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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.21

11th September 2020



Australian Government
 Department of Health

BE COVIDSAFE

CURRENT STATUS OF CONFIRMED CASES



29

CURRENT CASES
 INTENSIVE CARE UNITS (ICU)

ACT	NSW	NT	QLD	SA	TAS	VIC	WA
0	7	0	0	0	0	22	0

264

CURRENT CASES
 ADMITTED TO HOSPITALS

ACT	NSW	NT	QLD	SA	TAS	VIC	WA
0	13	0	12	0	0	238	1

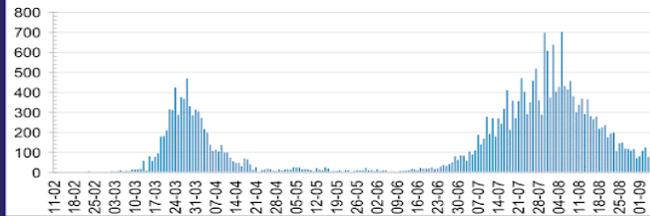
6,730,397

0.4% POSITIVE

TOTAL TESTS
 CONDUCTED

ACT	NSW	NT	QLD
84,235	2,350,649	38,938	978,869
POSITIVE	POSITIVE	POSITIVE	POSITIVE
0.1%	0.2%	0.1%	0.1%
SA	TAS	VIC	WA
404,963	92,521	2,412,092	368,130
POSITIVE	POSITIVE	POSITIVE	POSITIVE
0.1%	0.2%	0.8%	0.2%

DAILY NUMBER OF REPORTED CASES

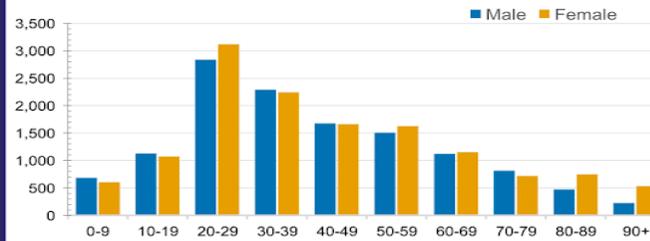


CASES IN AGED CARE SERVICES

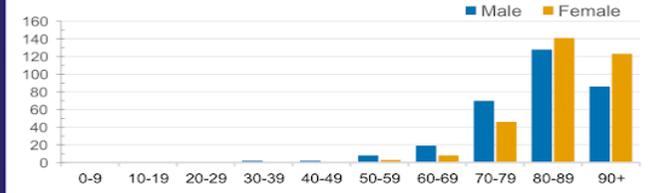
Confirmed Cases	Australia	ACT	NSW	NT	QLD	SA	TAS	VIC	WA
Residential Care Recipients	1963 (790)	0	61 (32)	0	1 (1)	0	1 (1)	1900 (758)	0
In Home Care Recipients	80 (59)	0	13 (13)	0	8 (8)	1 (1)	5 (3)	52 (34)	1 (1)
	(7)						(2)	(4)	

Cases in care recipients [recovered] (deaths)

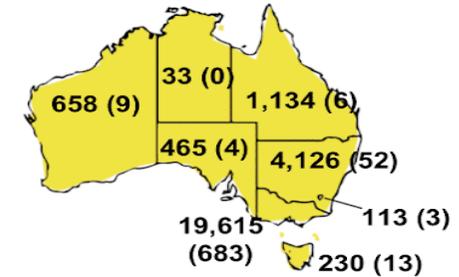
CASES BY AGE GROUP AND SEX



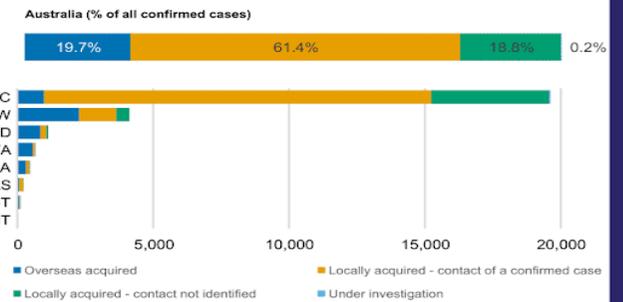
DEATHS BY AGE GROUP AND SEX



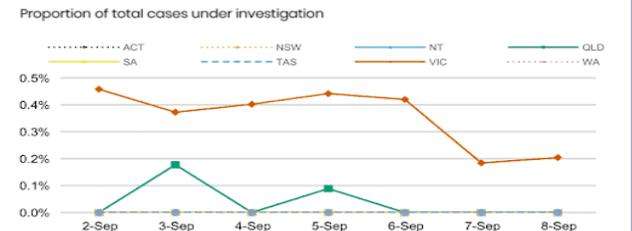
CASES (DEATHS) BY STATE AND TERRITORIES



CASES BY SOURCE OF INFECTION



PUBLIC HEALTH RESPONSE MEASURE



Last updated 8 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 8; cited 2020 September 9]. Available from: <https://www.health.gov.au/resources/collections/coronavirus-covid-19-at-a-glance-infographic-collection>

GUEST EDITORIAL

Professor Suzanne Garland - Reproductive & Neonatal Infectious Diseases, Department of Obstetrics and Gynecology, University of Melbourne; Director Centre Women's Infectious Diseases Research; Honorary Research Fellow, Infection & Immunity, Murdoch Children's Research Institute

The 21st edition of the COVID-19 Kids Evidence Update coincides with the 5th week of Stage 4 lockdown in Melbourne. Whilst many in the community may have wished for a cessation to the Stage 4 lockdown, given the 14-day average of cases of around 100 in the past two weeks, it is not surprising that the Premier announced on Sunday 6th of September, an extension, from the 13th to the 28th September, before Victoria could move to a second step towards reopening. And encouragingly, Monday 7th September, for the first time in almost two months, we have seen a 14 day average in double digits. We have been given a roadmap of 'slow, steady and safe'. We have been given a "countdown out of lockdown", much of which will be driven by the average weekly new case numbers over the next few weeks.

Seeing an upsurge of cases in Europe, with over 7,000 cases per day for example in France, over 10,000 per day for Spain, and upward surges in the U.K. and USA, the hard work in Victoria to bring numbers down is pertinent and commendable. Sweden has one fifth the population of Australia. Compared with neighbouring Scandinavian countries, Sweden's softer approach to restrictions was loose. Unfortunately, by the end of July 2020, Sweden had the highest per capita death rate in the world - about 10 times larger than its Nordic neighbours. To date, Sweden has had about over 85,500 confirmed cases of COVID-19, and about 5,800 people have died. In contrast, Australia, with a population of ~25 million, has lost 762 people to COVID-19 - it could have been many thousands. It is noteworthy that even with lighter lockdowns, Sweden has suffered economic losses almost as severe as its Nordic counterparts.

Clearly, to bring down case numbers fast requires rapid case identification, then comprehensive and thorough contact tracing with isolation/quarantine as appropriate, coupled with hand hygiene and physical distancing. Basic education of infection control practices is needed across the community. I have therefore focused on the various papers published this week with infection prevention or prevention of viral transmission.

The first topic is that of the value of wearing masks and appropriateness or not of face shields. We have seen much debate on the mandatory wearing of masks in the control of COVID-19, particularly when physical distancing is an issue. In this week's update the value of a multidisciplinary approach to understanding transmission routes and actions to mitigate spread is noted: an engineering approach and the study of the physics of fluids and the virus. Whilst evidence has shown the value of masks used appropriately, some have introduced clear plastic face shields or masks equipped with exhalation valves for easier exhalation. In medical practice face shields are largely used to protect against sprays and splashes when in close proximity to patients, protecting the mucous membranes and eyes.

