Covid-19

Ivermectin may significantly impact COVID-19 Infection prevention and treatment

Ivermectin, an anti-parasitic with antiviral and anti-inflammatory properties has been tested by researchers for its efficacy in reducing mortality and in chemoprophylaxis, among people with, or at high risk of, COVID-19 infection. A meta-analysis of 15 clinical trials found with moderate certainty that ivermectin reduced risk of death compared with no ivermectin. They also found, with low-certainty evidence, that ivermectin prophylaxis reduced COVID-19 infection by an average 86%. Effect estimates for "improvement" and "deterioration" favored ivermectin use, and severe adverse events in the treatment trials were rare. The researchers concluded that ivermectin is likely to have a significant impact on the SARS-CoV-2 pandemic globally owing to the proven efficacy, safety and low cost.

Bryant A, Lawrie TA et al. Ivermectin for Prevention and Treatment of COVID-19 Infection: A Systematic Review, Meta-analysis, and Trial Sequential Analysis to Inform Clinical Guidelines. Am J Ther. 2021 Jun 17. doi: 10.1097/MJT.0000000000001402. Epub ahead of print. PMID: 34145166.

Berberine and Obatoclax inhibit SARS-Cov-2 replication in primary human nasal epithelial cells

There is growing excitement about herbal medicines in the treatment of COVID19, for example, the now popular "Covidex" (a berberine-containing herbal medicine) in Uganda. Elsewhere, studies on two herbal compounds: berberine and obatoclax were conducted. Berberine, a plant-derived alkaloid inhibited SARS-CoV-2 at micromolar concentrations and obatoclax, originally developed as an anti-apoptotic protein antagonist was effective at sub-micromolar concentrations. Researchers found that Berberine acted on the late stages of the viral life cycle, strongly reducing the infectious viral titers while obatoclax acted on the early stage of the infection. Both obatoclax and berberine inhibited SARS-CoV-2 replication in primary human nasal epithelial cells in vitro. Researchers proposed berberine and obatoclax as potential antiviral drugs against SARS-CoV-2 that may need further efficacy testing.

Varghese, Finny S et al. "Berberine and Obatoclax Inhibit SARS-Cov-2 Replication in Primary Human Nasal Epithelial Cells In Vitro." Viruses vol. 13,2 282. 11 Feb. 2021, doi:10.3390/v13020282

Increased risk of clinical sequelae after the acute phase of SARS-CoV-2 infection

A group of researchers set out to evaluate the excess risk of clinical sequelae associated with SARS-CoV-2 infection. Through a large retrospective cohort study in the United States, participants aged 18-65years diagnosed as having SARS-CoV-2 infection were compared to 3 groups and excess risk after acute infection calculated. 14% of those infected with SARS-CoV-2 developed at least one new type of clinical sequelae that required medical care after the acute phase of the illness, which was 4.95% higher than the 2020 comparator group. Although older individuals were at greatest excess risk, younger adults with covid-19 also had an increased risk of developing new clinical sequelae, noted across a range of organ systems. This finding is relevant for healthcare planning.

BMJ 2021;373:n1098 http://dx.doi.org/10.1136/bmj.n1098

Tofacitinib in Patients Hospitalized with Covid-19 Pneumonia

Tofacitinib is an orally administered drug that suppresses cytokine production, hence the need to study its role in ameliorating the cytokine storm observed among patients with severe COVID-19. The safety and efficacy of tofacitinib in patients hospitalized with covid-19 pneumonia has been unclear. Researchers randomized 289 patients to receive either tofacitinib at a dose of 10 mg or placebo twice daily for up to 14 days or until hospital discharge. The primary outcome was the occurrence of death or respiratory failure through day 28. The cumulative incidence of death or respiratory failure through day 28 was lower (18.1%) in the tofacitinib group than the placebo (29.0%). Lower deaths from any cause through day 28 occurred in the tofacitinib group (2.8%) than the placebo (5.5%). In conclusion, tofacitinib led to a lower risk of death or respiratory failure through day 28 compared to placebo.

