Prevention

Aspirin for primary prevention of cardiovascular disease?

There is good evidence for the role of aspirin as secondary prevention for patients who have had a previous heart attack, coronary stent, coronary artery bypass graft surgery and stroke. The evidence on the role of aspirin for primary prevention of cardiovascular disease (CVD) is not conclusive yet millions of people without CVD take low dose aspirin. Researchers in a recent meta-analysis that included large trials leading to a sample size of 164,225 patients, found no difference in the risk of all-cause and cardiovascular mortality between patients who took aspirin and those who did not. Risk reduction for development of a major adverse cardiovascular event was only attained for males on statin treatment who were non-smokers. The relative risk for major bleeding events was raised by 46% in the group that took aspirin.

Gelbenegger G, Postula M, Pecen L et al. Aspirin for primary prevention of cardiovascular disease: a meta-analysis with a particular focus on subgroups. BMC Med 17, 198 (2019). https://doi.org/10.1186/s12916-019-1428-0

Dosing of Aspirin for prevention of preeclampsia in twin pregnancies

International guidelines recommend use of low dose aspirin for prevention of preeclampsia among pregnant women at high risk. The evidence for aspirin use and the appropriate dosing for women with twin pregnancies is not very clear. Researchers through a retrospective cohort of high risk twin pregnancies compared the efficacy of 75mg and 150mg daily dosing for prevention of preeclampsia. They found a significantly reduced incidence of hypertensive disorders in pregnancy among women with high risk twin pregnancies who took 75mg/day compared to those who did not take any aspirin. The researchers also found that 150mg/day of aspirin was associated with a much lower incidence of hypertensive disorders compared to 75mg/day.

Kalafat E, Shirazi A, Thilaganathan B, Khalil A. The role of aspirin in prevention of preeclampsia in twin pregnancies: does the dose matter? Am J Obstet Gynecol. 2020;223(3):457-458. doi:10.1016/j.ajog.2020.03.005

PPE preventing SARS-CoV-2 infection among health workers

Health care workers are at particularly increased risk for exposure to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Lack of or inadequate appropriate personal protective equipment (PPE) has left increasing numbers of health workers exposed to SARS-CoV-2 infection. Researchers studied the protective effect of standardised appropriate PPE, including protective suits, masks, gloves, goggles, face shields, and gowns among health workers who took care of and performed aerosolising procedures for patients admitted with Covid 19. None of the 420 health workers who had direct contact with the patients and performed at least one aerosolising procedures developed Covid 19 symptoms or tested positive for infection. The researchers emphasised the urgent need for provision and adequate training on use of appropriate PPE for health workers.

Min Liu, Shou-Zhen Cheng, Ke-Wei Xu et al. Use of personal protective equipment against coronavirus disease 2019 by healthcare professionals in Wuhan, China: cross sectional study. BMJ 2020;369:m2195. http://dx.doi.org/10.1136/bmj.m2195

Whole grains and risk for diabetes

Researchers have studied further the role of whole grain consumption in prevention of diabetes. Previous evidence has placed whole grains as favorable healthy food with a key role in prevention and control of many metabolic diseases including diabetes. This recent large study assessed the evidence from three large well defined cohorts of health professionals followed for more than 30 years. They assessed for the association between intake of whole grain as a whole and that for individual commonly eaten whole grains and the incidence of diabetes. These researchers found that consumption of whole grains in general and of several normally consumed individual whole grains such as whole grain breakfast cereal, oatmeal, brown bread, brown rice, among others, was associated with a significantly lower risk for type 2 diabetes. The researchers added to the pool of evidence for recommendation of diets rich in whole grains.

Hu Yang, Ding Ming, L Sampson et al. Intake of whole grain foods and risk of type 2 diabetes: results from three prospective cohort studies. BMJ2020;370:m2206. https://doi.org/10.1136/bmj.m2206

COVID-19

Saliva as a sample for COVID-19 diagnosis

The recent outbreak of COVID-19 in Wuhan, China, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has become a global emergency. The disease is currently being diagnosed by the reverse transcription polymerase chain reaction (RT-PCR) using a sample collected by the naspharyngeal swab. Recent evidence has demonstrated a role for the less invasive, quicker and less risky saliva sample for diagnosis, using RT-PCR. Researchers through a systematic review of nine studies carried out on patients with COVID-19 found that reverse transcription polymerase chain reaction carried out on self-collected saliva was both accurate and reliable. They recommend further studies on the subject because use of saliva may have implications for reduced health worker exposure, reduced invasiveness and a quicker sample collection process, among other benefits.

