

## Prevention

### Does hand hygiene reduce SARS-CoV-2 transmission?

An ophthalmology group in Hong Kong shared their experience of stepping up infection control measures to minimise COVID-19 infection of both healthcare workers and patients, and emphasised universal masking, hand hygiene, and appropriate use of personal protective equipment (PPE). However, whether hand hygiene is “particularly important” for SARS-CoV-2 infection control needs further study. For the moment, we can however draw conclusions with inference to past studies. Aiello et al determined the value of hand hygiene for influenza or influenza-like illness prevention, and found “hand washing habits were the same in both the facemask only and control groups, which suggests that mask use alone may provide a reduction in respiratory illness regardless of hand washing practices.” After adjustment for covariates, only the facemask with hand hygiene group showed a significant reduction. Hand washing mechanically removes pathogens from hands underlining its importance as SARS-CoV can survive on surfaces for extended periods.

Yang C. Does hand hygiene reduce SARS-CoV-2 transmission? Vol. 258, Graefes Archive for Clinical and Experimental Ophthalmology. Springer; 2020. p. 1133–4.

### WHO recommended hand rub formulations for SARS-CoV-2

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is responsible for Covid-19, which is characterised by severe respiratory distress, fever, and cough and high rates of mortality. Human-to-human transmission of SARS-CoV-2 is efficient. Because no antiviral drugs or vaccines are available, prevention of infection is the current highest priority. The original WHO hand hygiene formulations (80% (vol/vol) ethanol, 1.45% glycerol, and 0.125% hydrogen peroxide) OR (75% (vol/vol) 2-propanol, 1.45% glycerol, and 0.125% hydrogen peroxide) failed to meet the efficacy requirements of European Norm 1500. Suchomel et al suggested modified versions with increased concentrations of ethanol: 80% (wt/wt) or isopropanol, 75% (wt/wt). In their findings, the original and modified versions of the formulations were able to inactivate SARS-CoV-2 within 30

seconds with dilutions of up to >40% still efficient. They concluded that both the original WHO formulations and the modified formulations were able to reduce viral titers to background level within 30s.

Kratzel A, Todt D, V'kovski P, Steiner S, Gultom M, Thao TTN, et al. Inactivation of Severe Acute Respiratory Syndrome Coronavirus 2 by WHO-Recommended Hand Rub Formulations and Alcohols. *Emerg Infect Dis*. 2020 Jul 1;26(7).

### Droplets and aerosols and the rationale of wearing masks in transmission of SARS-CoV-2

Anfinrud et al used laser light scattering to illustrate how liquid droplets exhaled during speech can linger in the air. The large particles to which they refer remain airborne only briefly before settling because of gravity; but may still be inhaled by persons close by into nasal or oral passages. From here they may be removed in nasal secretions or carried upward by the mucociliary escalator, to be expelled or swallowed. Breathing and talking also produce smaller particles known as aerosols. These particles are too small to settle because of gravity. They are carried by air currents and turbulence and can penetrate to the depths of the lungs. The possible contribution of infective aerosols to the current pandemic suggests the advisability of wearing suitable masks and providing adequate ventilation of enclosed spaces where such persons are known to be or may have been.

Meselson M. Droplets and aerosols in the transmission of SARS-CoV-2 [Internet]. Vol. 382, *New England Journal of Medicine*. Massachusetts Medical Society; 2020 [cited 2020 Jun 27]. p. 2063.

### Hydroxychloroquine for SARS-CoV 2 postexposure prophylaxis?

With no currently identified curative treatment for Covid-19, public health measures for control of the global epidemic are largely focused on disease prevention. The disease is caused by exposure to the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). The current standard of care for exposed individuals is observation under quarantine for 14 days. Small observational studies previously reported promising results with use of hydroxychloroquine, a drug with in-vitro action against the virus, for preventing Covid-19 following exposure to SARS-CoV-2. A recent well-powered randomised, double-blinded, placebo-controlled trial in the USA and Canada studied the use of hydroxychloroquine for postexposure

prophylaxis among adults with moderate and high-risk exposure to patients with confirmed Covid-19. Hydroxychloroquine was administered within four days after exposure. They found no significant difference in development of Covid-19 between the group that received hydroxychloroquine and those who received a placebo.

