unintended consequences of COVID-19. The Figure and Table below illustrate the very real impact on communities, families, and children. It is worth noting the disproportionate burden on children living in disadvantaged circumstances, with increases in adverse experiences such as abuse, food insecurity, and poverty. All references have been included previously, but provide a sense of how research could inform necessary policy and practice responses, as the impact of the long tail of COVID-19 is yet to come for children, young people, and their families.

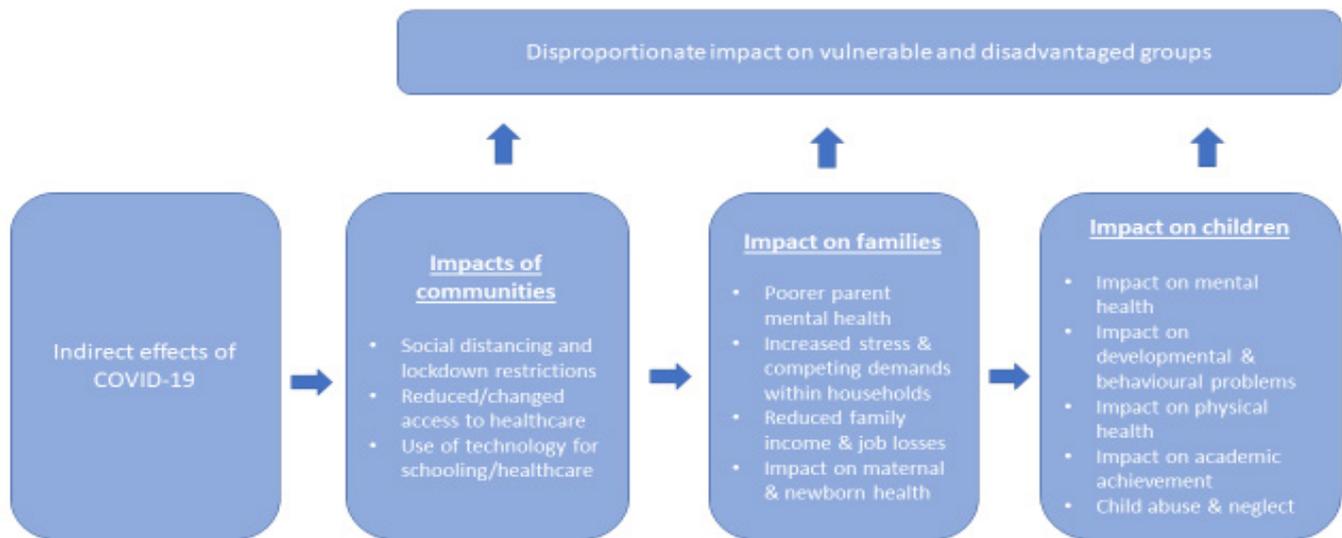


Figure 1: Indirect effects of COVID-19

Impacts on communities	Impacts on families	Impacts on children
<ul style="list-style-type: none"> > Lockdown and physical distancing requirements are likely to cause stress, anxiety and confusion for children, decrease social interactions with peers, disrupt routines which result in negative psychological and behavioural changes.^{1,2} > In Australia, around four million students were affected by school closures since March 2020. Long-term school closures are associated with high economic and social costs, and will have an unquantifiable impact on children's health, educational outcomes, and future productivity and earnings³ > Access to healthcare heavily impacted: Routine health checks have been missed, scheduled childhood vaccinations delayed, paediatric emergency department visits also decreased substantially.⁴ > The use of technology in schools for remote learning, staying connected via phone calls or video chats, in healthcare through telehealth.^{1,5} 	<ul style="list-style-type: none"> > Previous research on pandemics and disasters has shown some of the impacts of poor parent mental health on children. These events may impact parent mental health for several years, which could create a lower quality home learning environment. > Many families are struggling to support their children's remote learning needs and other childcare demands, while also balancing employment demands (including WFH requirements) or unemployment and financial instability.^{4,6} > Due to deteriorating economic circumstances resulted from COVID-19, an additional 42-66 million children worldwide will be living in extreme poverty over the coming year.⁷ This pandemic has placed many children into social and educational disadvantage for the first time.⁷ > There have been reports of increased anxiety and depression among pregnant women and those in the early postnatal period during the COVID-19 pandemic e.g. anxiety about visiting hospital, increased hospital restrictions, physical distancing rules after discharge etc.⁸ 	<ul style="list-style-type: none"> > The pandemic is having a large effect on children's wellbeing and mental health; affect their entire lives and inherit the aftermath. Impacts include separation from their caregivers, remote learning causing emotional distress, further exacerbation of mental health disorder symptoms.^{9,10,11} > Physical health has been indirectly affected particularly while schools, parks, and sports centres are closed in many countries. In particular, the implications for children with additional health care needs may be even greater, with limited access to healthcare, special education schools, and support services. > Student engagement is key, with disengaged students at risk of poorer academic achievement.⁶ There have been learning losses (and delays in cognitive gains and achievement) during remote learning as part of COVID-19 restrictions, and only 35% of Australian teachers reported that their students were learning well during this time.¹² > Physical distancing and lockdown restrictions are expected to lead to increased levels of family violence including greater non-accidental injury, sexual violence and mental trauma in children. Greater risk of family violence amongst vulnerable and disadvantaged groups.¹³

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13. Greeley CS. [Child Maltreatment Prevention in the Era of Coronavirus Disease 2019](#). JAMA Pediatrics. 2020:e202776-e202776.

HIGHLIGHTS

- > Three major lay-person concerns around a COVID-19 vaccine discussed.
- > Russian candidate vaccines broadly safe and immunogenic in a small cohort of predominantly male volunteers; results from studies that were neither randomised nor controlled.
- > IgG declines significantly from the peak by 8-10 weeks post-positive PCR.
- > Compared with women, a higher proportion of men had extremely high anti-SP IgA antibodies, which may contribute to the higher mortality risk in men (e.g. through an increased inflammatory response).
- > Population wide masking may increase the proportion of asymptomatic SARS-CoV-2 infections in the population and increase population-wide immunity without more severe illness or deaths.
- > No difference in hospitalisation rates, ICU admission rates, and mechanical ventilator use between children with COVID-19 and those with seasonal Influenza.
- > Obese COVID-19 patients more likely to require intensive services or die compared with obese influenza patients.
- > Further evidence using experimental study designs may be required regarding the behavioural, environmental, social, and systems interventions for pandemic prevention.
- > Diversion of healthcare resources from maternal health to the COVID-19 response in Kenya.
- > Genomic sequencing can aid decision making in public health management of the pandemic.
- > Nosocomial acquisition of COVID-19 was rare in a Boston medical centre during the height of the pandemic.
- > Presence of SARS-CoV-2 reactive antibodies in human milk could provide passive immunity to breastfed infants, but further study is required.
- > Seropositivity rates were similar in students and staff, suggesting children do get infected as frequently as adults, but may be more likely to have asymptomatic or mild disease (England primary school study).
- > Strict ventilation of classrooms and face masks used in schools, both, inside and outside classrooms would help maintain low transmission rates in schools and childcare facilities (German study).
- > Young children are capable of transmitting COVID-19 as evidenced in the epidemiological tracing study of three childcare facilities in Salt Lake City, Utah, USA (American Study).