Fakheran O, Dehghannejad M, Khademi, A. Saliva as a diagnostic specimen for detection of SARS-CoV-2 in suspected patients: a scoping review. Infect Dis Poverty 9, 100 (2020). https://doi.org/10.1186/s40249-020-00728-w

Surgery with perioperative COVID-19

In a recent international multicenter cohort study involving 24 countries researchers assessed 30-day mortality and the rate of pulmonary complications in 1128 patients diagnosed with COVID-19 within 7 days before (26.1%) or 30 days after (71.5%) having surgery. Most (74%) operations were due to emergencies and 74.6% were major. Thirty-day mortality was 23.8%. Over half of the patients (51.2%) had pulmonary complications and these accounted for 82.6% of deaths. Male sex, age≥70, malignancy, and emergent or major surgery were associated with higher risk for mortality. The study acknowledged limitations including; having no control group and a lack of standardised universal testing that may have introduced bias in patient selection. The researchers concluded that patients with perioperative COVID-19 have a high risk for poor outcomes and recommend deferring of non-emergent procedures and consideration for non-operative management.

COVIDSurg Collaborative. Mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection: an international cohort study. Lancet 2020; 396: 27–38. https://doi.org/10.1016/S0140-6736(20)31182-X

Does HIV infection reduce or increase risk for COVID-19?

Evidence on the risk, clinical and radiological characteristics and the outcome of COVID-19 among patients infected with HIV is still very scarce. Researchers from Madrid-Spain reported findings from the largest prospective cohort to date, involving 51 consecutive HIV infected patients admitted with COVID-19 to a single hospital. Compared with 1,288 people living with HIV (PLWH) who did not have COVID-19, patients with COVID-19 were more likely to have a comorbidity, including; a higher BMI, hypertension, diabetes, chronic kidney disease or chronic liver disease. PLWH who had COVID-19 were also more likely to have been on Tenofovir-based anti-retroviral therapy prior to the COVID-19 diagnosis. No differences were observed in the clinical features, the laboratory abnormalities, and the radiographic changes among PLWH who had COVID-19 and those of HIV negative patients with COVID-19. There was no significant association between CD4 count and clinical outcomes. ART regimen also did not change the risk of COVID-19 disease severity. In conclusion, there is not enough evidence for a difference in risk of COVID-19 among PLWH or a protective effect from any ART regimen. PLWH should receive the same protective and treatment interventions as the general population.

Vizcarra P, Pérez-Elías MJ, Quereda C, et al. Description of COVID-19 in HIV-infected individuals: a single-centre, prospective cohort. Lancet HIV 2020; 7: e554–64. https://doi.org/10.1016/S2352-3018(20)30164-8

Comorbidities identified among patients dying from COVID-19

As of today, more than 900,000 people have died from COVID-19 and the death toll is increasing. It is becoming increasingly urgent to study the predictors of mortality. Researchers in the United States studied the association between documented comorbidities and mortality among a retrospective cohort of 31,461 patients with COVID-19 using medical records from 24 facilities. This cohort of patients had a median age of 50 years and the most frequent comorbidities were chronic pulmonary disease (17.5%) and diabetes (15%). They found that older age, being male, black ethnicity, having a history of a myocardial infarction, heart failure, dementia, chronic pulmonary disease, liver disease, renal disease or a metastatic solid tumor were all significantly associated with increased mortality. Older age, male sex and black ethnicity remained significant even after stratification by age. The study recognised the limitations of using medical records and also reported unknown ethnicity in 24% of the participants and possible incomplete recording of mortality occurring out of the facility. These findings still provide important hypothesis generating data.

