COVID-19 KIDS RESEARCH EVIDENCE UPDATE

WHAT THE MELBOURNE CHILDREN'S CLINICIANS, SCIENTISTS, EPIDEMIOLOGISTS, AND MEDICAL STUDENTS HAVE BEEN READING THIS WEEK
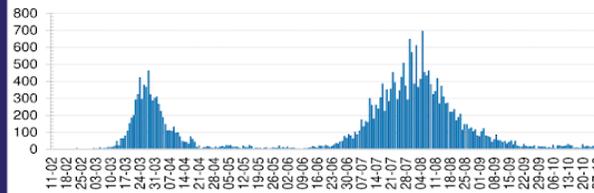
Weekly Update No. 28
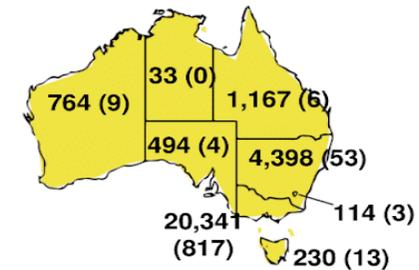29th October 2020

Australian Government
Department of Health

BE COVIDSAFE

CURRENT STATUS OF CONFIRMED CASES

27,541	905	25,055
Total cases	Total deaths	Cases recovered

1

CURRENT CASES
INTENSIVE CARE UNITS (ICU)

ACT	NSW	NT	QLD	SA	TAS	VIC	WA
0	1	0	0	0	0	0	0

15

CURRENT CASES
ADMITTED TO HOSPITALS

ACT	NSW	NT	QLD	SA	TAS	VIC	WA
0	8	0	2	0	0	5	0

8,598,558

0.3% POSITIVE

TOTAL TESTS CONDUCTED

ACT	NSW	NT	QLD
105,163	3,000,641	57,069	1,219,570
POSITIVE 0.1%	POSITIVE 0.1%	POSITIVE 0.1%	POSITIVE 0.1%

SA	TAS	VIC	WA
538,497	115,108	3,081,980	480,530
POSITIVE 0.1%	POSITIVE 0.2%	POSITIVE 0.7%	POSITIVE 0.2%

DAILY NUMBER OF REPORTED CASES

CASES IN AGED CARE SERVICES

Confirmed Cases	Austra lia	ACT	NSW	NT	QLD	SA	TAS	VIC	WA
Residential Care Recipients	2049 [1365] (683)	0	61 [33] (28)	0	1 (1)	0	1 (1)	1986 [1332] (653)	0
In Home Care Recipients	82 [74] (8)	0	13 [13]	0	8 [8]	1 [1]	5 [3] (2)	54 [49] (5)	1 (1)

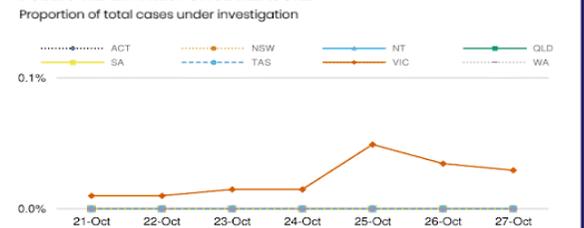Cases in care recipients [recovered] (deaths)

CASES BY AGE GROUP AND SEX

Male / Female

DEATHS BY AGE GROUP AND SEX

Male / Female

CASES (DEATHS) BY STATE AND TERRITORIES

764 (9)
33 (0)
1,167 (6)
494 (4)
4,398 (53)
20,341 (817)
114 (3)
230 (13)
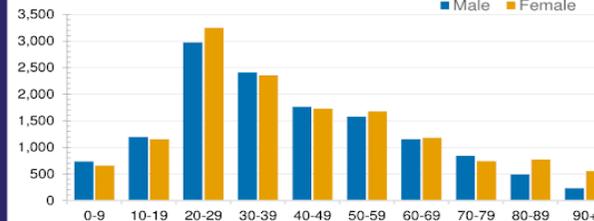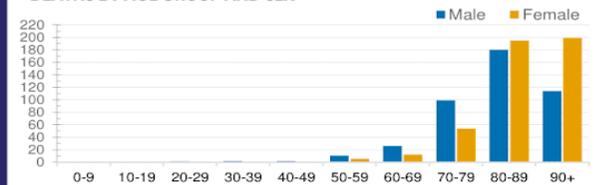
CASES BY SOURCE OF INFECTION

Australia (% of all confirmed cases)

20.01%	62.24%	17.73%	0.02%

VIC, NSW, QLD, WA, SA, TAS, ACT, NT

0 — 7,000 — 14,000 — 21,000

- Overseas acquired
- Locally acquired - contact of a confirmed case
- Locally acquired - contact not identified
- Under investigation

PUBLIC HEALTH RESPONSE MEASURE

Proportion of total cases under investigation

ACT NSW NT QLD SA TAS VIC WA

21-Oct 22-Oct 23-Oct 24-Oct 25-Oct 26-Oct 27-Oct

Last updated 27 October 2020

This infographic is updated every afternoon based on the data we receive by 3.00pm from states and territories

Source: Australian Government: Department of health [Internet]. 2020 [updated 2020 October 27; cited 2020 October 28]
Available from: https://www.health.gov.au/resources/collections/coronavirus-covid-19-at-a-glance-infographic-collection

GUEST EDITORIAL

Professor Susan Sawyer - Group Leader, Population Health, Adolescent Health, Murdoch Children's Research Institute; Director, Centre of Adolescent Health, Royal Children's Hospital; Chair of Adolescent Health, Department of Paediatrics, The University of Melbourne

The 28th edition of the COVID-19 Kids Research Evidence Update is finally coinciding with good news; the Melbourne lockdown, one of the world's longest and most gruelling, will soon be coming to an end. Never has the number zero looked as sweet as it did for Victorians when earlier this week, we experienced our first day for many months of zero new cases and zero deaths. A milestone for Victoria, albeit bittersweet in the context of around 20,000 COVID-19 cases and over 800 deaths this year. Notwithstanding the controversies and challenges along the way, there is widespread appreciation that Victoria's success has been achieved as a result of consistent political leadership, a solid public health system, community support for evidence-informed decision making, and good old-fashioned grit.

Yet as we emerge out of this strict lockdown, for how long will we remember this long COVID-19 winter? In lightening up, we will still be required to limit social contact, maintain physical distancing, wear face masks and wash our hands frequently. How well will we comply? Some countries have managed well, such as South Korea, whose experience is reported this week (1). However, the authors of this report urge caution around translating their success to larger populations with more geographically widespread epidemics, where managing clusters through finding, testing, and isolating cases may be more difficult.

Certainly, global experience from Europe suggests that different parts of our population may struggle to comply, especially young people whose lives have so extraordinarily been put on hold. And while all Victorians have had their lives upended by COVID-19, it increasingly doesn't feel that "we're all in this together"; families, children and young people whose lives are disadvantaged by poverty, job insecurity, poor mental health, poor education and poor internet connections have been much worse off.

In my weekly clinic, I marvel at the resilience of many of my adolescent patients as they have negotiated the impact of this topsy-turvy year on their schooling, friendships, sports and cultural pursuits. Yet while the elderly bear the brunt of fatal COVID-19 disease, it is young people who will carry the long-term scars of the pandemic from disruptions to their education and future employment and the weight of national economic debt that their generation will inherit.