However, in medical practice face shields are used in conjunction with a mask. To test whether face shields protect the wearer or those around them, the physics of fluid and the virus has been adopted in the article “Visualizing droplet dispersal for face shields and masks with exhalation valves.” <https://aip.scitation.org/doi/full/10.1063/5.0022968>

These researchers employed a mannequin and simulated cough and sneeze and used qualitative visualisations to measure dispersal of aerosolised droplets. Face shields blocked the initial forward motion of droplets, but also expelled droplets in a wide area, in both lateral and longitudinal directions. The authors were able to demonstrate that depending on the ambient temperature and air flow, the extent of dispersal varied (there are embedded movies to watch this, if you are interested). Thus, alternatives to regular masks such as face shields could have an adverse effect on mitigation efforts. Although surgical masks with exhalation valves permit easier breathability, the valve reduces the effectiveness of the mask as a source of control significantly, as a large number of droplets pass through the valve unfiltered. Hence, they are not recommended.

A second topic is the role of asymptomatic carriage of SARS-CoV-2 fueling the pandemic. Silent COVID-19 transmission in the community, with prolonged excretion of virus is described in the article

<https://jamanetwork.com/journals/jamapediatrics/fullarticle/2770150> [Clinical Characteristics and Viral RNA Detection in Children with Coronavirus Disease 2019 in the Republic of Korea.] This study was conducted in 20 hospitals and two non-hospital isolation facilities across South Korea from 18th February to 31st March, 2020. The study included children who had a history of close contact with confirmed cases, were epidemiologically linked to COVID-19 outbreaks, arrived from abroad, or had symptoms suspicious of COVID-19 as judged by physicians. During the entire observation period, 22% of children were asymptomatic. Of note, there was a shorter mean period of virus RNA detected in asymptomatic children (14.1 days) compared with symptomatic children (19 days).

The third topic is faecal-oral route as a potential transmission from toilet flushing via pipe drainage systems in a high-rise tower, <https://www.acpjournals.org/doi/10.7326/M20-0928> [Probable Evidence of Fecal Aerosol Transmission of SARS-CoV-2 in a High-Rise Building]. Given that SARS-CoV-2 can be found in faeces, it is unsurprising that the faecal-oral route, either directly or via aerosols, could be another form of transmission as described in this particular tower outbreak. In their investigation, researchers included airflow and dispersion tests using a tracer as a surrogate for virus-laden droplets in gas in the drainage systems. Other researchers have adopted computational fluid dynamics to explore and visualise the characteristics of fluid flow during toilet flushing, and the influence of flushing on the spread of virus aerosol particles. This was found to be a potential route of transmission too.

The issue of potential reinfection is raised in the article of one case study: COVID-19 re-infection by a phylogenetically distinct SARS-coronavirus-2 strain confirmed by whole genome sequencing. <https://academic.oup.com/cid/advance/doi/10.1093/cid/ciaa1275/5897019>. Whilst the patient described was symptomatic at the first infection, the second infection 142 days later was only picked up because of entry screening requirements in arriving back into the country from Europe - the patient had no symptoms whatsoever. Although the viral genomes from first and second episodes belonged to different clades/lineages, there was no evidence for a transcriptionally active infection, no measures of a T-cell response, and despite being performed, culture results were not available at the time of writing. The only serum collected for serology from the first episode was taken at 10 days post diagnosis, and although negative, it was too early to conclude that there was no specific response.

It may be that the case was colonised the second time round, but not actively infectious. I believe we need to see all these parameters measured before we can say there has been true reinfection.

Update on Perinatal outcomes: In this week's edition we read with interest the living systematic review and meta-analysis in the BMJ of coronavirus disease 2019 in pregnancy: <https://www.bmj.com/content/370/bmj.m3320>. This is a systematic review of 77 cohort studies reporting the clinical manifestations, risk factors, and maternal and perinatal outcomes of COVID-19. Overall, pregnant and recently pregnant women diagnosed with COVID-19 in hospital were found to be less likely to manifest symptoms of fever and myalgia than non-pregnant women of reproductive age. This might relate to many obstetric centres having universal screening rather than symptom-based testing. However, of those positive for SARS-CoV-2, there was an observed increase in admissions to the intensive care unit and need for invasive ventilation, compared with non-pregnant women of reproductive age with COVID-19. Risk factors for severe COVID-19 in pregnancy included increasing maternal age, high body mass index, and pre-existing co-morbidities such as chronic hypertension and pre-existing diabetes. Pregnant women with COVID-19 were more likely to experience preterm birth and their neonates are more likely to be admitted to a neonatal unit, compared with pregnant women without COVID-19. The real strength of this article is that this is a living systematic review and meta-analysis, with the ability for regular search and analysis updates, so is placed ideally to assess the impact of new findings on the rapidly growing evidence base of infection in pregnancy.

HIGHLIGHTS

- > Nationwide South Korean study among adults found higher BMI is associated with a higher risk of COVID-19.
- > Vitamin D deficiency was associated with positive COVID-19 test results in the U.S.
- > Screening for symptoms among children does not identify most COVID-19 cases in South Korea.
- > Weather may affect COVID-19 dynamics, but only marginally.
- > WHO calls for COVID-19 response strategies to include policies to protect children from violence.
- > In Spain, early summer outbreak coincided with social/leisure activities, and among workers in vulnerable occupational settings.
- > Reflections on World Water Week (24th – 28th August) - will the COVID-19 pandemic promote water resource governance to increase access to WASH?
- > In the Caribbean, lessons learnt from extreme weather events have proved useful in response to COVID-19.
- > Gaps in access to medical oxygen are being exposed by the COVID-19 pandemic; sustainable measures to address this issue would be of benefit post-COVID-19.
- > COVID-19 threatens to reverse gains made in countries with high HIV, tuberculosis, and malaria burdens.
- > SARS-CoV-2 infection rate among healthcare workers at the Royal Children's Hospital and Murdoch Children's Research Institute (0.6%) was similar to that in Victoria's overall (0.7%) before July 2020.
- > Face shields and masks with exhale valves likely less effective than regular face masks; widespread use of shields and valved masks, rather than regular masks, may impact COVID-19 mitigation efforts adversely.
- > Faecal aerosol transmission may have caused a community outbreak of COVID-19 in a high-rise building in Guangzhou, China.
- > The Fair Priority Model proposes equitable distribution of a COVID-19 vaccine, and aims to benefit people, limit harm, prioritise the disadvantaged, and recognise equal concern.
- > A SARS-CoV-2 recombinant spike protein nanoparticle vaccine has no safety concerns and is immunogenic; Phase 3 is in preparatory stages.
- > Whole genome sequencing of respiratory specimens from a single COVID-19 patient, together with epidemiological, clinical, and serological analyses, confirmed SARS-CoV-2 reinfection in a single patient in Hong Kong.

- > High proportion of children with a close contact were found to become positive to SARS-CoV-2 (76%) with children aged 6-13 years most frequently asymptomatic (38%).
- > Children with COVID-19 may present with a wide range of symptoms and signs, which were not specific enough to prompt diagnostic testing or anticipate disease severity (South Korea).
- > Triage tools to predict severity of illness and requirement for admission in paediatric emergency settings may be useful if high rates of COVID-19 community transmission and limited E.D. capacity, but not in settings with minimal or decreasing community transmission and/or spare E.D. capacity (such as Australia at present).
- > Slower increase in IgG and persistence of IgM in persons may predict mild COVID-19 but more definitive characterisation is needed.
- > Health related anxiety during a global pandemic is a normal response, and most of the time will not require treatment.
- > Pregnant and recently pregnant women are less likely to manifest COVID-19 related symptoms of fever and myalgia but potentially more likely to need intensive care and ventilation.

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ADULT MEDICINE

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

Association between body mass index and risk of COVID-19: a nationwide case-control study in South Korea

<https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1257/5897045>

When controlling for socio-demographic, co-morbidity, laboratory, and medication data, having a higher BMI is associated with a higher risk of contracting COVID-19.