Harrison SL, Fazio-Eynullayeva E, Lane DA, Underhill P, Lip GYH. Comorbidities associated with mortality in 31,461 adults with COVID-19 in the United States: A federated electronic medical record analysis. PLoS Med 17(9) (2020): e1003321. https://doi.org/10.1371/journal.pmed.1003321

Renin-Angiotensin-Aldosterone blockers and COVID-19 risk

Previous research has demonstrated that corona viruses use the Angiotensin Converting Enzyme 2 (ACE2) aminopeptidase that is abundant in the lungs as a receptor for cell entry. Angiotensin-receptor blockers (ARBs) and ACE inhibitors (ACEIs) increase the expression of ACE2 and are being studied as potential risk modulators for COVID-19. In a population-based case-control study in Italy, 6272 confirmed cases with COVID-19 were matched on age, sex and residence with 30,759 controls. Information on drug use and clinical profile was obtained from regional medical databases. Researchers found that in this predominantly male (63%) population with a mean age of 68±13 years the cases were more likely to have hypertension and to taking ARBs, ACEIs, other antihypertensives and other non-hypertensive drugs. The cases also had a worse clinical profile. However, they did not find any association between ARBs or ACEIs with risk of COVID-19

Mancia G, Rea F, Ludergnani M, Apolone G, Corrao G. Renin-Angiotensin-Aldosterone System Blockers and the Risk of COVID-19. N Engl J Med. 2020;382(25):2431-2440. doi:10.1056/NEJMoa2006923

COVID-19 and diabetes: reasons for the worse outcomes

With the increasing evidence about COVID-19 it has become clear that patients with diabetes are at increased risk for severe forms of the disease and for mortality. Much of the evidence is from studying patients with type2 diabetes but there's a similar trend observed with type1 diabetes. Whether the poor outcomes are attributable to diabetes alone or to other common comorbidities among patients with diabetes is not yet very clear. Researchers in a recent review explained some of these reasons. They emphasised the syndromic nature of diabetes as a likely explanation for multifaceted reasons for a worse prognosis. They explained that age, sex, ethnicity, comorbidities like obesity, hypertension and cardiovascular disease, prevalent pro-inflammatory and pro-coagulative state may collectively contribute to the risk for a worse prognosis. In addition, they note potential limitations in use of glucose lowering drugs and a need to properly study potential interaction between these drugs and COVID-19 treatments. Importantly they also note the direct negative effects on β-cell function caused by the severe acute respiratory syndrome coronavirus 2 that can lead to worsening of diabetes control, new onset hyperglycemia and even new-onset diabetes.

Apicella M, Campopiano MC, Mantuano M et al. COVID-19 in people with diabetes: understanding the reasons for worse outcomes. Lancet Diabetes Endocrinol 2020: 8; 782–92. https://doi.org/10.1016/S2213-8587(20)30238-2

COVID-19 in Uganda: patient characteristics and outcomes

The clinical profile and outcome of patients with COVID-19 in sub-Saharan Africa has not been well categorised. Researchers in Uganda described clinical characteristics and treatment outcomes of a prospective cohort of the first 56 patients admitted with COVID-19 at the Mulago National specialised hospital and Entebbe regional referral hospital; the largest treatment centers in the country at the time of the study. Primary outcomes included admission to intensive care, mechanical ventilation or in-hospital mortality. This cohort with more than half (57.1%) being asymptomatic, had a median age of 34.2 years, were predominantly male (67.9%) and 14.6% were children. Fever was the commonest symptom (21.4%), followed by cough (19.6%), rhinorrhea (16.1%), headache (12.5%), muscle ache (7.1%) and fatigue (7.1%). Pre-existing comorbidities included; hypertension (10.7%), diabetes (10.7%), HIV (7.1%) and obesity (36.6%). Laboratory derangements included; leucopenia (10.6%), lymphopenia (11.1%) and thrombocytopenia (26.3%) and 14.3% had abnormal chest X-rays. None of the patients reached the

clinical end points and even though 29 (51.8%) were treated with hydroxychloroquine, this did not significantly change the time to recovery.