- > Systemic corticosteroid use in critically ill patients with COVID-19 is associated with a reduced 28-day all-cause mortality rate, compared with usual care or placebo.
- > Evidence in support of skin-to-skin contact and early breastfeeding for mothers and neonates, as long as infection control measures are followed

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

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ADULT MEDICINE

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

Characteristics and outcomes of 627,044 COVID-19 patients with and without obesity in the United States, Spain, and the United Kingdom (not peer reviewed)

<https://www.medrxiv.org/content/10.1101/2020.09.02.20185173v1>

- > Six databases are covering three different countries.
- > 627,044 COVID-19 patients identified between January and June 2020: 33% diagnosed were obese (BMI 30 or greater, and/or weight > 120 kg), 40% hospitalised were obese.
- > 4,549,568 influenza patients diagnosed and hospitalised in influenza season of 2017-2018: 15% diagnosed were obese, 28% hospitalised were obese.
- > Overall, obese patients with COVID-19 had adverse events more frequently than non-obese.
- > Obese COVID-19 patients more likely to have prior comorbidities, present with cardiovascular and respiratory events during hospitalisation, require intensive services or die compared with non-obese COVID-19 patients.
- > Obese COVID-19 patients are more likely to require intensive services or die compared with obese influenza patients.
- > Limitations:
 - This is a descriptive study, and statistical testing and modelling were not performed.
 - Selection bias of COVID-19 cases cannot be excluded due to underreporting and asymptomatic cases.
 - No information on BMI as a continuous variable, preventing authors from investigating impact of different categories of obesity in COVID-19 outcomes.
 - Differences found in COVID-19/seasonal influenza comparison may have been influenced by vaccination for Influenza, temporal changes in clinical practice standards and coding.

Reviewed by: Dr Martin Wright

CLINICAL PAEDIATRICS

Sophia Moshegov - 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Comparison of clinical features of COVID-19 vs seasonal influenza A and B in US children

<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2770250>

- > Retrospective cohort study comparing children diagnosed with laboratory-confirmed COVID-19 between 25th March and 15th May 2020, and children diagnosed with laboratory-confirmed seasonal Influenza between 1st October 2019, and 6th June 2020 at the Children's National Hospital in the District of Columbia, Washington, DC.
- > Aimed to compare COVID-19 vs seasonal Influenza according to rates of hospitalisation, admission to ICU, mechanical ventilator use, the association with underlying medical conditions, and clinical symptoms using information collected from chart review of the medical records.
- > The study included 315 patients with COVID-19 (median age 8.4 years) and 1,402 patients with seasonal Influenza (SI) (median age 3.9 years).
- > Both groups had similar hospitalization rates (17% COVID-19 vs 21% SI), ICU admission rates (6% COVID-19 vs 7% SI) and use of mechanical ventilators (3% COVID-19 vs 2% SI).
- > More patients with COVID-19 than those with Influenza A reported fever, diarrhoea or vomiting, headache, body ache, myalgia and chest pain, but no significant differences with those with Influenza B.
- > No difference between groups in terms of reported cough and dyspnoea.
- > 65% of patients with COVID-19 had at least one underlying medical condition (mainly neurological issues - global developmental delay or seizures), significantly higher than the 42% with SI.
- > Two patients with Influenza A died, no deaths among patients with COVID-19 or Influenza B.
- > Children with COVID-19 infection and symptoms tended to be older, and a greater proportion of patients with COVID-19 had underlying neurological issues.
- > No difference in hospitalisation rates, ICU admission rates, and mechanical ventilator use between children with COVID-19 and those with seasonal Influenza.
- > Children hospitalised with COVID-19 were more likely to be symptomatic, but overall had a very similar profile of symptoms to those with seasonal Influenza
- > Findings from this study highlights the need for prompt identification and treatment of children with respiratory viral infections in health care facilities.

- > Limitations:
 - Retrospective study.
 - Findings are subject to recall bias or missing information introduced during patient encounters.
 - Lack of important demographic information, symptoms (such as anosmia), and potential risk factors (such as obesity).
 - Single centre study influences generalizability.

Reviewed by: Dr Martin Wright

CLINICAL TRIALS

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

We need better evidence on non-drug interventions for COVID-19
<https://www.bmj.com/content/370/bmj.m3473>

- > This opinion piece argues that there is a lack of evidence for non-drug interventions for COVID-19.
- > "Non-drug interventions" refer to behavioural, environmental, social and systems interventions for pandemic prevention. These include physical distancing, face coverings and patterns of school re-opening, among other strategies.
- > Almost 1,300 controlled trials have been registered for drug interventions for COVID-19. By comparison, only ten controlled trials of non-drug interventions have been registered, with three reported.
- > Suggests that controlled trials of non-drug interventions currently lack for three reasons:
 - Non-drug interventions are considered to be harmless.
 - Non-drug interventions are considered too difficult to investigate.
 - Non-drug interventions are considered too obviously beneficial to bother with trials.
- > The article argues that these assumptions are false and that we are missing a rare opportunity to gather a strong evidence base on non-drug interventions for pandemic control.
- > Non-drug intervention trials would affect significantly more people than drug-trials, may reduce unnecessary harm at a population level, and are likely to increase population trust in government decision-making.

