COVID-19 KIDS RESEARCH EVIDENCE UPDATE

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

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COVID-19 KIDS EVIDENCE UPDATE
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WEEKLY UPDATE NO. 26

GUEST EDITORIAL

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“It is wrong always, everywhere, and for anyone, to believe anything upon insufficient evidence”
(William Kingdon Clifford, mathematician/philosopher, 1877)

This 26th edition of the COVID-19 Kids Research Evidence Update represents the six-month mark of its production; a significant milestone in the dissemination of evidence to a wider audience. The editorial team and medical student reviewers have committed an enormous amount of time and energy into its production, and half a year of summaries has made me think about what all that effort enables us to achieve.

The interaction between opinion and evidence is often opaque, and the limitations of opinion have been clearly displayed during the COVID-19 pandemic. Public health response to communicable disease is by its very nature imperfect; rapid decision making when the nature of the organism is not well known is required. Over time as more evidence emerges public health priorities and messaging change, early mistakes can be corrected, and the public health response moves on. The “empty space” between early decisions and the gathering of evidence has proven fertile ground for opinion and argument.

Clinicians are not innocent in this regard; there are a myriad of examples of well-meaning clinicians publishing opinion in the absence of evidence. Opinions have appeared both for and against lockdowns, school closures, the use of facemasks in public, various types of PPE, coronavirus treatments, border closures, curfews, limitation on public movement, and various other measures. This messaging from “experts” has proven confusing and has dominated discussion of the public health response to Coronavirus. There has never been a more important time in recent memory for clinicians to produce evidence to support those who are making decisions.

Early indicators during the pandemic showed a dramatic reduction in children presenting to emergency departments(1), and the opinion that unwell children were not presenting to emergency due to fear of exposure to Coronavirus was stated widely. A case series from Italy fuelled concern that we were seeing the delayed presentation of unwell children(2). Recent evidence has highlighted that rates of minor communicable diseases such as gastroenteritis and respiratory illness have markedly decreased, and very few children truly have a delayed presentation(3). Some presentations to emergency have actually remained static (neonates) or increased (mental health)(4). In this edition, local evidence from a single centre is presented suggesting some children with DKA in type 1 diabetes may have presented late in the early stages of the pandemic. Clearly, motivators for emergency department presentations are multifactorial, and the true effects of the pandemic are unlikely to be known for some time.
Also in this edition, further evidence emerges that the reopening of schools is likely safe(5). One month after school reopening in Italy, 90% of schools which reported a case had only one, suggesting that transmission within schools is low in the context where schools close for case investigation. Evidence, including that produced by researchers at the Murdoch Children’s Research Institute(6), have enabled the reopening of schools in Victoria at a much earlier point than other parts of our society.

Whilst on the topic of reopening, enough jurisdictions have attempted to reopen their societies to enable an analysis of their success(7). We now have access to published recommendations across a comparative framework consisting of knowledge of infection status, community engagement, public health capacity, health system capacity, and measures for border control. The publication of evidence such as this enables us to challenge opinions that run contrary to experience as we attempt to transition from the acute response to a “second wave” to a more normal future.

I am acutely aware of the irony in being given the opportunity to write an editorial decrying the danger of opinion, but I think the broader point holds. As clinicians and researchers, part of our role in society is the dissemination and translation of knowledge. We must stay informed to enable us to rebut those who would push an agenda in the absence of evidence, or use imperfect evidence to draw incorrect conclusions. If you have a hypothesis; test it, and resist the temptation to publish it as expert opinion in the absence of evidence.


HIGHLIGHTS

> A systematic review found that asymptomatic patients appear to have low secondary attack rates, which suggests limited infectiousness or duration of infectiousness. Pre-symptomatic patients appear to transmit efficiently, especially within households.

> An Italian study found low transmission of SARS-CoV-2 within schools, at least among younger students, as schools were closed for investigation if a case occurred in the school setting.

> Rooming-in is safe for term/near-term infants born to asymptomatic/mildly symptomatic mothers with COVID-19 in conjunction with infection control measures.

> A survey of healthcare workers and administrators in Denmark found a seroprevalence of 3.4%.

> The drug combination lopinavir-ritonavir does not improve clinical outcomes for patients admitted to hospital with COVID-19, as found by the RECOVERY trial (United Kingdom).

> The European Centre for Disease Prevention and Control (ECDC) has set forth five objectives for testing: control transmission, monitor incidence and trends to assess severity over time, mitigate the impact of COVID-19 in health and social care settings, identify clusters or outbreaks in specific settings, and prevent re-introduction into regions/countries with sustained control of virus transmission.

> A decrease in obstetric triage visits during COVID-19 may contribute to an increasing rate of stillbirths observed in London hospital compared with the prior year.

> COVID-19 has created challenges in children’s routine sleep practices due to interruption of regular schedules and activities, and parents can use sleep hygiene strategies to help get back on track.

> Increase in diabetic ketoacidosis presentations to an Australian tertiary centre during the COVID-19 pandemic.

> COVID-19 recovery efforts should combat the disproportionate burden of longer-term poor health and mortality which children, particularly those from poor countries, will face because of the pandemic.

> A retrospective study found that children with COVID-19 had significantly lower vitamin D levels compared with healthy children. Low vitamin D was associated with fever but not disease severity.

> Observations of the COVID-19 exit strategy from nine countries yields important lessons in how to reach our new COVID-19 normal on a policy level.

> IgG antibody levels peak at around 8-12 weeks post-infection, and fall below positive cut-offs at ~week 20.

> In June 2020 American adults were more likely to remember to wash their hands after experiencing respiratory symptoms (cough, sneezing or nose-blowing), before eating in a restaurant and before eating at home than in October 2019. However, <75% participants washed their hands in these situations.
> When governance is not inclusive of gender, geography, sexual orientation, race, socio-economic status or disciplines within and beyond health the healthcare system becomes broken.