Guimarães PO et al. Tofacitinib in patients hospitalized with Covid-19 pneumonia. N Engl J Med 2021 Jun 16; [e-pub]. (https://doi.org/10.1056/NEJMoa2101643)

Bleeding and clotting disorders after vaccination with Oxford-AstraZeneca ChAdOx1-S in Denmark and Norway: population-based cohort study

Whether reports about the bleeding disorders seen in Oxford-AstraZeneca recipients represent an excess over the expected rate is unclear. Researchers compared the rates of venous thromboembolic events (VTEs) in the first 28 days among Oxford-AstraZeneca recipients with rates observed in the general population. 59 VTEs were observed in the vaccinated cohort compared with 30 expected based on the incidence rates in the general population, corresponding to 11 (5.6 to 17.0) excess events per 100000 vaccinations. A higher-than-expected rate of cerebral venous thrombosis was observed, an excess of 2.5 (0.9 to 5.2) events per 100000 vaccinations. Researchers observed increased rates of VTEs in vaccine recipients but noted that the absolute risk was small, and should be interpreted in light of the proven vaccine benefits.

BMJ 2021;373:n1114 http://dx.doi.org/10.1136/bmj.n1114

Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons

Preliminary findings on the safety of two messenger RNA (mRNA) coronavirus disease 2019 (Covid-19) vaccines among pregnant persons; Pfizer–BioNTech and Moderna were documented. Studies involving 35,691 participants aged 16- 54 years identified as pregnant were conducted. Injection-site pain was reported more frequently among pregnant persons than among nonpregnant women, whereas headache, myalgia, chills, and fever were reported less frequently. Calculated proportions of adverse pregnancy and neonatal outcomes in persons vaccinated against Covid-19 who had a completed pregnancy were similar to incidences reported in studies involving pregnant women that were conducted before the Covid-19 pandemic. Researchers hence found no obvious safety signals among pregnant persons receiving mRNA- Covid-19 vaccines. Similar studies in the Oxford-AstraZeneca counterpart available in LMICs are crucial.

Shimabukuro TT, Kim SY et al. Preliminary Findings of mRNA Covid-19 Vaccine Safety

in Pregnant Persons. N Engl J Med. 2021 Jun 17;384(24):2273-2282. doi: 10.1056/NEJMoa2104983. Epub 2021 Apr 21. PMID: 33882218; PMCID: PMC8117969.

Safety and Efficacy of Hydroxychloroquine for Treatment of Non-Severe COVID-19: Evidence from Uganda

Hydroxychloroquine (HCQ), a repurposed drug for the treatment of COVID-19, has not been found efficacious in a number of studies. Researchers in Uganda conducted a randomized open label Phase II clinical trial from October -December 2020 and studied adult patients diagnosed with COVID-19 using RT-PCR within the last 3 days. Patients received either HCQ 400mg twice a day for the first day followed by 200mg twice daily for the next 4 days plus standard of care (SOC) treatment or SOC treatment alone. They found that viral clearance did not differ by treatment arm. There were also no significant differences in secondary outcomes (symptom resolution and adverse events) and in adverse events such as elevated alkaline phosphatase, prolonged QTc interval on ECG, among patients in the intervention arm as compared to the control arm.

Pauline Byakika-Kibwika et al. Safety and Efficacy of Hydroxychloroquine for Treatment of Non-Severe COVID-19 in Adults in Uganda: A Randomized Open Label Phase II Clinical Trial, 04 June 2021, PREPRINT (Version 1) available at Research Square [https://doi.org/10.21203/rs.3.rs-506195/v1]

General

Treatment outcomes of drug resistant tuberculosis patients with poor prognostic indicators in Uganda: A countrywide 5-year retrospective study

Treatment outcomes for patients with drug resistant tuberculosis (DR – TB) with poor prognostic pointers such as comorbid conditions are not been well studied. Researchers in Uganda studied predictors of treatment success and mortality by reviewing records of DR – TB patients from 16 treatment units who had a treatment outcome documented in 2014–2019 and had at least one of 15 pre-defined poor prognostic indicators. The indicators included; HIV co-infection, diabetes, heart failure, malignancy, psychiatric illness/symptoms, severe anaemia, alcohol use, cigarette smoking, low body mass index, elevated creatinine, hepatic dysfunction, hearing loss, resistance to fluoroquinolones and/or second-line aminoglycosides, previous exposure to second-line drugs (SLDs), and pregnancy. Majority (71.8%) of the 1122 patients achieved treatment success, 18.4% died, 8.6% were lost-to-follow-up and 1.2% had treatment failure. Anaemia and previous exposure to SLDs were predictors of treatment failure and every additional poor prognostic indicator increased the odds of mortality. There is a need for optimization of DR – TB treatment when first initiated, especially for patients with anaemia.

