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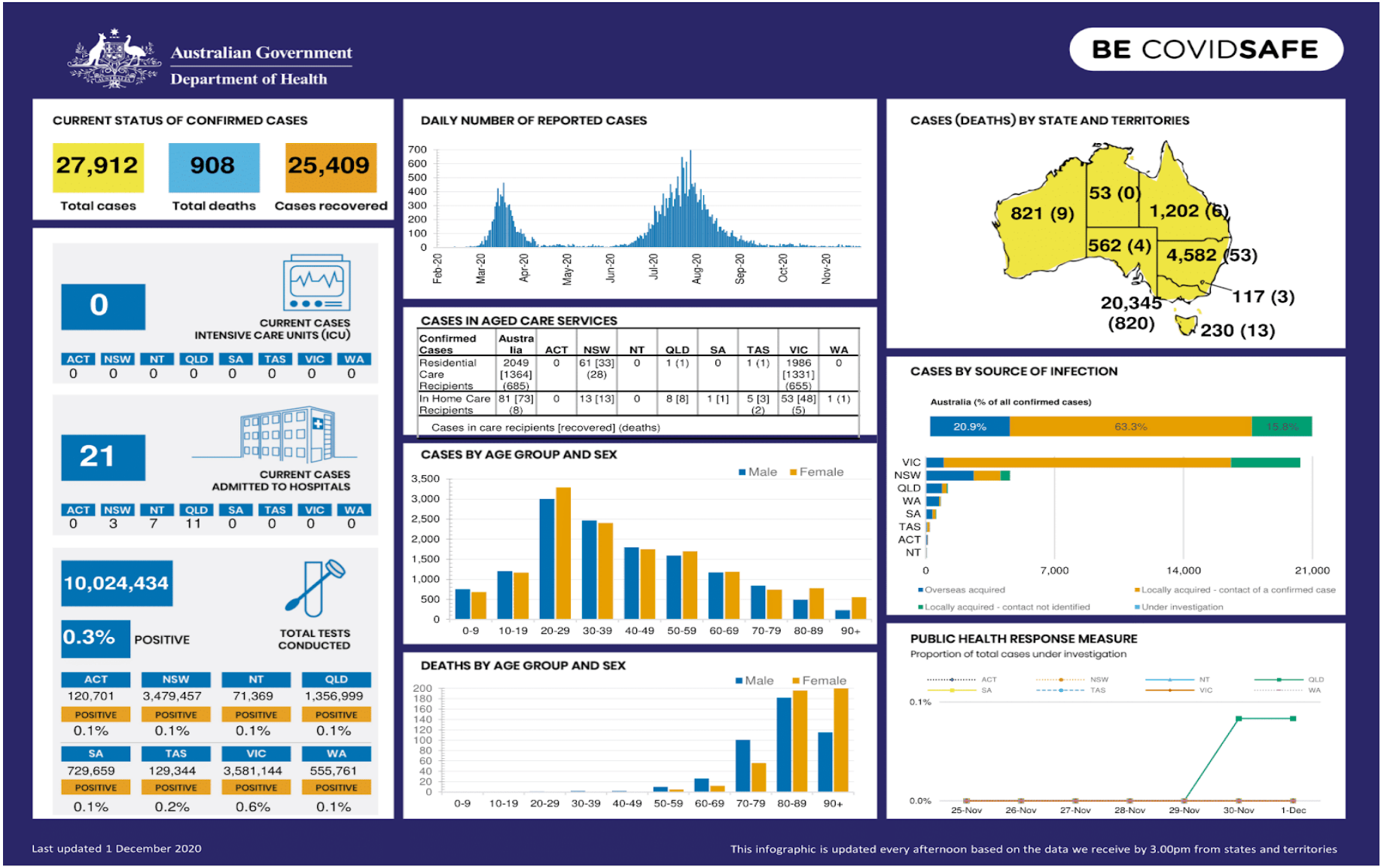
COVID-19 KIDS RESEARCH EVIDENCE UPDATE

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

Weekly Update No.31
4th December 2020



Source: Australian Government: Department of health [Internet]. 2020 [updated 2020 December 1; cited 2020 December 2]
Available from: https://www.health.gov.au/resources/collections/coronavirus-covid-19-at-a-glance-infographic-collection

GUEST EDITORIAL

Dr Louise Crowe[1-3], PhD MAPS and Prof Vicki Anderson[1-3], PhD MAPS
[1]Brain and Mind, MCRI, Melbourne, Australia
[2]Psychology Service, RCH, Melbourne, Australia
[3]School of Psychological Sciences, UoM, Melbourne, Australia

The impact of the COVID-19 pandemic on children with pre-existing medical and psychological conditions

The restrictions on movement, stay at home orders, and limitations on socialisation have meant a great upheaval for children and adolescents. It is expected that this will translate into a negative effect on child mental health and wellbeing. Anecdotal reports, and media coverage, highlight that children with pre-existing medical and psychological conditions have experienced additional concerns including loss of medical support and services because of healthcare changes (i.e., telehealth appointments only, no respite services or allied health therapies) and reduced access to home-based health services (e.g., nursing, allied health, respite care). While we anticipate that these children may be more vulnerable to stresses, such as those presented in the COVID-19 pandemic, resulting in higher levels of psychological symptoms compared with healthy children (1), it is likely that a proportion of children and families will be resilient and cope well with the challenges of 2020. While research on the impacts of the COVID-19 pandemic for this group of children is yet to emerge, data from previous disasters, such as Hurricane Katrina, have shown that children with chronic health conditions demonstrate negative psychological consequences including behaviour change and increased reporting of sadness and withdrawal (2). The additional burden of having a child with a chronic health condition has been reported by Van Tilburg et al., (3) who demonstrated that these parents had higher levels of stress and physical symptoms related to stress (i.e., stomach aches) than parents of healthy children. Children with chronic health conditions represent a large percentage of the patient population at the Royal Children's Hospital, the major tertiary paediatric hospital in Melbourne. Our study, investigating the mental health of children with pre-existing medical and psychological conditions, has analysed the responses of the first 50 children and their families during the COVID-19 pandemic. These findings confirm that children have experienced more loneliness, have been more fatigued and more worried. Parents reported that the most stressful element of the pandemic for children was the social isolation from their friends and extended family. Parents also reported that their children's healthcare needs were not being met as they were prior to the pandemic. Children were spending significantly more time on screens and watching T.V., for example prior to the pandemic only 10% of children were on screens more than 4 hours a day which went up to 40% during the pandemic. The study intends on following the children up again at 3 and 6 months, and it will be interesting to see if these symptoms resolve over this time or whether there is a long-term post-stress phase.