> While the primary spread of SRS-CoV-2 appears to be via aerosol and respiratory droplets, fomites and the effect of temperature on the persistence of virus may be an essential factor in the transmission of the pathogen.
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Response to COVID-19 and any other medical condition at this time is based on science that is new, often uncertain, subject to change, and dependent on context.

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

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

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CHILD DEVELOPMENT

Julia Sweet – 3rd Year Medical Student, University of Ottawa
Current and COVID-19 challenges with childhood and adolescent sleep
https://jamanetwork.com/journals/jamapediatrics/fullarticle/2770795

- Disrupted sleep is a common problem in childhood, made even more common due to the disruption of COVID-19 on regular schedules, including through school closures.
- This article reminds clinicians of strategies to optimise sleep hygiene.
- Recommended that children get the appropriate amount of sleep for their age: 3-5 years: 10-13 hours; 6-12 years: 9-12 hours; 13+ years: 8-10 hours.
- Sleep hygiene strategies: Maintain a consistent bedtime and wake-up times and routines; Turn off all electronics within one hour of a child’s bedtime; Avoid consumption of caffeine in children; Gradually move bedtime earlier by ten minutes every 3-4 days or once the child is able to fall asleep within 30 minutes of going to bed; Avoid naps in older children.
- Contact paediatrician for follow-up if a child displays sleeping behaviours of loud snoring, gasping, kicking, or excessive sleepiness as these may indicate a medical problem.

Reviewed by: Dr Martin Wright

Chelsea Haliburton – 3rd Year Medical Student, University of Ottawa
Leveraging cross-sector partnerships to preserve child health: a call to action in a time of crisis
https://jamanetwork.com/journals/jamapediatrics/fullarticle/2771108

- Health is inherently social, and the effects of catastrophic events are not uniformly distributed. At the commencement of the COVID-19 epidemic, the Department of Paediatrics at the University of Rochester shifted its focus to enhance and leverage existing partnerships so that children and families could continue to receive necessary community-based health and welfare services. The main objective was to collaborate across sectors to identify issues and develop timely and coordinated responses.
- To diminish viral transmission, they partnered with local accountable care organisations and private paediatric and family medicine practices to develop a unified community-wide paediatric plan to limit foot traffic through clinics. In-person visits were limited to essential preventative visits defined as screenings and immunisations for children up to two years. Other clinical services changed to telehealth.
- As practices and the healthcare system faced loss of revenue secondarily to limiting in-person visits, they partnered with the Monroe County Medical Society and local accountable care organisations to successfully increase reimbursement for telemedicine encounters as well as advocated for reimbursement to healthcare professionals on historical rather than actual claims. In addition, they worked with local banks and the small business development corporation to help practices receive loans and grants through the US Federal Coronavirus Aid, Relief, and Economic Security (CARES) Act.
> To assess and manage children with behavioural health concerns, they coordinated with local school districts, mental health counsellors, and community-based organisations to develop a tiered approach.

> To address the issue of child nutrition, they collaborated with the funders to allow new enrollees to join the Women, Infants, and Children program via telephone rather than the required in-person interviews.

> They collaborated with the regional public transportation system to organise safe transport to necessary health interactions for low-income families - allowing only one family per ride, requiring all to wear face masks and maintaining safe physical distances when possible.

> The extent of the solutions successes remains to be fully seen; however, they hope to provide insight to their efforts for preserving children’s health during the coronavirus pandemic to allow other communities to make necessary changes.

Reviewed by: Dr Martin Wright
Is Vitamin D deficiency a risk factor for COVID-19 in children?  

> Several studies have shown that vitamin D deficiency is a risk factor for acute respiratory distress syndrome and increases the risk of respiratory infections, including respiratory syncytial virus, tuberculosis and influenza. There is also some evidence suggesting a potential protective role of vitamin D against COVID-19 infection, including suppression of an adhesion molecule that aids viral host cell entry and reduction of inflammatory cytokines that predict worse disease outcomes in severe COVID-19.

> The aim of this retrospective study, from Turkey, was to determine the prevalence and clinical outcomes of vitamin D deficiency in children and adolescents hospitalised with COVID-19.

> A total of 85 children between the ages of 1 month and 18 years were included. Of those, 40 children were hospitalised with RT-PCR confirmed SARS-CoV-2 disease while the remaining 45 were healthy and acted as the control group. Children with chronic diseases and co-morbidities were excluded.

> Vitamin D deficiency and insufficiency were defined as 25-hydroxycholecalciferol \[25(OH)D\] level of <12ng/ml and between 12-20ng/ml, respectively. Normal vitamin D was defined as \[25(OH)D\] level of ≥20ng/ml.

> Results:

– Compared with the healthy control group, children with COVID-19 had significantly lower median vitamin D levels (13.14 vs 34.81 ng/ml; p<0.001). 29/40 (72.5%) of children with COVID-19 were vitamin D deficient or insufficient versus 11/45 (24.4%) in the control group.

– There was no significant difference in the distribution of disease severity according to vitamin D levels (p=0.097).

– No significant correlations were found between clinical parameters and vitamin D level, except for fever which was found more frequently with low vitamin D level.

– None of the children died.

> Limitations: Small sample size, certain clinical parameters including anosmia and loss of taste were not assessed for every patient, the relationship between vitamin D deficiency and mortality could not be assessed as there were no deaths in the study.

> Conclusion: Levels of vitamin D were significantly lower in children with COVID-19 compared with healthy children. Low vitamin D levels were only associated with fever, but no correlation was found between disease severity and vitamin D levels. Further studies are needed in children to characterise the effect of vitamin D deficiency on the clinical outcomes of COVID-19 disease.