- > BMI levels and risk of COVID-19 infection was assessed from 3,788 cases of confirmed infection (via positive PCR results) and compared to 15,152 age and sex matched controls.
 - The mean age of study participants was 53.7 (13.8) years - 62.1% were women, 87% were urban residents, 13.7% had at least one comorbid disease.
 - Case patients overall were likely to reside in rural regions, have lower income levels, and have a higher prevalence of the comorbid disease.
 - Matched controls were likely to be current smokers, have higher systolic blood pressure, higher lipid levels, and a higher eGFR.
- > Anthropometric data was collected at every health visit between 2015 and 2017 in which results were averaged over the three years - BMI was calculated accordingly.
 - Normal weight BMI category of 18.5 - 22.9 kg/m² was chosen as the reference because it included the largest number of participants and allowed for the most precise comparison with higher and lower BMI categories.
- > Multivariate logistic regression models demonstrated a graded association between higher BMI levels and a higher risk of COVID-19 infection.
 - 13% and 25% higher risk of COVID-19 in overweight and obese individuals, respectively.

Reviewed by: Dr Wonie Uahwatanasakul

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

What is the recovery rate and risk of long-term consequences following a diagnosis of COVID-19? A harmonised, global longitudinal observational study (not peer reviewed)

<https://www.medrxiv.org/content/10.1101/2020.08.26.20180950v1>

- > Protocol development for an international, open-access prospective cohort study.
- > Aims: to characterise the physical consequences post-COVID-19 infection, and to estimate the frequency of and risk factors for post-COVID-19 medical and psychological sequelae.

- > This protocol builds upon the existing ISARIC/WHO COVID-19 clinical characterisation protocol and database, which has been collecting data on >85,000 COVID-19 patients across 42 countries.
 - Consenting patients from the pre-existing cohort who are aged 16+ and are 28 days (-0/+3 months) post-discharge will be eligible.
 - Patients or their proxies will complete an online form detailing their clinical progress at 28 days and 3-6 months post-discharge. This form will include questions about hospital stay & readmissions, all-cause and cause-specific mortality, medical complications (such as DVT and P.E.), ongoing symptoms, quality of life and socioeconomic impacts.
 - Newly collected data will be linked to existing data on patient demographics, treatment and co-morbidities.
 - Data will be analysed for differences in clinical outcomes across demographic groups (age categories, sex, ethnicity, socioeconomic status, co-morbidities), specific exposures (severe infection, ICU admission, ventilation) and initial sequelae (complications arising during index admission).
- > Conclusion: the authors hope that this study will help to inform clinical and public health management strategies, to reduce overall morbidity and improve outcomes of COVID-19.
- > Limitations: as patient follow-up is quite resource intensive, this study may be biased towards countries/sites with greater health care capacity and funding.

Reviewed by: Professor Allen Cheng

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

Association of vitamin D status and other clinical characteristics with COVID-19 test results

<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2770157>

- > A single-centre retrospective cohort study in the U.S. to determine whether vitamin D status (reflected by both vitamin D levels and treatment) is associated with risk of COVID-19 infection.
- > 489 patients who had their vitamin D levels measured within a year before being tested for COVID-19 from 3rd March to 10th April 2020 were included.
- > Deficient vitamin D was defined as the last measured level of 25-hydroxycholecalciferol < 20 ng/mL or 1.25-dihydroxycholecalciferol < 18 pg/mL before COVID-19 testing.
- > Vitamin D treatment changes in the period between the date of the last measured vitamin D level and 14 days before COVID-19 testing were also taken into consideration to determine the final vitamin D status.
- > Results: Demographics: mean age 49.2 years, 75% women

- Vitamin D status:
 - 124/489 (25%) likely deficient with no increase in treatment
 - 287/489 (59%) likely sufficient with no decrease in treatment
 - 78/489 (16%) uncertain (last level deficient but treatment increased or the last level sufficient and treatment decreased)
- 71/489 (15%) tested positive for COVID-19. Those with deficient vitamin D were more likely to test positive compared to those with sufficient levels (R.R.: 1.77; 95% CI 1.12-2.81; P = 0.02), with estimated COVID-19 rates being 21.6% in the deficient group vs 12.2% in the sufficient group.
- > Conclusion: Deficient vitamin D status was associated with positive COVID-19 test results. Randomised clinical trials are needed to determine whether Vitamin D treatment in deficient and at-risk groups could be a potential strategy to decrease COVID-19 incidence.
- > Limitations: Vitamin D deficiency may be associated with other factors that increase COVID-19 risk; including age, obesity, diabetes and chronic illness. Although the study adjusted for many of these factors, there still remains a potential for confounding, making it difficult to predict the true impact of vitamin D status on COVID-19 outcomes from observational studies alone.

Reviewed by: Dr Wonie Uahwatanasakul

CLINICAL PAEDIATRICS

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

Clinical characteristics and viral RNA detection in children with coronavirus disease in 2019 in the Republic of Korea

<https://jamanetwork.com/journals/jamapediatrics/fullarticle/2770150>

- > This case series aimed to analyse the full clinical course, and duration of SARS-CoV-2 RNA detectability in children confirmed with COVID-19 in the Republic of Korea.
- > Children were tested for COVID-19 when they had a history of close contact with confirmed cases, were epidemiologically linked to COVID-19 outbreaks, arrived from abroad, or had symptoms suspicious of COVID-19 as judged by physicians.
- > Conducted in 20 hospitals and two non-hospital isolation facilities across the country from 18th February to 31st March 2020. Included children < 19 years with COVID-19 confirmed via SARS-CoV-2 RNA in a combined nasopharyngeal and oropharyngeal swab or sputum by RT-PCR.
- > 91 children were included, median age 11 (0-18) (76.5% of total cases in South Korea, excluding those associated with an outbreak in a specific religious group in Daegu).
- > 22% of children were asymptomatic during the entire observation period.
- > 78% symptomatic cases:
 - 66% of children had unrecognised symptoms before diagnosis.
 - 25% developed symptoms after diagnosis.
 - 9% were diagnosed at the time of symptom onset.
- > Symptomatic children developed a wide range of symptoms including fever (39%), respiratory symptoms (60%), gastrointestinal symptoms (18%), and loss of taste or smell (16%).
- > The severity of disease varied from mild (65%) and moderate (28%) to severe (3%).
- > Mean duration of the presence of SARS-CoV-2 RNA in upper respiratory samples was 17.6 days.
 - Virus RNA detected for mean 14.1 days in asymptomatic children.
 - Virus RNA was detected for mean 18.7 days in those with URTIs, and 19.9 days in those with LRTIs (no significant difference).
- > 15% of children were treated with lopinavir-ritonavir and/or hydroxychloroquine
- > 85% of patients did not receive treatment.
- > There were no fatal cases.

- > Children with COVID-19 presented with a wide range of symptoms and signs, which were not specific enough to prompt diagnostic testing or anticipate disease severity.
- > Unapparent infections in children may be associated with silent COVID-19 transmission in the community due to prolonged excretion of virus. Heightened surveillance using laboratory screening will allow detection in children with unrecognised SARS-CoV-2 infection.

Reviewed by: Dr Martin Wright

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

SARS-CoV-2 Infections Among Children in the Biospecimens from Respiratory Virus-Exposed Kids (BRAVE Kids) Study (not peer reviewed)

<https://www.medrxiv.org/content/10.1101/2020.08.18.20166835v2>

- > Prospective cohort study of children and adolescents (<21 years of age) who had close contact infected with SARS-CoV-2 (n=382) describing clinical and epidemiological characteristics of the transmission.
- > Population: Included participants attending a US-based health service between 7th April and 16th July 2020.
 - Close contacts of an individual with respiratory confirmed SARS-CoV-2 infection, defined as unprotected exposure within six feet to a confirmed case between two days before and seven days after symptom onset or laboratory confirmation of SARS-CoV-2 infection in asymptomatic contacts. Close contacts included parents, siblings, other caregivers, partners, and relatives.
- > Infected with SARS-CoV-2 289/382 (76%).
 - More likely to be Hispanic than uninfected children (88% vs 58%, p<0.0001).
 - Less likely to have a history of asthma than uninfected children (7% vs 16%, p=0.009), but no significant difference in obesity (30% vs 24%).
 - More likely to have an infected sibling contact than uninfected children (50% vs 29%, p=0.0007).
 - Children aged 6-13 years were frequently asymptomatic (38%) and had respiratory symptoms less often than younger children (30% vs 49%, p = 0.008) or adolescents (30% vs 59% p<0.0001).
 - Only one child admitted to the hospital.
 - Adolescents compared with children more frequently reported.
 - influenza-like symptoms (61% vs 39%, p = 0.002)
 - gastrointestinal symptoms (26% vs 9%, p = 0.003)
 - sensory symptoms (43% vs 9%, p<0.0001)
 - prolonged illnesses [median (IQR) duration: 7 (4, 12), vs 4 (3, 8) days, p= 0.004]
 - No association between viral load and age or symptoms.