1. Brady AM, Deighton J, Stansfeld S. Psychiatric outcomes associated with chronic illness in adolescence: A systematic review. J Adolesc. 2017;59:112-123. doi:10.1016/j.adolescence.2017.05.014
2. Rath B, Donato J, Duggan A, et al. Adverse health outcomes after Hurricane Katrina among children and adolescents with chronic conditions. J Health Care Poor Underserved. 2007;18(2):405-417. doi:10.1353/hpu.2007.0043
3. A L van Tilburg M, Edlynn E, Maddaloni M, van Kempen K, Díaz-González de Ferris M, Thomas J. High Levels of Stress Due to the SARS-CoV-2 Pandemic among Parents of Children with and without Chronic Conditions across the USA. Children. 2020;7(10):193. Published 2020 21st October. doi:10.3390/children7100193

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INTERVIEWS WITH EXPERTS

Click to watch interviews with our Melbourne Children's Campus paediatricians, child development paediatrician, child and adolescent psychiatrist, and vaccinologists on what they have learned about COVID-19

- Associate Professor Pete Azzopardi on Adolescent Health: https://youtu.be/2OMNN96-G-Y
- Professor Sharon Goldfeld, on Child Development: https://youtu.be/G5OS5q30V9I
- Professor Jim Buttery on Clinical Paediatrics: https://youtu.be/V4_z_a_sdhE
- Dr John Cheek on Clinical Paediatrics: https://youtu.be/XBGvXBV6wCI
- Professor Harriet Hiscock on Telehealth and Mental Health: https://youtu.be/-gwYxhinZ0o
- Professor Dave Coghill on Child and Adolescent Mental Health: https://youtu.be/YmgMQ18HLPg
- Dr Danielle Wurzel on Respiratory Medicine: https://youtu.be/nHO90IuanXk
- Dr Shidan Tossif on Transmission: https://youtu.be/C_Xv2N2MXb4
- Associate Professor Margie Danchin on Vaccines: https://youtu.be/ul00xSpOayo
- Associate Professor Nigel Crawford on Vaccines: https://youtu.be/TB2Xf5q30_s
- Podcast with Associate Professor Nigel Crawford on Vaccines: https://mvec.mcri.edu.au/media-library/covid19-road-to-a-vaccine/
- Professor Terry Nolan on Vaccines on Dr Norman Swann's Coronacast: https://www.abc.net.au/radio/programs/coronacast/why-the-next-big-vaccine-milestone-might-be-only-4-6-weeks-away/12828484

HIGHLIGHTS

- MIS-C is distinct from the cytokine storm seen in adults with severe COVID-19 and from hyper inflammation in children with Kawasaki disease.
- A case report finds acute ischemic stroke may be associated with SARS-CoV-2 and MIS-C.
- Consensus-based clinical recommendations and research priorities for anticoagulant thromboprophylaxis in children hospitalised for COVID-19-related illness are described.
- SARS-CoV-2 may trigger an inflammatory process that promotes aberrant beta-cell destruction and development of diabetic ketoacidosis.
- Nasal strip sampling may be more appropriate for collection in paediatric populations as it is non-invasive and more comfortable.
- A new smartphone application HealthBuddy+ allows users to ask questions, report rumours, and undertake polls regarding COVID-19 in their own countries.
- In Sweden, the groups most negatively impacted by COVID-19 were older adults and those living in socioeconomically deprived areas with a higher proportion of young people.
- Post-lockdown SARS-CoV-2 PCR screening in nearly 10 million residents in Wuhan revealed no symptomatic cases, 300 asymptomatic cases and no evidence of transmission to close contacts by asymptomatic positive patients.
- US CDC found that 18-29-year-olds have the lowest compliance with COVID-19 mitigation behaviours by age group.
- Those living below the poverty line are more likely to suffer from a mental, behavioural, or developmental disorder.
- A case report of a fetal death associated with the intrauterine transmission of SARS-CoV-2 infection.
- In Nepal, birth rates declined by almost 50% and that between January and May 2020, institutional neonatal mortality increased by more than 200% in certain hospitals.
- A decision-making framework to guide the re-opening of schools should begin with strong in-school mitigation measures, and then consider other community factors such as incidence, community mitigation measures, and factors that influence transmission and disease severity.
- A prospective population-based study of COVID-19 in preschool and school settings after re-opening in northern Italy found transmission occurred in a small number of cases and was more common in secondary schools.
- An adolescent, in the absence of any mitigation measures, led to 116 people testing positive at a summer school—but there were no cases in teachers who wore masks and adopted other mitigation measures.
- A study into the dispersion of evaporating cough droplets in tropical outdoor environments found that despite the fact that low inhalation exposure based on a single cough, infection risks may still manifest through successive coughs or high viral load.

- A study Switzerland explored household transmission using seropositive individuals to highlight how biological and social factors combine to shape the risk of SARS-CoV-2 infection.
- A phase 1 RCT found acceptable safety profiles and promising immunogenicity for 2 COVID-19 vaccines, BNT162b1 and BNT162b2.
- The Russian Sputnik V vaccine for SARS-CoV-2 found promising results in a phase 2 trial and has progressed to phase 3 trials.
- Pharmaceutical companies are requiring financial commitment and protection against liability in the event of adverse reactions to the vaccine. The COVAX Facility was developed to increase global access and create a program for compensation to allow all countries to access the vaccine and are exploring options regarding COVAX procured vaccines.
- A national household survey in the U.S. showed that only 63% of parents are likely to vaccinate their children or themselves against COVID-19.
- With the potential for the release of numerous COVID-19 vaccines in the coming months, the question of who should receive the vaccine after healthcare workers comes into question.

CLINICAL PAEDIATRICS

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

New Insights on COVID-19's hyper inflammation in children
https://jamanetwork.com/journals/jama/fullarticle/2771915

- There is a rare, life-threatening hyperinflammatory syndrome that develops in some children after COVID-19.
- Most children with SARS-CoV-2 have a mild or asymptomatic course of illness; however, some develop a Kawasaki-like syndrome called multisystem-inflammatory syndrome in children (MIS-C) about 4-6 weeks post-infection.
- This commentary describes a study that investigated and compared the immunological response in:
  - 41 children with mild COVID-19; 13 children with MIS-C; 28 who were treated for Kawasaki before the pandemic.
- MIS-C is distinct from the cytokine storm seen in adults with severe COVID-19 and from hyper inflammation in children with Kawasaki disease.
  - MIS-C was associated with less interleukin-17A mediated inflammation and distinct autoantibodies compared with children who had Kawasaki disease.
- Better knowledge of the pathogenesis is necessary for developing optimal treatments.
- No critical appraisal of the study was provided.

Reviewed by: Dr Martin Wright

COVID-19 associated arterial ischaemic stroke and multisystem inflammatory syndrome in children: a case report
https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(20)30314-X/fulltext

- Nine year-old female admitted to PICU with a history of high-grade fever for 14 days, throbbing frontal headache, vomiting and progressive weakness on the right side of her body for five days, bilateral non-purulent conjunctivitis, high-grade fever, blood oxygen saturation 98% and H.R. 64bpm, tachypnoea and hypertension, GCS 11.
  - SARS-CoV-2 was detected via nasopharyngeal swab.
  - Further examination showed clinical findings consistent with the presentation of ischemic stroke.
    - Upper motor neuron right sided seventh cranial nerve palsy, complete hemiplegia, brisk deep tendon reflexes and extensor plantar response on the right.
  - Suspected diagnosis: COVID-19 related ischemic stroke.

  - Satisfies the WHO criteria of Multisystem Inflammatory Syndrome in Children (MIS-C).
    - MIS-C is an emerging life-threatening non-respiratory complication of COVID-19 presenting at any time during the course of illness secondary to uncontrolled cytokine storm.