Reviewed by: Dr John Cheek

CRITICAL CARE

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

Association between administration of systemic corticosteroids and mortality among critically ill patients with COVID-19: a meta-analysis

<https://jamanetwork.com/journals/jama/fullarticle/2770279>

- > A prospective meta-analysis of seven randomised controlled trials conducted in 12 countries examining the association between administration of systemic corticosteroids and mortality rate in critically ill patients with COVID-19.
- > The studied population (n=1,703) had a median age of 60 and was predominantly male (71%).
 - 678 patients in the intervention groups received systemic corticosteroids (dexamethasone - low and high dose, hydrocortisone - low dose or methylprednisolone - high dose), while the remaining 1,025 received usual care or placebo.
 - 222 deaths within the intervention groups and 425 deaths within the control groups corresponded with an absolute 28-day all-cause mortality risk of 32% and 40% respectively. (OR 0.66; 95% CI 0.53-0.82; P < 0.001).
 - Subgroup analyses showed greater benefits from systemic corticosteroids in lowering the mortality rate in patients not receiving invasive mechanical ventilation. However, the effects were similar between men and women, individuals above and below 60 years old, and individuals exhibiting longer and shorter duration of symptoms.
- > There was no evidence for an increased risk of serious adverse events.
- > Optimal dose and duration of corticosteroids could not be assessed, but there were no data suggested higher doses had greater benefit.
- > Limitations:
 - The analysis was expedited after the publication of the RECOVERY trial demonstrated a benefit from steroids, and many ongoing RCTs were suspended.
 - Selective reporting or publication bias due to the prospective nature of studies.
 - Small study size of one included RCT (n=47).
 - Lack of data on long-term/post-discharge mortality.
 - Inconsistent definition of 'severe adverse event' across included studies.

Reviewed by: A/Professor Amy Gray

EPIDEMIOLOGY & PUBLIC HEALTH

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

Common paediatric respiratory infectious diseases may serve as an early predictor for SARS-CoV-2 new wave of infections (letter to the editor)

<https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1359/5902551>

- > Letter to the editor from a French emergency physician who describes that respiratory illnesses in children may predict SARS-CoV-2 transmission by several weeks.
- > After the start of national lockdown in France (from 17th March) which lasted ten weeks, there was a significant reduction in common paediatric infections transmitted through respiratory and faecal-oral routes.
- > The reduction in viral gastroenteritis, bronchiolitis, acute otitis media and the common cold preceded the fall of SARS-CoV-2 infection by several weeks.
- > After eight weeks of lockdown, the restrictions were eased (from 11th May), and the lockdown ended one month later.
- > Data was collected by the authors from 2017-2020 to estimate the difference in infection rates after lockdown compared with previous years.
 - There was a significant increase in airborne transmitted illnesses observed two weeks after the lockdown ended, with the number of common colds, bronchiolitis and acute asthma exacerbations (often triggered by viral illness) back to the expected levels. A few weeks later, there was an increase in SARS-CoV-2 transmission observed.
 - The amount of gastrointestinal infections remained low after lockdown.
- > These results indicate that acceptable hand hygiene practices are still being followed by the general public, as shown by the ongoing lower than expected number of gastrointestinal infections.
- > However, less popular public health measures such as masks and social distancing were likely not followed as closely by the public after lockdown, as evidenced by the rebound rates of respiratory illnesses.
- > Therefore, it may be useful to monitor the prevalence of common respiratory infections closely as they could predict a rise in SARS-CoV-2 transmission by several weeks.

Reviewed by: Dr Claire von Mollendorf

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

healthcareCOVID: A national cross-sectional observational study identifying risk factors for developing suspected or confirmed COVID-19 in UK healthcare workers (not peer reviewed)

<https://www.medrxiv.org/content/10.1101/2020.08.28.20182295v1>

- > A cross-sectional observational study (in the form of an online survey) to determine the prevalence and risk factors for developing suspected or confirmed COVID-19 infection among healthcare workers in the UK.
- > 6,152 healthcare workers aged ≥ 18 years working between 1st February – 25th May 2020 in both primary (community/social care facilities) and secondary (hospitals) care.
 - 2,516 (40.9%) nurses/midwives/associated staff.
 - 1,770 (28.8%) doctors.
 - 1,118 (18.2%) allied health professionals.
 - 198 (3.2%) dentists/dental staff.
 - 550 (8.9%) other.
- > The primary study outcome was a composite endpoint of laboratory-confirmed SARS-CoV-2 infection, or self-isolation, or hospitalisation due to suspected or confirmed COVID-19.
- > The overall prevalence of the composite endpoint over the study period was 29.4%.
 - 1,776 (28.9%) self-isolated due to COVID-19 symptoms or positive SARS-CoV-2 test. Total number of days of self-isolation for the cohort was between 11,870 – 21,158 days, which approximately equals 71-127 working days lost per 1000 working days (assuming a 40-hour workweek per healthcare worker).
 - 459 (7.5%) tested positive for SARS-CoV-2 (77.2% were not tested).
 - 49 (0.8%) hospitalized.
- > Risk factors for the main composite outcome was:
 - Increased frequency of contact with suspected/confirmed COVID-19 cases without wearing adequate PPE (strongest risk factor).
 - 1,382 (22.5%) reported lack of access to adequate PPE. Main reasons for this were: patient not suspected/confirmed case, lack of PPE availability, senior instruction.
 - Comorbidities (cancer, respiratory disease, obesity).
 - Using public transportation for work.
- > Adequate training and correct use of PPE were protective factors.
- > Nearly 1/3 of healthcare workers had suspected or confirmed COVID-19 infection, with the strongest risk factor being inadequate PPE during clinical encounters. Policymakers need to develop strategies to protect healthcare workers, including ensuring adequate access to PPE.

- > Limitations: survey format carries a risk of selection/recall bias, all data collected were subjective, and results did not account for those who died from COVID-19 or were too ill to participate.

Reviewed by: Dr Claire von Mollendorf

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

Tracking the COVID-19 pandemic in Australia using genomics
<https://www.nature.com/articles/s41467-020-18314-x>

- > Genomic sequencing may be used to investigate the source of individual cases of COVID-19 and place them in the context of known transmission chains.
- > Method: integration of genomic sequencing of 80% of cases in Victoria between 6th January and 14th April 2020 (total of 1,333 cases) with epidemiological and phylodynamic data.
- > Majority of cases (827/1,333, 62%) were identified in returned travellers, 360 (27%) were found in known contacts, and 134 (10.1%) were from an unknown source.
- > 1,242 samples from 1,045 patients (80.7%) were sequenced. Following removal of duplicates and based on quality control parameters, 903 samples were included in final analyses.
- > 76 distinct genomic clusters were obtained, 34 contained overseas travellers only, with a further 34 clusters from both overseas and locally-acquired cases.
- > Of the cases with an epidemiologically unknown source of acquisition, 88% were subsequently identified within 24 genomic clusters, which provided insights into potential sources of acquisition.
- > The phylodynamic analysis estimated a decrease in R_e (0.48 from 1.63) following the introduction of stage three restrictions and hotel quarantine.
- > Genomic analysis was used to investigate infections amongst healthcare workers and patients. It excluded interfacility healthcare transmission and showed that transmission was not occurring at that time in one health service—this reduced requirements for infection control and contact tracing investigations at that facility.
- > 98 patients had more than one sequence in for the study, which demonstrated little intra-patient SARS-CoV-2 genomic diversity.
- > The study demonstrates the role of returned travellers in driving the transmission in Australia and the effectiveness of social restrictions. Hence, genomic sequencing can aid decision making in public health management of the pandemic.

