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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.23

24th September 2020



Australian Government
 Department of Health

BE COVIDSAFE

CURRENT STATUS OF CONFIRMED CASES



10



CURRENT CASES
 INTENSIVE CARE UNITS (ICU)

ACT	NSW	NT	QLD	SA	TAS	VIC	WA
0	2	0	0	0	0	8	0

109



CURRENT CASES
 ADMITTED TO HOSPITALS

ACT	NSW	NT	QLD	SA	TAS	VIC	WA
0	11	0	4	0	0	94	0

7,296,252

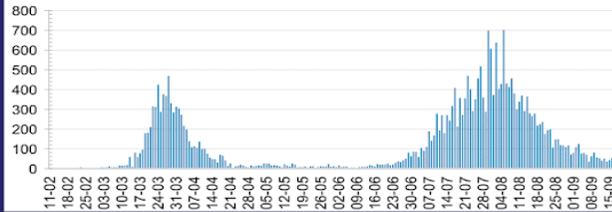


TOTAL TESTS
 CONDUCTED

0.4% POSITIVE

ACT	NSW	NT	QLD
89,963	2,584,683	43,758	1,065,078
POSITIVE	POSITIVE	POSITIVE	POSITIVE
0.1%	0.2%	0.1%	0.1%
SA	TAS	VIC	WA
443,097	98,814	2,575,457	395,402
POSITIVE	POSITIVE	POSITIVE	POSITIVE
0.1%	0.2%	0.8%	0.2%

DAILY NUMBER OF REPORTED CASES

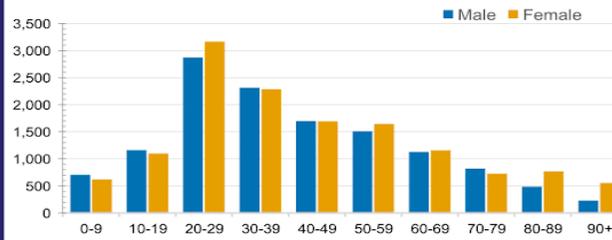


CASES IN AGED CARE SERVICES

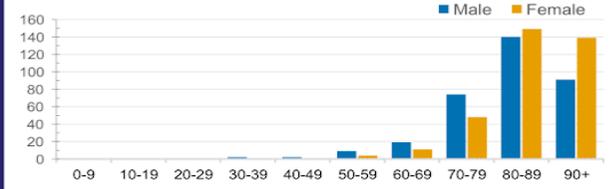
Confirmed Cases	Australia	ACT	NSW	NT	QLD	SA	TAS	VIC	WA
Residential Care Recipients	2041 [1170] (633)	0	61 [33] (28)	0	1 (1)	0	1 (1)	1978 [1137] (603)	0
In Home Care Recipients	82 [71] (7)	0	13 [13] (0)	0	8 [8] (1)	1 [1] (2)	5 [3] (4)	54 [46] (4)	1 (1)

Cases in care recipients [recovered] (deaths)

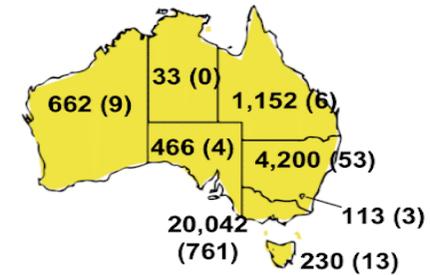
CASES BY AGE GROUP AND SEX



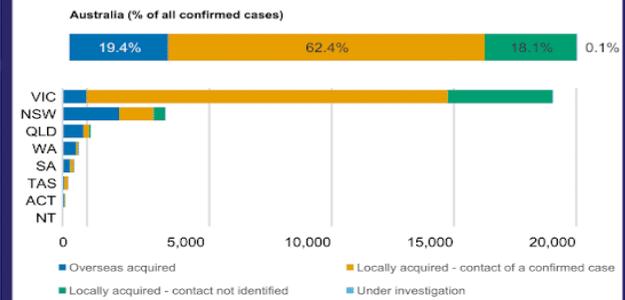
DEATHS BY AGE GROUP AND SEX



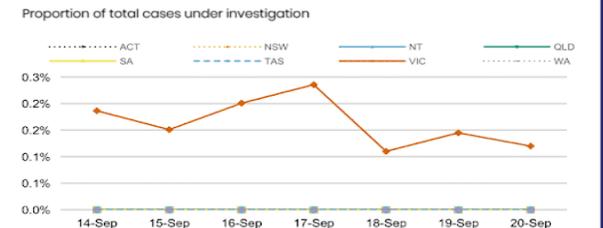
CASES (DEATHS) BY STATE AND TERRITORIES



CASES BY SOURCE OF INFECTION



PUBLIC HEALTH RESPONSE MEASURE



Last updated 20 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 21; cited 2020 September 22]. Available from: <https://www.health.gov.au/resources/collections/coronavirus-covid-19-at-a-glance-infographic-collection>

GUEST EDITORIAL

Professor Andrew Steer - General Paediatrician, Theme Director, Infection and Immunity, Murdoch Children's Research Institute; Department of General Medicine, Royal Children's Hospital; Paediatric Infectious Diseases Physician, Department of General Medicine, Royal Children's Hospital; Principal Research Fellow, Centre for International Child Health, Department of Paediatrics, University of Melbourne; Honorary Senior Lecturer, Menzies School of Health Research.

Welcome to the 23rd edition of The Weekly. This week's papers include two important topics: a World Health Organization framework to guide the equitable distribution of COVID-19 vaccines; and the potential role of mass testing to control viral transmission, linked to the development of new virus detection assays.

The WHO Strategic Advisory Group of Experts on Immunization (SAGE) outlined a framework for the allocation and prioritisation of COVID-19 vaccination.(1) The framework is values-based, anchored to the ideal that COVID-19 vaccines contribute to the equitable protection and promotion of human well-being among all people of the world. The framework provides six core principles to guide distribution: human well-being, equal respect, global equity, national equity, reciprocity and legitimacy. Such an approach is critical to equitable and ethical decision-making, and similar documents are being produced from academic groups across the world, (2) and in individual countries, including the United States. (3) As academics and global citizens, we must do our best to advocate key international organisations such as WHO, COVAX and CEPI, vaccine producers and national governments for fair and equitable distribution of COVID-19 vaccines.

However, the timing of the availability and deployment of vaccine/s is unknown, and there are many uncertainties along the path, including results of efficacy studies, concerns around vaccine safety, capacity for vaccine production, individuals' appetite for vaccine uptake and the ability of agencies to deliver the vaccine. In the meantime, governments, policymakers and academics continue to pursue strategies to reduce transmission of SARS-CoV-2 and to minimise the clinical and socio-economic impacts of COVID-19. As we have seen across the globe, these strategies are many and varied. Mass testing is one such strategy.

This week, the British Medical Journal reported on "Operation Moonshot", a plan by the U.K. government to do a mass population testing programme for COVID-19, with the aim to test the whole U.K. population each week, starting early 2021.(4) REF Mass testing has been advocated by several experts, including by a group of academics across the U.K. in early May.(5) Some, including Paul Sax, Professor of Medicine at Harvard Medical School, have suggested that mass testing will be critical in controlling the pandemic before a vaccine is available.(6)

The theory behind this approach is “test, test, test” – that is: test to detect people who may have the virus during the period before becoming symptomatic; test as many people as possible to detect as many cases as is possible; and test people where it is easy for them to do so, for example, at home. Michael Mina, a virologist and epidemiologist at the Harvard School of Public Health, advocates for a rapid test that people can do at home before leaving for the day – a “COVID check”, if you will – Prof Mina gives an easily digestible summary of this approach here:

<https://www.youtube.com/watch?v=AZWuyvBAWWQ>

New rapid tests are being developed at pace. Highlighted in this week’s Weekly, investigators at M.I.T. describe the development of a rapid test for detection of SARS-CoV-2 that combines simple extraction of viral R.N.A. with isothermal amplification, and CRISPR (clustered regularly interspaced short palindromic repeats) mediated detection. (7) The test, known as STOP (SHERLOCK in a pot) takes less than one hour and has a similar sensitivity to reverse-transcription-quantitative polymerase-chain-reaction (RT-qPCR) assays. This is an exciting advance.