Different parts of the world are grappling with different versions of the same challenges. On an International Association for Adolescent Health webinar about COVID-19 and adolescents last week, a young Indonesian medical student described how much her life had changed over these past few months. She shared photographs of her pre-COVID-19 life where, just like Australian medical students, long hours of study were happily interspersed with fun times socialising with friends, eating out, and travel to interesting places.

Fast forward, and her current photos were all tinged with the pale blue of PPE. She described huge case numbers and the daily fear of infection - not for herself, but for her older relatives.

In this editorial I wish to highlight three papers reviewed by our capable medical students which underline some of the common elements required by communities to maintain behavioural limit setting, namely the importance of poverty reduction, education and wider aspects of institutional trust.

The first is a study from the U.S. that reports short-term effects of COVID-19 on parent-child psychological well-being (2). Undertaken in the USA early in the pandemic, the authors utilised a sample of casually employed adults who had coincidentally been surveyed about their employment conditions before the health crisis. A subsample of parents with children aged 2-7 years were subsequently asked a set of questions about the impact of the pandemic on employment and financial stress and other worries on parent and child well-being. Even in the very short term, there was significant deterioration in parent-reported daily negative mood since the start of the crisis. Many families had experienced multiple hardships including job losses, income loss, caregiver burdens, and illness. Both parents' and children's well-being was strongly associated with the number of crisis-related hardships that the family experienced.

This work is consistent with previous studies about economic downturns which reveal that adult mental health worsens in response to long-term deterioration in economic conditions (3, 4), and that family poverty affects children's and adolescents' mental health (5, 6). Victorian health services are experiencing significantly increased presentations of children and adolescents with various forms of emotional distress. Studies like this (2) are a reminder that while mental health services are needed, the economic measures that have been put in place in Australia to support jobs and safeguard family income are incredibly important protectors of parent and child mental health, both in the short- and longer-term.

The second paper explores factors associated with belief in misinformation about COVID-19 and its broader public health implications (7). Beyond implanting false information, the particular concerns of the "infodemic" are that these beliefs then contribute to the rejection of information from expert authorities with risks to public health, including vaccine hesitancy. The study used five national samples from the UK, Ireland, Spain, Mexico and the USA to examine predictors of belief in the most common statements about the virus that contain misinformation. Reassuringly, the authors found that public belief in misinformation (e.g. that COVID-19 was manufactured in a laboratory in Wuhan) was not particularly common. However, in each country, a substantial proportion viewed misinformation as highly reliable. Importantly, the authors found that increased susceptibility to misinformation negatively affected people's self-reported compliance with public health guidance about COVID-19 and belief in the value of a COVID-19 vaccine. Across the surveys, higher trust in scientists and higher numeracy skills were associated with lower susceptibility to coronavirus-related misinformation.

The third paper is a commentary in the New England Journal of Medicine that addressed the emotional well-being of clinicians (8). Even before the pandemic, the authors, who are experienced providers of peer support in the workplace, describe unacceptably high rates of burnout and suicide among clinicians. However, during the pandemic, grief from seeing so many patients die, personal fears of contracting the virus and infecting family members, and anger over health care disparities and other systems failures have added to the personable toll for clinicians. For some, these stressors have caused or exacerbated burnout, depression, or post-traumatic stress disorder, and have been implicated in suicides. The authors affirmed that clinicians' emotional stress often comes from workplace issues that should be mitigated, such as inadequate resources; unsustainable clinical volume and hours; colleagues' unprofessional and problematic behaviours, including racist and sexist behaviour; and persistent health care disparities.

Just as trust in leadership has been critical to bringing the Victorian community along with the required behavioural changes during our prolonged lockdown, this commentary explicitly acknowledges the importance of institutional trust and the role of leadership. The authors noted that statements from organisational leaders about their desire to reduce clinician burnout will only erode trust in the absence of efforts to address its root causes. The authors also argue that institutional leadership should be accountable for clinician well-being. They suggested that leaders should empower clinicians to speak up about unsafe, highly stressful, or morally challenging workplace conditions and ensure that concerns are listened to and acted on. While the authors presented a range of strategies to respond to emotional distress, they highlighted the obligation of organisations to assess and address concerns in order to treat the root causes of emotional stress rather than merely treating symptoms.

In moving beyond our harsh lockdown, I hope that these papers may help us reflect on some of the reasons that have enabled our community to respond as well as it has. They may also serve as a reminder of how we cannot take this for granted but must continue to invest in strategies that will recharge our community's ability to remain resilient in the face of future adversity.

1.   Dighe, A., Cattarino, L., Cuomo-Dannenburg, G. et al. Response to COVID-19 in South Korea and implications for lifting stringent interventions. BMC Med 18, 321 (2020). https://doi.org/10.1186/s12916-020-01791-8.

2.   Gassman-Pines A, Ananat EO, Fitz-Henley J 2nd. COVID-19 and Parent-Child Psychological Well-being. Pediatrics. 2020 Oct;146(4):e2020007294. doi: 10.1542/peds.2020-007294. Epub 2020 6th August. PMID: 32764151; PMCID: PMC7546085.

3.   Ananat EO, Gassman-Pines A, Francis DV, Gibson-Davis CM. Linking job loss, inequality, mental health, and education. Science. 2017 16th June;356(6343):1127-1128. doi: 10.1126/science.aam5347. PMID: 28619903.

4.   Catalano R, Goldman-Mellor S, Saxton K, Margerison-Zilko C, Subbaraman M, LeWinn K, Anderson E. The health effects of economic decline. Annu Rev Public Health. 2011;32:431-50. doi: 10.1146/annurev-publhealth-031210-101146. PMID: 21054175; PMCID: PMC3855327.

5.   Rutter M. Poverty and child mental health: natural experiments and social causation. JAMA. 2003 15th October;290(15):2063-4. doi: 10.1001/jama.290.15.2063. PMID: 14559963.

6.   Najman JM, Hayatbakhsh MR, Clavarino A, Bor W, O'Callaghan MJ, Williams GM. Family poverty over the early life course and recurrent adolescent and young adult anxiety and depression: a longitudinal study. Am J Public Health. 2010 Sep;100(9):1719-23. doi: 10.2105/AJPH.2009.180943. Epub 2010 15th July. PMID: 20634459; PMCID: PMC2920957.

7.   Roozenbeek J, Schneider CR, Dryhurst S, Kerr J, Freeman AL, Recchia G, van der Bles AM, van der Linden S. Susceptibility to misinformation about COVID-19 around the world. Royal Society Open Science. 2020;7(10):201199.

8.   Shapiro J, McDonald TB. Supporting Clinicians during Covid-19 and Beyond - Learning from Past Failures and Envisioning New Strategies. N Engl J Med. 2020 14th October. doi: 10.1056/NEJMp2024834. Epub ahead of print. PMID: 33053277

HIGHLIGHTS

> A study from the U.K. found a high prevalence of acute kidney injury in children with paediatric

> An increased presentation to emergency departments for physical and mental health-related issues post-COVID-19 in adults.

> Point-of-care testing for COVID-19 has reduced the time to availability of results, compared with centralised laboratory PCR, improving patient flow and allocation to COVID-19 wards.

