

General

Cardiovascular outcomes in adults with hypertension with evening versus morning dosing of usual antihypertensives in the UK (TIME study)

Evening dosing with antihypertensive therapy has been thought to result in better cardiovascular outcomes than morning dosing. Researchers, through this large study compared morning and evening dosing in patients with hypertension. A total of 21104 were randomly assigned (1:1) to either take all their medications in the morning or evening and followed up for a mean duration of 5 years. The primary outcome was cardiovascular death or hospitalization for myocardial infarction or stroke. By the end of the follow-up, the researchers found no significant difference in the occurrence of primary outcome events in the evening or morning groups (3.4% versus 3.7% respectively). The researchers hence concluded that patients be advised to take their antihypertensive medications at a convenient time that minimizes undesirable effects.

Reference

Mackenzie IS, et al. Cardiovascular outcomes in adults with hypertension with evening versus morning dosing of usual antihypertensives in the UK (TIME study): a prospective, randomised, open-label, blinded-endpoint clinical trial. *Lancet*. 2022 Oct 22;400(10361):1417-1425. doi: 10.1016/S0140-6736(22)01786-X. Epub 2022 Oct 11. PMID: 36240838; PMCID: PMC9631239.

Rivaroxaban treatment for six weeks versus three months in patients with symptomatic isolated distal deep vein thrombosis: randomised controlled trial

Isolated distal vein thrombosis accounts for a majority of all deep vein thromboses (DVT), with a high frequency of recurrence. The optimal duration for anticoagulant treatment is controversial. Researchers compared the efficacy and safety of two treatment durations with rivaroxaban (6 weeks Vs 3 months) in 402 adult patients with symptomatic isolated distal DVT. They were equally randomized to receive either rivaroxaban or placebo for additional 6 weeks after standard 6-weeks therapy and followed up to 24 months. The efficacy outcome was a recurrence of venous thromboembolism (VTE) whereas the safety outcome was major bleeding during follow-up. Recurrence of VTE occurred less in the 3-months arm (11%) compared to 6 weeks-arm (19%). Researchers hence confirmed that 3 months of rivaroxaban treatment reduced the risk of VTE without increasing the risk of hemorrhage.

Reference

Agno W, BertÃ L, et al. Rivaroxaban treatment for six weeks versus three months in patients with symptomatic isolated distal deep vein thrombosis: randomised controlled trial *BMJ* 2022; 379 :e072623 doi:10.1136/bmj-2022-072623

Intermittently Scanned Continuous Glucose Monitoring for Type 1 Diabetes

Fingerstick blood glucose testing is the most practiced way of glucose monitoring. Whether continuous glucose

monitoring is more beneficial is uncertain. Researchers, through a study involving 156 participants with type 1 diabetes and high glycated hemoglobin levels, compared the efficacy of intermittent scanned continuous glucose monitoring (intervention arm) to fingerstick testing (usual care). Participants were randomised in a ratio of 1:1 and followed up to 24 weeks. The primary endpoint was glycated hemoglobin (HbA1c) level at 24 weeks. The researchers found that the HbA1c decreased more in the intervention arm than in the usual arm 8.7% to 7.9% versus 8.5% to 8.3% respectively. The researchers hence concluded that continuous glucose monitoring resulted in significantly lower HbA1c levels than fingerstick testing.

Reference

Leelarathna L, et al. Intermittently Scanned Continuous Glucose Monitoring for Type 1 Diabetes. *N Engl J Med*. 2022 Oct 20;387(16):1477-1487. doi: 10.1056/NEJMoa2205650. Epub 2022 Oct 5. PMID: 36198143.

Allopurinol versus usual care in UK patients with ischaemic heart disease (ALL-HEART)

Small observational studies have reported the cardiovascular benefits of allopurinol, a drug licensed for the treatment of gout. This finding had not been confirmed in a large, prospective controlled study. Researchers through this large, multi-centric randomized trial compared cardiovascular outcomes in patients aged 60 years or older with ischemic heart disease (IHD) but no history of gout treated with allopurinol versus usual care. A total of 5721 participants were included in the study and followed up for a mean duration of 4.8 years. The primary outcome was a composite of myocardial infarction, stroke, or cardiovascular death. The researchers found no difference between allopurinol or usual-care groups in terms of primary end-point (11.0% versus 11.3% respectively). The findings hence don't support allopurinol use in patients with IHD, without gout.