However, such technology is not what is needed for a mass testing approach. What is needed is a cheap, accurate, super-rapid, easy to use, home-based, paper antigen test – a bit like an over-the-counter pregnancy test. These tests, by their nature, will not be as sensitive as the STOP test or the RT-PCR tests, but advocates argue that this is acceptable for two reasons: 1) detection of SARS-CoV-2 by these tests are in the range of viral copies per mL consistent with the transmissible virus; and 2) these tests will be repeated frequently in individuals so that if the tests fail to detect the virus on one day, it will detect it the following day. (8)

Whilst a mass testing approach may sound good in theory, there is currently little detail behind the U.K. plan, and there are some fairly large barriers. First, the type of test described above is not yet readily available. (9) Second, there is the cost – the B.M.J. report suggests that GBP100 billion (~AUD175 billion) has been budgeted for the program. Third, the sheer capacity of testing is mind-boggling – Operation Moonshot aims to increase testing in the U.K. from the current 350,000 to up to 10 million tests per day – this will require a massive scale-up in production, distribution, reporting and tracking of tests. Fourth, false positives present a concerning ethical issue – even if the test has a specificity of 99%, thousands of people will be incorrectly given a diagnosis of SARS-CoV-2 infection. Finally, beyond modelling, there is no empirical evidence base to support such an approach. (10)

What happens with Operation Moonshot remains to be seen. Editorials in the B.M.J. with titles such as “Flying before we can walk” reflect scepticism from some, but thinking continues on how to best prevent and control the transmission of SARS-CoV-2 while we wait for a safe and effective vaccine. (11) Many will argue that we must continue to do our best with the approaches that have been shown to work so far in the pandemic.

Finally, a huge congratulations and thanks to the Editorial Team and reviewers involved in producing the Weekly, especially the medical student committee and contributors. The Weekly is a great read and a fantastic contribution from the Melbourne Children’s Campus.

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2. Emanuel EJ, Persad G, Kern A, Buchanan A, Fabre C, Halliday D, et al. [An ethical framework for global vaccine allocation](#). Science (New York, NY). 2020;369(6509):1309-12.
3. Toner E, Barnill A, Krubiner C, Bernstein J, Privor-Dumm L, Watson M, et al. [Interim Framework for COVID-19 Vaccine Allocation and Distribution in the United States](#). Johns Hopkins Bloomberg School of Public Health; 2020 2020 August 19.
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7. Joung J, Ladha A, Saito M, Kim NG, Woolley AE, Segel M, et al. [Detection of SARS-CoV-2 with SHERLOCK One-Pot Testing](#). The New England journal of medicine. 2020.
8. Larremore DB, Wilder B, Lester E, Shehata S, Burke JM, Hay JA, et al. [Test sensitivity is secondary to frequency and turnaround time for COVID-19 surveillance](#). medRxiv. 2020:2020.06.22.20136309.
9. Mahase E. [Operation Moonshot: Testing plan relies on technology that does not exist](#). B.M.J. (Clinical research ed). 2020;370:m3585.
10. Deeks JJ, Brookes AJ, Pollock AM. [Operation Moonshot proposals are scientifically unsound](#). B.M.J. (Clinical research ed). 2020;370:m3699.
11. Ladher N. [Covid-19: Flying before we can walk](#). B.M.J. (Clinical research ed). 2020;370:m3598.

HIGHLIGHTS

- > The Victorian Commission for Children and Young People have found a massive disruption in the lives of children and youth in Victoria due to the COVID-19 pandemic.
- > WHO provides a Values Framework for COVID-19 vaccine prioritisation intended for policymakers and expert advisors at the global, regional and national level about decisions on COVID-19 vaccine allocation.
- > Children need to be left out of the mandatory vaccine debate, as too little is known about the COVID-19 vaccine candidates & the epidemiology of SARS-CoV-2 in children.
- > The Lancet COVID-19 commission offers ten priority actions on suppression of the pandemic by pharmaceutical and non-pharmaceutical interventions, overcoming humanitarian emergencies caused by the pandemic, restructuring public and private finances and rebuilding a sustainable global economy.
- > A commentary highlighting the gaps in our understanding of COVID-19 in children.
- > A consensus guideline on the management of PIMS-TS has been developed.
- > A scoping review suggests that SARS-CoV-2 is an opportunistic airborne infection which frequently contaminates the air with SARS-CoV-2 R.N.A., but the virus is rarely viable.
- > Serological assays can identify paediatric infections missed by symptom-based administration of viral tests as most children are asymptomatic and have milder disease than adults.
- > In closed environments with recirculating air conditioning, the high potential for airborne transmission of COVID-19 raises the need for public health preventive and control measures.
- > Biomarkers including lymphopenia, thrombocytopenia, and raised C.R.P., P.C.T., C.K., A.S.T., A.L.T., creatinine, L.D.H., and D-dimer are all associated with increased COVID-19 severity
- > Compared with adult patients, C.T. chest imaging abnormalities in children with COVID-19 were less frequent and less severe
- > In a U.S. surveillance study, about half of hospitalised pregnant women with COVID-19 had symptoms and severe outcomes, including I.C.U. admission, mechanical ventilation, and death
- > A case-control study found that daily wearing of eyeglasses is associated with reduced susceptibility to COVID-19 infection, although the study used historical control.
- > A prospective cohort study found that the low molecular prevalence and lack of viable SARS-CoV-2 in fomites and air samples implied low nosocomial risk SARS-CoV-2 transmission through inanimate objects or aerosols.

- > A study of domesticated cats found no evidence of human-to-feline transmission
- > Early-symptomatic transmission of COVID-19 accounts for 39% of transmission in a model, highlighting the importance of rapid-testing, and early, strict infection control/isolation measures at the first sign of mild, potentially COVID-19 related symptoms.
- > Multilayered public health prevention and mitigation strategies in an overnight U.S. school camp can identify and prevent SARS-CoV-2 transmission.
- > In Hong Kong, there have been reported cases of COVID-19 in school children but no outbreaks in schools.

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ADULT MEDICINE

Thang Dao – 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Biomarkers and outcomes of COVID-19 hospitalisations: systematic review and meta-analysis

<https://ebm.bmj.com/content/early/2020/09/14/bmjebm-2020-111536>

Summary: Lymphopenia, thrombocytopenia, and raised C.R.P., P.C.T., C.K., A.S.T., A.L.T., creatinine, L.D.H., and D-dimer are associated with COVID-19 severity.

- > This systematic review and meta-analysis assessed the association of multiple laboratory biomarkers and outcomes in COVID-19 hospitalised patients.
- > Poor outcomes were defined as intensive care unit admission, severe disease, invasive mechanical ventilation use, SpO₂ <90%, and in-hospital mortality.
- > The review identified 32 observational studies with 10,491 confirmed COVID-19 cases from 1st December 2019 to 15th August 2020.
- > Comparing with the better outcomes, these biomarkers were associated with a higher risk of poor outcomes in COVID-19 patients:
 - Thrombocytopenic patients (platelet count <150,000 cells / μ L).
 - Raised levels of C-reactive protein (C.R.P.) (>10 mg/L), procalcitonin (P.C.T.) (>0.5 ng/mL), and creatinine kinase (C.K.) increased poor outcomes by approximately fourfold, sixfold, and threefold respectively.
 - For metabolic markers, elevated aspartate aminotransferase (A.S.T.) (>40 IU/L), alanine aminotransferase (A.L.T.) (>40 IU/L), and creatinine (>1.18–1.5) values were associated with nearly threefold, twofold, and threefold more at risk of poor outcomes.
 - Raised lactate dehydrogenase (L.D.H.) and D-dimer (\geq 0.5 mg/L) were associated with a nearly fivefold and threefold higher risk of poor outcomes.
- > There were two main limitations: Heterogeneity of the included studies due to differences in methods, such as definitions of severity and cut-off values. The role of this heterogeneity on outcomes evaluated in a sensitivity analysis. Data on the changing levels of biomarkers during the disease course.
- > Conclusion: The variation and profile of specific early biomarkers based on laboratory measures that are less expensive, easy and fast, may assist the development of a risk-stratified approach to the management of COVID-19 hospitalised patients.