- > Conclusion: A high proportion of children with close contact became SARS-CoV-2 positive.
 - Differences in symptoms (% symptomatic, nature of symptoms, duration of symptoms), but not viral nasopharyngeal load, occur across age groups.

Reviewed by: Dr Martin Wright

DIAGNOSTICS & SAMPLING

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

**Research Article: Pooling saliva to increase SARS-CoV-2 testing capacity
(not peer reviewed)**

<https://www.medrxiv.org/content/10.1101/2020.09.02.20183830v1>

- > As saliva collection is non-invasive, extending this strategy to test pooled saliva samples from multiple individuals could thus provide a simple method to expand testing capacity.
- > However, hesitation towards pooled sample testing arises due to the dilution of positive samples, potentially shifting weakly positive samples below the detection limit for SARS-CoV-2 and thereby decreasing the sensitivity.
- > This article investigated the potential of pooling saliva samples by 5, 10, and 20 samples prior to RNA extraction and RT-qPCR detection of SARS-CoV-2.
- > Based on samples tested, authors conservatively estimated a reduction of 7.41%, 11.11%, and 14.81% sensitivity, for each of the pool sizes, respectively.
- > Sensitivity can be increased by increasing the extraction volume, and potentially other testing factors.
- > Economic and sensitivity analyses were performed for different population prevalences.
- > In tested populations with greater than 3% prevalence, testing samples in pools of 5 requires the least overall number of tests.
- > Below 1% prevalence, however, pools of 10 or 20 are more beneficial and likely more supportive of ongoing surveillance strategies.
- > Rather than the sensitivity of specific pool size, the sensitivity of a testing program should be considered. Even if a larger pool has less sensitivity, it allows more frequent testing of a population (such as attending secondary school) with subsequent overall higher sensitivity of the testing program.
- > Testing strategies need to be varied depending on factors such as population prevalence.

Reviewed by: Dr Martin Wright

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

Salivary detection of COVID-19

<https://www.acpjournals.org/doi/10.7326/M20-4738>

- > Previous studies have investigated the use of self-collected saliva tests in populations with symptoms and/or who have been hospitalised. This study compared the SARS-CoV-2 detection performance between the standard sampling (nasopharyngeal and/or oropharyngeal swab) and a self-collected, commercial saliva sampling kit (OMNIgene•ORAL, OM-505 [DNA Genotek]) in a general population, including asymptomatic individuals.
- > The highlights of using the saliva OMNIgene•ORAL collection kit are:
 - A patient takes the saliva samples themselves.
 - Other self-collected tests have had difficulty with the instability of RNA in a raw saliva specimen; however, this saliva test uses a preservative and virucidal fluid which enhanced the stability of the sample and allows safe storage and transport.
- > Both saliva and swabs from 1,939 participants were processed using the same RNA extraction and PCR protocols to detect the SARS-CoV-2 envelope (E) gene.
- > Results:
 - The SARS-CoV-2 E gene was present in 70 samples - 80% with swabs and 68.6% with the saliva test.
 - 34 participants (48.6%) tested positive for SARS-CoV-2 on both swab and saliva samples.
 - Discordant results were seen in some participants - 22 (31.4%) tested positive for swabs alone and 14 (20%) tested positive for saliva only.
- > Limitations are that there was no true gold standard reference, no random of use swabs depending on the availability at the lab and recruitment rate was only 50% of the population targeted.

Reviewed by: Dr Lien Anh Ha Do

EMERGENCY MEDICINE

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

Prognostic accuracy of emergency department triage tools for children with suspected COVID-19: The PRIEST observational cohort study (not peer reviewed)

<https://www.medrxiv.org/content/10.1101/2020.09.01.20185793v1>

- > This article aimed to estimate the accuracy of triage tools for predicting severe illness in children presenting to the emergency department (E.D.) with suspected COVID-19 infection.
- > They undertook a mixed prospective and retrospective observational cohort study in 44 E.D.s across the United Kingdom (U.K.) and used presenting data to determine the results of assessment using the WHO algorithm, swine flu hospital pathway for children (SFHPC), Paediatric Observation Priority Score (POPS) and Children's Observation and Severity Tool (COAST).
- > Collected data from 1,530 children, including 26 (1.7%) with an adverse outcome.
- > Using pre-specified thresholds, the WHO algorithm had the highest sensitivity (0.85) and lowest specificity (0.75), but POPS and COAST could optimise sensitivity (0.96 and 0.92 respectively) at the expense of specificity (0.25 and 0.38 respectively) by using a threshold of any score above zero instead of the pre-specified threshold.
- > Existing triage tools have good but not excellent prediction for adverse outcome in children with suspected COVID-19. POPS and COAST could achieve an appropriate balance of sensitivity and specificity for supporting decisions to discharge home by considering any score above zero to be positive.
- > The limits on sensitivity/specificity mean they may be useful in settings with high rates of community transmission and limited E.D. capacity, but not in settings with minimal or decreasing community transmission and/or spare E.D. capacity (such as Australia at present).

Reviewed by: Dr John Cheek

EPIDEMIOLOGY & PUBLIC HEALTH

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

Misconceptions about weather and seasonality must not misguide COVID-19 response

<https://www.nature.com/articles/s41467-020-18150-z>

- > This commentary highlights how the weather may only marginally affect COVID-19 dynamics, and that misconceptions have shaped risk perceptions for both policymakers and citizens.
- > No human-settled area is protected from COVID-19 transmission by virtue of weather. Indoor transmission remains likely everywhere, and outdoor transmission is possible if other precautions are not taken.
- > Many scientists expect COVID-19 to be seasonal in the long term, conditional on a significant level of immunity. Seasonality could lead to worse outcomes in winter, but summer is unlikely to prevent epidemics.
- > All pharmaceutical and non-pharmaceutical interventions are believed to have a stronger impact on transmission than any environmental driver.
- > With current data, COVID-19 interventions and responses cannot be planned around seasonality.

Reviewed by: Dr Martin Wright

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

COVID-19 response measures and violence against children

<https://www.who.int/bulletin/volumes/98/9/20-263467.pdf>

- > This is an editorial. Before COVID-19, over one billion children experienced sexual, physical or emotional violence each year. These numbers have intensified during epidemics as previously observed during Cholera and Ebola outbreaks.
- > Already, during the COVID-19 pandemic, some countries have reported an increase in calls to helplines for violence against children whilst others have described a reduction in teacher-reported incidents due to school closures. These are inaccurate measures of underlying violence, and the true effects are not known.
- > The global response to COVID-19 has involved measures that aim to reduce overall physical interactions amongst the population thus increasing caregiver stress (a risk factor for violence against children), increasing contact with violent caregivers, and a reduction in formal and informal support structures that aim to prevent and/or respond to violence against children.

- > Policies such as paid sick leave for caregivers, childcare support and child feeding programs have already been implemented in some countries as a way to ease carer stress.
- > Other policies currently in consideration include alterations in stay-at-home orders, phone helplines, smartphones apps, access to shelters and integration of child protection into existing health services.
- > In conclusion, the COVID-19 response strategy should include policies to protect children against violence to prevent immediate and long-term implications on health, development and rights.