Boulware DR, Pullen MF, Bangdiwala AS, et al. A Randomized Trial of Hydroxychloroquine as Postexposure Prophylaxis for Covid-19 [published online ahead of print, 2020 Jun 3]. *N Engl J Med*. 2020;NEJMoa2016638. doi:10.1056/NEJMoa2016638

## Treatment

### Dexamethasone for Covid-19 patients

The majority of Covid-19 patients will be either asymptomatic or have only mild disease. There is a smaller portion of patients admitted requiring oxygen therapy or invasive mechanical ventilation (IMV). In this group of patients, there has not been much promise in the way of treatments improving mortality. These are patients believed to be in the hyperinflammatory pulmonary phase of disease. One theoretical option that Horby PW et al tested was the administration of dexamethasone to this group of patients. In this randomised open label clinical trial, 6mg of dexamethasone was administered to the intervention group. They found that in patients hospitalised with Covid-19, dexamethasone reduced 28-day mortality among those receiving invasive mechanical ventilation or oxygen at randomisation but not among patients not receiving respiratory support. This is the first treatment to be shown to reduce mortality in patients with Covid-19 requiring oxygen or ventilator support.

Dexamethasone for COVID: The RECOVERY trial - First10EM [Internet]. [cited 2020 Jun 27].

### Hydroxychloroquine or chloroquine for treatment of COVID-19-retracted study

Chloroquine, an antimalarial and hydroxychloroquine its derivative, have been redirected for treatment of Covid-19. The drugs have in-vitro antiviral activity against severe acute respiratory syndrome coronavirus 2 (SARS-CoV 2) which is responsible for the devastating Covid-19 pandemic. They have been widely advocated for and used following a few small uncontrolled trials and observational studies before evidence from well performed randomised con-

trolled trials. There are concerns, however, for potential causation of ventricular arrhythmias especially when used in combination with macrolides given both drug classes can cause the cardiovascular adverse effect of Q-T interval prolongation. A recent multinational registry analysis of data from 96,032 patients at 671 hospitals in six continents reported that hydroxychloroquine or chloroquine, used independently or in combination with a second generation macrolide such as Azithromycin did not confer benefits on in-hospital outcomes and were independently associated with increased in-hospital mortality and new onset ventricular arrhythmias. Such evidence from a large study published in a high impact journal would be expected to inform and maybe influence practice. The study, however, has since been retracted following concerns over the accuracy of the primary data sources. These findings influenced the pause of some clinical trials studying hydroxychloroquine, and its use for Covid-19 treatment is still a contentious topic.

Mehra MR, Desai SS, Ruschitzka F, Patel AN. Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis. *Lancet* 2020; published online May 22. [https://doi.org/10.1016/S0140-6736\(20\)31180-6](https://doi.org/10.1016/S0140-6736(20)31180-6).

Mehra MR, Desai SS, Ruschitzka F, Patel AN. RETRACTED: Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis [published online ahead of print, 2020 May 22] [retracted in: *Lancet*. 2020 Jun 5;:null]. *Lancet*. 2020;S0140-6736(20)31180-6. doi:10.1016/S0140-6736(20)31180-6

### Hydroxyurea dose escalation for Sickle Cell Anaemia in Children

Hydroxyurea is an efficacious and safe oral treatment for sickle cell anaemia. It increases production of fetal Haemoglobin, which reduces sickling of red blood cells. Hydroxyurea also improves other blood cell parameters and reduces complications, admissions and mortality attributable to sickle cell anaemia. Previous studies have demonstrated that Hydroxyurea dose escalation to the maximum tolerated dose is associated with better clinical outcomes. Increased dosage, however, may have potential for increased toxicity posing challenges of regular laboratory monitoring. A recent double-blinded randomised trial in Uganda compared a standard fixed daily dose of about 20mg per Kilogram body weight with an escalated daily dose of about 30mg per Kilogram body weight among children. They found children who received an escalated dose had better clinical outcomes, fewer

clinical events, reduced need for blood transfusion and fewer hospital admissions. Laboratory confirmed toxicities were comparable in the two arms. The authors concluded that for treatment of sickle cell anaemia among children in sub-Saharan Africa, Hydroxyurea dose escalation had better efficacy than fixed dosage, with comparable safety.