Joseph Baruch Baluku et al. Treatment outcomes of drug resistant tuberculosis patients with multiple poor prognostic indicators in Uganda: A countrywide 5-year retrospective study, Journal of Clinical Tuberculosis and Other Mycobacterial Diseases,Volume 23,2021,100221,ISSN 2405-5794,https://doi.org/10.1016/j.jctube.2021.100221.

Comparative Effectiveness of Aspirin dosing in Cardiovascular Disease

The appropriate dose of aspirin in patients with established atherosclerosis is still debatable. Through a large clinical trial, participants were randomly assigned to a strategy of 81mg or 325mg daily aspirin. The primary effectiveness outcome was a composite of death from any cause, hospitalization for myocardial infarction, or hospitalization for stroke; and the primary safety outcome was hospitalization for major bleeding. The primary effectiveness outcome occurred in 590 patients (7.28%) in the 81mg group and 569 patients (7.51%) in the 325mg group, while the safety outcome occurred in 53 (0.63%) versus 44 (0.60%) patients respectively. In conclusion, a strategy of 81-mg of daily aspirin was as effective as a 325-mg strategy, with better long-term adherence.

Jones WS, Mulder H et al. Comparative Effectiveness of Aspirin Dosing in Cardiovascular Disease. N Engl J Med. 2021 May 27;384(21):1981-1990. doi: 10.1056/NEJMoa2102137. Epub 2021 May 15. PMID: 33999548.

Final report of a trial of Intensive versus standard blood-pressure control

It is unclear whether intensive systolic blood pressure (SBP) control leads to better outcomes than the standard. Researchers enrolled 9,361 participants who were at increased risk for cardiovascular disease and assigned them to adhere to an intensive treatment target (SBP, <120mmHg) or a standard target (SBP, <140mmHg). The primary outcome was a composite of myocardial infarction, other acute coronary syndromes, stroke, acute decompensated heart failure, or death from cardiovascular causes. During the trial, the rate of the primary outcome were significantly lower in the intensive treatment arm than in the standard arm, but with severe adverse events, more frequent in the former. The researchers demonstrated that intensive SBP control resulted in lower rates of major adverse cardiovascular events than targeting a SBP of less than 140 mmHg.

SPRINT Research Group, Lewis CE et al. Final Report of a Trial of Intensive versus Standard Blood-Pressure Control. N Engl J Med. 2021 May 20;384(20):1921-1930. doi: 10.1056/NEJMoa1901281. PMID: 34010531.

Treatment timing and the effects of rhythm control strategy in patients with atrial fibrillation

Data on the prognostic effect of rhythm control treatment are inconclusive. Through a nationwide observational cohort study conducted in Korea, 22635 adults with atrial fibrillation (AFib) and cardiovascular conditions, newly treated with rhythm control or rate control strategies were followed up. The primary outcome was a composite outcome of death from cardiovascular causes, ischaemic stroke, admission to hospital for heart failure, or acute myocardial infarction. Rhythm control was associated with a lower risk of primary outcome occurrence than rate control among patients with early treatment AFib. The researchers found that early initiation of rhythm control treatment was associated with a lower risk of adverse cardiovascular outcomes than rate control treatment in patients with recently diagnosed atrial fibrillation.

Kim D, Yang PS et al. Treatment timing and the effects of rhythm control strategy in patients with atrial fibrillation: nationwide cohort study. BMJ. 2021 May 11;373:n991. doi: 10.1136/bmj.n991. PMID: 33975876; PMCID: PMC8111568.

Sudden cardiac death and myocardial fibrosis, determined by autopsy, in persons with HIV

The incidence of sudden cardiac death and sudden death caused by arrhythmia as determined by autopsy in persons with HIV has not been clearly

established. Researchers prospectively identified new deaths due to out-of-hospital cardiac arrests among persons aged 18 to 90 years with and without HIV infection. Postmortems were done and incidence rates of sudden cardiac death and sudden death caused by arrhythmia were compared between groups. Observed incidence rates of presumed sudden cardiac death were 53.3 deaths per 100,000 person-years among persons with known HIV infection versus 23.7 in those without known HIV infection; rates of sudden death caused by arrhythmia were 25.0 versus 13.3 deaths per 100,000 person-years, respectively. Many HIV-related sudden cardiac deaths were due to an occult drug overdose.