Kirenga B, Muttamba W, Kayongo A, et al. Characteristics and outcomes of admitted patients infected with SARS-CoV-2 in Uganda. BMJ Open Resp Res 2020;7:e000646. doi:10.1136/ bmjresp-2020-000646

General

Dolutegravir and hyperglycaemia

In low-income and middle-income countries, dolutegravir-based regimens have replaced older anti-retroviral therapies (ART) as the preferred alternative. The Ugandan government recommended initiating dolutegravir-based regimens among ART-naive patients and transitioning eligible treatment-experienced patients from various first-line regimens. After noting that some patients developed symptomatic hyperglycemia following transition to dolutegravir, researchers at the Infectious Disease Institute at Makerere University set out to characterise these events. A comparison between ART-naïve and treatment-experienced patients who were transitioned to dolutegravir-based first-line regimens between April 1, 2018, and March 31, 2019 (the case group); and patients on first-line regimens that did not include dolutegravir during the same period (the control group) revealed an incidence over 12 months of 4.7 versus 0.32 hyperglycemia diagnoses per 1000 patients respectively (i.e. 16 of 3417 patients in the case group had new-onset hyperglycemia, versus 1 of 3230 patients in the control group). Median time from dolutegravir initiation to hyperglycemia onset was 4 months, hyperglycemia events were more severe in the case group and majority were preceded by weight loss. The underlying mechanism for hyperglycemia with dolutegravir in this population wasn't known and the researchers recommended further research including to investigate genetic polymorphisms influencing glucose metabolism.

Lamorde M, Atwiine M, Owarwo NC, et al. Dolutegravir-associated hyperglycaemia in patients with HIV. Lancet HIV. 2020;7(7):e461-e462. doi:10.1016/S2352-3018(20)30042-4

Inhaled triple therapy for COPD

Triple therapy with an inhaled glucocorticoid, a long-acting muscarinic antagonist (LAMA), and a long-acting β2-agonist (LABA) has been shown to be superior to dual therapies in the management of chronic obstructive pulmonary disease (COPD). Adverse events associated with inhaled glucocorticoids include pneumonia, bone fractures, and cataracts; the magnitude of which may depend on the dose, duration, and type of inhaled glucocorticoid treatment. Studies at two dose levels of inhaled glucocorticoid were lacking. A year-long randomised trial was conducted to evaluate the efficacy and safety of triple therapy at two dose levels of inhaled glucocorticoid (320 µg or 160 µg of budesonide) in comparison to two dual therapies (18 µg of glycopyrrolate plus 9.6 µg of formoterol or 320 µg of budesonide plus 9.6 µg of formoterol) in patients with moderate to very severe COPD. The findings re-affirmed benefits of triple therapy with a budesonide-glycopyrrolate-formoterol combination over dual therapy with glycopyrrolate–formoterol or budesonide–formoterol. The researchers also found that triple therapy with a 320-µg dose of budesonide resulted in a lower all-cause mortality than glycopyrrolate–formoterol dual therapy. Triple therapy with a 160-µg dose of budesonide was an effective treatment option for COPD, and this lower-dose inhaled glucocorticoid triple-therapy regimen showed greater efficacy than the higher-dose inhaled glucocorticoid–formoterol dual regimen, with lower rates of exacerbations, greater reductions in symptoms, and greater improvement in health-related quality of life.

Rabe KF, Martinez FJ, Ferguson GT, et al. Triple Inhaled Therapy at Two Glucocorticoid Doses in Moderate-to-Very-Severe COPD. N Engl J Med. 2020;383(1):35-48. doi:10.1056/ NEJMoa1916046

Test-guided tuberculosis treatment for HIV patients

Despite recommendations by WHO that people living with HIV infection be screened for tuberculosis (TB), a diagnosis of TB remains challenging in HIV-infected adults, especially when they are severely immunosuppressed. Mortality after anti-retroviral therapy (ART) initiation is high in these patients, and TB and invasive bacterial diseases are common causes of death. It was not yet known if empirical treatment for TB would avert these deaths as compared to testing-guided treatment. A multinational randomised clinical trial was conducted in Ivory Coast, Uganda, Cambodia and Vietnam to compare systematic empirical treatment for TB to treatment guided by testing in HIV- infected adults who had not previously received ART and had CD4+ T-cell counts below 100 cells per cubic millimeter. The researchers found that systematic empirical treatment for TB and treatment guided by specific testing had similar effects on the rate of death or invasive bacterial disease in a population of HIV-infected adults with CD4+ T-cell counts below 100 cells per cubic millimeter. An important observation made was that the systematic empirical treatment for TB approach was associated with more grade 3 or 4 adverse events.