Reference

Mackenzie IS, et al; Allopurinol versus usual care in UK patients with ischaemic heart disease (ALL-HEART): a multicentre, prospective, randomised, open-label, blinded-endpoint trial. *Lancet*. 2022 Oct 8;400(10359):1195-1205. doi: 10.1016/S0140-6736(22)01657-9. PMID: 36216006.

Efficacy of awake prone positioning in patients with covid-19 related hypoxemic respiratory failure: systematic review and meta-analysis of randomized trials

Prone positioning is known to be life-saving in patients receiving invasive ventilation for non-COVID-19 respiratory distress syndrome. Its utility in spontaneously breathing patients with COVID-19 related respiratory failure is uncertain. Researchers conducted a systematic review involving 17 randomized trials comparing prone-positioning to usual care in adults with COVID-19-related hypoxemic respiratory failure. The primary outcome measure was endotracheal intubation, with secondary ones including mortality, ventilator-free days, and hospital stay days, among others. Awake-prone positioning reduced the risk of endotracheal intubation (24.2%) compared with usual care (29.8%) but didn't

significantly affect secondary outcomes. Researchers hence concluded that awake-prone positioning as compared to usual care reduces the risk of endotracheal intubation in COVID-19-related hypoxemic respiratory failure with little or no effect on mortality.

Reference

Weatherald J, Parhar K K S, et al. Efficacy of awake prone positioning in patients with covid-19 related hypoxemic respiratory failure: systematic review and meta-analysis of randomized trials BMJ 2022; 379 :e071966 doi:10.1136/bmj-2022-071966

Safety and Efficacy of a Monoclonal Antibody against Malaria in Mali

In the absence of an efficacious vaccine to control malaria infection, new methods are needed to augment existing countermeasures. Researchers tested in a malaria-endemic region a monoclonal antibody CIS43LS that had shown promise in a phase-1 clinical trial. A total of 330 participants were randomly assigned to 3 groups to receive a single intravenous infusion of 10mg/kg, 40mg/kg body weight of CIS43LS, or placebo and followed-up for 24 weeks. The primary end-point was the first plasmodium falciparum (P.falciparum) infection detected on blood-smear. The outcome occurred most in the placebo group (78.2%), 10mg/kg of CIS43LS group (35.5%), and least in the 40mg/kg of CIS43LS group (18.2%). The researchers hence found CIS43LS protective against P.falciparum infections over a 6-month malaria season without safety concerns.

Reference

Kayentao K, Ongoiba A, et al; Safety and Efficacy of a Monoclonal Antibody against Malaria in Mali. N Engl J Med. 2022 Nov 17;387(20):1833-1842. doi: 10.1056/NEJMoa2206966. Epub 2022 Oct 31. PMID: 36317783.

A 24-Week, All-Oral Regimen for Rifampin-Resistant Tuberculosis

In rifampin-resistant tuberculosis, the standard-care treatment is long, inconvenient, and with serious safety concerns. Shorter, safer, and more efficacious alternatives are needed. Researchers compared a 24-week all-oral regimen of bedaquiline, pretomanid, linezolid, and moxifloxacin (BPaLM) to 9-20-months standard-care regimen in 15 years and older patients with rifampin-resistant pulmonary tuberculosis. A total of 301 participants were randomly assigned to either group. The primary outcome was an unfavorable status, including death, treatment failure et cetera at 72 weeks. The study found that 11% of patients in the BPaLM group and 48% in the standard-care arm had primary outcome events, with significantly fewer adverse events (19% versus 59%). The researchers concluded that a 24-week all-oral regimen was non-inferior to the standard with a better safety profile.

Reference

B.-T. Nyang'wa, et al; A 24-Week, All-Oral Regimen for Rifampin-Resistant Tuberculosis. New England Journal of Medicine 2022 Vol. 387 Issue 25 Pages 2331-2343 DOI: 10.1056/NEJMoa2117166

Association of Direct-Acting Antiviral Therapy with liver and non-liver complications and long-term mortality in patients with chronic Hepatitis C

Chronic hepatitis C (CHC) infection and its complications are associated with high rates of morbidity and mortality globally. It's uncertain if directly-acting antiviral (DAA) therapy improves outcomes in these patients. Researchers, through this large retrospective study involving 245,596 adult patients with CHC, compared the incidence of hepatocellular carcinoma, liver decompensation, non-liver events, and mortality; between patients treated and not treated with DAA medications. The study found all liver events, relevant non-liver events, and mortality to be significantly lower in patients treated with DAA medications. The researchers hence concluded that antiviral therapy improves both liver and non-liver outcomes as well as mortality.