Reviewed by: Professor Julie Bines

CLINICAL PAEDIATRICS

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

Acute appendicitis in Multisystem Inflammatory Syndrome in Children with COVID-19

https://journals.lww.com/pidj/Citation/9000/Acute_Appendicitis_in_Multisystem_Inflammatory.96050.aspx

- > This case series from South Africa highlights the possible link between appendicitis and multisystem inflammatory syndrome in children (MIS-C), otherwise known as paediatric inflammatory, multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS).
- > Here, three children had surgically proven appendicitis and were PCR positive for SARS-CoV-2, whilst a fourth child was diagnosed with appendicitis and SARS-CoV-2 infection but did not require surgical intervention nor developed MIS-C.
- > Authors question whether there could be a link between viral entry and inflammation leading to both pathologies, noting that appendicitis has also been associated with Kawasaki disease.
- > They recommend awareness of the association between acute appendicitis, COVID-19, and MIS-C.

Reviewed by: Dr John Cheek

Grace Newman – 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne and
Celina DeBiasio - 3rd Year Medical Student, University of Ottawa

Safeguarding children's right to health in the hospital during COVID-19 (commentary)

[https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642\(20\)30300-X/fulltext](https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(20)30300-X/fulltext)

- > This is a commentary from The European Children's Hospitals Organisation calling on children's hospitals and public health systems to ensure the rights of children are central in the new normal of COVID-19.
- > There is concern that a falling rate of vaccine uptake may lead to a resurgence of vaccine-preventable diseases.
- > Preparation is essential to prepare for future surges in COVID-19 as well as predictable increases in seasonal illness.
- > General and complex paediatric services have been discontinued or limited during the pandemic. It is important to maintain safe access to children's hospitals, so children have consistent and timely access to care.

- > Healthcare providers need to be mindful of both the benefits and limitations of telemedicine, including challenges with quality, confidentiality and exacerbation of existing health inequities.
- > Consolidating paediatric hospital care in fewer locations (specific children's hospitals) can reduce the need for children and families to visit high-risk areas (such as joint emergency departments) and tells communities that children's hospitals are safe and ready to care for patients, as well as increasing space for adult care.
- > It will be essential to have rapid systems to address resource needs such as improving access, rapid identification of COVID-19 positive cases, robust digital health systems including the capacity for cross-border data sharing, and cross-training and education for staff.
- > It is important to develop clear communication strategies for the community to ensure they seek timely care for children.

Reviewed by: Dr Martin Wright

Juliana Wu - 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

The evolving picture of SARS-CoV-2 and COVID-19 in children: critical knowledge gaps (commentary)

<https://gh.bmj.com/content/5/9/e003454>

- > This is a commentary from the staff of UNICEF highlighting the gaps in our understanding about COVID-19 in children.
- > Most widely collected data by country does not include age, and when it does, children are often broadly classified as < 20 years. Thus, reports considering what would appear to be quite significant differences within different age groups (in incidence, symptomatology, and severity) are based on much smaller samples.
- > In addition, risk factors for infection and disease severity are not nearly as well defined in children as in adults.
- > Biological factors influencing differences in COVID-19 infection for children are only partly understood, and the epidemiology of spread from and to children also. As a result, there is still much uncertainty about how and when to re-open schools.

Reviewed by: Dr Martin Wright

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

A national consensus management pathway for paediatric inflammatory, multisystem syndrome temporally associated with COVID-19 (PIMS-TS): results of a national Delphi process

[https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642\(20\)30304-7/fulltext](https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(20)30304-7/fulltext)

- > National consensus management pathway for the U.K. to provide guidance for clinicians caring for children with Paediatric inflammatory, multisystem syndrome temporally associated with COVID-19 (PIMS-TS).
- > PIMS-TS is a novel condition that emerged during COVID-19 pandemic.

- > Consensus management pathway was developed through a three-phase online Delphi process and virtual meeting.
- > 140 consensus statements that describe the initial investigation of children with suspected PIMS-TS.
 - Children suspected should undergo first-line blood tests to determine if they meet diagnostic criteria; subsequent tests to determine the severity of the disease, exclude important differential diagnoses and screen for cardiac involvement.
 - Multidisciplinary team essential facet of care.
 - Therapeutic choices are dependent on presenting phenotype and high-risk features or severity of disease; the stepwise pathway of IV immunoglobulin, followed by methylprednisolone and biological therapy recommended.
- > Management pathway is based entirely on expert opinion and should be updated as new evidence emerges.

Reviewed by: Dr John Cheek

DIAGNOSTICS & SAMPLING

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

Detection of SARS-CoV-2 with SHERLOCK One-Pot Testing

<https://www.nejm.org/doi/10.1056/NEJMc2026172>

- > The authors describe a new simple test (SHERLOCK One-Pot testing) for detection of SARS-CoV-2, that combines a simplified viral R.N.A. extraction with loop-mediated isothermal amplification (LAMP) and CRISPR (clustered regularly interspaced short palindromic repeats)-mediated detection.
- > Briefly, samples were extracted for viral R.N.A. by adding a D.N.A. QuickExtract lysis buffer with 5 min heating at 95°C and then purified by a magnetic beads system. The extracted and purified R.N.A. was later under a LAMP-based amplicon generation step where the LAMP primer sets targeted to the viral gene N, encoding the SARS-CoV-2 nucleocapsid protein, to generate SARS-CoV-2 LAMP amplicons. AapCas12b guide R.N.A.s (a guide R.N.A. helps AapCas12b recognise and cut target D.N.A.) were to induce and amplify the fluorescence signal. The reaction was performed at 60°C and fluorescence was read out by a commercial fluorescence reader device (after 45 min of reaction) or by a lateral flow readout with detection strips (after 80 mins).
- > The SHERLOCK One-Pot testing (also named as STOPCovid v.2) had a sensitivity of 93.1% and a specificity of 98.5% when compared with C.D.C. protocol - a two-step test (R.N.A. extraction followed by RT-qPCR).
- > STOPCovid v.2 has a similar limit of detection to Cobas 6800 RT-PCR (Roche) when using the cycle threshold (Ct) value cut-off at 40.3.

Reviewed by: Dr Lien Anh Ha Do

EPIDEMIOLOGY & PUBLIC HEALTH

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

The timing of COVID-19 transmission (not peer reviewed)

<https://www.medrxiv.org/content/10.1101/2020.09.04.20188516v2>

- > Understanding the timing of SARS-CoV-2 transmission is vital when determining the epidemic curve and the potential impact of interventions on the spread of the epidemic. This article explores transmission events with regards to exposure and symptom onset by analysing currently available datasets of transmission pairs:
- > A key parameter in designing control measures for COVID-19 is the fraction of transmissions occurring while the source is asymptomatic, which is difficult to measure.
- > Another challenging parameter to capture is transmission occurring before or shortly after symptom onset (pre-symptomatic or early symptomatic).
- > Digital and traditional contact tracing requires a reliable estimate of the temporal profile of infectiousness to assess which contacts are at risk of infection.
- > The study used transmission pairs from four datasets in the literature (contained date of symptom onset and exposure intervals) and a fifth dataset to check the robustness of results (serial intervals only).
- > Four key time intervals:
 - Incubation period: the time between infection & onset of symptoms.
 - Serial interval: the interval between the time of onset of symptoms in index & secondary cases (can be directly measured, but is subject to bias).
 - Mean of 5.1 days for all datasets (4.1 days without fifth dataset).
 - Generation time: the interval between the time of infection of the index case and time of infection of the secondary case (harder to estimate).
 - Inferred by maximum likelihood estimation; best fit Weibull distribution; mean of 5.5 days.
 - Time from onset of symptoms to transmission (TOST): time elapsed between onset of symptoms in the index case, and transmission from index to the secondary case (positive for symptomatic transmission, negative for pre-symptomatic transmission).