Reviewed by: Dr Celeste Donato

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

Child maltreatment during the COVID-19 pandemic: consequences of parental job loss

<https://www.sciencedirect.com/science/article/pii/S0145213420303641>

- > The pandemic has caused unprecedented rates of unemployment. This study investigated whether parental job loss was associated with child maltreatment and if cognitive reframing was protective against child maltreatment.
- > 342 American parents, with children aged 4-10 years and currently in a relationship, were recruited via Facebook and Amazon Mechanical Turk to complete online questionnaires that assessed experiences during the pandemic, psychological maltreatment and physical abuse of children, cognitive reframing and parental depression.
- > Two binary logistic regressions were performed to assess predictors of physical abuse or psychological maltreatment by parents.
- > Parents were more likely to psychologically maltreat their children during the pandemic if they lost their job (OR=4.86, 95% CI [1.19, 19.91], p=0.03), were depressed (OR=1.05, 95% CI [1.02, 1.08], p<.01) or had previously psychologically maltreated their children (OR=111.94, 95% CI [28.54, 439.01], p<.001).
- > Parents who had psychically abused their children in the past year were more likely to do so during the pandemic (OR=20.10, 95% CI [7.60, 53.18], p<.001).
- > Engaging in reframing coping did not make physical abuse less likely (OR=0.94, 95% CI [0.94, 1.15]), however, the more that parents engaged in reframing coping following job loss, the lower the probability of physical abuse (OR=0.76, 95% CI [0.59, 0.99], p=.04).
- > Limitations: Participants were recruited via crowdsourcing platforms and may not be representative of the general population, cross-sectional design may not capture the extent of child maltreatment during the pandemic, self-report data may introduce recall bias.

Reviewed by: Professor. David Coghill

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

Transmission dynamics of COVID-19 outbreaks associated with child care facilities - Salt Lake City, Utah, April-July 2020

<https://www.cdc.gov/mmwr/volumes/69/wr/mm6937e3.htm>

- > Reports suggest that children aged ≥ 10 years can efficiently transmit SARS-CoV-2; however, limited data are available on SARS-CoV-2 transmission from young children, particularly in child care settings.
- > To explore this, contact tracing data collected from three COVID-19 outbreaks in three child care facilities in Salt Lake County, Utah were retrospectively reviewed to explore attack rates and transmission patterns.
- > 184 people (110 children) had a known epidemiological link to one of the three facilities.

- Among these, 31 confirmed COVID-19 cases occurred (13 in children, all children had mild or no symptoms).
 - The transmission was observed from 2 of 3 children with confirmed, asymptomatic COVID-19.
 - Detailed contact tracing data show that children can play a role in transmission from child care settings to household contacts.
- > An outbreak at a child care facility was defined as two or more laboratory-confirmed COVID-19 cases within 14 days among staff members or attendees at the same facility.
 - > Analysis of the contact tracing data of these facilities identified outbreaks linked to index cases in adults and associated with transmission from children to household and non-household contacts.
 - > 54% of the cases linked to these facilities occurred in children.
 - > To help mitigate this, the use of masks is recommended in people > 2 years of age old, particularly of staff in child care settings.
 - > Although COVID-19 is less severe in children than it is in adults, children still play a role in transmission.
 - > Having testing available with timely results and testing contacts of patients in childcare settings regardless of symptoms, can all help to prevent transmission.

Reviewed by: Dr Wonie Uahwatanasakul

GLOBAL HEALTH

Experiences of vulnerable urban youth under COVID-19: the case of youth with disabilities

<https://www.gage.odi.org/publication/experiences-of-vulnerable-urban-youth-under-covid-19-the-case-of-youth-with-disabilities/>

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

<https://ourworldindata.org/coronavirus>

WHO COVID-19 dashboard

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

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

The ramifications of COVID-19 on maternal health in Kenya

<https://www.tandfonline.com/doi/full/10.1080/26410397.2020.1804716>

- > Kenya is in its third epidemic phase and to date has reported 17,603 cases and 280 deaths, a case fatality rate of 1.6%.
- > The under-resourced healthcare system has been placed under significant additional pressure during the pandemic, characterised by:
 - A lack of medical and technical expertise utilised in the government's pandemic response.
 - A significant number of healthcare workers have been infected whilst at work.
 - A lack of access to PPE, resulting in workers refusing to provide care.
 - Reliant on the global market for the distribution of medical supplies.
 - Community healthcare resources are poorly utilised in Kenya, and community health workers have received no PPE and little additional funding to assist with the COVID-19 response.
 - Diversion of healthcare resources normally allocated for maternal health to the COVID-19 response.
- > Pregnant women during this time have been affected in a number of ways:
 - Expectant mothers have been confused and unsure where to access maternity services.
 - The night curfew has meant some women need to birth at home with the use of traditional birth experts or the help of relatives.
 - Some women have died from postpartum haemorrhage.
 - A marked reduction in women accessing maternity services, owing to the fear of contracting COVID-19.

- A lack of PPE and so increased risk of transmission from healthcare workers to mothers and vice versa.
- > Measures are taken to improve maternal care:
 - Registering pregnant women so that they can travel during the curfew times.
 - A hotline established which enables transportation assistance and free medical advice for pregnant women, as ambulances are not easily accessible. The program is inequitable however as it is restricted to Nairobi and some drivers won't travel to less affluent areas because of safety concerns.
 - The provision of four telehealth maternity services (in addition to four face-to-face services).
 - Extension of prescriptions for regular medications for chronic illness so that pregnant women can avoid unnecessary travel.
- > The existing measures need to be made accessible to all pregnant women. More advocacy and input is required to improve the pandemic response and by extension improve maternal health services.