Reference

Ogawa E, Chien N, et al. Association of Direct-Acting Antiviral Therapy With Liver and Nonliver Complications and Long-term Mortality in Patients With Chronic Hepatitis C. JAMA Intern Med. Published online December 12, 2022. doi:10.1001/jamainternmed.2022.5699

Pneumococcal Conjugate Vaccine use reduces hospitalization with Pneumonia in Medicare beneficiaries 65 years or older

Globally, there is an increasing burden of vaccine-preventable pneumococcal pneumonia contributing to mortality and morbidity among adults. This has resulted in recommendations for pneumococcal vaccination in adult patients. It's unclear if a 13-valent pneumococcal conjugate vaccine (PCV13) is effective. Researchers in this US cohort study involving over 24 million Medicare beneficiaries evaluated the association of PCV13 with pneumonia hospitalisations in adults 65 years or older. After 3 years of follow-up, the researchers found that vaccinated individuals had a 6.7% lower risk of pneumonia hospitalization compared to those who didn't receive any pneumococcal vaccines. The researchers hence concluded that increased higher-valent pneumococcal vaccine coverage and use could avert more pneumonia hospitalisations in adults.

Reference

Kobayashi M, et al. Association of Pneumococcal Conjugate Vaccine Use With Hospitalized Pneumonia in Medicare Beneficiaries 65 Years or Older With and Without Medical Conditions, 2014 to 2017. JAMA Intern Med. Published online December 05, 2022. doi:10.1001/jamainternmed.2022.5472

Comparative effectiveness of prophylactic strategies for preeclampsia: a network meta-analysis of randomized controlled trials

Various prophylactic strategies exist for preeclampsia, a common disorder of pregnancy. Their comparative effectiveness has, however, not been well evaluated. Researchers, through this meta-analysis involving 130 clinical trials, compared 13 prophylactic strategies with each other or with negative controls. The study found that low-molecular-weight heparin, vitamin D supplementation, and exercise were as efficacious as

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calcium supplementation and aspirin in preventing preeclampsia. In a head-to-head comparison, exercise was superior to aspirin and calcium supplementation in preventing pregnancy-induced hypertension. The researchers found that low-molecular-weight heparin, vitamin D supplementation, exercise, calcium supplementation, and aspirin all reduce the risk of preeclampsia but found no significant differences in effectiveness between them. They further noted that these needed to be reevaluated in more robust studies.

Reference

Liu YH, Zhang YS, et al. Comparative effectiveness of prophylactic strategies for preeclampsia: a network meta-analysis of randomized controlled trials. *Am J Obstet Gynecol.* 2022 Oct 23;S0002-9378(22)00819-5. doi: 10.1016/j.ajog.2022.10.014. Epub ahead of print. PMID: 36283479.

Association of checklist usage with adherence to recommended prophylactic low-dose aspirin for prevention of preeclampsia

Despite the recommendation of low-dose aspirin in patients at risk of preeclampsia, its utilization remains low according to recent findings. It's unclear if the use of a risk-factor checklist could increase low-dose aspirin use. In this cohort study, researchers compared rates of self-reported use of low-dose aspirin in patients referred by a specific provider group that routinely administers a checklist versus that among patients referred by other providers. Higher rates of low-dose aspirin use were reported in the checklist group than in the other provider group; 78% versus 52% and 68% versus 22% in high and moderate risk-factors groups respectively. The researchers hence recommended the use of these checklists to identify candidates for low-dose aspirin, and other checklists to improve patient outcomes.

Reference

Zhou MK, Combs CA, et al. Association of checklist usage with adherence to recommended prophylactic low-dose aspirin for prevention of preeclampsia. *Am J Obstet Gynecol.* 2022 Dec 1;S0002-9378(22)02208-6. doi: 10.1016/j.ajog.2022.11.1302. Epub ahead of print. PMID: 36462540.

Vaginal cleansing before unscheduled cesarean delivery to reduce infection: A Randomized Clinical Trial

Infections following Cesarean delivery after labour are a common cause of maternal postnatal morbidity. It's unclear if vaginal cleansing with antiseptic could help avert these. Researchers in this study evaluated if vaginal cleansing with povidone-iodine before Cesarean delivery after labour reduces post-operative infections. A total of 608 participants were equally randomized to either vaginal cleansing or not and followed up for infectious morbidity including surgical site infection, fever, endometritis, or wound complications over 30 days. The study found no significant differences in outcome in the two groups (11.8% versus 11.5%). They further concluded that their findings don't support the routine use of vaginal cleansing for women undergoing Cesarean delivery after labour.