Tseng TH, et al. N Engl J Med. 2021;doi:10.1056/NEJMoa1914279.

Associations between statins and adverse events in primary prevention of cardiovascular disease

The efficacy of statins in preventing cardiovascular disease is well established. Their safety, however, is not fully described. Researchers conducted a meta-analysis of clinical trials in adults without a history of cardiovascular disease that compared statins with non-statin controls. Statins were associated with increased risk of self-reported muscle symptoms, liver dysfunction, renal insufficiency, and eye conditions, but no clinically confirmed muscle disorders or diabetes. The researchers concluded that for primary prevention of cardiovascular disease, the risk of adverse events of statins was low with the benefit of their use outweighing the risk. Information about the type and dose of statin to use was however still at large.

Cai T, Abel L, et al. Associations between statins and adverse events in primary prevention of cardiovascular disease: systematic review with pairwise, network, and dose-response meta-analyses. BMJ. 2021 Jul 14;374:n1537. doi: 10.1136/bmj.n1537. PMID: 34261627.

Delayed antibiotic prescribing for respiratory tract infections

Injudicious use of antibiotics is a driver of antimicrobial resistance, a growing public health threat. Clinical trials have previously suggested delayed antibiotic prescription for respiratory infections as safe but associated harm is not well understood. Researchers conducted a systematic analysis to compare delayed with immediate or no antibiotic prescription, overall and for subgroups such as children and those with comorbidities. Delayed prescribing was associated with similar symptom severity as no antibiotic but patient satisfaction was higher and reconsultation rates lower. Children younger than 5 years, however, had a higher symptom severity with delayed antibiotics than with immediate antibiotics. Researchers concluded that delayed antibiotics, as a strategy could reduce repeat consultations without an increase in symptom severity or duration except in children.

Stuart B, Hounkpatin H, et al. Delayed antibiotic prescribing for respiratory tract infections: individual patient data meta-analysis. BMJ. 2021 Apr 28;373:n808. doi: 10.1136/bmj.n808. Erratum in: BMJ. 2021 May 24;373:n1282. PMID: 33910882; PMCID: PMC8080136.

MCH

Continued versus discontinued oxytocin stimulation in the active phase of labour

Once in active labor, the labor process is known to continue even after oxytocin stimulation is halted. Whether discontinuation of oxytocin stimulation could result in a lower Caesarean section rate was not clear. Researchers compared discontinued with continued oxytocin stimulation on Caesarean section rates, through a randomized controlled trial involving over 1200 women stimulated with intravenous oxytocin infusion during the latent phase of induced labor. Discontinuation of oxytocin stimulation was associated with higher Caesarean section rates (16.6%) compared to continued oxytocin (14.2%), but with a reduced risk of hyper-stimulation, or fetal heart rate abnormalities. The researchers concluded that discontinuation of oxytocin stimulation slightly increases Caesarean section rates but significantly reduces the risk of uterine hyper-stimulation and abnormal fetal heart rate patterns.

BMJ 2021;372:n716 http://dx.doi.org/10.1136/bmj.n716

The impact of COVID-19 pandemic on maternal mortality in Brazil

Pregnant women have been excluded in most studies assessing the effects of SARS-CoV-2 infection yet there may be effects on maternal health outcomes. The relationship between the maternal mortality ratio (MMR) and the incidence of COVID-19 in Bahia, Brazil, 2020 was verified in a study. Researchers compared the expected MMR for 2020 based on the previous decade's predictions. In 2020 (year when COVID-19 hit Bahia), there was a rise in the annual MMR (59.46%) higher than the expected throughout the months of this year with 13.19% of the maternal deaths resulting from COVID-19. Therefore, the COVID-19 pandemic has both direct and indirect negative effects on maternal health that call for public health attention to minimise maternal mortality during the pandemic.