> Possible pathophysiology of acute ischemic stroke associated with COVID-19 includes immune-mediated or para-infectious events, a hypercoagulable state from systemic inflammation and cytokine storm, viral mimicry of the host resulting in autoantibodies, viral superantigen sequences, antibody or T-cell recognition of viral antigens or formation of immune complexes.

> This is the only case report today of MIS-C presenting with acute ischemic stroke (though an early case report of PIMS-TS resulting in death was associated with right MCA and ACA ischaemic infarcts).

> Recommendations:

  - Include SARS-CoV-2 on the differential in children presenting with new neurological symptoms, positive inflammatory markers and suggestive imaging findings.
  - Aggressive therapy to halt cytokine storm and relevant supportive care while investigating differential diagnosis is crucial for reaching positive outcomes in children.

Reviewed by: Dr Martin Wright

Consensus-based clinical recommendations and research priorities for anticoagulant thromboprophylaxis in children hospitalised for COVID-19-related illness: a case report
https://pubmed.ncbi.nlm.nih.gov/33174388/

> Multiple studies have shown the increased risk of thromboembolic events in adult patients with COVID-19 related illness. Evidence suggests that children are at greater risk also, however, a concise recommendation on the use of thromboprophylaxis in children is lacking.

> This scientific statement is based on an international survey of 20 experts in Paediatric Hematology and Critical Care (responses from 18) to develop a consensus-based recommendation for the use of anticoagulant thromboprophylaxis (in combination with mechanical thromboprophylaxis where possible) in children hospitalised for COVID-19 related illness.

> Recommendations:

  - Anticoagulant thromboprophylaxis be administered in children hospitalised with COVID-19 related illness who have superimposed clinical risk factors for hospital-associated VTE or markedly elevated plasma D-dimer levels, in the absence of contraindications.
  - Administration of low-dose low molecular weight heparin subcutaneously twice daily targeted to achieve a 4-hour post-dose anti-Xa level of 0.2 to < 0.5 U/mL in children hospitalised with COVID-19 related illness who are clinically stable without severe renal impairment.
  - Marked thrombocytopenia, hypofibrinogenemia, recent major bleeding and concomitant aspirin administration at doses > 5 mg/kg/d likely confer a heightened bleeding risk in associated with anticoagulant thromboprophylaxis.

  - Continued anticoagulant thromboprophylaxis post-discharge from the hospital be considered in children with COVID-19 related illness who have markedly elevated D-dimer levels at hospital discharge and superimposed clinical risk factors for VTE.
  - Anticoagulant thromboprophylaxis not be prescribed routinely in hospitalised children who have asymptomatic SARS-CoV-2 infection in the absence of clinical risk factors for hospital-associated VTE.

> Future research priorities:

  - Clearer characterisation of VTE risk factors in children with COVID-19 related illness
  - Determination of the safety and efficacy of anticoagulant thromboprophylaxis in children hospitalised with COVID-19 related illness with multicentre clinical trials
  - Investigation of the hypothesised pathophysiological mechanisms underlying the prothrombotic state of SARS-CoV-2 infection and immune response
  - Understanding the pathophysiological mechanism distinguishing the MIS-C phenotype from the primary respiratory phenotype of COVID-19 related illness in children

Reviewed by: Dr Martin Wright

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

New-onset diabetes with diabetic ketoacidosis in a child with multisystem inflammatory syndrome due to COVID-19
https://www.degruyter.com/view/journals/jpem/ahead-of-print/article-10.1515-jpem-2020-0426/article-10.1515-jpem-2020-0426.xml?tab_body=pdf-78589

> Multisystem inflammatory syndrome in children (MIS-C) is a unique clinical complication of SARS-CoV-2 infection observed in paediatric patients. COVID-19 is emerging as a potential trigger for the development of diabetes in children based on effects on pancreatic function observed in animals and adults.

> This is the first report of a child presenting with MIS-C and new-onset diabetes and discusses the implication and clinical management of these concomitant conditions.

> An obese eight-year-old female with a strong family history of T2 diabetes presented with hyperglycaemia, ketosis and metabolic acidosis consistent with diabetic ketoacidosis (DKA) in the setting of fever, rash, respiratory distress, hemodynamic instability, reduced systolic function with dilation of the left anterior descending artery, and positive SARS-CoV-2 antibodies suggestive of MIS-C

> The finding of these two conditions occurring simultaneously suggests the possibility that COVID-19 impacts beta-cell function mechanistically and potentially leads to hastened beta-cell death.

> For patients with MIS-C and post-inflammatory conditions, we suggest monitoring blood sugars and encourage vigilance of development of ketosis and acidosis.

> Hyperglycaemia and acute diabetes mellitus have been observed in the original SARS coronavirus infection in which the virus binds to angiotensin-converting enzyme two receptors in the pancreas leading to islet cell damage and reduced insulin release [8].

- Animal studies on other viruses have guided a theory that SARS-CoV antibodies can promote disease via antibody-dependent enhancement, which can facilitate continued viral entry and host inflammation.
- It can be postulated that antibodies against SARS-CoV-2 may trigger an inflammatory process that leads to beta-cell destruction and onset of diabetes. Such a mechanism could help explain why pancreatitis and new-onset diabetes mellitus with DKA have been observed in the setting of acute SARS-CoV-2 infection in adults.
- Further investigation is required to better understand exactly by what mechanism SARS-CoV-2 leads to aberrant beta-cell destruction and to understand whether it is a transient vs. permanent phenomenon
- Key learning points:
  - New-onset diabetes can present in the setting of the multisystem inflammatory syndrome in children.
  - Inflammatory syndromes may raise the risk of diabetes development.
  - Glycaemic monitoring and control should be considered in MIS-C management

Reviewed by: Dr Martin Wright

DIAGNOSTICS & SAMPLING

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

SARS-CoV-2 detection by nasal strips: a superior tool for surveillance of paediatric population (Journal Pre-Proof)
https://www.sciencedirect.com/science/article/pii/S0163445320307040

- Study population: 38 infected COVID-19 patients confirmed by two PCR targeting two regions of RdRp gene of SARS-CoV-2 were recruited in Hong Kong, including 20 adults aged 22-74 and 18 children or adolescents aged 6-17 of whom ten were asymptomatic.
- Materials and methods:
  - Sample collection: Nasal epithelial lining fluids were obtained by nasal strip (n=43) and compared against pooled nasopharyngeal and throat swabs (n=21) and deep throat saliva (n=22), collected 24 hours after the collection of nasal strips. There were also 13 paired nasal swabs collected with nasal strips.
  - Testing method: All samples were tested with a real-time PCR targeting nucleoprotein (N) gene.
- Results
  - Significant correlation between nasal strip and nasopharyngeal and throat swabs and between nasal strip and deep throat saliva and between paired samples.
  - Agreement between nasal strip samples and nasopharyngeal and throat swabs was 94.44% for positive swabs and 100.00% for negative swabs.
  - Significant correlation of Ct-value was found between the nasal strip and nasopharyngeal and throat swabs.
  - Agreement between the nasal strip and deep throat saliva was 93.3% for positive deep throat saliva and 14.3% for negative. Six of the negative deep throat saliva swabs were correctly identified as positive on nasal strips.
  - Nasal strip sampling achieved an accuracy of 95.2%, compared to nasopharyngeal and throat swabs.
  - Viral RNA remained detectable on nasal strips after 24 and 72 hours of storage at room temperature.
- Benefits of nasal strip sampling compared to nasopharyngeal and throat swabs
  - Nasal strips are less traumatic and irritating meaning there is a reduced risk of many sneezes and coughs during collection.
  - Nasal strips are non-invasive and more comfortable, meaning repeat sampling is feasible, and they are especially suitable for the paediatric population.