Reference

Temming LA, Frolova AI, Raghuraman N, Tuuli MG, Cahill AG. Vaginal Cleansing Before Unscheduled Cesarean Delivery to Reduce Infection: A Randomized Clinical Trial. *Am J Obstet Gynecol.* 2022 Nov 30;S0002-9378(22)02206-2. doi: 10.1016/j.ajog.2022.11.1300. Epub ahead of print. PMID: 36462539.

Effect of Pessary vs Surgery on Patient-Reported Improvement in Patients With Symptomatic Pelvic Organ Prolapse

With increasing life expectancy, pelvic organ prolapse in women is likely to increase hence a need for cost-effective treatment approaches. It's unclear if the pessary approach is as good as surgery in the management of symptomatic pelvic organ prolapse. Researchers compared these two modalities through a randomized clinical trial involving 440 female patients with symptomatic pelvic organ prolapse in the Netherlands. The outcome was patient-reported improvement at 24 months measured with a Patient Global Impression of Improvement scale. Improvement was reported in 76.3% of the pessary group and 81.5% of the surgery group, failing to meet the criteria for non-inferiority. The researchers also noted a high cross-over rate (54.1%) from the pessary to surgery group further complicating the interpretation of results.

Reference

Van der Vaart LR, Vollebregt A, Milani AL, et al. Effect of Pessary vs Surgery on Patient-Reported Improvement in Patients With Symptomatic Pelvic Organ Prolapse: A Randomized Clinical Trial. *JAMA.* 2022;328(23):2312–2323. doi:10.1001/jama.2022.22385

Risk Factors for Suffocation and Unexplained Causes of Infant Deaths

Sudden infant death syndrome (SIDS) and its risk factors are a growing research area of interest. Previous studies have not examined sleep-related suffocation and unexplained infant deaths separately. Researchers through this case-control study using CDC data included 112 sleep-related suffocation cases, and 300 unexplained infant death cases with their age-matched controls respectively. The study found that risk factors for unexplained infant deaths including non-supine position, soft bedding, not room sharing with a caregiver, and surface sharing were also risk factors for suffocation but with a larger magnitude of risk for suffocation. The researchers hence recommended the addition of suffocation risk into infant safe sleep education, as it may be much easier for caregivers to understand than death from unknown causes.

Reference

Parks SE, et al; Risk Factors for Suffocation and Unexplained Causes of Infant Deaths. *Pediatrics.* 2022 Dec 5:e2022057771. DOI: 10.1542/peds.2022-057771. Epub ahead of print. PMID: 36464994.

Serious Bacterial Infections in Young Febrile Infants with Positive Urinalysis Results

Whether febrile infants with positive urinalysis (UA) require routine lumbar punctures to rule out bacterial meningitis is not known. Researchers in this observational study set out to determine the prevalence of bacteremia and/or bacterial meningitis in febrile infants ≤60 days with positive UA results. Of the 7180 infants enrolled, 15.2% had positive UA results. The risk of bacteremia was higher in those with positive UA results (5.8%) compared to those with negative UA results (1.1%). There was however no difference in the prevalence of bacterial meningitis in positive or negative UA results in the first 2 months of life. The researchers concluded that in noncritical febrile infants with positive UA results, the

prevalence of bacterial meningitis wasn't increased.

Reference

Mahajan P, et al; Pediatric Emergency Care Applied Research Network (PECARN). Serious Bacterial Infections in Young Febrile Infants With Positive Urinalysis Results. *Pediatrics*. 2022 Oct 1;150(4):e2021055633. doi: 10.1542/peds.2021-055633. PMID: 36097858; PMCID: PMC9648158.

Surgery

Routine sterile glove and instrument change at the time of abdominal wound closure to prevent surgical site infection

Globally, surgical site infections (SSIs) are the most common complication of surgery. Routine change of gloves and instruments before wound closure has been suggested as an approach that could be beneficial in reducing SSIs. Researchers through this large multi-centric cluster randomized trial tested if this approach reduces SSIs. Clusters were randomized to either current practice (42) or intervention (39), where the intervention was a routine change of gloves and instruments before wound closure. The primary outcome was SSI within 30 days of surgery. The researchers found that the intervention reduced SSI by 13% (1 in 8 SSIs) at 30 days after surgery compared to the control. They recommended that evidence of this easily deliverable intervention be put into practice globally to avert SSIs.