Reviewed by: Dr Wonie Uahwatanasaskul
Acute disseminated encephalomyelitis in a COVID-19 paediatric patient

https://link.springer.com/article/10.1007%2Fs00234-020-02571-0

A case report from Brazil of a 12-year-old girl with acute disseminated encephalomyelitis (ADEM) presumed secondary to SARS-CoV-2 infection.

ADEM is an immune-mediated inflammatory neurological disease which results in inflammation of predominantly the white matter of the brain and spinal cord and is often post-viral.

Case timeline

- **D1**: headache, rash and fever. Headache and fever lasted one day, rash lasted six days.
- **D5**: onset of acute, progressive, bilateral and symmetrical motor weakness, sensory changes in lower limbs without sphincter abnormalities.
- **D6**: positive SARS-CoV-2 rRT-PCR on a nasopharyngeal swab.
- **D7**: the patient developed respiratory distress and went into respiratory failure, requiring intubation and ventilation. MRI brain/spine demonstrating features in keeping with ADEM (pseudo-leukodystrophy pattern).
- **D37**: the resolution of MRI white matter changes with scattered gliotic changes, ventricular dilatation and widespread widening of cerebral sulci.
- **D68**: evolution from flaccid to spastic paresis, with hyperreflexia and bilateral Babinksi’s signs. Significant improvement of strength but remaining weakness in all four extremities.

Investigations

- **Bloods**: Leukocytosis with neutrophilia, elevated creatine phosphokinase (CPK), deranged liver enzymes, elevated LDH of 373 U/L, normal CRP, elevated fibrinogen with normal d-dimer, elevated troponin of 5.5.
- **CSF**: rRT-PCR negative for SARS-CoV-2, Zika and Dengue 1-4 (endemic to the area). Protein, white cells, glucose normal.
- **MRI brain and spine D7**: extensive and bilateral restricted diffusion in the subcortical and deep white matter, as well as a T2-hyperintense lesion with restricted diffusion in the splenium of the corpus callosum. Extensive cervical myelopathy involving white and grey matter.
- **CT Chest**: no characteristic changes of COVID-19 (some atelectasis).

Treatment was with five day methylprednisolone, which was repeated due to persistent motor symptoms.

This case of ADEM in a patient with recent SARS-CoV-2 infection and negative testing for other viral illnesses suggests a causal relationship, although the authors do not specify viral testing performed, other than the endemic viruses.

Reviewed by: Associate Professor Amy Gray
Increased paediatric presentations of severe diabetic ketoacidosis in an Australian tertiary centre during the COVID-19 pandemic


> The study compared March to May 2020 (pandemic period) presentations to the same period in the previous five years at the John Hunter Children’s Hospital.

> Main results:

- New diagnoses of type one diabetes (T1DM): Comparable to pre-pandemic.
- Frequency of severe diabetic ketoacidosis (DKA) at T1DM diagnosis: Significant increase in the pandemic period (45% vs 5%; P<0.003).
- Overall DKA: Significant increase in pandemic period (73% vs 2%; p <0.007).
- 27% decrease in presentations to the emergency department of < 18-year-olds in the pandemic period (p <0.01).

> Healthcare advocacy for non-pandemic-related conditions must continue during the pandemic.

> Limitations: Small sample size.

Reviewed by: Dr Wonie Uahwatanasakul
DIAGNOSTICS & SAMPLING

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

SARS-CoV-2 seroprevalence survey among 17,971 healthcare and administrative personnel at hospitals, pre-hospital services, and specialist practitioners in the Central Denmark Region.

https://dx.doi.org/10.1093/cid/ciaa1471

> This was a seroprevalence survey on SARS-CoV-2 among Danish healthcare workers (HCWs) from 18th May to 19th June 2020 in the Central Denmark Region.

> All healthcare and administrative personnel at seven hospitals, pre-hospital services, and specialist practitioners were invited via email to be tested for SARS-CoV-2 antibodies.

    - A commercial SARS-CoV-2 total antibody ELISA based (Wantai Biological Pharmacy Enterprise, Ltd., Beijing, China) was used. The assay detects IgG, IgM and IgA against the SARS-CoV-2 receptor binding domain and has a sensitivity of 96.7%, a specificity of 99.5% with no observed cross-reactivity.

    - 360 anonymised plasma samples of blood donors (background population) from late June 2020 in the region were also tested for SARS-CoV-2 antibody.

    - PCR detecting SARS-CoV-2 was conducted earlier on a subset of HCWs having relevant COVID-19 symptoms or relevant risks of exposure.

    - HCWs were grouped in five geographical locations.

    - Results were reported as percentages and percentage point differences with 95% CIs. The Rogen Gladen estimator was used to estimate the true prevalence based on the estimates of sensitivity and specificity of the test. Predictors of risk were analysed by multivariable logistic regression analysis and presented as ORs with CIs.

> 29,950 healthcare and administrative workers were invited to participate, 17,987 showed up for antibody testing (69%).

    - After adjusting for assay sensitivity and specificity, the seroprevalence in this group was 3.4% (95% CI, 2.5%-3.8%).

    - Among the total 3.4% who tested positive, 64.8% had been previously tested for viral RNA PCR, and 50% had received a positive result.

    - Predictors of risks of having seropositive are young age (<30 years old), being employees of Regional Hospital West Jutland (RHWJ) and especially working at Emergency Department as well as being medical staff (medical doctors, nurses and biomedical laboratory scientists). The risk of infection was associated with the workplace rather than the place of living.