- Inferred by the maximum likelihood of transmission; best-fit Student t distribution (mean of -0.07 days) and skew-logistic distribution (mean of 0.02 days).
- > The peak of infectiousness depends on the onset of symptoms, rather than the time of infection. Most transmission events occurred a few days before and after the onset of symptoms.
- > Infectiousness increases gradually from time of infection to onset of symptoms. Time of symptom onset is the main determinant of when transmission occurs.
- > It remains unclear whether the magnitude of infectiousness depends on the incubation period.
- > Transmission events are closely tied to symptom onset.
- > Assessed the contribution of pre-symptomatic transmission by estimating the fraction of transmission on each individual day, including negative times (i.e. pre-symptomatic times) and the fraction of pre-symptomatic transmissions.
- > The fraction of pre-symptomatic transmissions as modelled in this study (using a Bayesian approach) was 41% (95% CI 31-50).
- > The peak of transmission occurs on the day of symptom onset +/- 20% of transmissions, and the day after symptom onset accounts for 16% transmission.
 - Bayesian analysis of individual pairs in dataset = 35% (95% CI 26-45).
- > However, symptomatic transmissions occurring two days or more days following symptom onset only accounted for 22% of transmissions (24% from Bayesian analysis).
- > These results highlight the importance of implementing non-pharmaceutical interventions to reduce pre-symptomatic transmission and strict infection control measures at the first sign of even mild, potentially related COVID-19 symptoms to reduce early symptomatic transmission.
- > Rapid or at-home testing and contextual risk information would facilitate efficient, early isolation.

Reviewed by: Dr Claire von Mollendorf

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

Serological identification of SARS-CoV-2 infections among children visiting a hospital during the initial Seattle outbreak

<https://www.nature.com/articles/s41467-020-18178-1>

- > In the U.S., children represent 22% of the population, but only 1.7% of confirmed SARS-CoV-2 cases as of 2nd April 2020.
- > This may reflect the strategy of symptom-based testing that is less likely to identify asymptomatic or mildly symptomatic infected children.
- > Aim: Assess the frequency of paediatric SARS-CoV-2 infection by serological screening of 1775 residual samples from Seattle Children's Hospital collected from 1076 children seeking medical care from 3rd March to 24th April 2020 which coincided with a temporal peak in cases of COVID-19 within the population.
- > Samples were tested by multi-stage ELISA approach, sero-positives were confirmed using pseudo-neutralisation assays.
- > A total of n=8 seropositive; period sero-prevalence of ~1%.
- > Most (6/8) seropositive children were not clinically suspected of having had COVID-19.
- > Only 2/8 had a positive viral PCR (also had symptoms), 2/8 had negative viral PCR, and 4/8 did not have a viral PCR test; and additional one patient had a positive PCR but negative serology.
- > Sera from all seropositive children neutralised the virus at > 1:25 dilution.
- > Limitations: Minimal numbers, convenient sample and may not be reflective of the population of Seattle, only 4/8 had received a viral PCR test, early in the temporal increase in cases so may not have sero-responded at time of sample collection or low/borderline positive.
- > Conclusions: Seropositivity was low (~1%) in a convenient cohort of children coinciding with the temporal increase in cases in this city despite a few positive viral PCR results.

Reviewed by: Professor Julie Bines

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

Transmission dynamics of COVID-19 in household and community settings in the United Kingdom (not peer reviewed)

<https://www.medrxiv.org/content/10.1101/2020.08.19.20177188v1>

- > This is a preprint of a prospective case ascertained study of the first few hundred cases of COVID-19 in the U.K. examining secondary attack rates (S.A.R.s) in household contacts (living/spending a significant amount of time in the same household).
- > Follow-up was through phone interviews (daily with contacts), and PCR testing when indicated.
- > 269 primary/co-primary cases in 233 homes were included.
- > In 10 households the primary/co-primary case was < 19 years.
- > There were 472 household contacts.

- > Overall household S.A.R. = 37% (including confirmed and probably secondary cases).
 - Lower S.A.R.s reported in larger households (5 or more people).
 - Higher S.A.R.s reported if the primary case was aged <18 years (however there were only three cases < 18 years without a co-primary, so there is considerable uncertainty about this finding).
 - China, Taiwan and South Korea reported household S.A.R.s ranging from 5-30%. This may be attributed to differences in isolation and infection control measures, though making a comparison across these studies is difficult.
 - Mean serial interval (time of 1st symptom onset in the primary case to time of 1st symptom onset in secondary case) = 4.67 days (range 0-11).
 - Mean incubation period = 4.5 days (using point-source exposure).
 - Household reproduction number (# households infected by each household) = 2.33.
 - $R_0 = 1.85$
- > Limitations: this was early in the pandemic and recommended isolation and infection control measures increased over time, likely missed asymptomatic cases, likely underestimated secondary infection rates in children (since rates of asymptomatic infection appear to be highest in children).
- > Takeaway: hygiene measures and distancing are essential in households, mainly if there are vulnerable members. High household S.A.R.s from primary paediatric cases suggest re-opening of schools needs careful monitoring.

Reviewed by: Dr Martin Wright

GLOBAL HEALTH

gage: 'I have nothing to feed my family...': covid-19 risk pathways for adolescent girls in low- and middle-income countries

<https://www.gage.odi.org/publication/i-have-nothing-to-feed-my-family-covid-19-risk-pathways-for-adolescent-girls-in-low-and-middle-income-countries/>

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

<https://ourworldindata.org/coronavirus>

WHO COVID-19 dashboard

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

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

Lancet COVID-19 commission statement on the occasion of the 75th session of the United Nations General Assembly

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)31927-9/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31927-9/fulltext)

- > This Lancet Commission aims to offer practical solutions to four major challenges that the world faces due to the COVID-19 pandemic: suppression of the pandemic by pharmaceutical and non-pharmaceutical interventions, overcoming humanitarian emergencies caused by the pandemic, restructuring public and private finances and rebuilding a sustainable global economy.
- > This initial statement is extensive and details 11 sections pertaining to all aspects of the COVID-19 pandemic. These range from the zoonotic origin of COVID-19 and mechanisms of pandemic suppression or control to large-scale downstream effects of COVID-19 and the U.N.'s central role in the global recovery.
- > The commission offers ten priority actions. Critically, it will measure the success of a global recovery via a new set of regularly published metrics which broadly align with these goals and priority actions.

Reviewed by: Dr Claire von Mollendorf

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

Brazilian child protection professionals' resilient behaviour during the COVID-19 pandemic

<https://www.sciencedirect.com/science/article/pii/S0145213420303562?via%3Dihub>

- > In Brazil, Child Protection Professionals (C.P.P.s; clinicians, psychologists, social workers) face a heavy workload and stressful working conditions, often relying on resilience strategies to prevent burnout.
- > COVID-19 and the transition to mainly online consultations in a resource-depleted country has challenged the resilience practices of individuals and the willingness of employers to support those practices.
- > The study had three aims, (1) survey working conditions during the pandemic, (2) analyse rates of resilience practices during the pandemic, and (3) consider individual predictors of these behaviours.
- > Resilience practices were divided into three domains:
 - Individual (“caring about own mental health,” “time available for hobbies, etc.”)
 - Familial (“family-work balance,” “shared household tasks”)
 - Career (“open communication,” “shared responsibility at work”)
- > Results indicated that personal belief of importance, and employer support were key for an individual maintaining resilience practices during the pandemic in all three domains.
- > A supportive work environment was a strong mediator of an individuals’ belief in the importance of resilience and the carrying out of adaptive behaviours.
- > Given the importance of the socio-ecological context of work, authors believe a supportive workplace is crucial to practices of resilience.
- > Limitations:
 - Self-reported surveys, therefore difficult to know if actual workplace support or individual interpretation of support that alters behaviour.
 - Studied C.P.P.s in large cities in mostly southern Brazil, C.P.P.s in small communities face different challenges.
 - Cannot draw conclusions about how resilience practices impact the C.P.P.s and their clients.