John CC, Opoka RO, Latham TS, et al. Hydroxyurea Dose Escalation for Sickle Cell Anemia in Sub-Saharan Africa. *N Engl J Med*. 2020;382(26):2524-2533. doi:10.1056/NEJMoa2000146

### Traumatic brain injury and anti-coagulant chemoprophylaxis

Venous thromboembolism (VTE) is a known, catastrophic complication of Traumatic Brain Injury (TBI). Anticoagulant chemoprophylaxis can be safely used to prevent VTE in surgical patients without significantly increasing the risk of bleeding. Guidelines are in place for proper use of anticoagulant chemoprophylaxis for many surgical patients but there are no globally established guidelines for patients with TBI. Spano et. al in a recent systematic review evaluated existing evidence for the efficacy and safety of pharmacological prophylaxis for VTE for patients with Traumatic Brain Injury. They found that timely chemoprophylaxis, between 24 to 72 hours reduced the risk of VTE without increasing the risk of intracranial hemorrhage for patients who had stable repeat Computer Tomography scans. This systematic review concluded that there is a need for further studies on this topic.

Spano, Paul J. II MS; Shaikh, Saamia JD; Boneva, Dessy MD, FACS; Hai, Shaikh MD, FACS; McKenney, Mark MD, MBA, FACS; Elkbuli, Adel MD, MPH Anticoagulant chemoprophylaxis in patients with traumatic brain injuries: A systematic review, *Journal of Trauma and Acute Care Surgery*: March 2020 - Volume 88 - Issue 3 - p 454-460 doi: 10.1097/TA.0000000000002580

## Obstetrics

### Risk of Preterm birth and asymptomatic short cervix

Preterm birth is associated with poor outcomes and the earlier the birth, the worse the outcomes. Extreme prematurity, which refers to birth before 28 weeks gestation is associated with significant risk for complications, high costs of care, and worse outcomes. Previous studies have linked asymptomatic short cervical length ( $\leq 25$ mm), diagnosed by ultrasound scan with preterm birth but there is limited evidence for this association for pregnancies between 23 and 28

weeks gestation. A recent retrospective cohort study of 126 pregnant women with asymptomatic short cervical length 23-28 weeks gestation examined for this association. Shorter cervical length was associated with higher risk for preterm birth and a shorter interval between enrolment and delivery. The risk was significantly higher for women with cervical length of  $\leq 10$ mm. Preterm births within one to two weeks from enrolment were, however, uncommon at all cervical lengths. The authors recommended that institution of management plans for preterm birth like the timing of corticosteroid administration for women with asymptomatic short cervical length at 23-28 weeks gestation be guided by additional indications

Gulersen M, Divon MY, Krantz D, et al. The risk of spontaneous preterm birth in asymptomatic women with a short cervix ( $\leq 25$  mm) at 23-28 weeks' gestation. *Am J Obstet Gynecol* 2020;2:100059.

### Pre-operative application of Chlorhexidine for Elective Caesarian delivery and infection

Postoperative surgical site infection (SSI) following caesarian delivery is associated with significant morbidity, postnatal depression and significant cost. Normal skin microflora are the most implicated pathogens and interventions to minimise these go a long way in preventing SSI. Previous studies reported mixed findings for the role of different modalities of Chlorhexidine Gluconate (CHG) topical applications in preventing SSI following different types of surgeries but its use for prevention of SSI after elective caesarian delivery has not been studied. This highly powered double blinded randomised placebo-controlled trial studied if pre-operative application of CHG cloths before (the previous night and the morning of) elective caesarian delivery reduced SSI within 6 weeks after the surgery. There were no significant differences between the two study arms and the authors recommended use of standard of care guidelines.

Stone J, Bianco A, Monro J, et al. Study To Reduce Infection Prior to Elective Cesarean Deliveries (STRIPES): a randomized clinical trial of chlorhexidine. *Am J Obstet Gynecol* 2020;223:113.e1-11.