Reviewed by: Dr Martin Wright

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

COVID-19 outbreaks in a transmission control scenario: challenges posed by social and leisure activities, and for workers in vulnerable conditions, Spain, early summer 2020

<https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.35.2001545>

- > A new national strategy was introduced in Spain on 9th June requiring all regions to notify at a national level every identified COVID-19 outbreak (3+ cases with active infection with a proven epidemiological link), except those involving only members of a single household, at the time of detection, where they were compiled into a database and analysed.
- > The State of Alarm ended on 21st June.
- > From mid-June to 2nd August there were 673 COVID-19 outbreaks affecting >8300 people.
 - 551 of these were still active on 2nd August (> 6200 people).
 - 76% were small outbreaks (≤ 10 cases), and 2% had >100 cases. The number of new outbreaks each week increased exponentially (12 during week 24, 70 in week 28, 234 in week 31)
 - Social settings comprised 35% of all active outbreaks, especially family gathering or private parties (112 outbreaks, 854 cases). Leisure venues (bars, restaurants, clubs etc.) accounted for 34 outbreaks with >1,230 cases.
 - Occupational settings represented 20% of active outbreaks abattoir and fruit and vegetable workers.
 - 17% of outbreaks had a mixed setting.
 - 7% of outbreaks were related to long term care facilities, 3% related to healthcare facilities and 6% to those involving other socially vulnerable groups.
- > The increase in cases was likely due to early detection of cases and contact tracing, as well as an increase in mobility.

Reviewed by: Professor Fiona Russell

GLOBAL HEALTH

Adolescent experiences of COVID-19 in Jordan: a participatory photo project
<https://www.gage.odi.org/multimedia/adolescent-experiences-of-covid-19-in-jordan/>

Our world in data: statistics and research: Coronavirus pandemic (COVID-19)
<https://ourworldindata.org/coronavirus>

WHO weekly epidemiological update: COVID-19 7th September 2020
https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200907-weekly-epi-update-4.pdf?sfvrsn=f5f607ee_2

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

Water and sanitation in a post-COVID world
[https://www.thelancet.com/journals/langlo/article/PIIS2214-109X\(20\)30368-5/fulltext](https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(20)30368-5/fulltext)

- > Editorial published in The Lancet Global Health, September 2020, in the wake of World Water Week (24th - 28th August).
- > We are two years into the Water Action Decade (2018-2028).
 - In 2010, the U.N. General Assembly recognised the human right to access safe, affordable water.
 - In 2015, the Sustainable Development Goal (SDG) 6 provided measurable targets for global communities to ensure availability and sustainable management of water and sanitation by 2030.
 - While 1.8 billion people gained access to basic services from 2000 to 2017, WHO/UNICEF reported in 2019 that 2.2 billion people still lacked access to safe drinking water, 4.2 billion lacked adequate sanitation, and three billion lacked sufficient handwashing resources.
- > Issues with water supply disproportionately impact middle-low income countries.
 - Sub-Saharan Africa in 2017 had the worst access to piped water and the highest rates of diarrhoeal death attributed to unsafe water.
 - Of healthcare facilities in 2016, one in eight had no water service, and one in five had no sanitation service.
 - The consequences of these inadequacies for infection prevention and control amid a pandemic are clear.
 - The usage of water is growing at twice the rate of the global population.

- Major cities - Cape Town, São Paulo, Chennai - have recently come very close to “Day Zero” when municipal water supply would be cut off.
- > The COVID-19 pandemic has prompted a major improvement in access to handwashing facilities in many African countries and has seen water security become a priority in many countries’ response plans.
- > It is hoped that these practices will continue and progress in a post-COVID-19 era.

Reviewed by: Professor Steve Graham

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

COVID-19 in the Caribbean small island developing states: lessons learnt from extreme weather events

[https://www.thelancet.com/journals/langlo/article/PIIS2214-109X\(20\)30291-6/fulltext](https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(20)30291-6/fulltext)

- > Despite positive economic development indicators, small island developing states in the Caribbean have limited capacity to respond to environmental and public health emergencies due to small sizes and geographical remoteness.
- > The Caribbean Community (CARICOM) is a regional collaboration organisation established to improve the states’ responsiveness to environmental and health emergencies, particularly extreme weather threats.
- > Within the 20 CARICOM member states.
 - First COVID-19 case in Jamaica on 10th March 2020.
 - 6,421 confirmed cases and 152 deaths by 17th June 2020.
 - The most affected country in Haiti contributed to 71% and 52% of all CARICOM cases and deaths, respectively.
 - Majority of national outbreak growth rates kept below 10%. Peak growth rate at 24%.
- > Effective transmission control compared to central and South America was thought to be contributed by many similarities are evident between the successful response in Pacific island countries and the Caribbean
 - Responsiveness of CARICOM public health measures: movement restriction, curfews, and stay-at-home orders with punishment for non-compliance.
 - Public familiarity and willingness to comply derived from frequent responses to seasonal hurricane activities.
 - Early border controls and manageable entry points to states.

Reviewed by: Professor Fiona Russell

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

COVID-19 and the oxygen bottleneck

<https://www.who.int/bulletin/volumes/98/9/20-020920.pdf>

- > Obtaining a reliable and steady supply of oxygen is a common healthcare challenge in many regions of Sub-Saharan Africa, South America and South Asia.
- > The primary method of obtaining oxygen in these regions is individually transporting oxygen cylinders from manufacturer to hospitals. This renders the supply vulnerable to many obstacles, including heavy traffic, unsuitable roads and limitations based on the expense of transport and fuel.
- > The challenge of the existing limited supply of oxygen has been exacerbated by the oxygen demand placed by the coronavirus pandemic.
- > To address this issue of oxygen demand, the World Health Organization (WHO) has procured around 14,000 oxygen concentrators and distributed them to 120 low and middle-income countries.
- > Oxygen concentrators are suit-case sized devices that can deliver oxygen at a maximum flow of 10 litres of oxygen per minute.
- > Although oxygen concentrators are helping meet increased demands during the pandemic, the low flow may not provide enough ventilatory support for critically ill patients.
- > Researchers are also looking to more sustainable oxygen systems
 - Several facilities are trialing a solar-powered concentrator system (SPO2) in several facilities which were initially developed to provide oxygen for children with severe pneumonia but may play an important role in the pandemic response.
 - Pressure swing adsorption oxygen plants, which allows oxygen to be generated with enough purity for medical use onsite at hospitals.
- > The caveat to pressure swing adsorption plants is that they are a large upfront investment, and there needs to be long-term maintenance following installation.
- > The interest in improving access to oxygen therapy for COVID-19 patients may mean that as the pandemic subsides, care for people with severe pneumonia and other conditions needing oxygen therapy will also improve.

Reviewed by: Dr Wonie Uahwatanasakul

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

HIV, tuberculosis, and malaria: how can the impact of COVID-19 be minimised?

[https://www.thelancet.com/journals/langlo/article/PIIS2214-109X\(20\)30317-X/fulltext](https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(20)30317-X/fulltext)

- > Commentary by Peter Sands, the executive director of the Global Fund to fight AIDS, Tuberculosis, and Malaria (GFATM).
- > Sands highlights the estimates from a modelling study by Hogan et al that deaths due to HIV, tuberculosis, and malaria could increase by 10%, 20%, and 36% respectively, over a five year period in high-burden settings as a secondary consequence of the COVID-19 pandemic - similar in magnitude to the direct impact - while noting that estimating the knock-on impact of a pandemic is difficult.
- > The GFATM conducts regular surveys across >100 countries and reports disruption to 85% of HIV, 78% of tuberculosis, and 73% of malaria programmes, with severe disruption in around 20% of these disease control programmes.
- > The findings by Hogan et al are consistent with those of the GFATM: the primary drivers of increased mortality are interruption of antiretroviral treatment for HIV, disruption of timely diagnosis and treatment of new cases for tuberculosis, and curtailment of mosquito net distribution for malaria.
- > The GFATM has been working since March with countries to try to ensure continuity of services, has introduced flexibility of existing funds, and has increased availability of additional funds.
- > Despite the one billion provided by the GFATM to support countries in responding to COVID-19, a suggested total of \$28.5 billion is required to fund an effective response to prevent the direct and knock-on impacts of the pandemic on these three diseases in the highest-burden countries.