Blanc FX, Badje AD, Bonnet M, et al. Systematic or Test-Guided Treatment for Tuberculosis in HIV-Infected Adults. N Engl J Med. 2020;382(25):2397-2410. doi:10.1056/ NEJMoa1910708

Renal-replacement therapy following acute kidney injury

Acute kidney injury is a common complication encountered in critically-ill patients, many of whom receive renal replacement therapy. It has been rather unclear when the most effective timing for initiation of this therapy should be. A multinational, randomised, controlled trial involving critically ill patients with severe acute kidney injury was conducted, to compare outcomes between an accelerated strategy of renal-replacement therapy (RRT) (in which therapy was initiated within 12 hours after the patient had met eligibility criteria) and a standard strategy (in which RRT was discouraged unless conventional indications developed or acute kidney injury persisted for >72 hours). The primary outcome for this study was death from any cause at 90 days. Researchers found that an accelerated renal-replacement strategy was not associated with a lower risk of death at 90 days than a standard strategy. Also noted was that a great percentage of survivors who received the accelerated strategy were dependent on RRT at 90 days and had adverse events; this finding suggests that greater exposure to RRT may compromise kidney repair and a return of endogenous kidney function.

STARRT-AKI Investigators; Canadian Critical Care Trials Group; Australian and New Zealand Intensive Care Society Clinical Trials Group, et al. Timing of Initiation of Renal-Replacement Therapy in Acute Kidney Injury. N Engl J Med. 2020 Jul 16;383(3):240-251. doi: 10.1056/ NEJMoa2000741. Erratum in: N Engl J Med. 2020 Jul 15;: PMID: 32668114.

Therapy versus glucocorticoid for osteoarthritis of the knee

With the global prevalence of osteoarthritis projected to increase

as the population ages, there's need to evaluate the extant treatment modalities for their effectiveness. Both physical therapy and glucocorticoid injections have been shown to confer clinical benefit with respect to osteoarthritis of the knee. It has been unclear whether the short-term and long-term effectiveness for relieving pain and improving physical function differ between these two therapies. A randomised trial involving 156 participants was conducted to compare these in a primary care setting in the U.S. Military Health System. The primary outcome was the total score on the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) at 1 year (scores range from 0 to 240, with higher scores indicating worse pain, function, and stiffness). The researchers found that patients with osteoarthritis of the knee who underwent physical therapy had less pain and functional disability at 1 year than patients who received an intra-articular glucocorticoid injection.

Deyle GD, Allen CS, Allison SC, Gill NW, Hando BR, Petersen EJ, Dusenberry DI, Rhon DI. Physical Therapy versus Glucocorticoid Injection for Osteoarthritis of the Knee. N Engl J Med. 2020 Apr 9;382(15):1420-1429. doi: 10.1056/NEJMoa1905877. PMID: 32268027.

Early rhythm-control therapy in patients with atrial fibrillation

There have been tremendous improvements in the management of atrial fibrillation, but despite these, patients with this condition remain at increased risk for cardiovascular complications. It has been rather unclear if early rhythm control therapy can reduce this risk. Through a multicenter randomised trial, researchers assessed if early rhythm control reduced the risk of cardiovascular complications compared to usual care, among patients with early atrial fibrillation (diagnosed ≤1 year before enrollment). The findings of the study were significant of an association between early rhythm-control therapy and lower risk of cardiovascular outcomes than usual care. The trial which was stopped for efficacy at the third interim analysis after a median of 5.1 years of follow-up per patient, had at the time of termination recruited and randomised 2789 patients with atrial fibrillation. Important to note however, is that the early rhythm control strategy was associated with more adverse events related to rhythm control therapy but incidence of the overall safety outcome events was similar in both groups. The researchers noted that these findings will be relevant to decisions regarding rhythm control therapy in patients with early atrial fibrillation.