### Excessive weight gain in pregnancy and persistent low back and pelvic pain

Persistent low back and pelvic pain (LBPP) with first onset during pregnancy has been associated with depression, chronic pain and absence from work. Excessive weight gain during preg-

nancy, which puts a greater burden on the musculoskeletal system, has been considered as a risk factor. Matsuda et al examined the association of excessive weight gain during pregnancy and persistent low back and pelvic pain after delivery. They defined persistent LBPP as pain at 4 months after delivery with an onset during pregnancy or within 3 weeks after delivery. They found that in a retrospective cohort of 330 women who had LBPP during pregnancy, the prevalence of persistent LBPP was as high as 34.1%. Women who gained  $\geq 15$  kg had a higher prevalence of persistent LBPP compared with those who gained  $< 10$  kg. They concluded that excessive weight gain during pregnancy is one of the risk factors for persistent low back and pelvic pain and recommended that appropriate weight control during pregnancy may help prevent persistent LBPP after delivery.

Matsuda N, Kitagaki K, Perrein E, et al. Association Between Excessive Weight Gain During Pregnancy and Persistent Low Back and Pelvic Pain After Delivery. *Spine (Phila Pa 1976)*. 2020;45(5):319-324. doi:10.1097/BRS.0000000000003271

### Maternal death due to Covid-19

Previous outbreaks of novel corona and influenza viruses were associated with worse outcomes for pregnant women but the outcomes in the current SARS-CoV-2 infection pandemic have not yet been adequately described. A retrospective case series study in Iran compared outcomes of 9 pregnant women in their second or third trimester admitted with laboratory confirmed CCovid-19, with 33 of their familial/household contacts. The pregnant women were identified as cases from voluntary reporting of maternal cases of Covid-19. The authors reported outcomes at death or after at least 14 days from admission with Covid-19. Seven of the nine women died, one remained ventilator dependent by the end of the reporting period and one recovered after a long hospital stay. Pregnant women admitted with COVID-19 had worse outcomes than their household/familial contacts. Important to note that not much is reported about the disease status/ severity of the contacts. The authors concluded that it is important to be cognisant of the potential for maternal death among pregnant women diagnosed with Covid-19 in their second or third trimester.

Hantoushzadeh S, Shamshirsaz AA, Aleyasin A, et al. Maternal death due to COVID-19. *Am J Obstet Gynecol* 2020;223:109.e1-16

### Maternal and perinatal outcomes with COVID-19: A systematic review

Eighteen articles reporting data from 108 pregnancies between 8 December 2019 and 1 April 2020 were included in the current study. Most reports described women presenting in the third trimester with fever (68%) and coughing (34%). Lymphocytopenia (59%) and elevated C-reactive protein (70%) were also observed. 91% of the women were delivered by caesarean section. Three maternal admissions to the intensive care unit were reported but no maternal deaths had been reported by 1st April 2020. One neonatal death and one intrauterine foetal death were reported. The authors emphasised that even though most of the mothers were discharged without major complications, severe maternal morbidity as a result of COVID-19 and perinatal deaths were reported and that vertical transmission of COVID-19 could not be ruled out. They recommended careful monitoring of pregnant women with COVID-19 and measures to prevent neonatal infection.

Zaigham M, Andersson O. Maternal and perinatal outcomes with COVID-19: A systematic review of 108 pregnancies. *Acta Obstet Gynecol Scand*. 2020;99:823–829. <https://doi.org/10.1111/aogs.13867>

## General

### Routine Point-of-Care Early Infant Diagnosis: Acceptability in African Countries

Only 59% of HIV exposed infants received a virologic test in 2018, despite the WHO's recommendation for all to receive testing within 4-6 weeks of birth. Significant delays in receiving early infant diagnosis (EID) results between 30 to 90 days have been reported in sub-Saharan Africa where most tests are done at a central laboratory, despite the WHO's recommendation of 4 weeks turnaround time (TAT). Delays in EID results causes delays in ART initiation and losses in the mortality benefits of early diagnosis and treatment. Point of care (POC) testing rolled out as a pilot has been successfully done and well accepted by health-workers and infant caretakers. It led to significantly shorter TAT and reduced delays in treatment initiation. A recent study sought the perspectives of healthcare providers, laboratory and program managers for EID in eight African countries before and after rollout of the POC testing. Participants

were supportive of wide scale rollout of POC testing for early infant diagnosis and recommended its incorporation into national EID algorithms.