Reviewed by: Professor Steve Graham

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

Pulse survey on continuity of essential health services during the COVID-19 pandemic

https://www.who.int/publications/i/item/WHO-2019-nCoV-EHS_continuity-survey-2020.1

- > Essential health services (i.e. health promotion, prevention services, diagnosis, treatment and rehabilitative and palliative services) are at risk of collapse during disease outbreaks.
- > The global pulse survey conducted by the World Health Organization (WHO) aimed to gain insight into the impact of the COVID-19 pandemic across 25 essential health services and therefore inform national and international policy discussion and decisions

- > A web-based questionnaire comprising eight questions was sent to offices in five WHO regions between May and July 2020. Three main sections were outlined – (i) availability of national essential health services, (ii) level of functioning during the pandemic and (iii) main priorities and technical assistance required to maintain essential health services during the pandemic.
- > 80% of 105 countries had defined essential health services pre-COVID-19 and were, therefore, more likely (69% vs 55%) to maintain these services during the pandemic. 55% of countries allocated additional government funding to these facilities.
- > Nine out of ten countries reported at least one disruption of essential services (89%) with >75% disruptions reported in low-income countries.
- > The most frequently disrupted services included routine immunisations – outreach services (70%) and facility-based services (71%), non-communicable disease diagnosis and treatment (69%), family planning and contraception (68%), mental health management (61%), antenatal care (56%) and cancer diagnosis and treatment (55%).
- > Emergency and critical care disruptions were the main indirect consequence of the pandemic in 20-25% of countries.
- > Disruptions were due to both (i) a fall in demand due to a reduction in outpatient attendance (76%), lockdowns (48%) and financial difficulties (33%) and (ii) a reduction in supply due to cancellation of elective care (66%), healthcare workforce difficulties (49%), outpatient clinical consultation and screening program closures (33-41%), lack of stock and PPE supply (30-44%) and changes in treatment policies (33%).
- > Most countries (76%) had identified their COVID-19 response priorities and implemented telemedicine consultations (63%), task shifting (57%), novel supply chain policies (54%) and redirected patients to alternative facilities (53%) to mitigate the impacts of the pandemic—only 14% of countries removed user fees.
- > Real-time monitoring of the impacts of the COVID-19 pandemic allows rapid identification and implementation of mitigation strategies at different stages of the pandemic.
- > Limitations: responses were self-assessed and not validated, the types of respondents differed from country to country, the data is unweighted, countries were at different stages of the pandemic when they responded, and the novelty of concepts related to service impact may have influenced respondents differently.

Reviewed by: Professor Fiona Russell

IMMUNOLOGY

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

Antibody Profiles According to Mild or Severe SARS-CoV-2 Infection, Atlanta, Georgia, USA, 2020

https://wwwnc.cdc.gov/eid/article/26/12/20-3334_article

- > It is currently unclear if mild and severe COVID-19 represented two interlinked stages on a severity continuum or two distinct phenotypes of an infectious process.
- > A cross-sectional analysis of IgM and IgG reactive against SARS-CoV-2 antigens (S1, RBD and E protein) was conducted on 28 participants hospitalised for severe COVID-19 and 15 participants who had recently recovered from mild COVID-19. Pre-2020 sera were used as a control for comparison.
- > Participants with severe COVID-19 seroconverted to IgG early following symptom onset (< 7 days) but not for mild patients (took an average of 29 days to reach the threshold for severe COVID-19 participants).
- > IgM but not IgE against S1 during the first 21 days post symptom onset predicted COVID-19 patients (mild and severe) (mean specificity and sensitivity of approx. 80%).
- > IgM levels against S1 and E proteins were increased regardless of the disease severity.
- > A subgroup of samples from each group was subjected to plaque-reduction neutralisation assays-elevated IgM and IgG are most predictive of neutralising antibodies.
- > A similar pattern was observed in a separate serosurveillance cohort.
- > A diagnostic algorithm of IgG from hospitalised participants performed poorly to detect mild COVID-19.
- > Mild COVID-19 cases may have delayed or low-to-medium neutralising antibody titres.
- > Mild cases do not necessarily represent an intermediate stage between severe and asymptomatic COVID-19.
- > The slow increase in IgG and persistence of IgM in persons may predict mild COVID-19, but the more definitive characterisation is needed.
- > Limitations: Small sample size; may be confounded by ethnic differences; IgG and IgM are performed on ELISA coated on different antigens.

Reviewed by: Dr Ryan Toh

INFECTION CONTROL

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

COVID-19 in healthcare workers: Testing and outcomes at a Victorian tertiary children's hospital

<https://onlinelibrary.wiley.com/doi/10.1111/jpc.15143>

- > To describe COVID-19 testing and infection in healthcare workers (HCW) at the Melbourne Children's Campus (Royal Children's Hospital, Murdoch Children's Research Institute, and the University of Melbourne) during the first five months of the pandemic.
- > HCW presenting for testing to the E.D. or respiratory infection clinic were included, and those who underwent external testing and informed the research team of their results were also included
- > 1,964 HCWs were tested for SARS-CoV-2 with 2796 tests performed.
 - 11 COVID-19 positive HCW 0.6% (11/1964): Clinical staff (n=2); <50 years old (n=8); Asymptomatic (n=2)
 - Risk factors amongst positive cases: Returned overseas traveller (n=3); Staff member detected on asymptomatic screening during an outbreak in NICU (n=1); No additional risk factors (n=7).
 - 73 staff placed into 14 days of quarantine following close contact with a SARS-CoV-2 positive patient or staff member.
 - Nine staff recovered at home without hospital admission with two still recovering at the time of publication.
 - HCW infection rate at Melbourne Children's campus (0.6%) similar to that of Victoria's overall rate (0.7%).

Reviewed by: Dr Samantha Bannister

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

Visualising droplet dispersal for face shields and masks with exhalation valves

<https://aip.scitation.org/doi/full/10.1063/5.0022968>

- > The use of face shields and masks with exhalation valves are increasing in popularity because of their comfort and ease. Of concern, this is becoming instead of wearing regular cloth or surgical masks.
- > This study used qualitative visualisations (videos) to examine the performance of face shields and exhalation valves in stopping the spread of aerosol sized droplets, with the purpose of educating the public on the reduced efficacy of these face coverings.

- > The visualisations are set up using a hollow manikin head, where a cough/sneeze is emulated via a pressure impulse applied using a manual pump. The pump is 500 ml, similar to the lower end of the total volume expelled during a cough. Aerosolised droplets are visualised using laser sheets.
- > The visualisations show that although face shields block the initial forward motion of the cough/sneeze, the aerosolised droplets can move around the shield easily. These droplets spread out with decreasing concentration over a large area (visualised at 91 cm) depending on air disturbances.
- > Visualisations with an exhalation valve show a large number of droplets pass through. The droplets are mostly directed downwards, however, the aerosolised droplets eventually dispersed over a larger area. Visualisations with N95 masks were also performed to allow comparison, demonstrating N95 masks only allow a small escape of droplets between the mask and the nose, with significantly less intensity.
- > The final visualisation was a comparison between different mask brands, showing that there is variability in preventing aerosol spread between brands.
- > This qualitative study highlights the importance of proper face protection and that widespread adoption of alternatives to regular face masks may adversely affect infection control.

Reviewed by: Professor Suzanne M Garland

MENTAL HEALTH

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

Health anxiety in children and young people in the context of the COVID-19 pandemic: a practitioner review

<https://doi.org/10.1017/S1352465820000636>

- > To date, little research has been conducted into the manifestation and treatment of health anxiety (H.A.) in children and adolescents.
- > Development level should be taken into consideration when understanding how H.A. may manifest, and how children or adolescents may be seeking reassurance.
- > Clinician administered measures and self-reported tools exist for diagnosing H.A. in adults; however, would need to be adapted for use in children.
- > Health-related anxiety during a global pandemic is a normal response, and most of the time will not require treatment.
- > For a small number of children and adolescents, treatment may be indicated, for which cognitive behavioural therapy (CBT) has shown the most efficacy in treating H.A. in adults and anxiety in children.
- > Involving parents in CBT may be of added benefit to children and young people.
- > Further research needs to be conducted to verify age-appropriate diagnostic criteria and tools for the assessment of H.A. in children and young people.