Reviewed by: Professor Steve Graham

IMMUNOLOGY

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

SARS-CoV-2 IgG and IgA antibody response is gender dependent; and IgG antibodies rapidly decline early on

[https://www.journalofinfection.com/article/S0163-4453\(20\)30567-3/fulltext](https://www.journalofinfection.com/article/S0163-4453(20)30567-3/fulltext)

- > A letter to the editor was focusing on the duration and gender bias of antibody response to SARS-CoV-2 in a cohort study in Switzerland.
- > IgG and IgA antibodies were tested against SARS-CoV-2 spike and N proteins in patients with a history of positive SARS-CoV-2 PCR test (n = 159; 52.2% female).
- > Antibodies tested every week in the first month, then after four weeks in the second month using ELISA assays.
- > Approximately 4.6-6.5% of participants have not developed anti-spike IgG or IgA and anti-N protein by a median of five weeks after the PCR test (95% CI 5-6 weeks).
 - Speculated to be due to delayed or missing primary humoral response.
- > Antibody response peaks 4-5 weeks after positive PCR in most individuals followed by a decline, which was significantly lower at week 8-10 post PCR test compared with levels at week 4-5.
- > Significantly higher antibody levels for anti-spike IgG and IgA, and anti-N protein were observed in men than in women three weeks post PCR test.
- > A subgroup of individuals had extremely high values of anti-SP IgA antibodies, with a higher proportion of men than women.
 - This may contribute to a higher mortality risk in men compared with women (e.g. through an increased inflammatory response),
 - The overall course of anti-SP IgA may be the result of an ongoing infection.
- > Limitations: clinical symptoms of participants were not mentioned (i.e. mild, moderate or severe); and no data on participants demographics.

Reviewed by: Dr Ryan Toh

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

Seroprevalence of SARS-CoV-2 antibodies in children: a prospective multicentre cohort study (not peer reviewed)

<https://www.medrxiv.org/content/10.1101/2020.08.31.20183095v1>

The objective of this multicentre cohort study in the UK was to report the presence of SARS-CoV-2 antibodies in healthy children of healthcare workers and to report the symptomatology of infection, including the asymptomatic rate.

- > Serum and/or plasma were tested using the commercial kits from Abbott, Roche and Diasorin.
- > 1,007 participants were enrolled, and 992 were included in the final analysis.
 - The median age of participants was 10.1 years (range 2.03-15.99 years).
 - An approximately equal proportion of boys and girls.
 - No children within this cohort had severe disease.
- > There were 68/992 (6.9%) participants with positive SARS-CoV-2 antibodies, and of these, 34/68 (50%) reported no symptoms.
- > Most commonly reported symptoms were fever (21/68, 31%), gastrointestinal symptoms (13/68, 19%), and headache (12/68, 18%).
- > Seroprevalence varied between five sites, ranging from 0.9% (in Belfast) to 11.6% (London).
- > No correlation between age and antibody titres.
- > Multivariate analysis identified four independent variables as significantly associated with SARS-CoV-2 infection:
 - Known infected household contact
 - Fatigue
 - Gastrointestinal symptoms
 - Changes in sense of smell or taste.
- > Age does not predict the presence and overall antibody levels in children.
- > Significance:
 - The current UK testing regime will miss the majority of paediatric SARS-COV-2 infections.
 - Young children were just as likely to be infected as older children and were capable of mounting a similar antibody response.
- > Limitations:
 - Children in this study only have mild disease.
 - Data may not represent the general population as children were recruited from healthcare workers.

Reviewed by: Dr Ryan Toh

INFECTION CONTROL

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

Incidence of nosocomial COVID-19 in patients hospitalised at a large US academic medical centre

<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2770287>

- > Aimed to assess the incidence of nosocomial COVID-19 in hospitalised patients at Brigham and Women's Hospital (Boston) in the 12 weeks after the first inpatient case was identified, and to assess the effectiveness of the infection control program at the hospital.
- > Cohort study, including 9,149 patients admitted over a 12 week period. Any patient who tested positive for SARS-CoV-2 by RT-PCR on hospital day three or later, or within 14 days of discharge, had their medical records reviewed.
 - The hospital's COVID-19 screening policy included screening all patients for COVID-19 symptoms on admission and then daily (initiated six weeks after first inpatient case), as well as RT-PCR testing initially for all symptomatic patients than for all patients at their admission (seven weeks after first inpatient case).
 - Visitors were restricted four weeks after the first inpatient case, and a few days later all visitors and patients were required to wear masks.
- > Of 9,149 admitted patients there were 697 confirmed COVID-19 cases.
- > 12/697 (1.7%) first tested positive on hospital day three or later (median day four, range 3-15 days).
 - Only one case was deemed to be definitely hospital-acquired. They developed symptoms on day 15 of admission and had been visited by an asymptomatic spouse who was diagnosed with COVID-19 1 week before the inpatient's symptoms began. This case occurred prior to visitor restrictions and universal mask-wearing being implemented.
 - Four cases deemed definitely community-acquired and seven cases likely community-acquired.
- > 11/8,370 (0.1%) patients with non-COVID-19 related hospitalisations tested positive within 14 days of discharge (median time to diagnosis six days, range 1-14 days) with
 - only one case was deemed likely to be hospital-acquired, but with no known exposures in the hospital, and
 - three cases attributed to delayed diagnosis or previous false-negative results with the progression of symptoms present at hospitalisation and seven cases with exposures post-discharge.

- > Nosocomial acquisition of COVID-19 was rare in this medical centre during the height of the pandemic.
- > Limitations:
 - Difficulty in identifying the source of infection in each case with certainty, the possibility of additional undetected nosocomial cases, the possibility of some patients being diagnosed after discharge outside the healthcare system studied, or patients who sought testing more than 14 days after discharge.
 - This study does not provide insight into the risk of nosocomial infection among healthcare workers, nor does it allow assessment of which measures implemented were most effective.
 - The adherence to basic infection control practices varies across hospitals, and thus findings may not be generalisable.

Reviewed by: Dr Samantha Bannister

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

Facial masking for COVID-19 - potential for "variolaion" as we await a vaccine
<https://www.nejm.org/doi/full/10.1056/NEJMp2026913>

- > Population-wide mask use is an important strategy to reduce both SARS-CoV-2 transmission and the severity of the disease, according to the authors of this perspective piece.
- > Asymptomatic people are essential sources of disease transmission. It has been suggested that viral inoculum plays a role in the severity of illness.
- > The authors hypothesise that reducing viral inoculum through a population wide mask increases the proportion of asymptomatic infected people. This is based on a higher proportion of asymptomatic infection observed in outbreaks in settings with widespread mask use compared with outbreaks in settings with lower mask use.
- > As we await a vaccine, population-wide masking may increase population-wide immunity without severe illness or deaths ("variolaion" hypothesis). Even mild or asymptomatic infection has been suggested to induce strong cell-mediated immunity.
- > To test the hypotheses, more studies comparing rates of asymptomatic infection in areas with and without universal mask use are needed as well as more studies on the durability of SARS-CoV-2-specific T-cell immunity in asymptomatic people versus symptomatic people with infection.
- > Ultimately, increasing evidence suggests that population-wide mask use reduces both transmission rates and disease severity, both important strategies to combat the pandemic.