Bianchi F, Clemens S, Arif Z, Sacks E, Cohn J. Acceptability of Routine Point-of-Care Early Infant Diagnosis in Eight African Countries: Findings From a Qualitative Assessment of Clinical and Laboratory Personnel. *J Acquir Immune Defic Syndr*. 2020;84 Suppl 1:S41-S48. doi:10.1097/QAI.0000000000002372

### Multisystem Inflammatory Syndrome in children with Covid-19

Multisystem inflammatory syndrome in children (MIS-C) is a life threatening systemic condition characterised by persistent fever, inflammation and organ dysfunction. Children with MIS-C present with features similar to Kawasaki syndrome, a form of childhood vasculitis that has been linked to infection. Multisystem inflammatory syndrome has been reported as case series in children with severe COVID-19 disease. The condition poses potentially devastating clinical and public health implications and understanding its epidemiology and clinical course is crucial. Targeted surveillance was done at paediatric health facilities in the USA and characteristics of 186 children and adolescents with evidence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and MIS-C were reported. Median age was 8.3 years and 73% were previously healthy. Median duration of hospitalisation was a week, 92% had at least four elevated biomarkers of inflammation and the gastrointestinal (92%), cardiovascular (80%), hematologic (76%), mucocutaneous (74%), and respiratory (70%) systems were involved. Use of immunomodulatory was common and 4 (2%) died. The authors concluded that Multisystem inflammatory syndrome caused life-threatening disease in previously healthy children and adolescents with COVID-19.

Cheung EW, Zachariah P, Gorelik M, et al. Multisystem Inflammatory Syndrome Related to COVID-19 in Previously Healthy Children and Adolescents in New York City. *JAMA*. Published online June 08, 2020. doi:10.1001/jama.2020.10374

### Sepsis and Empiric broad-Spectrum Antibiotic under-/over-use

Sepsis, a life-threatening organ dysfunction secondary to infection, is associated with poor outcomes. Early administration of active antibiotics significantly improves outcomes and national and international guidelines recommend immediate empiric administration of broad-spectrum antibiotics. Broad-spec-

trum antibiotics, however, need to be used rationally to avoid both under and over treatment that are associated with unfavourable outcomes. Understanding the epidemiology of antibiotic-resistant pathogens is a key step in rational broad-spectrum antibiotic use. A recent cohort study of 17430 adults admitted with culture-positive community onset sepsis at 104 hospitals in the US, determined the prevalence of antibiotic resistance, empiric broad spectrum antibiotic use and mortality associated with inadequate empiric antibiotic and unnecessary broad-spectrum antibiotic use. They found resistant gram-positive pathogens were isolated in only 13.6% and resistant gram-negatives in 13.2% of patients even though 67.0% of the patients received empiric broad-spectrum antibiotics. Inadequate and unnecessary broad-spectrum antibiotics were both associated with increased mortality. The authors concluded by emphasizing the need for better and quicker tests for identification of resistant pathogens to guide rational use of broad-spectrum antibiotics.

Rhee C, Kadri SS, Dekker JP, et al. Prevalence of Antibiotic-Resistant Pathogens in Culture-Proven Sepsis and Outcomes Associated With Inadequate and Broad-Spectrum Empiric Antibiotic Use. *JAMA Netw Open.* 2020;3(4):e202899. doi:10.1001/jamanetworkopen.2020.2899

### Factors associated with under nutrition among Children

Child undernutrition as assessed by three anthropometric inadequacies, including; wasting, stunting and underweight, is an important global problem and approximately 21.9% of children had stunting in 2018. The underlying mechanisms for child undernutrition are not completely understood as the current conceptual frameworks have been found lacking. Randomised studies on the same have studied only a few of the factors and multisite studies found marked heterogeneity. This cross-sectional study of 299 353 children aged 12 to 59 months from 35 low- and middle-income countries (LMICs), used Demographic and Health Surveys covering a period of 11 years to assess the strengths of associations of 26 factors with child undernutrition. Parental nutritional status (height and BMI) and household socioeconomic conditions were the leading factors for most countries, ranking first to fourth. Environmental factors, health behaviours, disease prevalence, and maternal reproductive care were infrequently

associated with child undernutrition and were quite heterogeneous across countries. The authors concluded contextually aligned strategies including poverty reduction, women's education, and nutrition programs for households could reduce child undernutrition.