Reviewed by: Dr Claire von Mollendorf

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

Addressing racial inequalities in a pandemic: data limitations and a call for critical analyses

[https://www.thelancet.com/journals/langlo/article/PIIS2214-109X\(20\)30360-0/fulltext](https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(20)30360-0/fulltext)

- > This correspondence refers to Baqui P et al. Ethnic and regional variations in-hospital mortality from COVID-19 in Brazil: a cross-sectional observational study. Lancet Glob Health. 2020; 8: e1018-e1026 - that has shown that COVID-19 mortality rates vary with race.
- > Brazil has a high COVID-19 burden and is a very diverse population racially. However, despite recognition for early on in the pandemic that the health of “Communities of Colour” have been disproportionately affected, there have been only three articles on racial inequality and COVID-19 from Brazil (compared to 302 from elsewhere) and as of 12th July, less than 0.01% of COVID-19 scientific papers referenced racial inequality. Reasons for this lack of published research may include: limited data collected and shared by public health agencies; incomplete data or data that are collected are undervalued; lack of perceived importance surrounding the topic; and lack of statistics reported by the government that includes race.
- > Baqui and colleagues excluded 38.7% of patients with SARS-CoV-2 because of missing data of race even though the collection of such data in Brazil is required by law - indicating that a legal requirement is being routinely ignored.
- > In Brazil, race is viewed as phenotypic and not ancestry based. Darker-skinned individuals have an increased incidence of racism and worse health indicators. The black community faces barriers to accessing health services and achieving better living conditions.
- > The COVID-19 pandemic has coincided with the Black Lives Matter movement. The public health responses are interrelated. A deeper critique of structural racism must be addressed for change. The lack of data and scientific analysis of the racial injustices in Brazil during the pandemic makes it even more challenging to create solutions. Proposed plan for the federal, state, and municipal authorities:
 - Ensure the collection of racial data.
 - Make data available to the general public and scientists.
 - Develop data-informed policies.
 - Implement these policies urgently.

Reviewed by: Professor Steve Graham

IMAGING

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

Paediatric lung imaging features of COVID-19: a systematic review and meta-analysis

<https://onlinelibrary.wiley.com/doi/abs/10.1002/ppul.25070>

- > A systematic review and single-arm meta-analysis, including 29 articles reporting on C.T. chest imaging findings in 1026 paediatric patients (0-18 years) with RT-PCR confirmed SARS-CoV-2 infection.
- > C.T. chest was normal in 35.7%. Most common abnormality was ground-glass opacities (37.2% of cases) followed by consolidations or pneumonic infiltrates (22.3% of cases). 27.7% had bilateral lung involvement. Other reported findings were very uncommon (< 1%) and included halo sign, interstitial abnormalities and interlobular septal thickening, bronchovascular bundle thickening, crazy paving pattern, lymphadenopathy, pleural effusion or pleural thickening.
 - Specific CT imaging findings reported in adults with COVID-19 including bronchiectasis, air bronchograms and pericardial effusion were not seen in children with COVID-19.
 - Typical lung imaging features of viral respiratory infections in the paediatric population (e.g. hyperinflation and increased perihilar infiltrates) were not reported in children with COVID-19.
 - Compared to adult patients, C.T. chest imaging abnormalities in children with COVID-19 were less frequent and less severe.
 - Paediatric patients with COVID-19 were approximately three times more likely to have a normal C.T. scan compared to adults with COVID-19 (35.7% vs 8.4-10.24%).
 - Children with COVID-19 were less likely to have bilateral lung lesions compared to adults with COVID-19 (27.7% vs 73.8-78.8%).
- > Conclusion: C.T. chest imaging findings in children with COVID-19 are less frequent and less severe compared to adults with COVID-19 and are distinct from the typical lung features of paediatric viral respiratory infections.
- > Limitations: lung imaging findings were not analysed in relation to clinical features and symptom severity of COVID-19. The terminology used to describe certain C.T. findings varied between the studies, potentially causing diverging or overlapping C.T. reporting. Lung imaging features of patients with the multisystem inflammatory syndrome were not included in this review.

Reviewed by: Associate Professor Simone Mandelstam

IMMUNOLOGY

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

Humoral Immune Response to SARS-CoV-2 in Iceland

<https://www.nejm.org/doi/full/10.1056/NEJMoa2026116?query=RP>

- > To assess SARS-CoV-2 seroprevalence in Iceland, as well as longitudinal changes in antibody, titres up to four months post-infection, and how these changes correlate with age, sex, other phenotypes, and COVID-19 symptom severity.
 - SARS-CoV-2 antibodies were measured in 30,576 persons using six established immunological assays (including two pan-Ig assays), targeting IgG, IgM, IgA against N, RBD and S1 subunit of the spike protein.
 - Positive results from both pan-Ig assays were required to be considered seropositive.
 - Antibodies were measured in two groups of known qPCR-positive persons, and six groups who had not been qPCR-tested or were confirmed qPCR negative.
- > Antibody response among SARS-CoV-2 qPCR positive persons.
 - >90% of recovered persons were seropositive 25 days after being diagnosed with COVID-19 via qPCR.
 - IgM anti-N protein antibodies increased after diagnosis and fell rapidly (not detectable at two months).
 - IgA anti-S1 antibodies decreased one month after diagnosis but remained detectable.
 - IgG anti-nucleoprotein and anti-S1 antibodies increased during the first six weeks after diagnosis, decreased slightly and then persisted over four months.
- > SARS-CoV-2 infection during quarantine.
 - 2.3% were seropositive among those who had not been qPCR-tested or confirmed qPCR negative.
 - Household exposure was 5.2 times more likely to be seropositive than those with other types of exposure.
 - About a quarter of quarantined individuals (26.6%) with household exposure were infected.
- > SARS-CoV-2 seroprevalence in Iceland.

- Estimated 0.9% of the population of Iceland has been infected by SARS-CoV-2.
 - 56% of all infections were diagnosed by qPCR.
 - 14% occurred in quarantine without being qPCR-tested or confirmed qPCR negative.
 - 30% of infections occurred outside quarantine and were not detected by qPCR.
- Estimated infection fatality risk of 0.3% based on the seroprevalence rate.
- Infection fatality risk was significantly lower in those 70 years and under (0.1%) compared with those above 70 years old (4.4%).
- > Factors affecting antibody response.
 - Women had lower antibody levels to some antigens (Pan-Ig anti S1-receptor-binding domain (RBD), and IgA anti-S1).
 - B.M.I., smoking and the use of anti-inflammatory medication were associated with lower antibody levels.
 - Clinical severity, hospitalisation and older people were associated with higher antibody levels.
- > Significance:
 - A substantial fraction of infections were not detected by qPCR despite extensive screening, indicating many infected individuals are asymptomatic or mild symptoms.
 - Household exposure was more likely to lead to infection.
 - Antibodies against SARS-CoV-2 are likely to persist for at least four months.
 - Low seroprevalence against SARS-CoV-2 in Iceland indicates that the Icelandic population is vulnerable to future infection.

Reviewed by: Dr Ryan Toh

INFECTION CONTROL

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

Airborne contamination of COVID-19 in hospitals: a scoping review of the current evidence (not peer reviewed)

<https://www.medrxiv.org/content/10.1101/2020.09.09.20191213v1.full.pdf>

- > This was a scoping review of articles detailing SARS-CoV-2 air contamination in hospital settings between 1/12/19 - 21/7/20.
 - Total of 2034 articles identified of which 17 were included in the review.
 - Descriptive analysis: positivity rate of SARS-CoV-2 R.N.A. detected by RT-PCR and viral culture, air sampling method, setting, clinical context, air ventilation system and distance from the patient.
- > Results: 646 air samples tested with RT-PCR across 17 studies.
 - Samples positive for SARS-CoV-2 RNA by RT-PCR: 27.5% (68/247) from close patient's environment, 23.8% (5/21) from patient's toilet/bathroom, 9.5% (20/221) clinical areas, 12.4% (12/121) staff areas, 34.1% (14/41) public areas.
 - Three studies included viral culture with a total of 78 samples: only three samples were positive in one study (3/39, 7.7%) in a close patient environment in a non-ICU setting.
- > Limitations: This study is a pre-print that has not yet undergone peer-review. It attempts to pool data from a heterogeneous group of studies with limited contextual information in many studies with a high risk of misclassification. This significantly limits the reliability of the pooled data analyses. For example, five studies in I.C.U. did not find any air contamination with viral R.N.A., while a further three found high rates of contamination (40.4-100%). There is incomplete data regarding the context (i.e. type of respiratory support, requirement or frequency of aerosol-generating procedures) in these studies that limit the interpretability of the pooled result.
- > Conclusions: In hospital settings, the air around COVID-19 patients is frequently contaminated with SARS-CoV-2 R.N.A. There is limited evidence regarding the viability of SARS-CoV-2 virus in the air and its role in transmission.