    - 26.7% of all participants had already been previously tested at some point for SARS-CoV-2 RNA via RT-PCR. Among these, 7.1% had tested positive, and 98% were subsequently seropositive in this study.
In blood donors, seroprevalence was low in both western and eastern part of the region, 1.2% and 0.6%, respectively.

Conclusions: High sensitivity and specificity of the Wantai test; High seroprevalence in HCWs having a high frequency of patient contacts due to in-hospital transmission as there was a significantly higher seropositive prevalence in HCWs than in blood donors (background population).

Limitations: Low study participation (69%) could under- or overestimate the true prevalence. No dynamic antibody concentration overtime. No available information about the PPE use and/or specific tasks of participants in order to estimate the associated risk of infections.

Reviewed by: Dr Lien Anh Ha Do
COVID-19 testing strategies and objectives

This technical report was developed by the European Centre for Disease Prevention and Control (ECDC) as a synopsis of COVID-19 testing strategies.

The report recommends five objectives for testing:

1. Control transmission
   - In all situations, populations to test include: All possible cases and close contacts of confirmed cases regardless of symptoms. If resources allow, consider re-testing close contacts of confirmed cases which test negative and remain asymptomatic.
   - In settings with widespread community transmission, consider testing of the entire population. Test all close contacts of confirmed cases regardless of symptoms. If resources allow, consider re-testing close contacts of confirmed cases which test negative and remain asymptomatic.

2. Monitor incidence and trends assess severity over time
   - If resources allow, all samples from healthcare settings should be tested both for SARS-CoV-2 as well as influenza in order to monitor incidence and trends. If this is not possible, patients with underlying conditions and the elderly should be prioritised for testing of both influenza and SARS-CoV-2.
   - In areas of no local transmission, populations to test include those presenting with compatible symptoms in primary care or hospital settings.
   - In areas of community transmission, populations to test include: All possible cases, those presenting with compatible symptoms in primary care or hospital settings, and all contacts of confirmed positive cases regardless of symptoms.
     - If testing capacity is exceeded, consider only testing a systematic sample of all detected possible cases and their contacts with symptoms.

3. Mitigate the impact of COVID-19 in healthcare and social care settings
   - In settings with no local transmission, test all possible cases among staff, residents, and visitors.
In settings with community transmission, populations to test include: All staff periodically (weekly to every two weeks) regardless of symptoms, all patients/residents upon admission, all possible cases, and all contacts of confirmed cases. If a case is detected, all staff and residents should be tested regardless of symptoms.

If resources allow, consider re-testing patients/residents that tested negative on admission, again on day 3-5, in combination with daily symptom monitoring for the first 14 days.

4. Identify clusters or outbreaks in specific settings

- Specific settings prone to outbreaks include: long-term care facilities, workplaces in confined spaces, schools and education centres, prisons, and migrant detention centres.
- In areas of no or low local transmission, populations to test include: all possible cases, all close contacts of confirmed cases regardless of symptoms, and all contacts exposed via high-risk settings/events.
- Wider testing should be performed in prisons, detention and reception centres, occupational centres where physical distancing is not feasible, education settings, etc. where a case has been confirmed.
- In areas of community transmission, testing strategies are the same as in areas of no or low local transmission. In addition, all incoming persons to such settings should be tested in addition to daily monitoring of symptoms.
- If resources allow, consider re-testing close contacts of confirmed cases who test negative initially and remain asymptomatic.

5. Prevent re-introduction into regions/countries with sustained control of virus transmission

- Countries or smaller areas where SARS-CoV-2 circulation has been essentially eliminated should consider testing and follow-up of any individuals coming from outside of the area.
- If in quarantine, incomers should be tested again at the end of their quarantine period (day 14).
- This recommendation only applies to areas where SARS-CoV-2 circulation is absent or low. It is not cost-effective to screen travellers to other regions.

This document also describes the SARS-CoV-2 incubation period, various test types and strategies (rapid test combined with later confirmatory testing, sample pooling, follow-up testing), specimen types, contact tracing strategies (contact testing, asymptomatic/pre-symptomatic impact, long-term carriers and reinfection), and current limitations of testing.

Reviewed by: Dr Claire von Mollendorf
Lessons learnt from easing COVID-19 restrictions: an analysis of countries and regions in Asia Pacific and Europe

The authors outline the observational findings of COVID-19 restrictions being scaled back and propose a framework for assessing the readiness to lift measures and resume a new COVID-normal.

> 186 countries have implemented local policies on population movement to slow the spread of COVID-19, including 82 with strict lockdown measures.

> With no clear COVID-19 exit strategy, countries have taken differing approaches in easing restrictions in order to balance public health measures and opening the economy.

> Countries such as Singapore, Norway, and Spain relaxed restrictions without publicly-known criteria, whereas countries such as Japan, Germany, New Zealand, and Australia have set thresholds and published plans in place.

> Experiences of SARS and MERS seem to have better prepared Asian countries compared with Europe with regards to public health infrastructure and pandemic adaptability.

> Through experiences of different countries, the authors have postulated several principles that should inform the exit strategy:

1. **Knowledge of infection status**
   - Countries should have a robust surveillance system in place.
   - This allows accurate measurement of \( R_{\text{eff}} \) to ensure the virus is not spreading widely.

2. **Community engagement**
   - Social distancing policies must be in place and well-communicated, perhaps initially with strict distancing before adopting the household/social bubble model.
   - Messaging around mandatory masks has been controversial and confusing, with most countries studied recommending it especially when social distancing is impossible.
   - Schools and workplaces must have COVID-safe protocols, with many countries opting for a staggered return.
   - Transparent communication from political leaders in certain countries (Germany, New Zealand, and South Korea) garnered public trust for community measures.
   - Vulnerable populations, such as those in aged care facilities, minority ethnic groups, and lower SES groups, should be protected to ensure the virus does not spread amongst these communities and beyond.
   - Economic stimulus measures, especially long-term sustained plans, are crucial to offsetting the effect of COVID-19 on those most disproportionately affected.
3. Public health capacity

- Initial testing was guided by narrow criteria, but most countries have now adopted broader testing strategies (including asymptomatic contacts) to stop the spread. Drive-through and home-based testing have increased testing capacity.