Li Z, Kim R, Vollmer S, Subramanian SV. Factors Associated With Child Stunting, Wasting, and Underweight in 35 Low- and Middle-Income Countries. *JAMA Netw Open.* 2020;3(4):e203386. doi:10.1001/jamanetworkopen.2020.3386

### Anthropometric measures of obesity and cancer risk

Previous evidence has demonstrated a causal association between obesity and certain cancers, referred to as obesity-related cancers. The exact mechanisms through which obesity increases cancer risk are not very well understood but obesity leads to an interplay of chronic low-level inflammation, increased DNA damage and reduced DNA repair, among other conducive factors for oncogenesis. Some of the obesity related cancers include; cancer of the colon, endometrium and post-menopausal cancer of the breast. Anthropometric body measures like Body Mass Index (BMI), Hip circumference, Waist circumference and Waist to Height ratio can be used to assess body fat composition. The association between these anthropometric measures and 16 obesity related cancers was studied and compared by sex, in a cohort of 45 to 69 year olds in the Framingham, USA. Obesity was a risk factor for cancer in both men and women. The waist-based anthropometric measures were stronger risk factors for men compared to women. Large waist and small hip sizes are both predictors of obesity related cancers among men.

Chadid, S., Kregar, B.E., Singer, M.R. et al. Anthropometric measures of body fat and obesity-related cancer risk: sex-specific differences in Framingham Offspring Study adults. *Int J Obes* 44, 601–608 (2020). <https://doi.org/10.1038/s41366-020-0519-5>

## Misc

### Low alcohol use may improve cognitive function in old age

There is no clear consensus on the association of low to moderate alcohol intake and cognitive function as previous studies have reported mixed findings. Many of the previous studies did not put into consideration the challenges of single measurements of cognition and the associated factors, for example the

association with age-related decline in cognitive function. A prospective cohort of 19, 887 predominantly female participants of the Health and Retirement Study in the US, with a mean age of 61.8 years filled at least three biennial surveys over a follow up period of 9.1 years. Results showed that compared to never drinkers low to moderate alcohol consumption (<8 drinks per week for women and <15 for men) was associated with higher cognitive function and a slower rate of cognitive decline. This association, however, was stronger for white compared to black participants. The authors concluded that there is a need to study the underlying mechanisms for the association of alcohol intake and cognition in this age group.

Zhang R, Shen L, Miles T, et al. Association of Low to Moderate Alcohol Drinking With Cognitive Functions From Middle to Older Age Among US Adults. *JAMA Netw Open.* 2020;3(6):e207922. doi:10.1001/jamanetworkopen.2020.7922

### Intimate Partner Violence among middle-aged women

Intimate partner violence (IPV), which refers to physical, psychological or sexual aggression by a current or former intimate partner, has been associated with undesirable mental and physical health outcomes such as sexually transmitted infections, injuries, heart disease, chronic pain, depression, post-traumatic stress disorder (PTSD) and substance use among others. Studies among women of reproductive age found that overall IPV was associated with higher utilisation of different healthcare services and high healthcare costs. Whether similar associations occur for middle aged and old women, has not been well studied. A recent study among a cohort of 4481 women aged at least 45 years, who are universally screened for past-year IPV found that IPV was prevalent and was associated with anxiety disorders, depression, PTSD, suicidal ideation and/or behaviour and substance use disorder. These associations were stronger for middle aged compared to older women. IPV among middle women was associated with increased psychosocial, primary healthcare and emergency department visits. Only psychosocial visits were increased for older women who experienced IPV.

Makaroun LK, Brignone E, Rosland A, Dichter ME. Association of Health Conditions and Health Service Utilization With Intimate Partner Violence Identified via Routine Screening Among Middle-Aged and Older Women. *JAMA Netw Open.* 2020;3(4):e203138. doi:10.1001/jamanetworkopen.2020.3138