- Conclusion: Nasal strip sampling would provide at least consistent qualitative results sufficient to identify potentially infectious individuals and susceptible contacts, as long as the PCR Ct value is within the range of an inferred infectivity.
- Limitations: Data was only collected from a single hospital. The impact of protease and RNase activity of individual subjects on sample stability was not fully elucidated. No information about the infectious titres of the virus was gathered.

Reviewed by: Dr Lien Anh Ha Do

EPIDEMIOLOGY & PUBLIC HEALTH

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

UNICEF ECARO and WHO/Europe launch HealthBuddy+ mobile application (promotional article)
https://www.unicef.org/eca/unicef-ecaro-and-whoeurope-launch-healthbuddy-mobile-application

- HealthBuddy+ is an interactive mobile application where participants can ask your questions, report rumours, and share thoughts on COVID-19.
- HealthBuddy+ provides essential and fact-checked information on COVID-19 and is continuously updated.
- The HealthBuddy+ app is currently available in English and Russian.
- Features:
  - Ask COVID-19 questions on the chatbot. HealthBuddy+ looks for answers in all the latest COVID-19 evidence, using artificial intelligence. If an answer is not available, app monitors will process the question individually and generate an answer
  - Report rumours using the to be verified and used to update the app
  - Share your thoughts on aspects of the COVID-19 response using the polls function. This will provide information to help develop solutions.
- Currently available from apple or google app stores.

Reviewed by: Dr Wonie Uahwatanasakul

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

High excess mortality in areas with young and socially vulnerable populations during the COVID-19 outbreak in Stockholm Region, Sweden
https://dx.doi.org/10.1136/bmjgh-2020-003595

- This study aimed to describe the distribution of excess mortality during the first weeks of the COVID-19 outbreak in the Stockholm Region of Sweden, stratified by age, sex, and sociodemographic context.
- Sweden is unique in that it has had no widespread lockdowns to mitigate the spread of COVID-19.
- Excess mortality was found by comparing observed mortality at the beginning of 2020 with the average rates during previous years.

- Excess mortality from 11th March 2020 (the date of the first recorded death due to COVID-19) to 17th May 2020 was 2110 deaths. Of this, 1942 were officially attributed to COVID-19.
- During the week of highest mortality, overall mortality exceeded average rates by 150%.
  - There was a 69% increase for those aged 0-64, 129% for those 65-79, and 165% for those over 80.
  - Excess mortality was observed to be higher in younger people of lower sociodemographic status. There was a 215% increase for those with the lowest income, 221% for those with the lowest education level, 198% for those with the lowest share of Swedish-born, and 232% for those with the lowest share of gainfully employed residents
- Conclusion: The groups most negatively impacted by COVID-19 were older adults and those living in socioeconomically deprived areas with a higher proportion of young people.
- Limitations:
  - Lack of individual-level data. The authors cannot determine the age of subjects contributing to the exceptionally high rates of excess mortality in deprived young neighbourhoods.
  - There was reduced observed mortality in the period before the pandemic, which may have accounted for increased mortality noted due to the 'pool' of frail persons during the pandemic.

Reviewed by: Dr Wonie Uahwatanasakul

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

COVID-19 mitigation behaviours by age group - the United States, April-June 2020 (CDC Morbidity and mortality report)
https://www.cdc.gov/mmwr/volumes/69/wr/mm6943e4.htm?s_cid=mm6943e4_w

- Prior to report: Recommended mitigation behaviours to prevent the spread of COVID-19 include wearing masks, hand washing, social distancing, and staying home when ill.
- Added by report:
  - Self-reported engagement in mitigation behaviours (mask-wearing, handwashing, physical distancing, crowd and restaurant avoidance, and cancellation of social activities) differed significantly by adult age group.
  - During April–June 2020, the prevalence of these behaviours was lowest among adults aged 18–29 years and highest among those aged > 60 years. Whereas mask-wearing increased over time, other reported mitigation behaviours decreased or remained unchanged.
- Improved communication and policy priorities are needed to promote recommended COVID-19 mitigation behaviours, particularly among young adults.

Reviewed by: Dr Wonie Uahwatanasakul

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

Post-lockdown SARS-CoV-2 nucleic acid screening in nearly ten million residents of Wuhan, China
https://www.nature.com/articles/s41467-020-19802-w

- This article reported the results of a citywide SARS-CoV-2 nucleic acid screening program in Wuhan following stringent lockdown measures between 23rd January and 8th April 2020.
- The study aimed to assess the post-lockdown risk of COVID-19, identify second wave prevention strategies and guide economic and social service policymaking.
- A total of 9,899,828 (92.9%) Wuhan residents received testing between 14th May and 1st June 2020. The following results showed that COVID-19 was well controlled in Wuhan in the post-lockdown setting.
  - Among the 34,424 participants who previously recovered from COVID-19, 107 tested positive again (re-positive rate 0.3%)
  - No symptomatic COVID-19 cases were detected among the 9,865,404 participants without a previous history of COVID-19 infection.
  - The asymptomatic positive rate was very low (0.303/10,000). All 300 cases returned with negative viral cultures, suggesting the absence of viable viral transmission, however at least 63% were infected with SARS-CoV-2 virus.
  - Elderly aged over 60 years had the highest asymptomatic positive rate, while children and adolescents under the age of 17 had the lowest.
  - Domestic and unemployed residents, retired adults and public service workers accounted for 57% of asymptomatic positive cases.
  - All 1174 close contacts of asymptomatic cases tested negative.
- Due to the cross-sectional nature of the study, long-term impacts of asymptomatic positive cases on Wuhan's COVID-19 control could not be assessed. However, the lack of infection detected in close contacts of asymptomatic cases suggests a very low probability of transmission in this group.

Reviewed by: Professor Jim Buttery

MENTAL HEALTH

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

Factors affecting children's mental health during the coronavirus disease 2019 pandemic
https://jamanetwork.com/journals/jamapediatrics/fullarticle/2773001

- This short letter to the editor discusses areas of interest regarding children's mental health concerns due to ongoing COVID-19-related changes.
- Studies thus far have shown a negative trend with regard to public mental health during the pandemic, and corresponding changes in how we approach and support mental health concerns are necessary.
- Cited study supporting that household income plays an essential role in children's mental health, and those below the poverty line are more likely to suffer from a mental, behavioural, or developmental disorder.
- These risk factors should be considered for future planning in approach and management for paediatric mental health during the pandemic.
- Behavioural disorders are more commonly diagnosed in children 6-11 years, whereas depression and anxiety disorders are more common in the older paediatric population.
- These should be examined in greater detail with larger studies to assess for residual confounding and hierarchical exploration to aid future policy decisions for supporting various age groups and populations.