- Contact tracing teams were overwhelmed in the initial phases of COVID-19. Successful systems such as in South Korea used multiple sources of data (e.g., credit card transaction, CCTV, mobile GPS) to confirm suspected contacts.

- Effective isolation is key; in many Asian countries, confirmed cases are isolated in hospitals or central facilities, whereas in European countries many cases isolate at home.

- Public health experts have played a key role in presenting evidence to drive policy, but the precarious position begs the question – what should come first?

4. Health systems capacity

- Adequate health-system capacity is vital. During surges, other spaces may be repurposed.

- There has also been a critical shortage of healthcare workers, leading to recruitment, redeployment, and reorganisation. Some countries also experienced shortages of PPE.

5. Measures for border control

- Many countries have instituted strict incoming border measures, including closing to visitors and requiring mandatory 14-day quarantine.

- Asian countries have overall been more strict than those in the European Union.

Reviewed by: Dr Claire von Mollendorf
GLOBAL HEALTH

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

Impact of the COVID-19 pandemic on global child health: joint statement of the International Child Health Group and the Royal College of Paediatrics and Child Health
https://adc.bmj.com/content/early/2020/10/05/archdischild-2020-320652.full

> A brief viewpoint that advocates for monitoring of impact and a "new era of investment" to strengthen family-based, integrated healthcare systems.

> The many indirect impacts of the pandemic on maternal, newborn, and child health, particularly in poor countries, with immediate and potential long-term adverse effects are again highlighted:

  − Outbreaks of vaccine-preventable diseases.
  − Increase in deaths due to infectious diseases such as malaria, HIV and tuberculosis due to interruption of prevention and treatment.
  − A major increase in food insecurity and malnutrition, disproportionately affecting children.
  − An estimated excess of >1 million child deaths over the next six months due to severely compromised maternal, neonatal and child health service delivery.
  − Negative impacts on children’s mental health and safety due to increased poverty, violence, dropping out of education (especially girls) and other factors.

> Therefore, the joint statement calls for investments in COVID-19 recovery that prioritise a family-centred model of health care and child health programmes.

Reviewed by: Professor Steve Graham

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

Symptoms of a broken system: the gender gaps in COVID-19 decision making
https://gh.bmj.com/content/5/10/e003549

This article provides quantitative data of 87 countries, highlighting the lack of women’s voices and opinions in COVID-19 decision-making bodies.

> COVID-19 has followed suite in the global trend of excluding women’s voices. Of the 115 identified COVID-19 decision making and expert task forces, only 3.5% have equal gender membership, 11.4% a female majority, and 85.2% are composed of a male majority.

> In this article, gender was determined based on prefixes, pronouns and online bibliographies.

> The authors note that information surrounding task force composition and membership criteria was not easily publicly accessible for the majority of United Nations Member States, which hindered the ability to hold countries accountable to previously made commitments regarding gender-inclusive global health governance.
> When governance is not inclusive of gender, geography, sexual orientation, race, socio-economic status or disciplines within and beyond health, the system becomes broken.

> Representation is necessary because the default governance mode is losing out on key perspectives and expertise. Women’s voices are important in decision making that affects women. This is because response measures often do not account for women’s increased exposure to domestic and sexual violence or their loss of access to essential health services. Furthermore, many lockdown policies do not consider maternal and reproductive health service as essential care.

> Effective and functional healthcare systems bold systemic changes that ensure gender-responsive and intersectional practices are the norm – rather than the exception.

> Closed-door traditional forms of governance must be transformed into open, inclusive and transparent communication and decision-making.

> Data collection and governance policies include sex and gender data and strive for an intersectionality approach that includes going beyond binary representation in order to produce results that are inclusive of the full gender spectrum.

Reviewed by: Professor Julie Bines
IMMUNOLOGY

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

SARS-CoV-2 antibody testing in a UK population: detectable IgG for up to 20 weeks post infection (not peer reviewed)
https://www.medrxiv.org/content/10.1101/2020.09.29.20201509v1

- Measuring SARS-CoV-2 specific antibodies is vital for building biobanks of convalescent sera for treatment, monitoring immune response to infection and assessing responses to vaccination programmes, but there is currently no standardised assay or reference standard to assess serological assays.

- This study reported on the longevity of IgG responses against SARS-CoV-2, and described a “pseudo gold standard” to evaluate serological assays, including the validation of a UK-RTC AbC-19 point of care lateral flow immunoassay (against S1 domain of the spike protein).

  - This “standard” is derived from testing of 880 pre-pandemic (n=223) and COVID-19 pandemic SARS-CoV-2 PCR+/PCR- blood samples (n=657) from within Northern Ireland using three commercial assays, Roche (IgG/IgM/IgA against N protein), Abbott (IgG against N protein), and Euroimmun (IgG against the S1 protein).

- IgG antibodies were detected in individuals across all three immunoassays used up to week 20 (day 140); median antibody levels for all tests had dropped below the positivity cut off by week 21.

- Pseudo gold-standard: seropositive: antibody positive by two or more immunoassays (n=348); seronegative: negative antibody result on two or more immunoassays (n=510).