Reviewed by: Dr Samantha Bannister

PERINATAL HEALTH

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

Protecting newborn infants during the COVID-19 pandemic should be based on evidence and equity

<https://pubmed.ncbi.nlm.nih.gov/32893895/>

During this time of global crisis, public health professionals have called for regulations to help limit the spread of the SARS-CoV-2 virus. As we try our best to reduce the risk of viral transmission, concerns have been expressed about the protection of vulnerable populations, including pregnant and postpartum women, newborn infants, and those healthcare professionals caring for them.

Due to a lack of effective testing capacity and personal protective equipment (PPE), families and healthcare providers have resulted in some potentially harmful measures related to infant care have been implemented for patients across multiple health systems, despite evidence indicating a low risk of transmission to newborns from asymptomatic and mildly symptomatic women and these include:

- > Reduced skin-to-skin contact and breastfeeding.
- > Separation of newborn infants from their mothers or other family members immediately after birth and as well as during inpatient care.
- > Reduced ability to provide informed consent for how their newborn child is cared for, and thus prevent families who are already marginalised from taking an active role in healthcare decision making.
- > Moreover, in some settings, PPE resources have not been distributed equitably across healthcare facilities leading to suboptimal infection control measures, especially in underfunded and overburdened facilities.
- > The reuse of PPE has further increased exposure risk at a family and community level.

To date, the evidence supports not separating mothers and their newborn infants and thus allowing the skin to skin contact and early and exclusive breastfeeding in almost all cases while ensuring appropriate infection control measures to reduce risk among family members and healthcare professionals.

- > Mothers who elect to practice skin-to-skin care and breastfeeding should be encouraged with education on proper infection control practices (washing hands and surfaces regularly).
- > Mothers with suspected or confirmed COVID-19 are still encouraged to initiate early contact - frequent hand washing, avoidance of sneezing or coughing directly on the infant, and the appropriate use of a face mask is recommended.
- > The evidence suggests that the benefits of maintaining mother to infant contact and breastfeeding outweigh the potential and likely minimal harms of COVID-19 transmission to the newborn.

- > There is a need for acceptable infection control practices to underpin effective interruption of viral transmission no matter the setting.
- > Evidence-based guidelines for providing mothers and newborn infants with high-quality care are evolving with increased information about COVID-19.
- > The World Health Organization (WHO) regularly publishes COVID-19 guidance that holistically considers the benefits of essential newborn care alongside emerging viral threats.

In most cases, having the newborn connect with the mother and other family members when necessary, encouraging close contact and breastfeeding, and practicing infection control measures allows for the best clinical care and is the safest option for the child, family, and healthcare workers.

Reviewed by: Professor Suzanne Garland

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

The difference in levels of SARS-CoV-2 S1 and S2 subunits- and nucleocapsid protein-reactive SIgM/IgM, IgG and SIgA/IgA antibodies in human milk
<https://www.nature.com/articles/s41372-020-00805-w>

- > This study evaluated the presence and levels of antibodies reactive to SARS-CoV-2 S1 and S2 subunits (S1 + S2), and nucleocapsid protein.
- > The levels of SARS-CoV-2 S1 + S2- and nucleocapsid-reactive SIgM/IgM, IgG and SIgA/IgA were measured in human milk samples from 41 women during the COVID-19 pandemic (2020-HM) and from 16 women two years before the outbreak (2018-HM).
- > The study compared antibody levels between vaccinated [for Influenza and/ Tdap in pregnancy 26] and unvaccinated mothers [15], as well as between women that had symptoms of viral respiratory infection(s) during the year and women without symptoms.
- > SARS-CoV-2 S1 + S2-reactive SIgA/IgA, SIgM/IgM and IgG were detected in 97.6%, 68.3% and 58.5% in human milk, whereas nucleocapsid-reactive antibodies were detected in 56.4%, 87.2% and 46.2%, respectively.
- > S1 + S2-reactive IgG was higher in milk from women that had symptoms of viral respiratory infection(s) during the last year, than in milk from women without symptom.
- > S1 + S2- and nucleocapsid-reactive IgG were higher in the 2020-HM group compared with the 2018-HM group.
- > SARS-CoV-2 S1 + S2-reactive IgG from vaccinated women was 2.9-fold higher than unvaccinated women ($p=0.004$).
- > The IgG responses seem distinct between unexposed and exposed women's samples.
- > The presence of SARS-CoV-2 reactive antibodies in human milk could provide passive immunity to breastfed infants and protect them against COVID-19 diseases.

- > Human milk antibodies with high polyreactive and cross-reactive properties against SARS-CoV-2 and other coronaviruses could be useful to neutralise and protect against future coronavirus pandemics, especially in vulnerable populations.
- > A limitation of this study was the absence of information on whether the mothers were previously infected with or exposed to SARS-CoV-2. However, they did not detect viral RNA from SARS-CoV-2 in any of the human milk samples using real-time RT-qPCR.
- > In conclusion, despite the high proportion of SARS-CoV-2 S1 + S2 antibodies in breast milk, the neutralising capacity and potential role of human milk antibodies reactive to SARS-CoV-2 S1 + S2 and nucleocapsid in providing passive immunity to infants remain to be seen.

Reviewed by: Professor Suzanne Garland

SCHOOLS

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

Prospective active national surveillance of preschools and primary schools for SARS-CoV-2 infection and transmission in England, June 2020 (sKIDs COVID-19 surveillance in school KIDs)

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/914700/sKIDs_Phase1Report_01sep2020.pdf

- > As schools re-open, there is concern that community transmission at school will increase, particularly as children are not expected to social distance. However, the actual risk of transmission in schools is unclear.
- > From the 1st June to mid-July 2020, Public Health England undertook a prospective national study in students and staff at preschool and primary schools to investigate infection and transmission of SARS-CoV-2.
- > Study design: The study had two arms, the first was weekly nasal swabs for 4-6 weeks at participating schools (n=86) and the second was blood sampling with nasal and throat swabs within the first two weeks of school re-opening in schools not participating in arm one and in regions where a paediatric investigation team could be formed (n=45). 12,026 participants across 131 schools were included in the study and 43,039 swabs taken.
- > Swab positivity rates were calculated at 3.9/100,000/week in students and 11.3/100,000/week in staff.
- > Only 3/43,039 swabs had SARS-CoV-2 infection.
- > SARS-CoV-2 antibody positivity rate was 10.6% (86/814, CI 8/5-12/9%) in students and 12.7% (167/1,316, CI 10.9-14.6%) in staff at the start of the summer term of school. This was similar to the seropositivity rate in the broader community at the time. Only 20.9% (18/96) of seropositive students reported COVID-19 like symptoms compared with 60.1% (101/168) of staff.
- > Non-white ethnicity (OR 3.48, CI 1.73-7.03), having a history of COVID-19 like symptoms (OR 2.03, CI 1.15-2.58) and having a healthcare worker in the household (OR 2.54, CI 1.33-4.88) were significantly associated (P=0.05) with seropositivity in both students and staff, but not school attendance or time spent in school during the lockdown.
- > Mass testing found three participants who initially tested positive but did not seroconvert, suggesting a false positive result and demonstrating the limitations of mass testing.
- > The positive cases identified could have been picked up through contact tracing and community testing based on their contacts and presence of symptoms.