> Reopening of college institutions poses a significant SARS-CoV-2 infection risk for college associated populations and their surrounding community.

> A study examining meat processing facilities in the U.S. with COVID-19 positive employees finds that racial and ethnic minority workers may be affected by COVID-19 disproportionately.

> South Korea's response involved rapid large-scale testing, social distancing measures, cluster-based contact tracing, and careful monitoring of high-risk contacts. Currently, it is not possible to estimate the extent to which each measure contributed to the low case counts in the country.

> The current estimate of deaths from COVID-19 in the U.S. may underestimate total mortality from the pandemic. There were 299,028 excess deaths occurring between 26th January - 3rd October 2020, of which 66.2% are estimated to be due to COVID-19.

> What is fake news? A survey examines the factors influencing false beliefs of COVID-19 and their effect on public health measure compliance and vaccine hesitancy.

> Community engagement is a fundamental component of outbreaks; however, there is concern over the lack of community involvement during the COVID-19 responses.

> Humoral and cellular immunity against SARS-CoV-2 was reviewed in the context of leading vaccine candidates - highlighting critical questions which remain unanswered.

> With over 90% of the population remaining susceptible to COVID-19, multiple interventions, including non-pharmacological, will need to be adopted.

> The COVID-19 pandemic has highlighted an urgent need to address the emotional well-being of clinicians by designing proactive support programs with peer support, timely access to services, and leadership accountability.

> An American study into the psychological well-being of parents and children during the COVID-19 pandemic found that both child and parent mental health deteriorated significantly and that paediatricians should screen for this, especially in vulnerable families.

> Series of case studies in Bangladesh support the need for early COVID-19 testing after birth, and that presence of severe comorbidities increase severity and mortality for COVID-19 positive neonates.

> Although there is limited high-quality evidence available to quantify the extent of SARS-CoV-2 transmission in schools, emerging evidence suggests that overall infection attack rates and SARS-CoV-2 positivity rates in schools are low.

> A retrospective cohort study from Guangzhou, China is the first study that provides epidemiologic and laboratory evidence that contaminated sewage might cause COVID-19 outbreaks.

> In a survey of 19 countries, current levels of readiness to accept a COVID-19 vaccine are insufficient to meet requirements for community immunity. Acceptance of a vaccine varies based on country, level of education, and age.

> Available data do not support more concern about vaccine associated-enhanced disease for COVID-19 vaccines that is appropriate for the development of any viral vaccine.

> Based on evidence from previous HIV-vaccine trials using an adenovirus-5 vector where there was an increased risk of HIV-1 acquisition among vaccinated men, there is concern regarding the use of this vector in a COVID-19 vaccine phase one trial.

CONTENTS

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ADULT MEDICINE

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

Residual clinical damage after COVID-19: A retrospective and prospective observational cohort study
https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0239570

> The aims of this study were to investigate whether COVID-19 leaves behind residual dysfunction and to identify patients who might benefit from post-discharge monitoring.

> The primary outcome was need of follow-up, defined as the presence at follow-up of at least one among respiratory rate (R.R.) >20 breaths/min, uncontrolled blood pressure (B.P.) requiring therapeutic change, moderate to very severe dyspnoea, malnutrition, or new-onset cognitive impairment, according to validated scores.

> Post-traumatic stress disorder (PTSD) and other psychiatric disorders served as secondary outcomes.

> Inclusion criteria were age >18 years and attendance at one Italian hospital (admitted or discharged from E.D.) from 25th February 2020 with confirmed COVID-19 infection. If patients had clinical and radiological findings of pneumonia, they were followed up in a specialised clinic. Included individuals attended that clinic between 7th April and 7th May.

> Hospital records were reviewed; further history is taken; examination performed; health status, nutritional status, and cognitive function evaluated; psychiatric evaluation performed.

> 185 patients were included. Median time from hospital discharge to follow-up was 23 days.

> At follow-up evaluation, 58 (31.3%) patients were dyspnoeic, 41 (22.2%) tachypnoeic, 10 (5.4%) malnourished, 106 (57.3%) at risk for malnutrition. Forty (21.6%) patients had uncontrolled BP requiring therapeutic change, and 47 (25.4%) new-onset cognitive impairment.

> A regression tree analysis, PaO_2/FiO_2, BMI at E.D. presentation, and age emerged as independent predictors of the need for follow-up. Patients with PaO_2/FiO_2 <324 and BMI ≥33 kg/m^2 had the highest odds to require follow-up. Among hospitalised patients, age ≥63 years, or age <63 plus non-invasive ventilation or diabetes identified those with the highest probability to need follow-up.

> PTSD was observed in 41 (22.2%) patients and was independently predicted by female gender and hospitalisation, the latter being protective (odds ratio, OR, 4.03, 95% confidence interval, CI 1.76 to 9.47, p 0.0011; OR 0.37, 95% CI 0.14 to 0.92, p 0.033, respectively).

> In total, 68.1% of patients had one of the primary or secondary outcomes requiring follow-up.

> Limitation; Only patients with pneumonia included.

> Conclusion; COVID-19 leaves behind physical and psychological dysfunctions. Follow-up programmes should be implemented for selected patients.

Reviewed by: Dr Martin Wright

DIAGNOSTICS & SAMPLING

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

Clinical impact of molecular point-of-care testing for suspected COVID-19 in hospital (COV-19POC): a prospective, interventional, non-randomised, controlled study
https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30454-9/fulltext

> This study describes the clinical impact and real-world diagnostic accuracy of point-of-care testing using the QIAstat-Dx Respiratory SARS-CoV-2 Panel (Qiagen, Hilden, Germany) in adults presenting with suspected COVID-19 during the first wave of the pandemic in the U.K.

  – Study design: prospective, interventional, non-randomised, controlled study.

  – Population: age 18 years or older, capacity to give consent, for whom a decision had been made for hospital admission in the acute medical unit, emergency department, or other acute areas, recruited within 24 hours of presentation, with acute respiratory illness, or otherwise suspected for COVID-19 infection.

  – Intervention: combined nose and throat swabs sample testing with the QIAstat-Dx Respiratory SARS-CoV-2 Panel platform in a dedicated testing hub in the acute medical unit detecting two target genes of SARS-CoV-2, ORF1b and the E gene, for which detection of either gene is reported as positive (n=500).

  – Comparator: an additional combined nose and throat swabs sample from the same individual was tested with laboratory PHE PCR platform targeting RdRp and E gene, for which detection of either gene is reported as positive (n=500).

  – Outcomes: Primary outcome - time to results. Pre-specified secondary outcomes: time from admission to arrival in a definitive clinical area, e.g., designated COVID-19 positive ward or negative ward based on test results, and among patients admitted for more than 24 hours: total number of bed moves before arriving in the correct location based on test results, duration of hospitalisation, the proportion of patients treated with antibiotics, the proportion of patients admitted to ICU, in-hospital and 30-day mortality, sensitivity, specificity, positive predictive value, negative predictive value, and overall diagnostic accuracy.

> Clinical utility

  – The median time to results during the study was 1.7 hours (IQR 1.6-1.9) in the point-of-care testing group and 21.3 hours (16.0- 27.9) with laboratory PCR in the control group, p<0.0001). The large difference in groups remained after controlling for sex, age, time of presentation, and severity of illness.