- When assessed against the pseudo gold standard,
  - Euroimmun: highest accuracy (sensitivity: 98.9%, specificity: 99.2%, accuracy: 99.1%).
  - Roche: highest sensitivity and high accuracy (sensitivity: 99.4%, specificity: 96.7%, accuracy: 97.8%).
  - Abbott: poor sensitivity but had the highest specificity (Sensitivity: 86.8%, specificity: 99.2%, accuracy: 94.2%).
  - AbC-19 LFIA: sensitivity of 97.7% and specificity of 100% and demonstrated strong correlation against the commercial assays (Abbott r=0.86; Euroimmun r=0.88; Roche r=0.83).

- IgG antibodies persisted for 20 weeks for the majority of individuals in this study, despite significant decline after 90 days.

- Further studies are needed on large cohorts with sequential antibody results performed on symptomatic and asymptomatic, as well as mild and severe COVID-19 individuals.

- Limitations: Potential biases in the recruitment, with a high number of positive participants (n=348; 40.9%). Feasibility of finger-prick LFIA not tested (use of venous blood in this study).

Reviewed by: Dr Ryan Toh
INFECTION CONTROL

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

Characteristics associated with adults remembering to wash hands in multiple situations before and during the COVID-19 pandemic — United States, October 2019 and June 2020

https://www.cdc.gov/mmwr/volumes/69/wr/mm6940a2.htm?s_cid=mm6940a2_w

> Hand hygiene is an important measure to prevent the spread of COVID-19, but little is known about how handwashing behaviour has changed since the start of the pandemic.

> Methods:

− An online survey conducted in October 2019 (n=3624, 77.5% response rate) and June 2020 (n=4053, 63.7% response rate) assessed situational handwashing in US adults.

− Participants were asked if they were likely to wash their hands in the following situations: after using a bathroom at home; after using a bathroom in public; after coughing, sneezing, or blowing one’s nose; before eating at home; before eating at a restaurant; before preparing food at home.

− Samples were weighted to match the US population across age, sex, annual household income, race/ethnicity, household size, education, US Census division and residence in a metropolitan area.

− Differences in percentages from 2019 to 2020 were considered statistically significant when confidence intervals were not overlapping; multivariate logistic regression was used to estimate odds ratios for the association between remembering to wash hands and year.

> Results:

− In 2020 participants reported higher rates of handwashing before eating at home and before eating at a restaurant, and after coughing, sneezing, or blowing their nose than in 2019. Despite the overall increase, <75% of participants washed their hands in these situations in 2020.

− Irrespective of year, men were less likely than women to remember to wash their hands before eating at a restaurant, before preparing food, after using the bathroom at home and after experiencing respiratory symptoms.

− Young adults (18-24 years) were less likely to remember to wash their hands before eating at a restaurant, before preparing food, and after having respiratory symptoms than adults aged 45-74 years.

− White participants were less likely to remember to wash their hands before eating at home, before eating in a restaurant, and after experiencing respiratory symptoms than Black and Hispanic participants.
> Limitations: cross-sectional design cannot evaluate if a change in handwashing was truly related to the pandemic; those who chose to participate in the survey may not be representative of the general population; self-reported answers may be affected by recall bias or social desirability bias.

> This study has highlighted the need to target certain socio-demographic groups to improve situational handwashing.

Reviewed by: Dr Samantha Bannister
PERINATAL HEALTH

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

Change in obstetric attendance and activities during the COVID-19 pandemic
https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30779-9/fulltext

> This article examines whether an increase in stillbirths at a large London hospital during the first wave of SARS-CoV-2 may have been related to decreased attendance and activities.

> Rates of prenatal care appointments, unscheduled triage service usage and the number of births were analysed from February to June of 2019 and compared with the same dates in 2020.
  - Subgroup analysis divided pre-lockdown and lockdown (late March to mid-June).
  - Results reported as incident rate ratios with 95% CI.

> The rate of prenatal care scheduled appointments did not change (IRR 0.98)
  - There were significantly fewer obstetrical triage visits in the 2020 time period (IRR 0.81)
  - The rate of hospital births decreased (IRR 0.94), but only significantly so for the lockdown period (IRR 0.89).

> Discussion: decrease in care-seeking (19% fall in obstetric triage visits with only 6% fall in birth rate) may contribute to the observed increased rate of stillbirths.

> Limitations: data from years prior to 2019 was unavailable and therefore, cannot rule out that the observed trend was present prior to COVID-19.

Reviewed by: Professor Suzanne M Garland

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

Rooming-in for well term infants born to asymptomatic mothers with COVID-19

> A small pilot trial to investigate if rooming-in is safe for term/near-term infants born to asymptomatic/mildly symptomatic mothers with COVID-19.

> Temporary separation of newborns from their mothers has been recommended due to COVID-19, but these recommendations have been questioned due to the risk of interruption of beneficial effects of bonding and breastfeeding.

> The American Academy of Pediatrics recommends rooming-in in a single room, maintaining a distance of at least six feet between mother and infant with a curtain barrier, and requiring the mother to wear a mask and perform hand hygiene before breastfeeding.

> 49 mother-infant dyads were included: Four mothers were mildly symptomatic, 45 were asymptomatic.
  - In this cohort, 48 infants tested negative for SARS-CoV-2 by RTPCR.
− The only infant that tested positive at 24 hours post-birth had a repeat test which was negative at 48 hours of age.

− At telehealth follow-up two weeks post-birth, all infants were asymptomatic, and none had respiratory distress.

> Conclusion: rooming-in can be considered for term/near-term infants with asymptomatic mothers with COVID-19 with appropriate infection control measures.

Reviewed by: Professor Suzanne M Garland
With children going back to school, here is a free online course aimed at teenagers and young adults, where 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

SARS-CoV-2 infections in Italian schools: preliminary findings after one month of school opening during the second wave of the pandemic (not peer reviewed)

https://www.medrxiv.org/content/10.1101/2020.10.10.20210328v1

- This study aims to provide preliminary information about the number of SARS-CoV-2 cases among students attending Italian schools.