de Carvalho-Sauer, R.d.C.O., Costa, M.d.C.N., Teixeira, M.G. et al. Impact of COVID-19 pandemic on time series of maternal mortality ratio in Bahia, Brazil: analysis of period 2011–2020. BMC Pregnancy Childbirth 21, 423 (2021). https://doi.org/10.1186/s12884-021-03899-y

Closed incision negative pressure wound therapy versus standard dressings in obese women undergoing Caesarean section

Surgical site complications after caesarean section are not uncommon, obesity being a major risk factor. Researchers through a large randomized controlled trial evaluated the effectiveness of a novel wound dressing modality, closed incision negative pressure wound therapy (NPWT) against standard dressing in preventing surgical site infections (SSIs) in obese women (pre-pregnancy body mass index of 30 or greater). Closed incision NPWT was found to be more effective than standard dressing at preventing SSIs, with a 24% risk reduction. The novel dressing modality was however associated with a small but significant increase in skin blistering. The researchers concluded that closed incision NPWT was superior but its use be weighed against an increase in both skin-blistering and economic considerations.

Hussamy DJ, Wortman AC, et al. Closed Incision Negative Pressure Therapy in Morbidly Obese Women Undergoing Cesarean Delivery: A Randomized Controlled Trial. Obstet Gynecol. 2019 Oct;134(4):781-789. doi: 10.1097/AOG.0000000000003465. PMID: 31503147.

The impact of COVID-19 on intrauterine foetal demise: a single system's experience

Some studies have shown an increase in intrauterine foetal demise (IUFD) during

the COVID-19 pandemic. A comparison of IUFD rates before and during the COVID-19 pandemic stratified by race showed that IUFD rates during the pandemic were similar to those before the pandemic period, with higher rates in tertiary care compared to a community hospital during both periods. This study also noted that blacks had higher IUFD rates than whites/Asians in both periods. Therefore, unlike findings from elsewhere, the healthcare system of the American south experienced no change in the IUFD rates during the pandemic. However, the racial differences in the IUFD rates especially at the tertiary hospitals call for more attention. Qualitative studies may be helpful to understand and devise culturally sensitive interventions for high-risk women who need specialised care.

Estin, Miriam, et al. "727 The impact of COVID-19 on intrauterine fetal demise: a single system's experience." American Journal of Obstetrics & Gynecology 224.2 (2021): S456.

Immediate "Kangaroo Mother Care "and Survival of Infants with Low Birth Weight

Most deaths among low birth weight babies occur before the babies are stabilized. It is not clear whether "Kangaroo mother care," (KMC) a type of newborn care involving skin-to-skin contact with the mother or other caregiver, which improves survival when initiated after babies are stabilized is safe and efficacious when initiated right after birth, before stabilization. Researchers through a randomized controlled trial in five countries (Ghana, India, Malawi, Nigeria, and Tanzania) compared mortality among low birth weight neonates assigned to receive immediate kangaroo mother care (intervention) or conventional care in an incubator or a radiant warmer until their condition stabilized and kangaroo mother care thereafter (control). They found that KMC initiated soon after birth, before stabilization was associated with a statistically significant reduction in neonatal death in the first 28 days of life. The associated reduced risk of death in the first 72 hours of life was not statistically significant.

https://www.nejm.org/doi/full/10.1056/NEJMoa2026486

Childhood overweight and obesity: a case-control study among school going children

Childhood obesity is a growing global public health problem that is associated with physical and psychosocial consequences. The burden and contributing factors, however, are not well understood. Researchers in Saudi Arabia through a case-control study involving 492 school children aged 5-9 years (246 overweight/obese children, and 246 normal weight control children) assessed for risk factors for childhood obesity. They found that an unemployed father, a father with overweight/obesity, wrong parental perception of child's weight status, cesarean delivery, daily time in active play of less than 30 min, frequent snacking and screen time use for more than 2 h per day outside of school were independent risk factors for being overweight or obese. They highlighted the need to focus on early identification and confrontation of these risk factors in order to prevent childhood overweight and obesity.

Aljassim, H., Jradi, H. Childhood overweight and obesity among the Saudi population: a case-control study among school children. J Health Popul Nutr 40, 15 (2021). https://doi.org/10.1186/s41043-021-00242-1

Engaging communities to combat COVID-19

Equipping community health workers with tools for COVID-19 interventions

Masks for all in the communities