  – Patients confirmed positive for COVID-19 were 197 (39%) of 499 patients in the point-of-care testing group having PCR positive for SARS-CoV-2, compared with 155 (28%) of 555 patients in the control group.

- Of those patients admitted to hospital for at least 24 hours, 313 (73%) of 428 in the point-of-care testing group and 242 (57%) of 421 in the control group were transferred from assessment areas to the correct definitive clinical area (i.e., a COVID-19 positive or COVID-19 negative ward) on the basis of their test results.

- The median time from presentation to arrival in a definitive clinical area was eight hours (IQR 6-15) in the point-of-care testing group and 28.8 hours (23.5-38.9) in the control group.

- The mean total number of bed moves between admission and definitive ward arrival was 0.9 (SD 0.5) in the point-of-care testing group and 1.4 (0.7) in the control group.

> Diagnostic accuracy

- The QIAstat-Dx Respiratory SARS-CoV-2 Panel returned positive results in 176 of 177 positive cases (sensitivity 99.4%) and negative results in 288 of 292 negative cases (specificity 98.6%) using a composite reference standard of detection (doubly validated PCR to determine true positive and negative cases for comparison).

- While during the first seven days of the study, the sensitivity of the laboratory PHE RdRp assay was found to be very poor (62·5% [40·6–81·2]; 15 of 24 cases) compared with the QIAstat-Dx Respiratory SARS-CoV-2 Panel. The sensitivity of the Laboratory PHE PCR with combining RdRp and E gene target was improved to be 89·5% (83·6–93·9; 137 of 153 cases).

> Long delays in centralised laboratory PCR testing presents challenges for allocation of COVID-19 patients to dedicated wards.

> The use of point-of-care testing led to a large reduction in the time to availability of results compared with laboratory PCR and was associated with improvements in infection control measures and patient flow, with patients spending around one day less in assessment areas.

Reviewed by: Dr Lien Anh Ha Do

EPIDEMIOLOGY & PUBLIC HEALTH

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

Excess deaths associated with COVID-19, by age and race and ethnicity — United States, 26th January-3rd October, 2020.
https://www.cdc.gov/mmwr/volumes/69/wr/mm6942e2.htm

> The current estimate (on 15th October) of 216,025 deaths from COVID-19 in the United States may underestimate the total impact of the pandemic on mortality. Mortality estimates may be limited by a number of factors, including the availability and use of testing and inaccurate or incomplete reporting of cause of death information on death certificates.

> Measures of excess deaths have been used to estimate the impact of public health pandemics or disasters, especially when there are concerns regarding under ascertainment of deaths directly attributable to a given event or cause.

> Excess deaths are defined as the number of deaths from any cause that is above the expected number of deaths for a given place and time.

> This study compared the weekly number of deaths by age group and race/ethnicity occurring in 2020, to the average number in the same week during the 2015-2019 period and calculated the percentage change in 2020.

> Expected deaths were calculated using provisional mortality data from CDC's National Vital Statistics System (NVSS). Over dispersed Poisson regression models were used with spline terms to account for seasonal patterns.

> This report focused on excess deaths occurring in the United States from 26th January 2020 to 3rd October 2020.

> Results:

  – There were a total of 299,028 excess deaths that occurred during the reporting period; 66.2% of these deaths were attributed to COVID-19 and the remainder to other causes

  – Average percentage change in deaths compared to previous years was greatest for those aged 25-44 years (26.5% above average) and Hispanic persons.

  – There was a 2.0% decrease in excess deaths in the <25 year age group, a 14.4% increase in the 45-64 year age group, a 24.1% increase in the 65-74 year age group, a 21.5% increase in the 75-84 year age group, and a 14.7% increase in the ≥85 year age group.

  – There was an 11.9% increase in excess deaths in White persons, a 53.6% increase in Hispanic persons, a 28.9% increase in American Indian or Alaska Native persons, a 32.9% increase in Black persons, a 36.6% increase in Asian persons, and 34.6% increase for those of other or unknown race/ethnicity.

> Limitations:

– The weighting of NVSS mortality data likely did not fully account for reporting lags, especially in more recent weeks.

– There is uncertainty in the models used to generate the expected numbers of deaths in a particular week.

– Different methods for estimating the expected number of deaths may lead to different results.

– Using average numbers of deaths from previous years might underestimate the total expected numbers because of population growth or aging, or because of increasing trends in other causes of mortality.

– Estimated excess deaths from COVID-19 may still underestimate actual numbers, because deaths from other causes may be due to misclassified COVID-19 or be indirectly caused by the pandemic.

Reviewed by: Dr Claire von Mollendorf

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

SARS-CoV-2 sequencing reveals rapid transmission from college student clusters resulting in morbidity and deaths in vulnerable populations (not peer reviewed)
https://www.medrxiv.org/content/10.1101/2020.10.12.20210294v1

> A substantial SARS-CoV-2 outbreak in La Crosse County, Wisconsin in September 2020 coincided with the return of students to in-person teaching at three local academic institutions.

> The authors identified two SARS-CoV-2 sub-strains associated with the outbreak using genomic sequencing.

> Molecular sequencing identified the transmission of the virus from college students into vulnerable non-student populations (two nursing facilities).

> The study only included SARS-CoV-2 positive nasopharyngeal swabs tested at the Gundersen Healthcare System's diagnostic laboratories.

> Results:

– The majority of cases were due to clusters related to two specific viral sub-strains.

– Over half of the 111 cases were identified in individuals 17-29 years of age. Nineteen (17.1%) cases due to these two sub-strains were identified in individuals 60 years or older.

– Phylogenetic trees identified four case groups of young people with five or more genetically identical genomes. This pattern was suggestive of rapid transmission of the SARS-CoV-2 virus amongst the younger age group most likely driven by student behaviours.

> Limitations: Nasopharyngeal swabs from other healthcare systems and or/public health laboratories were not tested. Swabs from college students living on-campus were not available.

> Conclusion:

– The authors' ability to establish direct genetic links using sequencing between a younger and older age group provides evidence that the risk of the rapid spread of SARS-CoV-2 among college-age individuals poses an immediate threat to older individuals in the surrounding community.

– This should be an additional factor considered with the reopening of college institutions.

Reviewed by: Dr Claire von Mollendorf

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

Coronavirus disease among workers in food processing, food manufacturing, and agriculture workplaces
https://wwwnc.cdc.gov/eid/article/27/1/20-3821_article

> Examined data from state health departments on COVID-19 positive U.S. workers in agricultural and meat processing facilities with findings of racial and ethnic minority workers being disproportionately affected by COVID-19.

> Methods:

– Data included: sex, age, race, and symptom status. Data on worker populations for each specific plant was unavailable, and so racial and ethnic distribution of COVID-19 positive employees as compared to the distribution of all workers in the industry.

> Results:

– 36 of 50 states provided data, and 33 of those had at least one confirmed COVID-19 case among food processing workers.

– 28/36 states reported racial data:

▪ Total employment rates: 52.6% White, 36.5% Hispanic or Latino, 5.9% Black, 3.5% Pacific Islander, 1.5% other.

▪ In employees positive for COVID-19, 72.8% were Hispanic or Latino, 16.8% White, 6.3% Black, 4.1% Pacific Islander.

– Overall, 83.2% of cases occurred among racial minorities in this study.