- As of 5th October 2020, a total of 1350 cases of SARS-CoV-2 infections have occurred in schools (involving 1059 students, 145 teachers and 146 other school members), for a total of 1212 out of 65,104 (1.8%) Italian schools involved.

- National schools reported only one case of SARS-CoV-2 infection in more than 90% of cases, and only one high school had a cluster of more than ten cases.

- The detection of one or more SARS-CoV-2 infections led to the closure of 192 (14.2%) schools, more frequently nursery/kindergartens.

- Findings support the low transmission of SARS-CoV-2 within schools, at least among younger students. However, entire schools are frequently closed in fear of larger outbreaks.

- Continuous monitoring of school settings are needed to better understand the impact of schools on the pandemic and provide guidelines that better consider different risks within different age groups.
Lopinavir–ritonavir in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial

https://www.thelancet.com/action/showPdf?pii=S0140-6736%2820%2932013-4

> The randomised evaluation of COVID-19 therapy (RECOVERY) trial is a large-scale randomised controlled trial that recruits patients from 176 hospitals in the UK. One arm of this trial investigated the drug combination lopinavir-ritonavir (n=1616 vs n=3424 usual care) as an antiviral treatment for COVID-19.

> Lopinavir is an HIV-1 protease inhibitor that also has in vitro inhibitory activity against SARS, MERS and SARS-CoV-2. Ritonavir increases the plasma half-life of lopinavir.

> Eligible patients had clinically suspected, or laboratory-confirmed SARS-CoV-2 and no medical history that would put the patient at substantial risk if they participated in the study.

> Intervention: Standard of care alone vs standard of care plus lopinavir 400 mg/ritonavir 10 mg orally every 12 hours for ten days or until discharge (if earlier). Patients were not blinded to the allocated treatment.

> The mean age of participants was 66.2 years, and the median duration of treatment was five days (IQR 2-8).

> Primary outcome:

  - No significant difference in 28-day mortality between both groups: 374/1616 (23%) lopinavir-ritonavir vs 767/3424 (22%) usual care (p=0.60).

> Secondary outcomes:

  - No significant difference in time to discharge alive from hospital between the two treatment groups (median 11 days [IQR 5 to >28] in both groups).

  - Disease progression requiring invasive mechanical ventilation was similar in both groups (risk ratio 1.09, 0.99-1.20, p=0.092).

  - No significant difference in requirement for haemofiltration, renal dialysis or frequency of new cardiac arrhythmias.

> Limitations:

  - Unclear whether the dose of lopinavir-ritonavir used would achieve inhibitory concentrations for SARS-CoV-2 in the lungs. However, pharmacokinetic analysis of a range of accepted SARS-CoV-2 antiviral drugs has predicted that the doses used would achieve effective concentration.

  - Few intubated patients were enrolled in the study as the administration of oral preparations to patients who cannot swallow is unreasonable, and crushing the medication to insert down a feeding tube results in unreliable bioavailability and potential tube blockage.

Reviewed by: Dr Amanda Gwee
TRANSMISSION

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

Scientific Brief: SARS-CoV-2 and potential airborne transmission

> CDC update on characteristics of SARS-CoV-2 transmission.

> Respiratory viruses are transmitted through three mechanisms: contact, droplet and airborne.

  - Contact: direct contact with an infected person.

  - Droplet: produced during exhalation (e.g. breathing, speaking, singing, etc.). Larger droplets fall out of the air rapidly within seconds to minutes close to the source (generally within six feet).

  - Airborne: small droplets and particles can remain suspended for many minutes to hours and travel far from the source (>6 feet). Airborne transmission means that there is exposure to small droplets and particles at greater distances over longer times.

  “Aerosol” refers to smaller droplets and particles, and also describes the collection of these particles in the air. Aerosol-generating procedures include intubation and bronchoscopy that produce small droplets/particles.

> People are primarily infected with SARS-CoV-2 through exposure to respiratory droplets as close contacts, not through airborne transmission.

> Airborne spread of SARS-CoV-2 is uncommon but possible. It has occurred in specific circumstances, where there has been an infected person producing droplets for >30 minutes - multiple hours in an enclosed space.

> Ventilation and avoidance of crowded indoor spaces are important for the prevention of airborne transmission of SARS-CoV-2.

> There is no current evidence to suggest that special engineering controls (such as those used to prevent measles and tuberculosis infection) are required in the healthcare setting. SARS-CoV-2 has a lower risk of airborne transmission compared with measles and tuberculosis, and transmission is similar to most other common respiratory viruses.

> There are still many features of SARS-CoV-2 that are not known - including the proportion of infections that are spread by airborne transmission and the infectious dose (number of virions required for infection to occur).

Reviewed by: Dr Wonie Uahwatanasakul
Defining the role of asymptomatic and pre-symptomatic SARS-CoV-2 transmission - a living systematic review (not peer reviewed)
https://www.medrxiv.org/content/10.1101/2020.09.01.20135194v2

> This systematic review summarises the secondary attack rates amongst the contacts of asymptomatic or pre-symptomatic individuals with SARS-CoV-2. The secondary attack rate is the probability an infected individual will transmit the disease to a susceptible individual. The findings would indicate their degree of contagiousness and their role in driving the pandemic.

> Using designated search terms and eight databases between 30th December 2019 and 21st May 2020, the authors identified 928 articles. Nineteen studies were included in the review.

> Nine studies reported the contact tracing of asymptomatic patients. 13 studies reported transmission during the pre-symptomatic period.

> Those who were asymptomatic throughout the disease course had fewer secondary infections than symptomatic and pre-symptomatic individuals.