Reviewed by: Dr Samantha Bannister

MENTAL HEALTH

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

New findings reveal the massive impact of COVID for children and young people in Victoria

<https://ccyp.vic.gov.au/news/new-findings-reveal-massive-impact-of-covid-for-children-and-young-people-in-victoria/>

- > The Victorian Commission for Children and Young People have published results documenting the massive disruption in the lives of children and youth in Victoria due to the COVID-19 pandemic.
- > Created in consultation with children, young people, and agencies involved in their care, there is hope these results will inform the response to COVID-19 to protect their well-being and meet increased needs.
- > The consultations focused on three main areas:
 - Safety:
 - Increasing conflict within families with children/youth unable to access normal means of escape, such as school or friends.
 - Vulnerable youth less visible, less access to support.
 - Many services, including Child Protection, either halted entirely or significantly reduced operations.
 - Concern for becoming infected with COVID-19.
 - Mental Health:
 - Mixed experiences during pandemic; some enjoyed opportunity to slow down and self-reflect, but the majority report negative experiences.
 - Most common reports of loneliness, isolation, and disruption of routines.
 - Increased numbers reporting first time mental health challenges and first time concerns of self-harm.
 - The majority prefer face-to-face services rather than online / telephone when initiating mental health support.
 - Agencies report a reduction in services and community-based programs, but that most are switching to online methods, however, the reductions have created long wait times.

- Education:

- Lack of COVID-19 information aimed directly at them.
- The stress of remote learning; limited support, lack of technology, and cost of technology.
- Most miss the social aspect of school, are easily distracted, and struggle to feel motivated to complete tasks while studying at home.
- Rural areas reported the most difficulties with access due to connectivity, while those living in urban centres reported cost as the major barrier.

Reviewed by: Professor David Coghill

PERINATAL HEALTH

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

Stillbirth rate rises dramatically during the pandemic

<http://nature.com/articles/d41586-020-02618-5>

- > Summary: Stillbirth rates have increased during the pandemic.
- > There have been several studies that have reported an increase in the number of stillbirths since the start of the SARS-CoV-2 pandemic.
- > A Lancet study of 9 hospitals and over 20,000 women in Nepal is the largest study to date looking at stillbirths during the pandemic.
 - It reported a 50% increase in stillbirths (before lockdown which occurred in March) from 14 to 21 per 1,000 births (late May).
 - The sharpest increase was noted in the first four weeks of lockdown when the restrictions were the most severe.
 - The average number of hospital births per week halved from 1261 to 651 (no data available on those delivering out of the hospital).
 - The rate of complications for hospital births increased.
- > Another study performed at a large London hospital found an almost fourfold increase in the incidence of stillbirths.
 - 2.38 per 1,000 stillbirths between October 2019 - late January 2020.
 - 9.31 per 1,000 stillbirths between February and mid-June 2020.
 - Studies in India have similarly reported an increase in stillbirths, with reduced women delivering in a hospital.
 - Scotland too has detected an increase in the rate of stillbirth in the months of the pandemic.
- > The cause of the increase in stillbirth rates is likely multifactorial.
 - Some antenatal appointments have been moved to telehealth and/or reduced, and women are having less physical exams to screen for antenatal complications.
 - Some women are avoiding the hospital environment due to fear of catching SARS-CoV-2. This may manifest in missing antenatal appointments or not presenting to the hospital early when they are concerned.
 - As seen in the Lancet study, more women are birthing at home, and there is a lack of data on whether these pregnancies have resulted in stillbirths or other pregnancy complications.

- > Women who want to attend their antenatal appointments may face difficulty in doing so because of hospital restrictions, difficulty catching public transport and may also face difficulties accessing maternal services.
- > The pandemic has widely impacted maternal services, and the increase in stillbirth rates is very concerning.
- > Further studies are required to look at the causes behind the increased rate of stillbirths, particularly studies that capture data on the increasing number of women birthing at home.
- > Studies in India have similarly reported an increase in stillbirths, with reduced women delivering in a hospital.

Reviewed by: Professor Suzanne Garland

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

Impact of SARS-CoV-2 antibodies at delivery in women, partners and newborns (not peer reviewed)

<https://www.medrxiv.org/content/10.1101/2020.09.14.20191106v1>

- > Pregnant women admitted for delivery are not often tested for SARS-CoV-2, and little research has gone into the prevalence in parturient women (& of their partners) of seropositivity for SARS-CoV-2, and impact on the infant.
- > This is a prospective Danish cohort study that aimed to identify a relationship between a SARS-CoV-2 infection and obstetric and neonatal complications.
- > Between 4th April 2020 and 3rd July 2020, pharyngeal swabs and blood samples were collected on admission for delivery from pregnant women, their partners and umbilical cord blood from their newborns. SARS-CoV-2 PCR RNA testing of the pharyngeal swabs and IgM and IgG analyses [YHLO's iFlash 1800 and SARS-CoV-2 IgM/IgG kits] were conducted on sera.
- > Overall, 75% of those delivering in the study period joined.
- > 29/1361 (2.2%) pregnant women had SARS-CoV-2 antibodies on admission with 52% reporting COVID-19 symptoms. These women were more likely to have an A negative blood type ($P=0.025$), and their babies had an 86% absolute increased risk of having SARS-CoV-2 antibodies at birth (95% CI 69%-104%; $P<0.001$).
- > 34/1236 (2.9%) partners had SARS-CoV-2 antibodies and were more likely to have previously tested positive for antibodies ($P<0.001$) and report symptoms at the time of their partner's admission ($P<0.001$). This translates to a 45.7% increased absolute risk for mothers living with a partner that has SARS-CoV-2 antibodies (95% CI 23.2%-68.2%).
- > 17/1342 (1.4%) newborns had positive SARS-CoV-2 antibodies (100% IgG, 0% IgM). However, there were no significant differences in meconium staining, newborn measurements, umbilical biochemistry, APGAR scores and gestation adjusted birth weight compared to their counterparts with no SARS-CoV-2 antibodies.

- > In conclusion, despite an increased absolute risk of SARS-CoV-2 infection when pregnant women cohabit with antibody-positive partners, there was no association between mild or asymptomatic COVID-19 and obstetric or neonatal complications.
- > Limitations: the study included young, non-smoking individuals of normal B.M.I. with asymptomatic or mild disease and therefore cannot be readily extrapolated to those ill with COVID-19, or with COVID comorbidities. Cord blood can be mixed with maternal blood so not necessarily representative of baby blood responses.