- > Seropositivity rates were similar in students and staff, suggesting children do get infected as frequently as adults but may be more likely to have asymptomatic or mild disease.
- > Limitations:
 - The study was undertaken after the easing of lockdown when SARS-CoV-2 rates were at their lowest.
 - The characteristics of those who consented to take part may be different from those who did not, increasing the risk of confounding factors.
 - Findings cannot be extrapolated to secondary schools.

Reviewed by: Dr Martin Wright

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

Transmission of SARS-CoV-2 in children aged 0 to 19 years in childcare facilities and schools after their re-opening in May 2020, Baden-Württemberg, Germany
<https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.36.2001587>

- > This study analysed data from SARS-CoV-2 infected children (age: 0–19 years), who had been to school/childcare facilities, after they re-opened in Baden-Württemberg Germany in May 2020.
- > Children returned to school with 50% class size and no face masks, plus cleaning of contact surfaces, regular ventilation of rooms, and exclusion of sick children.
- > In total, 557 cases of age 0–19 years were notified (17.9% of all 3,104 notified cases), and for 453 (81.3%) information on school attendance was available; 137 (30%) of these 453 cases attended school or childcare settings for at least one day in their infectious period whereas the remaining 316 were at home during their entire infectious period.
- > More than 2,300 nasopharyngeal swabs were taken from the close contacts (teachers and pupils) of the 137 index cases, and the close contacts of any secondary cases.
- > Swabbing usually occurred three to five days after the index cases' diagnosis.
- > 6/137 cases infected 11 additional pupils (one to three pupils per case; three in childcare facilities, one in primary school, four in secondary school and three in vocational school), whereas no secondary infections could be detected for the remaining cases despite extensive contact tracing and swabbing of school and childcare-facility contacts.
- > Aside from the 11 secondary cases and another four pupils who were infected by two teachers, all remaining cases with information on school attendance (n = 437) were caused by sources outside of school and childcare facilities.
- > This investigation suggests that child-to-child transmission in schools and childcare facilities is uncommon and not the primary cause of SARS-CoV-2 infection in children.

- > Based on the estimation, there could be one secondary case per roughly 25 infectious school days. This ratio of 1 in 25 might, however, overestimate the transmission risk in schools and childcare facilities, because some of the 104 index cases (i.e. $104 = 557 - 453$) for whom no information on school attendance was available, may have spent some time in school or a childcare facility while being infectious, yet without further generating any notified COVID-19 cases.
- > In order to gradually return to the regular school and childcare-facility life, larger classes will have to be accepted again. This will require more proximity between pupils. As a countermeasure, strict ventilation of classrooms, not only between lessons but within, should be implemented.
- > Additionally, face masks should be used in schools, both inside and outside of classrooms. Based on our current study findings, we anticipate that transmission rates in schools and childcare facilities would remain low under such interventions.

Reviewed by: Professor Fiona Russell

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

COVID-19, children, and schools: overlooked and at risk

<https://www.mja.com.au/journal/2020/covid-19-children-and-schools-overlooked-and-risk>

- > Emerging evidence suggests that children may transmit SARS-CoV-2 to a comparable degree as adults.
- > Children remain at a lower risk of severe disease from SARS-CoV-2, having low rates of hospitalisation and mortality. However, they may experience the severe post-infectious inflammatory syndrome.
- > There are several examples that demonstrate children to be as susceptible to SARS-CoV-2 infection.
 - In a Spanish study of 61,000 people, antibodies against the virus were demonstrated in 3.4% of children and 4.4-6% of adults.
 - In a household contact study conducted in China, children were equally as likely to be infected as adults.
- > The role that children play in the transmission is less clear.
 - Nasopharyngeal swabs from children (5-17 years old) had levels of viral RNA comparable to adults, whereas young children had levels 10-100 times that of adults.
 - Evidence from South Korea and Italy, suggests that contacts of children infected with SARS-CoV-2 are more likely to be infected than those of adults.
- > Re-opening of schools has been associated with significant outbreaks. In Israel, 153 students and 25 staff members tested positive in the setting of a heatwave. Similarly, an outbreak in Chile related to schools demonstrated the potential for a silent spread with, 18% of staff and 40% of students positive for SARS-CoV-2 and asymptomatic.

- > Limitations of studies involving children: most are conducted in lockdown periods, which are not indicative of normal conditions; quarantine/isolation protocols further limit spread to children, which may skew results; testing was limited to specific clinical criteria, which impairs detection of asymptomatic infection of children; children may be thought to be a contact rather than an index case.
- > Schools must implement risk minimisation strategies, such as masks, increased ventilation, strict hygiene measures and regular disinfection of shared surfaces.
- > In the setting of ongoing community transmission, schools should be closed so that risk of spread amongst children, and hence the wider community, may be limited.

Reviewed by: Dr Wonie Uahwatanasakul

VACCINES

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

"When Will We Have a Vaccine?" – understanding questions and answers about COVID-19 vaccination