> Asymptomatic cases transmitted SARS-CoV-2 to others at the secondary attack rates of 0% to 2.8%. In contrast, symptomatic cases had secondary attack rates between 0.7% and 16.2%.

> Secondary attack rates during the pre-symptomatic period ranged from 0% to 31.8%.

> Attack rates were lower in those wearing masks at 8.1% compared with 19.0% of those not wearing masks.

> Transmission events were associated with living with the patient or group activities such as sharing meals and playing board games.

> In household settings, it was difficult to differentiate between transmission during the pre-symptomatic period and symptomatic transmission.

> Implications: Pre-symptomatic transmission may contribute substantially to transmission in settings where people spend time together in the same environment, such as nursing homes, homeless shelters, prisons, cruise ships, and meat-packing plants. This implication highlights the importance of mitigation measures and surveillance to identify patients early in the disease course to prevent onward transmission inside the facility.

> The strengths of this systematic review were:

> It was a systematic living review examining SARS-CoV-2 transmission through contact tracing and outbreak investigation studies.

> The authors only included studies with clear case definitions.

> They included studies available in Chinese and clarified the symptomatology of the cases directly with the authors.

> The limitations of the review were: It excluded studies that had unclear case definitions or did not provide the contact number. They did not produce a summary estimate of the included studies due to anticipated heterogeneity. Limitations from the individual studies include imprecision from small study size or sources of bias in estimating the secondary attack rate. There was no age breakdown.
Research gaps: Future studies require a clear and comprehensive case definition that defines the major, minor, or atypical symptoms. This definition can help quantify more accurately the contribution of asymptomatic and pre-symptomatic SARS-CoV-2 transmission.

In conclusion, the low secondary attack rates of asymptomatic patients are suggestive of limited infectiousness or shorter duration of infectiousness. Pre-symptomatic patients appear to transmit efficiently, especially within households. This needs to be confirmed for children as well.

Reviewed by: Professor Fiona Russell
The effect of temperature on persistence of SARS-CoV-2 on common surfaces

The transmission of SARS-CoV-2 appears primarily to be via aerosols with recent data demonstrating the virus can remain infectious in airborne particles for more than three hours. Fomites transmission is also an important route of SARS-CoV-2 transmission, with handwashing having been recommended earlier at the beginning of the pandemic. This study provides additional environmental stability data of SARS-CoV-2 under different temperature and humidity conditions for a range of common surfaces.

> SARS-CoV-2 isolates provided by the Peter Doherty Institute (Victoria, Australia) were cultured with four passages on Vero E6 cells and diluted to a final concentration at 3.38 x 10^5/10 ul (which equates to a Ct-value ~14 for N, E and RdRp gene) in a defined organic matrix mimicking the composition of body secretions. 10uL of the suspension was inoculated onto coupons (1-1.5cm²) prepared from different surface materials. The coupons with virus inoculations were then exposed to different temperature and humidity conditions. After certain exposure times, the infectivity of recovered viruses from different surfaces and at different conditions was measured through cell culture by scoring cytopathic effects/ viral titre.

> **Non-porous surfaces**: glass, polymer banknotes, stainless steel, vinyl, paper banknotes

  - At 20°C, the virus was detectable for 28 days post inoculation from all non-porous surfaces.
  - At 30°C, the virus was detectable for 21 days post inoculation from paper bank notes (with 1 log reduction of virus recovered).
  - At 30°C, the virus was detectable for seven days post inoculation from stainless steel, polymer notes, and glass.
  - At 30°C, the virus was detectable for three days post inoculation from vinyl.
  - At 40°C, the virus was detectable for three days post inoculation from all non-porous surfaces (with 4-log reduction).

> **Porous surfaces**: cotton cloth

  - At 20°C, the recovery of virus on porous material was reduced compared with non-porous material with no infectious virus recovered after 14 days.
    - Viral reduction occurred soon after application of the virus to the cotton, suggesting an immediate absorption effect.
  - At 30°C, the virus was detectable for three days post inoculation from cotton cloth.
  - At 40°C, the virus was detectable for one day post inoculation from cotton cloth.
> **Conclusion:** the study provides crucial data for current mitigation strategies in reducing the viral transmission. The persistence of infectious viruses on non-porous surfaces (at least 28 days at 20°C and 50% humidity), especially on stainless steel, on glass and banknotes would be a potential source of transmission.

Reviewed by: Dr Lien Anh Ha Do
OTHER RESOURCES

All COVID-19 literature

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

Australian Government

Burnet Institute research findings, policy and technical reports
https://www.burnet.edu.au/covid-19//36_know_c19_hub

COVID-19 and the kidney, currently the recommended US resource
http://www.nephjc.com/covid19

Daily updates on COVID-19 literature compiled by Canadian medical students
https://docs.google.com/forms/u/0/d/e/1FAIpQLSfOxCoAuVLV0aJdf_z2uWV7r3FaPzAOir86q9ZXBcTZ1DcGE_Nw/formResponse

Focuses on paediatric clinical, epidemiological, transmission and neonatal aspects

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

National COVID-19 clinical evidence taskforce: continually updated evidence-based clinical guidelines
https://covid19evidence.net.au/

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

Oxford COVID-19 Evidence Service
https://www.cebm.net/oxford-covid-19/

https://phe.library.koha-pts.co.uk/covid19rapidreviews/

Retracted coronavirus (COVID-19) papers

Scimex.org – breaking science news portal: COVID-19 stories (research and expert commentary)
https://www.covid19-hpc-consortium.org/

University of Birmingham COVID-19 Research Briefing

Victorian Department of Health and Human Services

WHO Rolling updates on COVID-19

WHO COVID-19 dashboard
https://covid19.who.int/
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