Reviewed by: Professor David Coghill

PERINATAL HEALTH

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

Intrauterine transmission of SARS-CoV-2
https://wwwnc.cdc.gov/eid/article/27/2/20-3824_article

- A case report of fetal death associated with the intrauterine transmission of SARS-CoV-2 infection.
- A 42-year-old pregnant woman at 27 weeks gestation presented to the hospital in Brazil with dyspnoea, dry cough, high fever, anosmia, nausea, vomiting and diarrhoea for 2/7.
- Obstetric history
  - G7P3 (the patient had two abortions, ectopic pregnancy and three children).
  - The patient had hypertension in a prior pregnancy which resolved by delivery, and she was not hypertensive during this current pregnancy.
  - The current pregnancy was uncomplicated. The patient received routine tests and ultrasounds, with the last ultrasound at 25 weeks gestation.
- The patient tested positive for SARS-COV-2 and rhinovirus upon admission and received antiviral therapy [oseltamivir], prophylactic enoxaparin and corticosteroids for lung maturation. She had a C.T. chest which demonstrated changes consistent with SARS-CoV-2 infection. Her condition deteriorated, and she was ventilated 4/7 after admission and haemodynamic support.
- An ultrasound performed six days after admission demonstrated reduced amniotic fluid volume, no foetal movements or heart rate. After failed induction with misoprostol, the patient underwent a caesarean section where she delivered a stillborn fetus.
- Post-mortem findings
  - Autopsy demonstrated red serous effusions in the chest and abdomen, petechial haemorrhages in heart and lungs, hepatic discolouration and friability, and severe lung and kidney hypoplasia.
  - The placental disc was extremely small, with several recent infarcts, decidual vasculopathy, accelerated villous maturation, low placental weight, multifocal small intervillous thrombi and focal thrombosis of fetal placental vessels.
  - SARS-CoV-2 RNA was detected in the placenta (cotyledon samples, membranes and umbilical blood cord aspirate), suggesting fetal intrauterine viraemia and confirming transplacental transmission.
  - Immunohistochemistry staining with CD68 antibodies revealed multifocal chronic histiocytic intervillositis in the placenta, which has reported in other cases of pregnant women with COVID-19.

  - Microglial hyperplasia, mild lymphocytic infiltrate and oedema was noted in skeletal muscle and could suggest infection: however, no fetal tissue samples tested positive for SARS-CoV-2 infection.

> The patient's age and past history of gestational hypertension are risk factors that may have contributed to placental insufficiency and fetal demise, and some autopsy findings may have been caused by intrauterine asphyxia.

> However, the extent and rapid development of these findings in the context of a previously healthy pregnancy were likely contributed to by SARS-CoV-2 infection.

> Much about the congenital transmission of SAR-CoV-2 is still unknown in part due to the extensive investigations required to determine intrauterine infection. Placental and fetal gross and microscopic examination, as well as SARS-CoV-2 PCR on multiple tissue samples, are needed to detail the transmission and effects of SARS-CoV-2 infection in utero.

> Severe maternal vascular malperfusion injuries in the placenta, including substantial recent infarcts, decidual vasculopathy, accelerated villous maturation, low placental weight and multifocal small intervillous thrombi and focal thrombosis of fetal placental vessels point to infection contributing to vascular damage and fetal demise.

Reviewed by: Professor Suzanne M. Garland

SCHOOLS

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

School reopenings and the community during the COVID-19 pandemic
https://jamanetwork.com/channels/health-forum/fullarticle/2772568?utm_source=twitter&utm_campaign=content-shareicons&utm_content=article_engagement&utm_medium=social&utm_term=110120#.X54L_PNAUfM.twitter

- The approaches that various states and localities have taken to re-opening schools are highly variable. This variability is in part driven by differences in values and priorities.
- To be successful, school re-opening efforts must incorporate the values and characteristics of the communities in which those schools are embedded.
- This document outlines three community considerations deemed to be most important:
  1. School re-opening increases the risk of transmission within schools, households, workplaces, and the community as a whole.
     - Not only is there the opportunity for students and staff to transmit, or 'mix' with others outside of the school, but re-opening also allows parents to return to work where they will mix with their colleagues.
     - School reopenings would substantially contribute to a large second wave of COVID-19, unless accompanied by a robust test-and-trace-strategy for that community.
  2. Community disease prevalence affects in-school transmission risk.
     - Areas, where incidence is not well-controlled, are at risk of becoming hot-spots if schools re-open.
  3. Other community characteristics drive the potential impact of increased spread.
     - The success of school re-opening is highly dependent on the success of transmission mitigation measures taken in the wider community, such as social distancing and masking.
     - Risks also vary by population composition: transmission increases with the size and density of the school-aged population, whereas severity increases in older adults and those with comorbidities. Therefore, communities with large school-aged populations, elderly populations, or both, are at higher risk.
     - Other important characteristics include population density, ethnic/racial composition, and the prevalence of comorbidities in a community.
- A decision-making framework to guide the re-opening of schools should begin with strong in-school mitigation measures and then consider community factors.
     - Incidence of COVID-19 in the community should be low or on the decline.

  - The community must be willing to enforce community mitigation measures
  - The framework should consider the other factors that influence transmission and disease severity.

> Reopenings also provoke ethical questions. How can a community weigh its children's needs against those of its elderly and medically vulnerable?

> There are examples from Ireland, France, and Iceland that have kept schools open with community and school mitigation measures in place simultaneously. It is not one without the other.

Reviewed by: Professor Fiona Russell

Benjamin Watson – 4th Year Medical Student, Department of Paediatrics, The University of Melbourne & Maria Gladkikh – 3rd Year Medical Student, University of Ottawa

Secondary transmission of COVID-19 in preschool and school settings after their re-opening in northern Italy: a population-based study (not peer reviewed)
https://www.medrxiv.org/content/10.1101/2020.11.17.20229583v1.full.pdf+html

> School closures was one of the main measures undertaken to reduce the number of social contacts during the first wave of the pandemic.

> This study aimed to describe the data on the secondary transmission of SARS-CoV-2 among students and teachers/personnel after the re-opening of preschools and schools in Reggio Emilia, Italy.

> This prospective population-based study included all consecutive cases leading to a school investigation that were diagnosed from 1st September – 15th October 2020, in Italy.

> 994 students and 204 teachers (41 classes in 36 different schools) were tested due to notification of 43 primary cases (38 among students and five among teachers).

  - 39 secondary cases (attack rate 3.9%) were identified among the 994 tested children, in a total of 13 out of 41 classes. The largest cluster (22 secondary cases) occurred in a middle school.
  - The attack rate was higher in secondary schools (6.64%) than in primary schools (0.44%), and there were no secondary cases in preschool cases.
  - There were no secondary cases among tested teachers and staff members.
  - The majority of secondary cases did not report any previous close contact with a positive case.

> Limitations: low number of analysed clusters, cannot distinguish between transmission occurring in the classroom and those linked to activities and behaviours outside of school

> Conclusion: transmission at school occurred in a small number of cases and was more prevalent in secondary schools. Prompt testing and isolation of classmates may reduce the risk of transmission in classroom settings. Other school mitigation measures are important to prevent transmission.