> Conclusions:

– Employees must be on-site, and thus spend large amounts of time in a high-density workplace.

– Results indicate a disproportionate burden of COVID-19 likely due to environmental working conditions.

– When implementing workplace interventions, care should be taken to observe the cultural and linguistic needs of individual workplace.

– Strategies suggested include providing PPE and increasing sanitisation/disinfection protocols.

> Limitations:

– Study limited by demographics data.

—   Workers may have been hesitant to report illness or symptoms leading to underestimation of cases among workers.

—   Workers are also members of their community and may have contracted COVID-19 outside of the workplace.

Reviewed by: Dr Wonie Uahwatanasakul

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

Response to COVID-19 in South Korea and implications for lifting stringent interventions
https://bmcmedicine.biomedcentral.com/articles/10.1186/s12916-020-01791-8

> The authors systematically reviewed each daily update on COVID-19 in South Korea (published by the Korea Centers for Disease Control and Prevention) for the period from 20th January to 13th July 2020.

> South Korea brought the transmission of SARS-CoV-2 under control with less stringent national social distancing policies relative to countries such as Italy, France, and the U.K.

> It was estimated that Rt (time-varying reproduction number) dropped below one in early April. Although estimates rose above one in May and early June, it reflected transmissibility within highly localised clusters in the Seoul Metropolitan Region rather than widespread national transmission.

> In early June, Rt dropped below one and remained low until the end of the study (13th July).

> Social distancing:

    – South Korea had not implemented a national "lockdown" but rather enforced short-term localised lockdowns in high-incidence regions like Daegu, where residents were asked to refrain from leaving their homes for at least two weeks.

    – People were asked to leave their houses only for daily necessities, healthcare, work. Many community spaces were closed.

    – The country transitioned to remote learning on 23rd February 2020 and schools reopened in late May.

    – High-risk facilities (karaoke rooms, cafes, nightlife venues) were subject to gathering bans or limited operation with possible legal action against non-compliance.

> Testing:

    – Testing capacity rapidly increased to 15,000-20,000/day with a turnaround time of 6-24 hours by the end of March.

    – Mass testing was used in high-risk facilities such as hospitals and care homes since 18th March.

> Contact tracing:

    – Cluster contact tracing accounted for 2/3 of the identified cases, while individual case-based contact tracing accounts for only 10% of South Korea's cumulative cases.

    – Mass testing was employed in identified clusters.

> Isolation:

    – Based on severity and risk factors, confirmed cases were isolated in a hospital, at home, or a residential treatment centre, and were monitored by staff or public health managers twice a day.

    – Close contacts of confirmed cases were asked to self-quarantine for 14 days and were monitored daily by public health managers.

> Of note, the number of SARS-CoV-2 infections in South Korea was far smaller than the USA or most European countries, and over 2/3 of the cases were linked to a few major clusters that were quickly identified and mass tested. Cluster-based management is more difficult in settings of widespread infection. Furthermore, South Korea has additional legal powers for quarantine, surveillance systems, and digital technologies that were introduced after the 2015 MERS outbreak, which may be lacking in other countries.

> Conclusion: South Korea's response involved rapid large-scale testing, social distancing measures, cluster-based contact tracing, careful monitoring of high-risk contacts and frequent monitoring of confirmed cases. Currently, it is not possible to estimate the extent to which each measure contributed to the low case counts in the country.

Reviewed by: Professor Jim Buttery

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

Susceptibility to misinformation about COVID-19 around the world
https://royalsocietypublishing.org/doi/10.1098/rsos.201199

The authors explore the factors associated with belief in misinformation during COVID-19 and their broader public health implications.

> Information and communication have played a crucial role in public health response to the Coronavirus, and conversely, misinformation is a serious threat to health and international relations. The World Health Organisation has termed this second pandemic the "infodemic".

> Misinformation about the Coronavirus has been commonplace and problematic, with half of the British population surveyed reporting exposure to fake news, often on a daily basis. Extreme conspiracy theories have resulted in the mass destruction of technology and property. Misinformation has a "double-dosing" effect, where it not only implants false information but also results in some to reject information from expert authorities and to jeopardise the public health cause.

> Some "risk factors" to misinformation include older age, lower education attainment, identification of minority status, conservatism, and lower trust in science, mainstream media, and government. These were primarily in the contexts of vaccine hesitancy and the 2016 U.S. presidential elections.

> The authors conducted a survey across five countries (UK, Ireland, Spain, USA, Mexico) to explore the predictors of susceptibility to misinformation, the influence on compliance with public health guidelines, and the effect on vaccine hesitancy. 700 age- and gender-balanced participants were recruited from each country except the U.K., who recruited 1,050 + 1,150 participants in two surveys one month apart.

> In two or more of the countries studied, susceptibility to misinformation was associated with younger age, lower numeracy ability, minority group identification, politically conservative, and those who accessed information from social media. Interestingly, trust in scientists led to less misinformation, but trust in politicians' ability to deal with COVID-19 led to an increase. It is important to note that the age correlation is opposite to what was previously found.

> Those who were less likely to get vaccinated or recommend vaccination include those susceptible to misinformation, younger, female, and low trust in scientists.

> Higher susceptibility to misinformation was the only significant predictor for lower compliance with public health guidance in Mexico, Spain, and USA.

> Mexican and Spanish samples were most likely to rate COVID-19 misinformation as reliable.

> This study contributes to our understanding of the prevalence and risk of misinformation when combating COVID-19, international similarity and heterogeneity in risk factors. It helps inform future strategies to increase high-quality evidence delivery to at-risk groups.

Reviewed by: Professor Jim Buttery

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

Summary of the effectiveness and harms of different non-pharmaceutical interventions
https://www.gov.uk/government/publications/summary-of-the-effectiveness-and-harms-of-different-non-pharmaceutical-interventions-16-september-2020?utm_source=842ac590-9aa1-4f10-bbed-6e7c360f40bf&utm_medium=email&utm_campaign=govuk-notifications&utm_content=daily

> A review was undertaken by Public Health England.

> COVID-19 cases are increasing across many countries with the latest data suggesting the doubling time may be as low as seven to eight days.

> COVID-19 related hospitalisations and intensive care bed usage have started to increase.

> With over 90% of the population remaining susceptible, multiple interventions rather than a single will need to be adopted.

> Some non-pharmaceutical interventions that should be considered for immediate introduction include:

   – Short period of lockdown to return incidence to low levels.

   – Working from home if possible

   – Restricting all contact within the home with members outside their primary households (except members of a support bubble)

   – Closure of all bars, restaurants, cafes, indoor gyms, and personal services

   – All university and college teaching to be online unless absolutely essential

> Many of these interventions will affect the poorest members of society to a greater extent. Measures will be needed urgently to mitigate these effects and to achieve equity and social justice.

> The more rapidly these measures are used, the quicker their effect will be. Some measures will need to remain for a substantial period of time.

> Clear, consistent communications will be critical, and a consistent package of measures should be adopted that does not appear to promote contradictory goals.

Reviewed by: Professor Fiona Russell

GLOBAL HEALTH

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

Community engagement for COVID-19 prevention and control: a rapid evidence synthesis
https://gh.bmj.com/content/5/10/e003188

> Community engagement is a fundamental component of outbreaks; however, there's concern over the lack of community involvement during the COVID-19 responses.