Reviewed by: Professor Dave Coghill

PERINATAL HEALTH

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

Systematic Review: Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis

<https://www.bmj.com/content/370/bmj.m3320>

- > 77 studies were included. Overall, 10% of pregnant and recently pregnant women attending or admitted to hospital for any reason were diagnosed as having suspected or confirmed COVID-19.
- > Most common clinical manifestations of COVID-19 in pregnancy were fever (40%) and cough (39%).
- > Pregnant and recently pregnant women are less likely to manifest COVID-19 related symptoms of fever and myalgia than non-pregnant women of reproductive age and are potentially more likely to need intensive care and ventilation treatment for COVID-19. The lower rate of fever and myalgia may result from higher rates of asymptomatic presentation in this population, as the strategy of universal screening for COVID-19 in pregnancy and the low thresholds for testing than in non-pregnancy.
- > 0.1% overall mortality in pregnant women with COVID-19.
- > Pre-existing co-morbidities, high maternal age, and increased body mass index, pre-existing diabetes, chronic hypertension were associated with severe COVID-19.
- > Preterm birth rates are higher in pregnant women with COVID-19 than in pregnant women without the disease and at 6% in the former.
- > A quarter of all neonates born to mothers with COVID-19 were admitted to the neonatal unit.

Reviewed by: Professor Suzanne M Garland

TRANSMISSION

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

Probable evidence of fecal aerosol transmission of SARS-CoV-2 in a high-rise building

<https://www.acpjournals.org/doi/10.7326/M20-0928>

- > The presence of SARS-CoV-2 virus in stool has raised the potential for transmission of the virus via faecal aerosol in the pipe drainage systems of high rise buildings.
- > This a report of the investigation of an outbreak of nine patients from three families living in three vertically aligned flats connected by drainage pipes in master bathrooms in a high rise building in Guangzhou China.
- > Infection occurred during a period of social distancing.
- > Extensive close contact tracing, bathroom habits and elevator use by CCTV records were reviewed. Weather records and detailed site, floor and drainage system plans were reviewed.
- > Environmental detection measurements were conducted, including airflow and dispersion tests using ethane as a tracer surrogate for virus-laden droplets in gas in the drainage systems.
- > Infected families were all from vertically aligned flats (1502, 2502, 2702).
- > Infection source was probably the master bathroom of flat 1502, and faecal aerosols containing virus were thought to be produced in the vertical drainage stack during toilet flushing after use by the index patient.
- > Conclusion: The faecal aerosol transmission may have resulted in an outbreak of COVID-19 in this high-rise building.
- > Avoiding gas leaks from the drainage system to indoor spaces could reduce the risk of faecal aerosol transmission in high rise buildings, in particular, U-shaped water traps should not be allowed to dry out.
- > Transmission via faecal aerosolisation from leaks within the drainage system of a high rise building complex had been previously postulated as the source of an outbreak in Hong Kong during the SARS epidemic in 2003.

Reviewed by: Professor Julie Bines

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

Symptomatic and asymptomatic viral shedding in paediatric patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2): Under the surface (editorial)

<https://jamanetwork.com/journals/jamapediatrics/fullarticle/2770149>

- > Editorial extracting key points from Han MS, Choi EH, Chang SH et al. Clinical characteristics and viral RNA detection in children with coronavirus disease 2019 in the Republic of Korea. JAMA Pediatr. Published online 21st August 2020.
- > A large percentage of infected children may be asymptomatic or pre-symptomatic despite infection with SARS CoV-2 and that both asymptomatic and symptomatic individuals may shed virus for prolonged periods of time (2 to 3 weeks) regardless of symptoms.
- > It is estimated that up to 93% of infections would be missed if a detection strategy relied on testing of symptomatic children alone.
- > These findings are highly relevant to the development of public health strategies to mitigate and contain spread within communities, particularly as affected communities begin their recovery phases.
- > There are likely to be expanding scenarios for testing children as schools reopen and sports and other activities resume.
- > The method of sampling and type of test used need to be more closely considered as significant variation in test characteristics occur in real-life testing
- > Furthermore, a qualitative molecular test at a single point in time in each of these scenarios cannot be assumed to be equal; the degree of viral load or kinetics of shedding is very likely to be different in each of these, and formal studies to dissect this are needed to fill this knowledge gap.

Reviewed by: Dr Martin Wright

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

Seroprevalence of SARS-CoV-2 among frontline health care personnel in a multi-state hospital network: 13 academic medical centers, April-June 2020

https://www.cdc.gov/mmwr/volumes/69/wr/mm6935e2.htm?s_cid=mm6935e2_w

- > Cross-sectional serosurvey (3rd April to 19th June, 2020) using a convenience sample of 3,248 frontline healthcare personnel working with adult COVID-19 patients at 13 academic medical centres in the U.S. Participants had a serum sample collected for SARS-CoV-2 antibodies (IgG, IgA, IgM) and were asked to report previous symptoms consistent with COVID-19 (since Feb 2020), any previous testing for SARS-CoV-2, and PPE use in the past week/ security of access to adequate PPE.
- > SARS-CoV-2 antibodies were detected in 6% of all personnel (194/3248).
 - 29% of seropositive participants (56/194) did not report any symptoms in the preceding months.
 - 69% (133/194) did not report a previous COVID-19 diagnosis.

- Personnel who reported always wearing a face covering (surgical mask, N95 respirator, or powered air-purifying respirator) while caring for patients had a lower prevalence of antibodies compared to those who did not (5.6% vs. 9.0%).
- > Implications:
 - There is a high proportion of undetected and unrecognised SARS-CoV-2 infection among frontline healthcare personnel.
 - Essential strategies to reduce hospital transmission could be universal face mask use and lowering clinical thresholds for testing.
- > Limitations: selection bias (convenience sampling), reporting bias (some self-reported outcomes), possible underestimation of seroprevalence (if the antibody titres had declined since infection or if antibody response has not been mounted yet), inability to distinguish between hospital or community exposure, and confounders (e.g. differences in facility-level infection control) not adjusted for in the multivariate analysis.

Reviewed by: Dr Vanessa Clifford

VACCINES

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

An ethical framework for global vaccine allocation

<https://science.sciencemag.org/content/early/2020/09/02/science.abe2803.full>

- > Once effective COVID-19 vaccines are developed, it needs to be decided on how to distribute them fairly across countries.
- > The absolute priority for a country's own citizens is not ethical, and countries should not retain more vaccine than the amount needed to keep the rate of transmission below one.
- > The authors propose three key values: benefitting people and limiting harm, prioritising the disadvantaged and equal moral concern.
- > The authors offer an ethically defensible and practical proposal for the fair distribution of COVID-19 vaccine – the Fair Priority Model, which outlines three phases of vaccine allocation:
 - COVID-19 causes harm in three ways: death and permanent organ damage, indirect effects including an overburdened health system, mental health and decreased immunisation, and impacts on the global economy.
 - Phase 1: reduce premature deaths and other irreversible direct and indirect health impacts allocated based on Standard Expected Years of Life Lost (SEYLL) averted per dose of vaccine.
 - Phase 2: continue to address enduring health harms but also aims at reducing serious economic and social deprivations allocated based on SEYLL, the projected reduction in the absolute size of the poverty gap per dose of vaccine, projected absolute improvement in gross national income per vaccine dose.
 - Phase 3: reduce community transmission allocated based on country transmission rates.
- > Other suggested models (not supported by the authors) include:
 - WHO: countries receive doses proportional to population in phase I until every country has vaccinated 20% of its population.
 - Distribute vaccines to countries according to the number of front-line health care workers, the proportion of the population over 65 and the number of people with co-morbidities.
- > The Fair Priority Model contains ethical values to limit harms, benefit the disadvantaged, and recognise the equal concern.
- > The responsibility for implementing such a model rests with countries, international organisations, and vaccine producers.