Reference

NIHR Global Research Health Unit on Global Surgery. Routine sterile glove and instrument change at the time of abdominal wound closure to prevent surgical site infection (ChEETAH): a pragmatic, cluster-randomised trial in seven low-income and middle-income countries. *Lancet*. 2022 Nov 19;400(10365):1767-1776. doi: 10.1016/S0140-6736(22)01884-0. Epub 2022 Oct 31. PMID: 36328045.

Aqueous skin antiseptics before surgical fixation of open fractures: cluster-randomized, crossover trial

Povidone-iodine is usually the preferred agent of antiseptics before surgery on traumatic contaminated wounds. Whether chlorhexidine is suitable in similar surgical settings is not known. Researchers through this study conducted in Canada, Spain, and the USA compared aqueous 10% povidone-iodine with aqueous 4% chlorhexidine gluconate in adult patients with open extremity fractures requiring surgical fixation. The primary outcome was surgical site infection (SSI) within 30 or 90 days for superficial or deep infections respectively. Of the 1571 participants in whom the outcome was known, there was no difference in rates of SSI (7% in both groups). The researchers concluded that either povidone-iodine or chlorhexidine can be used in traumatic wound antiseptics with the choice based on availability, patient contraindications, or cost.

Reference

PREP-IT Investigators. Aqueous skin antiseptics before surgical fixation of open fractures (Aqueous-PREP): a multiple-period, cluster-randomised, crossover trial. *Lancet*. 2022 Oct 15;400(10360):1334-1344. doi: 10.1016/S0140-6736(22)01652-X. Erratum in: *Lancet*. 2023 Dec 17;400(10369):2198. PMID: 36244384.

Effect of Colonoscopy screening on risks of Colorectal Cancer and related death

Whether colonoscopy as a screening tool for colorectal cancer affects the risk of colorectal cancer and related death isn't known. Researchers conducted a randomised trial involving healthy men and women between 55 and 64 years of age from some population registries in Europe and randomized them to receive a single colonoscopy (invited group) or usual-care group (no invitation). The outcome measure was colorectal cancer and related death. At the 10-year follow-up, the risk of colorectal cancer was lower in the invited group (0.98%) compared to usual care (1.20%). There was however no difference in the risk of death from any cause across the two groups. The findings were supportive of colonoscopy as a screening tool for colorectal cancer.

Reference

Bretthauer M et al; Effect of Colonoscopy Screening on Risks of Colorectal Cancer and Related Death. *N Engl J Med*. 2022 Oct 27;387(17):1547-1556. doi: 10.1056/NEJMoa2208375. Epub 2022 Oct 9. PMID: 36214590.

Association between preoperative hemodialysis timing and postoperative mortality in patients with End-stage Kidney Disease

The optimal timing of hemodialysis before surgery among patients with end-stage kidney disease (ESRD) isn't known. Researchers, through this large cohort study assessed if the time interval between hemodialysis and subsequent surgery was associated with outcomes in ESRD patients. Intervals of 1-, 2-, or 3 days from the most recent hemodialysis to surgical procedure were evaluated on their impact on 90-day postoperative mortality. The study involving 346,828 patients found that longer intervals were significantly associated with a higher risk of 90-day mortality in a dose-dependent fashion that is 5.2%, 4.7%, and 4.2% for 3-, 2-, and 1-day intervals respectively. The researchers concluded that longer intervals are associated with higher mortality rates, especially in those not receiving hemodialysis on the same day as surgery.

Reference

Fielding-Singh V, Vanneman MW, Grogan T, et al. Association Between Preoperative Hemodialysis Timing and Postoperative Mortality in Patients With End-stage Kidney Disease. *JAMA*. 2022;328(18):1837-1848. doi:10.1001/jama.2022.19626

Safety and Efficacy of Robotic vs Open Liver Resection for Hepatocellular Carcinoma

With the rapidly evolving innovations in surgery, the utility of robotic surgery in surgical oncology remains underevidenced. Researchers in this study compared outcomes of robotic liver resection (RLR) to open liver resection (OLR) for hepatocellular carcinoma (HCC). The study included 398 patients; 106 RLR patients were compared with 106 OLR patients after propensity score matching. The study found that RLR patients had a significantly longer operative time; 295 versus 200 minutes, but with a shorter hospital stay, fewer admissions to the intensive care unit, and lower rates of post-hepatectomy liver failure compared to OLR patients. The 90-day survival rate was however comparable. The researchers concluded that RLR was a safer approach for HCC patients than OLR, and in patients with compromised liver function.