> This article performs a rapid review of the community engagement approaches in past epidemics to support more robust implementation within the COVID-19 response.

> For the review, three databases were searched in addition to extensive snowballing for grey literature. Previous epidemics were limited to Ebola, Zika, SARS, Middle East respiratory syndrome and H1N1 since 2000.

> Six main community engagement actors were identified: local leaders, community and faith-based organisations, community groups, health facility committees, individuals and key stakeholders.

> They worked on different functions including designing and planning, community entry and trust-building, social and behaviour change communication, risk communication, surveillance and tracing, and logistics and administration.

> There was a lack of documented engagement activities from high-income countries.

> The findings indicate that communities can play important and active roles in prevention and control.

> Accessing existing community engagement structures can help support acceptable and appropriate COVID-19 prevention and control measures.

Reviewed by: Dr Wonie Uahwatanasakul

IMMUNOLOGY

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

SARS-CoV-2 immunity: review and applications to phase 3 vaccine candidates
https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32137-1/fulltext

> This is a comprehensive review of the humoral and cellular immunity to SARS-CoV-2, and how this knowledge is applied to evaluate the COVID-19 vaccines currently in Phase 3 clinical trials.

> Current understanding of SARS-CoV-2 infection and development of immunity.

    – SARS-CoV-2 virion interacts with the ACE2 cellular receptor on host cells to gain entry into the cell.

    – Viral proteins can be recognised by pattern recognition receptors (e.g., TLR3, TLR4, and TLR7), leading to the release of danger-associated molecular patterns, the inflammatory response, and the activation of innate anti-viral pathways

    – The virus replicates in the cell and is released to infect more cells.

    – Recognition of the spike glycoprotein and nucleocapsid protein (structural proteins) by the B-cell receptor; B-cell produces antibodies and neutralising antibodies are targeting the spike glycoprotein.

    – Viral uptake by antigen-presenting cells, followed by activation of T cells; helper T cells (Th) produce cytokines (mainly IFNγ, IL-2, and TNFα), while CTL recognised and kill infected cells.

> Humoral Immunity to SARS-CoV-2

    – Spike glycoprotein consists of the receptor-binding domain (RBD) that interacts with ACE2; target for neutralising antibodies, which is important for viral neutralisation and viral clearance.

    – Most patients with COVID-19 or those who are convalescent generate virus-specific IgM, IgA, and IgG responses to viral surface glycoproteins; spike glycoprotein and the nucleocapsid protein.

    – Antibody titres were significantly higher in patients with the severe disease than they were in patients without the severe disease.

    – Longitudinal studies are needed to further understand the longevity of SARS-CoV-2-induced antibodies in populations and the role of antibodies in disease severity.

    – Sex and age influence antibody response; men and old age (60-85 years old) have higher anti-RBD and anti-spike glycoprotein than in women and young age (15-39 years old), respectively.

> Cellular immunity to SARS-CoV-2

- Most individuals develop T-cell responses (both Th and CTL) to SARS-CoV-2 within one to two weeks after symptom onset and produce mainly Th1 cytokines.

- Some individuals exposed to SARS-CoV-2 develop specific T-cell responses in the absence of specific antibodies.

- T-cells cross-reactive to SARS-CoV-2 spike glycoprotein have been documented in individuals who are not favourable for COVID-19, although the role of these cells in protection is unknown.

- Tfh and Th17 responses have also been documented, which may be important for antibody production and excessive inflammation, respectively.

- Frequency of CD4+ T-cells targeted to the spike glycoprotein correlates with neutralising antibody titres and may influence disease severity.

- Contribution of cellular immunity to protection against COVID-19 remains unclear.

> Vaccines against SARS-CoV-2

- Based on the US FDA guidelines, a COVID-19 vaccine would have to protect at least 50% of vaccinated people to be considered efficacious.

- A number of Phase 1 to 3 vaccine candidates were summarised; nine candidates are currently in Phase 3 trials, and details of each candidate are described in the paper.

- Most have exhibited acceptable safety profiles thus far, however concerns remain around the Gamelaya candidates (Russian Federation), and safety data has not been publicly released for the Johnson & Johnson candidate.

- Cold-chain requirements will post a significant logistical challenge for most candidates.

> Whilst there are concerns of antibody-dependent enhancement for SARS-CoV-2, there has been no evidence of this phenomenon found in animal or Phase 3 human studies to date.

> Critical questions remain unanswered, including the efficacy of vaccine candidates and the maintenance of immunity against SARS-CoV-2.

Reviewed by: Dr Ryan Toh

MENTAL HEALTH

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

Supporting clinicians during COVID-19 and beyond – learning from past failures and envisioning new strategies
https://www.nejm.org/doi/full/10.1056/NEJMp2024834

> The COVID-19 pandemic has highlighted an urgent need to address the emotional well-being of clinicians and has exposed the cultural and structural barriers causing exiting support systems to fail.

> Most existing frameworks are more reactive than proactive in anticipation of managing clinical, emotional pain associated with the challenging work of physicians.

> Strategies to design effective and useful emotional support programs for organisations:

– Create and provide funding for peer-support programs

– Prioritise reaching out to employees who may benefit from receiving help rather than relying on clinicians to seek help themselves

– Provide easily accessible and psychologically safe "reaching-in" services for clinicians – professional mental health services

▪ Confidential, affordable and accessible at any time

– Institutional leadership should be accountable for clinician well-being

▪ Empower other clinicians to speak up about unsafe, highly stressful or challenging workspace conditions

▪ Organisations have an obligation to assess and address concerns in order to treat the cause of the emotional distress

▪ Accountability among organisational leaders is vital

Reviewed by: Professor David Coghill

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

COVID-19 and Parent-Child Psychological Well-being
https://pediatrics.aappublications.org/content/146/4/e2020007294

> In this study researchers began with the hypothesis that the crisis has worsened parents' and children's psychological well-being. They also examine the extent of crisis-related hardships and evaluate the hypothesis that the accumulation of hardships will be associated with parent and child psychological well-being.

> Daily survey data were collected from hourly service workers with a young child (aged 2–7) in a large US city (N = 8,222 person-days from 645 individuals).

> Ordered models revealed that the frequency of parent-reported daily negative mood increased significantly since the start of the crisis.

> Many families have experienced hardships during the crisis, including job loss, income loss, caregiving burden, and illness.

> Both parents' and children's well-being in the post-crisis period was strongly associated with the number of crisis-related hardships that the family experienced.

> Consistent with the hypotheses, in families that have experienced multiple hardships related to the coronavirus disease 2019 crisis, both parents' and children's mental health is worse. As the crisis continues to unfold, paediatricians should screen for mental health, with particular attention to children whose families are especially vulnerable to economic and disease aspects of the crisis.

Reviewed by: Professor David Coghill

PERINATAL HEALTH

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

The direct and indirect impact of SARS-CoV-2 infections on neonates: a series of 26 cases in Bangladesh
https://pubmed.ncbi.nlm.nih.gov/33031143/

> Knowledge gap in the epidemiology of South Asian LMIC with COVID-19 cases, especially in neonates. This study examines 26 case reports of infected neonates in terms of clinical presentation and outcomes.