<https://www.nejm.org/doi/full/10.1056/NEJMp2025331>

- > In this NEJM "Perspective", authors discuss three main concerns around a COVID-19 vaccine: when can people be confident of a safe and effective vaccine, when will that vaccine be available to people, and when will we achieve vaccination rates that allow a return to a pre-COVID-19 "normal".
- > This perspective highlights the importance of repeatedly emphasising stringent safety requirements to develop confidence for clinicians and the public alike.
- > The need for clinicians and the public to have easy access to user-friendly materials that reference publicly available studies, data, and presentations related to safety and effectiveness and the need and planning for longer-term, post-licensure vaccine safety and monitoring systems need to be highlighted and made visible to the public and health care professionals.
- > Authors discuss the distribution of such a vaccine, including which groups might be prioritised and how this could translate to public acceptance.
- > The National Academy of Medicine (NAM) committee to formulate criteria to ensure equitable distribution of initial COVID-19 vaccines and to offer guidance on addressing vaccine hesitancy is vital, and other countries will need to do the same.
- > The discussion emphasises the importance of impeccable public health messaging to ensure broad uptake of a vaccine.
- > Communication about vaccine candidates and availability needs to be much more than just releasing expert-committee reports.
- > Investment needs to occur now not when uptake of newly recommended vaccines falls short of goals, as occurred with HPV vaccines - the point is made that not since the March of Dimes polio-vaccination efforts in the 1950s has there been major investment in public information and advocacy for new vaccines.
- > High uptake of COVID-19 vaccines among prioritised groups should not be assumed - many people in these groups will want to be vaccinated, but their willingness will be affected by what is said, the way it is said, and who says it.
- > Surveys in the USA suggest that physicians, nurses, and pharmacists remain the most highly trusted professionals - extensive, active, and ongoing involvement by clinicians is essential to attaining the high uptake.
- > The final point is clear and important - efforts to engage diverse stakeholders and communities in COVID-19 vaccination education strategies, key messages, and materials for clinicians and the public are needed now.

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

Safety and immunogenicity of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine in two formulations: two open, non-randomised phase 1 / 2 studies from Russia

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)31866-3/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31866-3/fulltext)

- > This report details two phase 1/2 studies of two different adenovirus vector SARS-CoV-2 spike protein vaccine formulations (one frozen and one freeze-dried/lyophilised). Each study investigated two different adenovirus vectors (rAd5 and rAd26). Neither study was randomised, blinded, nor controlled.
- > There were 38 individuals included in each trial. In each, nine individuals received each of the rAd5 or rAd26 vaccines (Phase 1), and 20 received the rAd26 vaccine on day 0 followed by the rAd5 vaccine on day 21 (Phase 2). The Phase 1 study of the frozen vaccine included only males, and only 30% of participants in both the Phase 2 trials were female.
- > The safety profile was documented for both trials - most adverse events were mild. All participants in the frozen formulation phase two study had at least a mild fever. Fewer adverse events were reported in the group which received the lyophilised formulation. There were no serious adverse events documented.
- > The immunogenicity of the vaccine candidates is described, although results were often pooled across both trials. The candidates were broadly immunogenic and comparable to convalescent plasma. The authors note that titres reported here are lower than those generated by other vaccine candidates (e.g. ChadOx1).
- > Large scale randomised controlled trials are needed to confirm the results in these studies.
- > The predominance of males in this study is particularly concerning, and future studies need to be carried out in more diverse populations.
- > The Russian government has provisionally approved the use of these vaccines for some at-risk groups and under strict pharmacovigilance based on these clinical (and pre-clinical) studies. This is inconsistent with the approach of other nations which await more robust phase 2 and 3 clinical trial results.

Reviewed by: A/Prof Margie Danchin

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

Mapping global trends in vaccine confidence and investigating barriers to vaccine uptake: a large-scale retrospective temporal modelling study

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)31558-0/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31558-0/fulltext)

- > Examination of global trends in vaccine confidence using data from 290 surveys completed between 2015 and 2019 across 149 countries, including 284,381 individuals.
- > Confidence remained low across Europe compared with other continents.
- > Confidence in importance, safety and effectiveness of vaccines fell in Afghanistan, Indonesia, Pakistan, the Philippines, and South Korea, mostly in relation to specific adverse events or safety scares, i.e. Dengvaxia in the Philippines.
- > Significant increase in strongly disagreeing that vaccines are safe in Afghanistan, Azerbaijan, Indonesia, Nigeria, Pakistan, and Serbia.
- > Confidence improved in Finland, France, Ireland and Italy.
- > This is the largest study of global vaccine confidence to date, allowing for cross-country comparisons and changes over time.
- > This study highlights the importance of regular monitoring of vaccine confidence to detect emerging trends in countries to prompt interventions to build and sustain vaccine confidence.
- > Countries should be encouraged to undertake their monitoring of vaccine confidence with calibrated tools to detect barriers to vaccine acceptance and access.

Reviewed by: A/Prof Margie Danchin

VIROLOGY

Min Zhang - 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

SARS-CoV-2 RNA viremia is associated with a sepsis-like host response and critical illness in COVID-19 (not peer reviewed)

<https://www.medrxiv.org/content/10.1101/2020.08.25.20154252v2>

- > Retrospective cohort study which aims to identify the potential role of the SARS-CoV-2 virus or its viral components in the pathogenesis of the "sepsis-like" clinical presentation observed in severe COVID-19.
- > The study population consisted of 250 adult patients with a positive nasopharyngeal swab PCR test for SARS-CoV-2 administered at participating hospitals in Spain from 16th March to the 15th April 2020.
- > These patients were recruited according to three categories, an outpatient group who were discharged from the hospital within 24 hours (n=50), a ward group who were hospitalised to pneumology, infectious diseases or internal medicine wards (n=100), and an ICU group (n=100).
- > Method: assessed the impact of SARS-CoV-2 RNA viremia on a number of biological parameters; examined the association between SARS-CoV-2 RNA in peripheral blood plasma and disease severity using multivariate ordinal logistic regression analysis and other methods.
- > SARS-CoV-2-RNA viremia was independently associated with:
 - High levels of ferritin, LDH and high levels of chemokines (CXCL10, CCL-2), cytokines (IL-15, IL-10, IL-1ra) and GCS-F.
 - CXCL10 was the most accurate identifier of viremia in plasma (AUC = 0.85 [0.80 – 0.89], P<0.001).
 - IL-15 was the cytokine which most accurately differentiated clinical ward patients from ICU patients (AUC: 0.82 [0.76 – 0.88], p <0.001).
 - Low lymphocyte, monocyte and platelet counts and low levels of IL-4 in plasma.
- > SARS-CoV-2-RNA viremia was a predictor of severity across all three categories [OR= 8.24, P< 0.001, (CI 95%= 4.71; 14.41)].
 - In hospitalised COVID-19 patients, the presence of SARS-CoV-2-RNA viremia translated to an eight-fold increase in the risk of presenting critical illness, independently of age, sex and significant comorbidities.
- > Implications:
 - Recognising severe COVID-19 as a sepsis-like disease suggests that targeting the virus as an infectious agent causing sepsis would require early intervention with antiviral strategies.

- Using CXCL-10 and IL-15 as surrogate biomarkers for SARS-CoV-2 RNA viremia and critical illness could facilitate indirect identification of the "septic-like" state, as proteins are easier to profile than viraemic RNA.

Reviewed by: Dr Celeste Donato

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/>

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>

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