Reviewed by: Professor Suzanne M Garland

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

Characteristics and maternal and birth outcomes of hospitalised pregnant women with laboratory-confirmed COVID-19 – COVID-NET, 13 States, March 1-August 22, 2020

<https://www.cdc.gov/mmwr/volumes/69/wr/mm6938e1.htm>

- > Population-wide surveillance of COVID-19 associated hospitalisations in the United States between 1st March and 22nd August 2020 (convenience sampling).
- > Main results:
 - 26.5% of hospitalised women aged 15-49 years with COVID-19 were pregnant in this study. Pregnant women are overrepresented in this age group of women compared to the general population, and of the pregnant women admitted with COVID-19, Hispanic and Black women are overrepresented.
 - Out of 598 hospitalised pregnant women with COVID-19, 55% were asymptomatic at admission.
 - Severe outcomes among symptomatic women (272 women) included I.C.U. admission (16%), mechanical ventilation (8%) and death (1%). Pregnant women admitted with acute illness may have more severe outcomes compared to pregnant women admitted for obstetric indications alone.
 - Pregnancy loss occurred in both symptomatic and asymptomatic women (2% of admitted women).
 - Among 445 pregnancies resulting in live births, 13% were preterm (<37 weeks), higher than the preterm birth rate of the general U.S. population in 2018 (10%). There was a higher proportion of preterm births in symptomatic women compared to asymptomatic women (23% versus 8%).
- > Limitations include that this study is based on a convenience sample of 29% of women aged 15-49 years, the possibility of the sample not being representative of the catchment area, the possibility of missed COVID-19 cases due to differences in testing (screening in pregnancy vs specific symptoms), incomplete follow up data in some cases, no reason for admission recorded for 46% of women and no follow-up of outcomes after discharge.
- > Overall, it is important to prevent and identify COVID-19 infection in pregnant women with standard infection prevention strategies and continued surveillance.

Reviewed by: Professor Suzanne Garland

SCHOOLS

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

Letter to the editor: COVID-19 cases among school-aged children and school-based measures in Hong Kong, July 2020

<https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.37.2001671>

- > This letter to the editor was written in response to an article from Stein-Zamir et al. regarding a major outbreak in an Israeli high school. Here the authors describe the situation in Hong Kong where there have been reported cases of COVID-19 in school children but no outbreaks in these schools.
- > Secondary schools re-opened in Hong Kong in late May, followed by primary schools, after a period without any local infections.
- > There were no cases in school-aged children until an increase in local transmission in early July, leading to a reclosure of schools on 13th July.
- > On 18th July there were 20 cases aged 5-17 with 15 of these being linked to case clusters in their own households, neighbourhood or an unknown source of infection. The remaining five were part of a secondary school or tutorial centre cluster.
- > There were no further cases related to these 20 cases, indicating possible introductions of COVID-19 into schools did not lead to onward transmission.
- > Infection control measures used in schools included daily temperature checks, face masks worn at all times, moving to half days by removing lunch hours, staggering of arrival and dismissal times, spacing desks, transparent partitions in some schools, limited group work and contact sports, cancellation of assemblies and extra-curricular activities, and staggered use of common facilities.

Reviewed by: Professor Fiona Russell

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

Preventing and mitigating SARS-CoV-2 transmission – four overnight camps, Maine, June-August 2020

https://www.cdc.gov/mmwr/volumes/69/wr/mm6935e1.htm?s_cid=mm6935e1_w

- > To prevent, identify, and mitigate the spread of COVID-19, four Maine overnight summer camps opened with pre-camp quarantine, pre- and post-arrival testing and symptom screening, cohorting, and physical distancing between cohorts.
- > Camps also required face coverings, enhanced hygiene, cleaning & disinfection practices, maximal outdoor programming, and early rapid identification of infection & isolation.
- > Three out of four camps mandated submission of COVID-19 test results before camp entry.

- > Campers and staff were monitored daily for symptoms and checked for fever with infrared thermometers.
- > PCR tests were repeated between four and nine days after camp arrival - attendees with positive results, or those with symptoms, were isolated immediately, and their cohort quarantine until the attendee received a negative test result.
- > Daily symptom checks identified 12 attendees with COVID-19 symptoms - all 12 received negative test results.
- > Three asymptomatic attendees at three different camps tested positive after arrival and were rapidly isolated, and cohorts quarantined for 14 days.
 - The quarantine cohort were retested on days three and four after the initial campers positive test result, no cohort members received a positive test result and were released from quarantine on day eight after asymptomatic campers positive test result - no secondary transmission was identified.
- > Multilayered public health prevention and mitigation strategies in an overnight camp can identify and prevent SARS-CoV-2 transmission.
- > Limitations of this report include adherence to these interventions was not measured; travel was not well documented; intermediate travel may change the risk level of various persons in the study.

Reviewed by: Dr Wonie Uahwatanasakul

Rafael Lee - 3rd Year Medical Student,
Department of Paediatrics, The University of Melbourne

Was school closure effective in mitigating coronavirus disease 2019 (COVID-19)? Time series analysis using Bayesian inference

<https://www.sciencedirect.com/science/article/pii/S1201971220305981>

- > To mitigate the risk of transmission of COVID-19, Japan called for a nationwide close of elementary, junior high, and high schools beginning 1st March 2020.
- > A time-series analysis was conducted on daily data of COVID-19 incidence in Japan from 29th February to 31st March, 2020.
- > School closure did not appear to significantly decrease the incidence of SARS-CoV-2 infection.
- > Limitations: A linear trend model may not be appropriate as school closure could have prevented stochastic clusters or outbreaks among school children. Estimated alpha value using data by the time of intervention effectiveness may not accurately predict alpha value after the intervention. Confidence intervals are wide and should be interpreted cautiously. It is not clear what other broader public health mitigation interventions were instigated in Japan at the same time of school closures. School closure combined with other measures - such as traffic limitations or city lockdown may be useful during rising case numbers.
- > Given the limitations, the authors did not claim school closures overall are ineffective in mitigating the COVID-19 epidemic, only that school closure in Japan did not demonstrate meaningful effectiveness in controlling the COVID-19 epidemic.

Reviewed by: Professor Fiona Russell

TRANSMISSION

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

Community outbreak investigation of SARS-CoV-2 transmission among bus riders in Eastern China

<https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2770172>

- > This retrospective cohort study investigates the transmission of COVID-19 in a closed environment with air recirculation in the context of a community outbreak among bus riders Eastern China.
- > The key event leading to the outbreak on 19th January 2020 was a 100-minute round trip bus ride with an infectious passenger aboard.
 - Two buses travelled to and from the same destinations at the same time for a worship ceremony. This mimicked the quasi-experiment where there was a control group (60 participants on bus 1; no infectious case on board) and the exposure group (68 participants on bus 2, 1 index case aboard).
- > Exposure data collected retrospectively via standard questionnaires on demographics, travel history and close contacts. Oropharyngeal swabs were collected for reverse transcription PCR or viral genome sequencing:
 - 50-minute one-way trip (total of 100 minutes roundtrip) with no seating changes.
 - Similar bus design, operating air-conditioning on recirculating mode throughout rides.
 - 150-minute worship ceremony and 30-minute luncheon where all attendees socialised freely before the return trip.
 - No masks were worn due to absent public awareness of COVID-19 at the time of the outbreak.
- > Outcomes:
 - Index case on bus 2 was presumed to be the source of infection based on recent close contacts and symptom appearance (cough, chills, and myalgia) while on the returning bus ride.
 - 24 out of 68 (35.3%) passengers on bus 2 contracted COVID-19, compared to 0 on bus 1.
 - Among the additional 172 individuals who attended the worship ceremony without being on the buses, 7 (4.1%) contracted COVID-19, all of which recalled close contact with the index case.
 - Bus seatings were classified as either high-risk (within 3 rows from index case) or low-risk based on existing definitions of close contacts. However, a high theoretical risk did not result in statistically higher infection rates.

- > Conclusion: In closed environments with recirculating air conditioning, the high potential for airborne transmission of COVID-19 raises the need for public health preventative and control measures.
- > Limitations: Alternative sources of infection during the ceremony could not be excluded, even though the chances are low. Acquisition of virus could not be attributed to airborne only; droplets and shared contact surfaces remained as possible modes of transmission.