Reviewed by: Professor Fiona Russell

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

COVID-19 outbreak at an overnight summer school retreat — Wisconsin, July-August 2020
https://www.cdc.gov/mmwr/volumes/69/wr/mm6943a4.htm?s_cid=mm6943a4_w

- This Morbidity and Mortality Weekly Report discusses an outbreak at an American summer camp where a single student infected with COVID-19 resulted in 76% of attendees (116 individuals) contracting the virus.
- This case documented rapid transmission of the virus among adolescent males in a non-socially distanced setting.
- Attendees were told to provide proof of a negative serologic test from < 3 months, or a PCR result from < 7 days before arrival, and were instructed to self-isolate at home for the seven days prior to travelling to the retreat.
- The single student who was the source of the virus had a negative PCR result from < 7 days prior but developed symptoms on his first day at the retreat.
- Notably, the four staff members who socially distanced and wore masks all tested negative by PCR testing.
- Many non-pharmaceutical measures, such as pre-arrival quarantine and testing, cohorting, symptom monitoring, physical distancing, mask use, enhanced hygiene measures, enhanced cleaning and disinfection, outdoor activities and programming, and early identification of infections with prompt isolation have been suggested in guidelines, but many of these were not utilised in this case.
- Limitations to the findings in this report:
  - RT-PCR was completed after the outbreak, likely leading to underestimation of the number of confirmed cases.
  - Baseline serology results not available for all attendees; therefore some positives found during the retreat may have been from older, undocumented infection.

Reviewed by: Professor Fiona Russell

THERAPEUTICS

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

A randomised trial of convalescent plasma in COVID-19 severe pneumonia
https://www.nejm.org/doi/full/10.1056/NEJMoa2031304

- Double-blind, placebo-controlled, multicentre trial at 12 sites in Argentina (PlasmAr trial) comparing convalescent plasma to placebo.
- Population:
  - Patients aged >18 years with COVID-19 confirmed via RT-PCR, radiologically-confirmed pneumonia, and further index of disease severity such as <93% O2 saturation (98.2% of patients met this criteria) or mSOFA>2.
  - 46% of patients had no detectable anti-SARS-CoV-2 IgG antibody level at baseline.
  - The median age of patient population 62 years (IQR 52-72). Major comorbidities included BMI >30, hypertension, diabetes, asthma, chronic kidney disease, haematologic disease, and congestive heart failure. Common medications at baseline included ACEi, ARB, NSAIDs, anticoagulants, corticosteroids, and NSAIDs.
- Intervention: Participants randomised in a 2:1 ratio with 228 in the intervention group and 105 in the placebo group. Convalescent plasma obtained from convalescent patients with a minimum SARS-CoV-2 total antibody titre of 1:400.
- Outcomes: Clinical status 30 days after the intervention, as represented by one of six categories adapted from the WHO clinical scale:
  1. Indicated death
  2. Invasive ventilatory support
  3. Hospitalised with supplemental oxygen requirement
  4. Hospitalised without supplemental oxygen requirement
  5. Discharged without a full return to baseline physical function
  6. Discharged with full return to baseline physical function.
- Primary outcome: no significant difference between convalescent plasma group and placebo group in the distribution of clinical outcomes (odds ratio 0.83, 95% CI 0.52 - 1.35, P =0.46)
- Secondary outcomes:
  - No significant difference in 30 day mortality in intervention group 25/228 (11%) vs controls 12/105 (11.4%). Risk difference -0.46 (95% CI, -7.8-6.8)

- No significant difference in: clinical status on the ordinal scale at day seven or day 14; median time from enrolment to hospital discharge; proportion of participants requiring ICU admission and invasive ventilatory support; proportion hospitalised with supplemental oxygen requirement.
- Similar rates of adverse events in both groups - infusion-related adverse events in the convalescent plasma group 11/228 (4.8%) vs controls 2/105 (1.9%).

> Conclusion: No significant difference in clinical status or mortality between intervention and placebo group.

Reviewed by: Dr Amanda Gwee

TRANSMISSION

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

Dispersion of evaporating cough droplets in tropical outdoor environment
https://aip.scitation.org/doi/10.1063/5.0026360

- To better understand airborne SARS-CoV-2 transmission, it is critical to fully understand the flow dynamics for both air flow and droplets as well as droplet evaporation. The role of the droplet composition in evaporative dispersion mechanisms of droplets remains unclear. This study modelled the evaporative droplet dispersion numerically under different tropical outdoor environmental conditions (e.g., relative humidity, wind speed) and the two recommended social distancing (e.g., 1 m and 2 m).
- Outdoor conditions were set up with the social distancing between a "cougher" and a "listener" model. The height of the cougher and listener are 1.70 m and 1.59 m. A typical flow rate at an angle of 27.5○ was rejected from the cougher, and both cougher and listener had normal breaths with a breath cycle proposed by Bulinska and Bulinsk. Salt was assumed to be the only non-volatile component in the droplet in this study. The total number of emitted cough droplets used in this study was 4897, which corresponds to a mass of 9.37 × 10−6 kg and a volume of 9.26 × 10−3 ml. Each droplet is assumed to constitute 93.5% water and 6.5% salt in terms of the mass fraction. The effects of fluid flow and heat transfer, droplet motion, as well as droplet evaporation, were investigated by three separated numerical models.
- Results:
  - The current numerical models were validated for single droplet evaporation and for three pure water droplet sizes at 1 µm, 10 µm, and 100 µm and three different relative humidity (R.H.).
  - Low inhalation exposure but large droplets deposition on the listener => potential risk for shorter persons, including children, who are less than 1 m away from a cougher.
  - The evaporation time depends significantly on different droplet diameters and the presence of salt in the droplet composition. At low R.H., a droplet has a high evaporation rate and shrinks quickly, leading to a longer life expectancy and travel distance.
    - The droplet size at ~75 µm was shown a special pattern e.g. ~50% of these droplets were suspended in the wake eventually depositing on the cougher, 45% settled to the ground rapidly due to the downward momentum of the cough jet, and the remaining 5% exited the simulation domain at around t = 15 s.
    - The travel distance for a 100 µm droplet can be up to 6.6 m under a wind speed of 2 m/s, the ambient air temperature at 30 ○C, R.H. = 0.84. It was found that the travel distance of a small droplet is relatively insensitive to relative humidity. For a millimetric droplet, the projected distance can be more than 1 m, even in still air.

        - The presence of salt in the droplet reduced the evaporation rate

    - Significantly greater droplets e.g. viral deposition, are found on a body 1 m away from a cougher, compared to 2 m.

    - Despite the fact that low inhalation exposure based on a single cough, infection risks may still manifest through successive coughs or a higher viral load.

Reviewed by: Dr Lien Anh Ha Do

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

Household transmission of SARS-CoV-2: insights from a population-based serological survey (not peer reviewed)
https://www.medrxiv.org/content/10.1101/2020.11.04.20225573v1

> This study applied household transmission models to data form a household based population serosurvey of 4534 people in Geneva, Switzerland to explore the relative role of transmission between household members compared to transmission in the community, and the infectivity of asymptomatic individuals as well as the effect of age on the susceptibility to infection.

> Peripheral venous blood from each consenting participant was collected and assessed for anti-SARS-CoV-2 IgG antibodies using an ELISA targeting the S1 domain of the spike protein.