> Methods

– Examined hospital records, lab results, imaging studies, and follow up of the 26 patients from Dhaka's largest paediatric hospital from 29th March to 1st July 2020, and then from the respective COVID-19 hospital if a patient was transferred. Nasopharyngeal specimens were collected for SARS-CoV-2 PCR testing.

> Results:

– 26/83 tested neonates [31%] were positive for COVID-19 and included in the study, and 62% were boys. A subset of caregivers was also tested. 14 babies (53%) were in their first five days of life, and the median age was eight days. All babies were born at term.

– 25 cases had detailed data available, and all 25 presented with an additional diagnosis: Seven had signs of early-onset neonatal sepsis [EONS], five late-onset neonatal sepsis, two pneumonia, 11 serious non-communicable diseases (such as malformations, congenital heart disease, etc.). They were followed up for 27-75 days.

– Of the 26 COVID-19 positive neonates, eight died, three were lost to follow-up, 12 were healthy at the last follow-up, three were still sick. One of the EONS patients had respiratory distress, requiring supplemental oxygen.

– Oxygen and showed signs of disseminated intravascular coagulation and eventually died on the sixth day of hospitalisation, at the age of eight days. One presenting with pneumonia was admitted with perinatal asphyxia and HIE stage two, and congenital pneumonia with bilateral crepitations. The child died after two days, at the age of three days.

– Immediate caregivers from nine neonates (eight mothers and one grandmother) provided nasopharyngeal swab specimens during the time of specimen collection from the neonates; eight of them tested positive for SARS-CoV-2.

> Discussion:

– Of the eight who died, six had serious comorbidities (ruptured myelomeningocele, perinatal asphyxia, congenital heart disease, etc.), therefore difficult to determine COVID-19 role in the death. In the other two deaths, COVID-19 was believed to be the main contributor. Both showed bilateral ground-glass opacity, one with metabolic acidosis and one with DIC.

- COVID-19 likely amplifies severity and mortality of neonates with other morbidities, therefore worsening the health of already vulnerable patients.

- Half of the positive cases were tested in the first five days of life, indicating that early testing is essential to lessen potential complications such as late-onset sepsis.

> Limitations:

- The hospital in this study does not have a maternity ward, and neonates are only admitted here with serious conditions, therefore biasing findings towards more severe outcomes.

- The study did not include neonates who were asymptomatic with COVID-19.

- Follow-up was only for 75 days, and studies have shown that children with the virus can have long-term health consequences in the months that follow, such as multisystem inflammatory response.

Reviewed by: Professor Suzanne Garland

SCHOOLS

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

What is the evidence for transmission of COVID-19 by children in schools? A living systematic review (not peer reviewed)
https://www.medrxiv.org/content/10.1101/2020.10.11.20210658v1

> A systematic review and meta-analysis 11 studies (five cohorts and six cross-sectional) to investigate the extent of SARS-CoV-2 transmission in schools.

> Study quality was deemed to be low, with the risk of performance bias and attrition bias. The majority of studies included in the review were not peer-reviewed. This limits confidence in the results.

> Findings:

  – The pooled infection attack rates (IAR) of total study participants was 0.08%. IARs for students were 0.15%. IARs and for school staff were 0.70%.

  – Random effect meta-analysis of the cross-sectional studies showed positivity rates of SARS-CoV-2 was 8.74% among students, compared to 13.68% among school staff.

  – Transmission rates of student-to-student, student-to-staff, staff-to-student and staff-to-staff were 0.31%, 0.97%, 1.49% and 4.38% respectively in NSW Australia, which did not close schools during the beginning of COVID-19 pandemic.

  – IARs for <6 years old = 2.25%, for 6-12 years old = 0.92%, and 12-18 years old = 0% in NSW.

  – Clusters in educational facilities were identified in 1/5 reporting countries, and they were limited in number and size.

  – No gender differences were found for secondary infection (OR 1.44, P=0.49) or for SARS-CoV-2 positivity (OR 0.90, P=0.36) in schools.

  – Among study participants, the most frequently reported symptoms were anosmia (84.27%), ageusia (79.58%), myalgia (30.61%), fever (29.88%) and diarrhoea (29.15%).

  – A study from Sweden in which schools remained opened suggests that 5-19 year old children (6%) had similar seroprevalence to 20-49 year old adults.

> Effective implementation of interventions such as physical distancing, small-size class, cancellation of mass gatherings, and hand hygiene will likely limit further ability to study school transmission of SARS-CoV-2. Therefore differences in mitigation measures between settings make it difficult to understand child transmission and compare studies.

> Conclusion: Although there is limited high-quality evidence available to quantify the extent of SARS-CoV-2 transmission in schools, emerging evidence suggests that overall IAR and SARS-CoV-2 positivity rate in schools are low. Serosurveillence studies need to be conducted to monitor SARS-CoV-2 infection during school opening.

Reviewed by: Professor Fiona Russell

TRANSMISSION

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

Sewage as a possible transmission vehicle during a coronavirus disease 2019 outbreak in a densely populated community: Guangzhou, China, April 2020
https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1494/5920983

> This study examined a COVID-19 outbreak that occurred in a densely populated community in Guangzhou, China - which was investigated to identify modes of transmission.

> Eight cases in the community of 2,888 residents were identified: Case 1 and 2 frequented a market with an ongoing outbreak, cases 3 to 8 never visited in the market, lived in separate buildings and did not interact with cases 1 and 2.

> The community immediately surrounding the first two positive cases was placed on a lockdown (212 residents) in a hotel with an independent sewage system; each person stayed in a single occupancy room and not able to leave.

> An additional 112 residents of surrounding buildings (within 20 m of the two initial cases) were placed under involuntary home quarantine, while the remaining 2,552 residents were given voluntary stay-at-home orders.

> Environmental sampling from frequently touched surfaces, as well as samples from stools, floor drains and sinks from the washrooms, were collected and tested with RT-PCR.

> In-depth interviews were conducted with the eight people who tested positive to identify potential risk factors of transmission.

   – Cases 3 to 8 had no contact with the first two positive cases, nor did they attend the market with the original ongoing outbreak.

   – The sewage pipe for the toilet of cases 1 and 2 had a hole located a few centimetres above the ground - the study demonstrated that pouring water into the toilet of case 1 and 2 resulted in the water spewing out of this hole, and soaking the floor of the entrances to the building where cases 3 to 8 lived.

> It was hypothesised that based on the spatial distribution, onset dates, and contract history, cases 3 to 8 were infected by cases 1 and 2 through the leaked sewage.

> This was further supported by genome sequencing of the virus, demonstrating 99.996% identity.

> Highlights the importance of sewage management in preventing COVID-19 outbreaks, especially in densely populated urban, low-income communities with poor sanitation and hygiene conditions.

Reviewed by: Dr Wonie Uahwatanasakul

VACCINES

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

A global survey of potential acceptance of a COVID-19 vaccine.
https://www.nature.com/articles/s41591-020-1124-9

> This study surveyed 13,426 people in 19 countries to determine factors that could influence the acceptance of a COVID-19 vaccine and to determine possible acceptance rates.

> Respondents who reported higher levels of trust in information provided by their government were more likely to accept a vaccine and to take their employer's advice to take a vaccine.

> In total, 71.5% of respondents reported that they would be very or somewhat likely to accept a COVID-19 vaccine that was 'proven safe and effective'. 61.4% reported they would do so if their employer recommended it.