Reviewed by: Dr Celeste Donato

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

Association of daily wear of eyeglasses with susceptibility to coronavirus disease 2019 infection

<https://jamanetwork.com/journals/jamaophthalmology/fullarticle/2770872>

- > A case-control study is investigating the relationship between daily eyeglass wearing and susceptibility to COVID-19.
- > Participants were 276 COVID-19 patients, admitted between 27th January and 13th March 2020, in the northern Hubei province of China.
 - The median age was 51 (IQR 41-58) years, and 155 patients (56.2%) were male.
- > Methods involved comparing the proportion of COVID-19 patients who wore eyeglasses for more than 8 hours each day with the proportion of students aged 7 to 22 years with myopia in the Hubei province, from a 1985 community survey.
- > All 16 of 276 patients (5.8%; 95% CI 3.04%-8.55%) who were found to be daily wearers of glasses for more than 8 hours a day also had myopia.
 - Their symptoms, underlying disease, and COVID-19 severity were not significantly different from those of other patients.
 - The proportion of daily eyeglass wearers was lower than that of the local population (5.8% vs 31.5%).
 - Suggests that daily wearers of eyeglasses may be less susceptible to COVID-19.
 - Explanations may be that eyeglasses prevent or discourage wearers from touching their eyes, thus avoiding transferring the virus from the hands to the eyes.
- > Limitations: The study only evaluated a single-centre using a small sample size. The proportion of eyeglass wearers was based on data from previous literature and was not calculated from current local populations. The myopia rate obtained from previous studies included a small number of people with myopia who did not wear eyeglasses.

Reviewed by: Dr Martin Wright

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

Environmental and aerosolised SARS-CoV-2 among hospitalised COVID-19 patients
<https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiaa575/5903399>

- > During April and May 2020, this study observed 20 hospitalised COVID-19 patients, their hospital rooms (fomites and aerosols), and six close contacts for molecular and culture evidence of SARS-CoV-2 virus.
- > Rooms only had minimal surface cleaning as required during a patient's stay, though the room ventilation was better than recommended with high air exchange frequency.
- > Among the more than 400 clinical samples and of air and surfaces, we found molecular evidence of the virus in most sample types, especially the nasopharyngeal (N.P.), saliva, and faecal samples, but the prevalence of molecular positivity among fomites and aerosols was low (and decreased over the duration of hospital stay).
 - The agreement between N.P. Swab and saliva positivity was high (89.5%, Kappa 0.79).
 - Two N.P. Swabs collected from patients on one and seven days post-symptom onset had evidence of infectious virus (2 passages over 14 days in Vero E6 cells).
 - The low molecular prevalence and lack of viable SARS-CoV-2 virus in fomites and air samples implied low nosocomial risk SARS-CoV-2 transmission through inanimate objects or aerosols.
- > Limitations: Patients were on average, ten days from symptom onset when enrolled, so one would expect to be less infectious. Small sample size and larger than average air quality makes the results hard to generalise. Larger airborne particles may not have been as well sampled from the air, but surfaces near the patient likely to be contaminated were swabbed.
- > Conclusion: Whilst findings support the position that fomite and aerosol transmission were of relatively low risk among these COVID-19 patients, results may also be consistent with aerosol transmission occurring early on in the course of the disease, well before COVID-19 patients are ill enough to require hospitalisation. This requires further assessment.

Reviewed by: Dr Martin Wright

SARS-CoV-2 in quarantined domestic cats from COVID-19 households or close contacts, Hong Kong, China
https://wwwnc.cdc.gov/eid/article/26/12/20-2786_article

- > Naturally occurring human-to-animal transmission of severe acute respiratory syndrome (SARS) coronavirus was reported during 2003
- > This study tested 50 cats from coronavirus disease households or close contacts in Hong Kong, China, for SARS-CoV-2 R.N.A. in respiratory and faecal samples.
- > This study found 6 cases of apparent human-to-feline transmission involving healthy cats. Virus genomes sequenced from 1 cat and its owner were identical.

- > The timeline of infection in cat one and the finding of an identical SARS-CoV-2 genome sequence in a human from the same household is consistent with the human-to-animal transmission. In support of these findings, the cat had no outdoor access.
- > Although feline-to-human transmission is theoretically possible, this study did not find any evidence of this transmission.

Reviewed by: Dr Celeste Donato

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 values framework for the allocation and prioritisation of COVID-19 vaccination

https://apps.who.int/iris/bitstream/handle/10665/334299/WHO-2019-nCoV-SAGE_Framework-Allocation_and_prioritization-2020.1-eng.pdf?sequence=1&isAllowed=y

- > The framework is intended to be helpful to policymakers and expert advisors at the global, regional and national level as they make allocation and prioritisation decisions about COVID-19 vaccines.
- > Provides six core principles that should guide distribution and 12 objectives based on:
 - Human Well-Being: Protect and promote human well-being, including health, social and economic security, human rights and civil liberties, and child development.
 - Equal Respect: Recognise and treat all human beings as having equal moral status and their interests as deserving of equal moral consideration.
 - Global Equity: Ensure equity in vaccine access and benefit globally among people living in all countries, particularly those living in low-and middle-income countries.
 - National Equity: Ensure equity in vaccine access and benefit within countries for groups experiencing greater burdens from the COVID-19 pandemic.
 - Reciprocity: Honor obligations of reciprocity to those individuals and groups within countries who bear significant additional risks and burdens of COVID-19 response for the benefit of society.
 - Legitimacy: Make global decisions about vaccine allocation and national decisions about vaccine prioritisation through transparent processes that are based on shared values, best available scientific evidence, and appropriate representation and input by affected parties.
- > The Values Framework needs to be complemented with information about specific characteristics of available vaccine(s), the benefit-risk assessment for different population groups, the amount and pace of vaccine supply, and the current state of the epidemiology, clinical management, and economic and social impact of the pandemic. Hence, the final vaccination strategy will be defined by the characteristics of vaccine products as they become available.

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

Should we mandate a COVID-19 vaccine for children? (viewpoint)

<https://jamanetwork.com/journals/jamapediatrics/fullarticle/2770123>

- > This viewpoint suggests that children may be a potential target for mandatory vaccination, given that several vaccines are already mandatory to attend school.
- > They suggest in this article that the approach to the influenza vaccine (not mandatory) should inform the approach to a COVID-19 vaccine.
- > One important difference between COVID-19 & influenza is the role children play in transmission; children have been well documented in spreading influenza; however initial reports suggest children transmit SARS-CoV-2 less easily than the influenza virus, and this is an area undergoing intensive research internationally.
- > Despite this, SARS-CoV-2 appears to spread more efficiently than influenza, which the authors' reason may make SARS-CoV-2 a good candidate for a mandatory vaccine.
- > There are nine criteria to consider when evaluating antigens for inclusion in mandatory school immunisation programs:
 - Experience with the vaccine containing this antigen indicates that it is safe, and has an acceptable level of adverse effects (prioritised criterion).
 - An antigen is effective as measured by immunogenicity and population-based prevention.
 - A vaccine is as cost-effective as other vaccines.
 - A vaccine should bear some relationship to increasing safety in the school environment.
 - A vaccine prevents disease with significant morbidity/mortality in at least some subset of the population.
 - Vaccinating the infant, child, or adolescent against disease reduces the risk of person-to-person transmission.
 - A vaccine is acceptable to the medical community & the public.
 - Administrative burdens of delivery are reasonable.
 - The burden of adherence for the vaccine is reasonable for parent/caregiver.
- > With the above framework of criteria, the article concludes that too little is known about the performance of any of the candidate COVID-19 vaccines, and the epidemiology of SARS-CoV-2 in children to make a firm judgement on mandating a vaccine.
- > A major limitation of the paper is that it does not highlight that children do not get severe COVID-19 disease at anywhere near the rates of older adults and making a vaccine mandatory for certain groups should relate to both individual and community (herd) protection.

- > Lastly, this paper does not mention the lack of clinical SARS-CoV-2 vaccine trials that include children. The large Phase 3 trials being operated internationally have, to-date, largely excluded children, recruiting adults > 18 years. We should not even be considering making COVID-19 vaccine mandatory in children until we see that they are safe and efficacious in this population. Due to vaccine supply constraints, it is unlikely children will be part of the 1st phase of vaccine roll-out. Mandatory vaccination is a contentious issue and can have an impact on vaccine confidence, especially when there is a lack of evidence in that target group. Let's leave children out of the mandatory vaccine debate, at least until we have seen the data.

Reviewed by: Associate Professor Nigel Crawford

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 U.S. 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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