> The presence of antibodies has been shown to be a reliable marker of infection; therefore, the study deemed seropositive participants infected.

> 6.6% of the individuals in the study tested positive for SARS-CoV-2 anti-S1 IgG antibodies - 9.8% of the study population had at least one positive household member.

> The positivity rate was 4.8% in 2 person households, 17% in three-person households, and relatively constant in larger households.

> Seropositive household members not reporting symptoms had 0.25 times the odds (OR = 0.25) having another infected household member compared to those reporting symptoms.

> The study estimated that 18.8% of all infections occurred in the household, with the proportion of infections attributable to household transmission increasing with household size.

> The study is consistent with other literature finding reduced risk of infection from household exposures among young children, an elevated risk of infection among those 65 or older.

    - This reduced risk in children is only true for children 5-9, 10-19-year-olds had similar risk profiles to working-age adults.

> Limitations to this study include self-reporting of symptoms and unknown time of infection, meaning they may not have been a result of SARS-CoV-2.

> The study highlights how biological and social factors combine to shape the risk of SARS-CoV-2 infection - the trend in infection risk by age and increased transmissibility of symptomatic individuals are fundamental attributes of the pandemic.

Reviewed by: Professor Jim Buttery

VACCINES

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

Safety and immunogenicity of two RNA-based COVID-19 vaccine candidates
https://www.nejm.org/doi/full/10.1056/NEJMoa2027906

- This is a randomised, placebo-controlled, observer-blinded phase 1 trial conducted in the United States that tested the safety and immunogenicity of 2 COVID-19 vaccines, BNT162b1 and BNT162b2.
- 195 healthy adults between the ages of 18 and 55, and between 65 and 85 were randomised to receive two doses of 10-µg, 20-µg, or 30-µg of BNT162b1 or BNT162b2 (or placebo), 21 days apart. Another group of adults aged 18 to 55 received a single dose of either 100-µg of BNT162b1 or placebo.
- Safety
  - 75-92% of participants reported mild-to-moderate injection site pain. No reports of redness or swelling
  - Dose-dependent systemic effects such as fever were present in up to 75% of participants. Reactions to BNT162b2 were milder than those to BNT162b1.
  - No reports of serious adverse events.
- Immunogenicity
  - Immunogenicity assessments were conducted at seven and 21 days after the first dose and seven and 14 days after the second dose. Neutralisation assays were performed to obtain 50% and 90% neutralisation titres. These were compared against serum samples from 38 donors recovered from moderate severity COVID-19.
  - BNT162b1 and BNT162b2 elicited similar serological responses, which decreased with age.
  - Clear benefits from a second dose in both younger and older adults.
- Limitations: Unclear characterisation of humoral and cellular immunity with regards to COVID-19 protection. Although the 2 vaccinations showed promising serum neutralising responses compared to which elicited by natural infections, the level of COVID-19 protection in vivo remained unclear. Serum panels used by vaccine developers were not standardised across labs to allow lab comparisons of results.
- Phase 2-3 trials will address the above limitations in up to 44,000 participants.

Reviewed by: Professor Jim Buttery

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

Understanding COVID-19 vaccine efficacy
https://science.sciencemag.org/content/early/2020/10/21/science.abe5938.full

> There are two ways by which a COVID-19 vaccine could protect high-risk populations:

1. Direct protection – i.e. high-risk persons received the vaccine and then are protected from contracting the illness.
2. Indirect protection – i.e. persons in contact with high-risk persons receive the vaccine and then are prevented from transmitting the illness onto them.

> Phase 3 vaccine trials serve to assess individual-level safety and efficacy. Their primary endpoint is usually confirmed, symptomatic disease, whereas secondary endpoints can include infection or viral shedding.

> This article outlines two of the significant questions that may not be answered by vaccine trials.

1. How effective will the vaccine be in protecting those at highest risk (i.e. the elderly and those with comorbidities)?
   - Vaccine trials are typically not designed to establish subgroup-specific efficacy. Randomised control trials can provide early estimates, but we will still be left with significant uncertainty. This could be addressed by:
     - Ensuring that high risk adults are well-represented in the trial population.
     - Maintaining blinded follow-up to assess long-term efficacy and safety to gather more age-specific effects (however, it may become unethical to ask trial participants to forego access to an available vaccine).
     - If phase 3 trials identify more than one safe, effective vaccine, there could be individual, or community level randomised trials to compare different active vaccines without a control arm. Sub-group specific evidence could be amassed via post-approval observational studies.
2. Will vaccines prevent infection? Or reduce contagiousness?
   - A vaccine that prevents infection entirely would reduce transmission. Vaccines that reduce severity can also be useful in reducing the respiratory tract viral load (infectiousness) and therefore transmission (by decreasing sneezing, coughing, etc.)
   - A worst-case scenario is a vaccine that reduces disease while permitting viral shedding; this may even increase transmission if symptoms are suppressed
   - The following could be ways to assess a vaccine's impact on infectiousness
     - Examine the amount or duration of viral shedding in confirmed participants. This would require regular testing of all participants in order to capture both symptomatic and asymptomatic cases.
     - Add-on household studies can follow household members or close contacts of infected participants to assess the vaccine's effects on infectiousness
     - By designing trials in which indirect effectiveness is a primary outcome

> Other open questions about a COVID-19 vaccine include long term safety data, rare adverse events, use in different populations than trial populations, duration of protection, the efficacy of series or lower dosing, protection against severe infection and death, efficacy by baseline serostatus, and the potential for the virus to escape the vaccine by evolving.

Reviewed by: Professor Jim Buttery

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

What defines an efficacious COVID-19 vaccine? A review of the challenges assessing the clinical efficacy of vaccines against SARS-CoV-2
https://www.thelancet.com/action/showPdf?pii=S1473-3099%2820%2930773-8

> Any vaccine that reduces infection, disease, or transmission could contribute to disease control.

> The World Health Organisation suggested a ~50% point estimate against disease, severe disease, and/or shedding/transmission as the minimum criterion for an acceptable vaccine.

> The United States Food and Drug Administration suggests a lower threshold of 50% laboratory-confirmed COVID-19 endpoint estimate for placebo-controlled efficacy trials.

> Trials must be adequately randomised and powered to account for confounding factors and meet efficacy endpoints in addition to informing about efficacy in different populations.

> Standardised, quantifiable endpoints are essential to allow comparison of vaccine candidates for effective use of vaccines.

> Trials may reach their endpoints earlier with the use of different study designs or studying populations with increased incidence rates.

> Controlled human infection models (CHIMs), where participants are exposed to infectious pathogens, can substantially reduce the time required to reach phase 3 studies endpoints and may be utilised to provide immunological insights.

> Various endpoints have their own difficulties such as the expense and participant burden with the detection of asymptomatic infection or the unclear association between quantitative RT-PCR and infectious virus with transmission as an endpoint.

> Severe disease and mortality are the most important efficacy endpoints due to their burden on healthcare systems; however, these are difficult to assess in phase 3 trials due to unpredictable and varying incidence rates. They may, however, be deduced from surrogate endpoints.

> Vaccine efficacy does not always predict vaccine effectiveness as it does not account for other factors such as herd protection and efficacy in populations not studied.