> Respondents from China reported the highest proportion of positive responses (88.6%) and the lowest proportion of negative responses (0.7%) if the vaccine was safe and effective. Respondents from China also reported the highest proportion of positive responses (83.7%) and the lowest proportion of negative responses (3.7%) if the vaccine was recommended by their employer.

> Respondents from Poland reported the highest proportion of negative responses (27.3%) if the vaccine was safe and effective.

> Respondents from Russia reported the lowest proportion of positive responses (54.9%) if the vaccine was proven safe and effective. Respondents from Russia also reported the highest proportion of negative responses (40.9%) and the lowest proportion of positive responses (27.1%) if the vaccine was recommended by their employer.

> Higher levels of education were positively associated with vaccine acceptance to both government and employer recommendations.

> Persons aged 18-24 years were the least likely to accept the vaccine.

> In most of the countries surveyed, current readiness to accept a COVID-19 vaccine is insufficient to meet requirements for community immunity.

> Recommendations:

 – Future vaccine communication strategies should build vaccine literacy and address specific concerns and misconceptions of different groups.

 – Employers should promote voluntary acceptance as opposed to mandatory vaccines.

 – Governments should focus on clear and consistent communication to build public confidence. They should explain how vaccines work and how they are developed.

> Limitations: This survey represents a snapshot in time as vaccine opinions are very dynamic. Subsequent surveys suggest that public hesitancy towards a COVID-19 vaccine has increased since this study.

> Most importantly - trust in government is strongly associated with vaccine acceptance and can contribute to public compliance with recommended actions.

> To build increased trust among the general population, the elements that define and build trust must be understood, and interventions crafted accordingly.

Reviewed by: Associate Professor Margie Danchin

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

Prospects for a safe COVID-19 vaccine
https://stm.sciencemag.org/content/early/2020/10/16/scitranslmed.abe0948/tab-pdf

> This study reviewed the literature and evaluated the possibility of enhanced disease caused by COVID-19 vaccines.

> For this review, the authors defined immune-associated enhanced disease as an infection that is made worse because the person has a pre-existing immune response against the pathogen.

> Vaccine associated-enhanced disease (VAED) was defined as an immune response to a vaccine that is causally linked to a higher risk of adverse outcomes upon infection compared to infection without prior vaccination.

> The phenomena of VAED was observed in the 1960s when children were given formalin-inactivated whole virus vaccines against RSV.

– Hospitalisation rates for severe RSV were higher in the formalin-inactivated vaccine group during these clinical trials.

– Potential mechanisms of VAED suggested that antibodies directed at non-protective fusion protein epitopes, a failure to elicit high-avidity neutralising antibodies to RSV fusion protein, aberrant antibody response to RSV proteins, activation of the complement pathway, and abnormal T-cell responses.

> A formalin-inactivated measles vaccine in the 1960s was also withdrawn because some children developed atypical measles with high fever, unusual petechial/papular rash and atypical pneumonia.

> An extensive study of the annual influenza vaccines has not revealed correlations between more severe illnesses and pre-existing immunity.

> Vaccines made from inactivated viruses do not have an intrinsic potential to elicit deleterious immune responses.

> So far, animal models of SARS-CoV-2 infection have not shown evidence of VAED after immunisation.

> Several COVID-19 vaccines expressing the SARS-CoV-2 spike protein have now been tested in rhesus macaque SARS-CoV-2 challenge models.

> Vaccines tested include:

– DNA vaccines

– An inactivated virus vaccine with an alum adjuvant

– An adenovirus vector vaccine

– A vaccine comprising mRNA encapsulated in lipid nanoparticles

> Protective efficacy has correlated with the titres of neutralising antibodies against the spike protein, although further analysis of T-cell immunity is needed.

> Analysis of serological signatures in COVID-19 revealed functional antibody responses to SARS-CoV-2, nucleocapsid proteins were elevated in those who died, whereas spike-specific antibody responses were enriched among convalescent individuals.

> In COVID-19, disease severity and death have been associated with higher amounts of inflammatory markers in the blood and increased concentrations of serum inflammatory cytokines and chemokines.

> Phase 3 trials will follow participants for at least one year to monitor efficacy outcomes and safety in the context of ongoing SARS-CoV-2 infection.

> In phase 2 and 3 trials using the chimp adenovirus vector vaccine, there have been early reports of two possible cases of transverse myelitis in trial participants, and this trial has been paused in the U.S. at the time of this review (19th October 2020).

> If judged safe and effective by regulating bodies based on efficacy clinical trials that could include up to 30,000 participants per trial, COVID-19 vaccines could be made more rapidly available to far larger numbers of people.

> The capacity to produce and deliver millions of vaccine doses has been accelerated in order to gain control of the pandemic. As a result, many people may be vaccinated before longer-term follow-up is possible.

> The foremost opportunity to identify whether a COVID-19 vaccine candidate has a risk of VAED will be in randomised, placebo-controlled phase 3 clinical trials.

> If data from phase 3 efficacy trials demonstrate that vaccine candidates meet the safety, efficacy, and quality standards set by regulators, then vaccine candidates may be licensed for use.

> The authors conclude available data do not support more concern about VAED for COVID-19 vaccines that is appropriate for the development of any viral vaccine.

Reviewed by: Associate Professor Margie Danchin

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

Use of adenovirus type-5 vectored vaccines: a cautionary tale

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)32156-5/fulltext?utm_content=143499475&utm_medium=social&utm_source=twitter&hss_channel=tw-27013292

> There is concern regarding the use of an adenovirus type-5 (Ad5) vector for a COVID-19 phase 1 vaccine trial.

> The STEP and PHAMBILI phase 2b trials that evaluated an Ad5 vectored HIV-1 vaccine both found an increased risk of HIV-1 acquisition among vaccinated men.

> Non-HIV vaccine trials that used similar Ad5 vectors in areas of high HIV prevalence could lead to an increased risk of HIV-1 acquisition in the vaccinated population.

   – This risk appears to be limited to men

> Non-human primate challenge study:

   – Rhesus macaques were injected with Ad5 then immunised with Simian Immunodeficiency Virus (SIV; based on Ad5 increased the risk of SIV acquisition from low-dose SIV penile challenge.

> Therefore, the authors are concerned about the use of Ad5 vector for SARS-CoV-2 as it could similarly increase the risk of HIV-1 acquisition among men who receive the vaccine.

Reviewed by: Professor Fiona Russell

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/

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

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

Public Health England COVID-19 Rapid Reviewed - Knowledge & Library Service
https://phelibrary.koha-ptfs.co.uk/covid19rapidreviews/

Retracted coronavirus (COVID-19) papers

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

Scimex.org – breaking science news portal: COVID-19 stories (research and expert commentary)
https://www.scimex.org/info/2019-20-coronavirus
https://www.covid19-hpc-consortium.org/

University of Birmingham COVID-19 Research Briefing
https://www.birmingham.ac.uk/university/colleges/mds/Coronavirus/COVID-19-research-briefing.aspx

Victorian Department of Health and Human Services
https://www.dhhs.vic.gov.au/coronavirus-covid-19-daily-update

WHO Rolling updates on COVID-19
https://www.who.int/emergencies/diseases/novel-coronavirus-2019/events-as-they-happen

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

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