Reviewed by: Associate Professor Margie Danchin

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

The end-to-end process needed for a SARS-CoV-2 vaccine

<https://www.who.int/bulletin/volumes/98/9/20-030920.pdf>

- > Dr Melanie Saville is the director of vaccine research and development at the Coalition for Epidemic Preparedness Innovations (CEPI). Here, Dr Saville discusses her career in industry, the role of CEPI, as well as the manufacturing, financial and global challenges to bringing a successful candidate to market.
- > CEPI supports vaccine research and development on key diseases, working to ensure vaccine availability to low-income countries.
- > They currently support nine COVID-19 vaccine candidates. Whilst their focus is on those with potential for rapid development and scalability, CEPI remains adamant that stringent safety criteria must be met.
- > CEPI advocates for immediately increasing the number and capacity of manufacturing facilities to support the production of an eventually successful vaccine candidate.
- > Dr Saville discusses the ACT Accelerator, which focuses on the cooperative “end-to-end” approach of bringing CEPI, Gavi and the WHO together to rapidly bring a successful vaccine to market.
- > Importantly, Dr Saville highlights the disadvantages posed by individual nations making bilateral agreements for vaccine procurement. The absence of funding from some of these key countries compromises the ACT Accelerator’s global endeavour to bring a vaccine to people everywhere, as opposed to only those from countries with the means to make these agreements and who happen to back a successful candidate.

Reviewed by: Associate Professor Margie Danchin

Phase 1-2 Trial of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine

<https://www.nejm.org/doi/full/10.1056/NEJMoa2026920>

- > This was a randomised, placebo-controlled, phase 1-2 trial of NVX-CoV2373 (Novavax), a recombinant SARS-CoV-2 nanoparticle vaccine composed of trimeric full-length spike glycoproteins, which was administered both with and without a Matrix-M1 adjuvant.
- > Each healthy adult (18-59 years) received an injection on day zero and day 21. Of 131 participants, 82 were administered either five or 25 microgram doses of the vaccine with or without adjuvant. 26 participants received only one dose of the vaccine, then placebo, whilst 23 received placebo for both injections. Safety and immunogenicity were assessed at day 35.
- > The safety profile was broadly acceptable: local reactions were common. Systemic adverse events included headache, fatigue and myalgia.
- > Two doses of rSARS-CoV-2 with adjuvant led to antibody levels and neutralisation responses comparable with convalescent serum of patients infected with COVID-19. Authors suggest that their study is evidence in support of a two-dose vaccine/adjuvant schedule with three weeks between doses.

- > This study documents another promising vaccine candidate for COVID-19, which was broadly safe and immunogenic.
- > The vaccine will progress to phase 3 trials. More diverse populations and longer-term follow-up data will be important in properly assessing the safety and immunogenicity of all promising vaccine candidates.

Reviewed by: Professor Fiona Russell

VIROLOGY

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

COVID-19 re-infection by a phylogenetically distinct SARS-coronavirus-2 strain confirmed by whole genome sequencing

<https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1275/5897019>

- > It is unclear if true re-infection occurs. Recent studies have shown that neutralising antibodies, which develop rapidly after infection, begin to decline 1-2 months after infection.
- > Method: whole genome sequencing was conducted on respiratory specimens collected from the same patient (33 year old male from Hong Kong) during two episodes of COVID-19. Comparative genome analysis was used to distinguish between reinfection and prolonged viral shedding. Serum IgG against SARS-CoV-2 was also analysed.
- > The patient was symptomatic in his first episode (March 2020) and was asymptomatic in his second episode (August 2020).
- > Serial serum specimens were taken and were negative for SARS-CoV-2 IgG ten days after the first episode and one to three days after the second episode. The serum of the second episode returned positive on day five.
- > Genome analysis demonstrated that the first viral genome belonged to a different lineage to the second. The first viral genome was closely related to strains from the U.S. or England collected in March-April 2020, contrasting to the second which related to strains found in Switzerland and England collected from July to August 2020.
- > The patient's clinical parameters, such as CRP, viral load and seroconversion in the second episode suggests that he was having acute infection with SARS-CoV-2, e.g. reinfected with SARS-CoV-2. Furthermore, an interval of 142 days between episodes makes persistent viral shedding unlikely.
- > The results suggest that SARS-CoV-2 may continue to circulate amongst the community despite herd immunity (obtained via infection or vaccination).
- > Further studies of patients with re-infection is important for vaccination development.
- > Limitations: single patient, only serum specimen was collected in the first episode, no data on T-cell roles in the first and second episodes.

Reviewed by: Dr Lien Anh Ha Do

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_z2uWV7r3FaPzAOr86q9ZXBcTZ1QcCE_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/>

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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Professor Fiona Russell
Dr Wonie Uahwatanasakul
Dr Amy Gray

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REVIEWERS

Professor Fiona Russell	Director of the Child and Adolescent Health PhD Program, Department of Paediatrics, The University of Melbourne; Group Leader Asia-Pacific Health Research, MCRI
Dr Wonie Uahwatanasakul	Paediatrician- Immunization service RCH, MD Child and Adolescent Health Program Lead Coordinator, Department of Paediatrics, The University of Melbourne
Dr Amy Gray	Consultant paediatrician, General Medicine Director of Medical Education and the Education Hub, RCH A/Professor, Department of Paediatrics, The University of Melbourne
Professor Allen Cheng	Deputy Chief Medical Officer , DHHS , Medical Adviser, Melbourne Vaccine Education Centre, Infectious Diseases Epidemiology Director of the Infection Prevention and Healthcare Epidemiology, Alfred Health, Infectious diseases and an epidemiologist, Department of Epidemiology and Preventive Medicine at Monash
Dr Martin Wright	Paediatrician, Joan Kirner Women's and Children's, Sunshine Hospital and Senior Lecturer, Department of Paediatrics, The University of Melbourne
Dr Lien Anh Ha Do	Virologist New Vaccines, Infection & Immunity Theme, MCRI and Honorary Fellow, Department of Paediatrics, The University of Melbourne
Dr John Cheek	Deputy Director Emergency Medicine at The Royal Children's Hospital Melbourne, Research Associate at MCRI, Honorary Senior Fellow Department of Paediatrics at the University of Melbourne
Professor Steve Graham	Centre for International Child Health, Department of Paediatrics, The University of Melbourne, MCRI
Dr Ryan Toh	Post-doctoral researcher, New Vaccines, Infection & Immunity Theme, MCRI and Honorary Fellow, Department of Paediatrics, The University of Melbourne
Dr Samantha Bannister	Paediatric Registrar, The Royal Children's Hospital, Melbourne, Graduate Research Student, Murdoch Children's Research Institute, PhD Candidate, Department of Paediatrics, The University of Melbourne
Dr Claire von Mollendorf	Senior Research Officer, New Vaccines and Asia-Pacific Health Research Groups, MCRI and honorary Senior Fellow, Department of Paediatrics, The University of Melbourne

Professor Sue Garland

Reproductive & Neonatal Infectious Diseases, Department of Obstetrics and Gynecology, University of Melbourne; Director Centre Women's Infectious Diseases Research; Honorary Research Fellow, Infection & Immunity, Murdoch Children's Research Institute

Professor David Coghill

Financial Markets Foundation Chair of Developmental Mental Health, The University of Melbourne

Professor Julie Bines

Paediatric Gastroenterologist, RCH; Lead Enteric Disease Group MCRI; Victor and Loti Smorgon Professor of Paediatrics, The University of Melbourne and Dr Celeste Donato- Virologist, Enteric Diseases Group, MCRI; Lecturer, Department of Paediatrics, The University of Melbourne

Dr Vanessa Clifford

Infectious Diseases physician and Microbiologist, RCH/RWH; Honorary Research Fellow in the Infection and Immunity Group, MCRI: and honorary Senior Fellow, Department of Paediatrics, The University of Melbourne

A/Professor Margie Danchin

General and Immunisation Paediatrician, Department of General Medicine, RCH, Group Leader, Vaccine Uptake, MCRI, Clinician Scientist Fellow, Department of Paediatrics and School of Population and Global Health, The University of Melbourne