> Dedicated paediatric trials will be required as adult trials are not predictive of vaccine safety and efficacy in paediatric populations, however, these may be limited to phase 2 immunogenicity and safety trials.

> Vaccine efficacy against a particular SARS-CoV-2 variant in a region is likely to predict efficacy in other regions; however, surveillance for a viral escape from vaccine-induced immunity is important.

> Clinical trials may not be able to detect serious adverse events or vaccine associated enhanced respiratory disease if they are uncommon.

Reviewed by: Professor Jim Buttery

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

Second interim analysis of clinical trial data showed a 91.4% efficacy for the Sputnik V vaccine on day 28 after the first dose: vaccine efficacy is over 95% 42 days after the first dose (press release 24th November 2020)
https://sputnikvaccine.com/newsroom/pressreleases/second-interim-analysis-of-clinical-trial-data-showed-a-91-4-efficacy-for-the-sputnik-v-vaccine-on-d/

- The efficacy of the Sputnik V vaccine is 91.4%, based on the second interim analysis of data obtained 28 days after administering the first dose (the primary outcome was not clearly stipulated regarding the severity of disease)
- Preliminary data from volunteers obtained 42 days after the first dose (corresponds with 21 days after the second dose) indicates the efficacy of the vaccine above 95%.
- Minor adverse events such as pain at the injection point and flu-like symptoms including fever, weakness, fatigue, and headache were reported, but no data was provided
- Currently, 40,000 volunteers are taking part in Phase III double-blind, randomised, the placebo-controlled clinical post-registration study of the Sputnik V vaccine in Russia, of whom more than 22,000 volunteers were vaccinated with the first dose and more than 19,000 volunteers with the first and second doses.
- There were no unexpected adverse events during the trials. Monitoring of the participants is ongoing.
- The uniqueness of the Russian vaccine lies in the use of two different human adenoviral vectors which allows for a stronger and longer-term immune response as compared to the vaccines using one and the same vector for two doses.
- More information is needed to interpret the trial findings.

Reviewed by: Associate Professor Margie Danchin

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

No-fault compensation for vaccine injury - the other side of equitable access to COVID-19 vaccines
https://www.nejm.org/doi/full/10.1056/NEJMp2030600

- There is an ongoing race to find a safe and effective vaccine for COVID-19
- Wealthy governments have invested in vaccines candidates and made bilateral agreements with developers to reserve doses for the highest income countries – a phenomenon known as “vaccine nationalism.”
  - This leaves individuals living in poorer countries at a disadvantage and vulnerable to COVID-19 and lack of access to vaccines.
- The COVAX Facility was created in response to vaccine nationalism in an attempt to financial support leading vaccine candidates and ensure access to vaccines for lower-income countries.
- Financial agreements are only half of the solution; offering companies protection against potential liability is also very important.

  - As the vaccine will likely be distributed worldwide, there is an inevitable risk of adverse events, even with a safe product. These events may not come to light until enough of the population is vaccinated.
  - The International Federation of Pharmaceutical Manufacturers and Associations publicly demanded that manufacturers be granted protection from lawsuits associated with vaccine-related adverse events if they were going to participate in pandemic responses.
  - Offering immunity to all pharmaceutical companies developing a COVID-19 vaccine in all countries is impossible; some countries refuse to remit the responsibility of pharmaceutical companies to provide a safe product.

> Suggested solution: leverage existing no-fault vaccine injury regimens and construct a third regimen under COVAX's authority.

  - Existing policies for no-fault vaccine injury are in place for 24 Countries worldwide; the COVID-19 vaccine could be added to this current policy.
    - These programs could be adapted in regard to funding and distributing compensation.
  - WHO has an insurance mechanism for vaccines deployed under emergency use authorisation; the WHO provides compensation to people with a serious adverse event.
    - This existing program is small but could be useful for small countries.
  - COVAX Facility could develop a procedure to manage the high volume of claims worldwide and to compensate people who have a serious adverse event; they would do this by requiring countries to include plans for post-marketing safety surveillance.
    - The compensation system could be funded by earmarking committed resources from higher-income countries or by charging manufacturers a per-dose tax.

> COVAX believes that the global community that promotes immunisation as a collective interest, knowing that people will be injured, must share the burden of the injuries' costs. Their program proposal for the COVAX Facility addresses this concern to provide global access while providing compensation for serious adverse events.

> Australia does not have a no-fault vaccine injury compensation scheme, with COVID-19 providing a timely opportunity to establish one to ensure ongoing public trust and confidence in vaccines.

Reviewed by: Associate Professor Margie Danchin

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

Parents' likelihood to vaccinate their children and themselves against COVID-19 (not peer reviewed)
https://www.medrxiv.org/content/10.1101/2020.11.10.20228759v1.full.pdf+html

> This national household survey conducted in the United States from 5th - 10th June analysed the likelihood of parents immunising their children and themselves against COVID-19.

> The survey had a 50% completion rate (n=1008). Parents were asked two vaccination-specific questions, and responses were dichotomised into "Likely" and "Unlikely".

- Results:
  - 63% of parents (95% CI 59 - 66) were likely to vaccinate their children against COVID-19, and 60% of parents (95% CI 57 - 64) were likely to get a vaccine themselves (Pearson's r=0.89, high correlation).
  - In bivariate analyses, parental age, sex, marital status, education level and income were associated with parents' likelihood to vaccinate their children/themselves.
  - In bivariate analyses, parent employment status, child age, and state-level population-adjusted COVID-19 case incidence/mortality rates were not associated with likelihood to vaccinate.
  - In multimodal analyses, older parents were significantly more likely than younger parents to vaccinate their children and themselves against COVID-19.
  - In multimodal analyses, parents with bachelor's degrees were more likely to vaccinate their children/themselves than parents with high school or less education, as were Hispanic parents compared with non-Hispanic White parents ($P < 0.05$).
- Limitation: study sample included a disproportionately high number of high-income respondents.
- Vaccine concerns among different population groups need to be understood to ensure tailored communication strategies to improve vaccine uptake

Reviewed by: Associate Professor Margie Danchin

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

Who should be prioritised for COVID-19 vaccination?
https://protectau.mimecast.com/s/qmFDCmOxr6sj8YxY1FQDEzK?domain=url310.tandfonline.com

- COVID-19 vaccines are being developed and set to be released at a rapid pace.
- There is a general consensus that healthcare workers (HCW) should be the first group to receive vaccinations, but the subsequent groups hold societal and ethical dilemmas.
- The authors of this article explore the arguments regarding priority vaccination for the elderly who are at most risk of serious illness or age groups that transmit the virus frequently and who make up a significant portion of the economic workforce.
- Vaccinating those who are most likely to get infected and transmit the infection, may provide herd immunity and aid in helping the workforce to function.
- If vaccinating according to risk, variation in epidemiology by country and ethnicity need to be considered.
- If more antigen/doses are needed in certain populations to create the required immune response, issues regarding supply may arise.
- The authors argue that for high-income countries, the priority groups for vaccination should be to prevent deaths and severe disease and are therefore likely to be HCW, the elderly and those with comorbidities.
- There needs to be a call to action for research on the epidemiology of COVID-19 especially for children and pregnant women.

Reviewed by: Associate Professor Margie Danchin

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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