Kirchhof P et al. for the EAST-AFNET 4 Trial Investigators. Early rhythm-control therapy in patients with atrial fibrillation. N Engl J Med 2020 Aug 29; [e-pub]. https://doi.org/10.1056/NEJMoa2019422

MCH

Stillbirth and long-term renal disease

There is evidence that women who experience stillbirths are at greater risk of long-term cardiovascular disease. Little, however is known about the risk of chronic kidney disease and end-stage renal disease in this patient group. A population-based cohort study (the largest about this research question to date) was conducted using nationwide data from the Swedish Medical Birth Register, National Patient Register, and Swedish Renal register. All women who had live births and stillbirths from 1973 to 2012 were included. Women with preexisting renal disease were excluded. There was a significant association observed between stillbirth and chronic kidney disease and end-stage renal disease, with women who had experienced at least 1 stillbirth having a greater risk of developing chronic kidney disease and end-stage renal disease compared with women who only had live births. These associations persisted even after removing all stillbirths that occurred in the context of preeclampsia, and small for gestational age or congenital malformations. The researchers concluded that further research was required to determine if affected women would benefit from closer surveillance and follow up for future renal disease.

Barrett PM, McCarthy FP, Evans M, et al. Stillbirth is associated with increased risk of long-term maternal renal disease: a nationwide cohort study. Am J Obstet Gynecol. 2020;223(3):427.e1-427.e14. doi:10.1016/j.ajog.2020.02.031

Pregnancy outcomes for women with pulmonary hypertension

Previous research reported an association between pulmonary hypertension in pregnancy and poor maternal and fetal outcomes. Researchers recently performed a meta-analysis using data from studies on this topic published over the recent decades, including the period 1st January 1990 to 31st May 2018. Primary outcomes studied included maternal mortality and any pregnancy loss. Twenty studies that described 610 pregnancies were included. Findings included maternal mortality of 11.5% (95% CI; 7.6-17.2) and the prevalence of pregnancy loss was 22.8% (95% CI; 16.2-31.1). The prevalence of prematurity and intrauterine growth restriction/small for gestational age (IUGR/SGA) which were reported by 7 and 8 studies, respectively was 51.7% (95% CI; 37.6-65.7) and 29.3% (95% CI; 20.9-39.5). Prevalence of cesarean delivery and general anesthesia was 72.1% (95% CI; 60.6-81.93) and 40.1% (95% CI; 26.4-55.5), respectively. The researchers concluded that fetal and maternal outcomes among pregnant women with pulmonary hypertension have improved over the recent decades and the findings impact pre-conception counseling for this category of patients.

Jha N, Jha AK, Mishra SK, Sagili H. Pulmonary hypertension and pregnancy outcomes: Systematic Review and Meta-analysis. Eur J Obstet Gynecol Reprod Biol. 2020 Aug 24;253:108-116. doi: 10.1016/j.ejogrb.2020.08.028. Epub ahead of print. PMID: 32862030.

Amoxicillin treatment for childhood pneumonia

The World Health Organization (WHO) recommends oral amoxicillin as first line for children with pneumonia and no general danger signs. Evidence for the appropriate duration of treatment with this antibiotic in low-resource settings in Africa, where the greatest burden is accommodated is lacking. Through a randomised controlled trial involving over 3000 study participants aged 2 to 59 months done in Malawi, researchers evaluated if treatment with amoxicillin for 3 days was less effective than treatment for 5 days in children with chest indrawing pneumonia. Participants were followed for 14 days with the primary outcome being treatment failure by day 6. The results indicated that the 3-day treatment course was not inferior to the 5-day treatment course in HIV-uninfected Malawian children. This finding could likely improve early identification of children failing on first-line and who need to be promptly transitioned to appropriate second-line treatment.

Ginsburg AS, Mvalo T, Nkwopara E, et al. Amoxicillin for 3 or 5 Days for Chest-Indrawing Pneumonia in Malawian Children. N Engl J Med. 2020;383(1):13-23. doi:10.1056/NEJMoa1912400