

General

Metformin Compared to Sulfonylurea Reduced the Development of Osteoarthritis in Patients with Type 2 Diabetes

Preclinical studies and some observational studies suggest a protective role of metformin in the development of osteoarthritis (OA). Researchers, through this nationwide retrospective study enrolled patients with type 2 diabetes aged 40 years and older and determined the risk of OA and joint replacement with metformin or sulfonylurea. After matching, the metformin and sulfonylurea group each included 20937 individuals. The researchers found that metformin reduced the risk of OA development by 24% compared to the control (sulfonylurea) but with no statistical difference in joint replacements. The researchers hence concluded that metformin use is associated with reduced risk of OA development and suggested further intervention studies to confirm this finding.

Reference

Baker, M.C. et al. (2023) 'Development of Osteoarthritis in Adults With Type 2 Diabetes Treated With Metformin vs a Sulfonylurea', *JAMA Network Open*, 6(3), pp. e233646–e233646. Available at: <https://doi.org/10.1001/JAMANETWORKOPEN.2023.3646>.

Hydrocortisone in Severe Community-Acquired Pneumonia

The benefit of glucocorticoids in severe infections for instance severe pneumonia has long been controversial. Researchers, through this multi-center, double-blind, randomized controlled trial compared 28-day mortality among patients admitted to the intensive care unit with severe pneumonia who received intravenous hydrocortisone with those who received a placebo. At analysis, the researchers found that death by 28 days was less frequent in the intervention group (6.2%) compared to the placebo group (11.9%). They also found that endotracheal intubation and vasopressor use was higher in the placebo group, with no difference in hospital-acquired infections or gastrointestinal bleeding. They concluded that in ICU patients admitted with severe pneumonia, hydrocortisone was associated with a lower risk of death compared to placebo.

Reference

Dequin, P.-F. et al. (2023) 'Hydrocortisone in Severe Community-Acquired Pneumonia.', *The New England journal of medicine* [Preprint].

Acute effects of Coffee consumption on health among ambulatory adults

The acute health effects of coffee, one of the most consumed beverages in the world, are uncertain. It has been suggested that it should be avoided owing to its associated proarrhythmic effects but evidence for this is lacking. In a prospective study involving 100 adults, researchers examined the effects of caffeinated coffee on cardiac ectopy and arrhythmias, daily step counts, sleep minutes, and serum glucose levels. The primary outcome was the mean number of premature atrial contractions (PACs). The researchers found that caffeinated coffee

consumption was associated with a mean PACs of 58 versus 53 when caffeine was avoided. They thus concluded that consumption of caffeinated coffee didn't result in significantly more PACs than caffeine avoidance.

Reference

Lingani, M. et al. (2023) 'Effects of maternal antenatal treatment with two doses of azithromycin added to monthly sulfadoxine-pyrimethamine for the prevention of low birth weight in Burkina Faso: an open-label randomized controlled trial', *Malaria Journal*, 22(1), pp. 1–9

Long-term outcomes of monitoring, surgery, or radiotherapy for localized prostatic cancer

Researchers evaluated the effectiveness of different treatment strategies for localized prostatic cancer, including active monitoring, prostatectomy, and radiotherapy through this long-term follow-up of patients in a randomized controlled trial. A total of 1610 patients were randomized: 545 to receive active monitoring, 553 to undergo a prostatectomy, and 545 to undergo radiotherapy. The primary outcome measure was death from prostatic cancer; with death from any cause, metastases, disease progression, and initiation of long-term deprivation therapy as secondary outcomes. After 15 years of follow-up, overall prostatic-specific death was found to be low (2.7%) and didn't vary between treatment groups. The researchers recommended based on this observation that the choice of therapy for localized prostatic cancer, be determined by weighing the benefits and harms of the strategy.

Reference

Hamdy, F.C. et al. (2023) 'Fifteen-Year Outcomes after Monitoring, Surgery, or Radiotherapy for Prostate Cancer', <https://doi.org/10.1056/NEJMoa2214122> [Preprint]. Available at: <https://doi.org/10.1056/NEJMoa2214122>.

Sepsis-Induced Hypotension: Restrictive or Liberal Fluid Management?

Patients with sepsis-induced hypotension are commonly treated with intravenous fluids and/or vasopressors, but data on prioritizing between these two is lacking. A recently published trial compared a restrictive fluid strategy (prioritizing vasopressors) to a liberal fluid strategy (prioritizing higher volumes of fluids) over a 24-hour resuscitation period. A total of 1563 patients were enrolled and equally randomized to either group. The primary outcome measure was all-cause mortality before discharge home by day 90. The primary outcome was similar in both groups occurring in 14.0% in the restrictive fluid strategy, and 14.9% in the liberal fluid group. The authors hence concluded that the restrictive fluid strategy wasn't superior to the liberal strategy in patients with sepsis-induced hypotension.

Reference

Early Restrictive or Liberal Fluid Management for Sepsis-Induced Hypotension' (2023) *New England Journal of Medicine* [Preprint]. Available at: <https://doi.org/10.1056/NEJMoa2212663>.

An Intervention to Improve Acute Heart Failure Outcomes

Acute heart failure presents a challenge in clinical practice. It's not known if a strategy to support clinicians

to make decisions on whom to admit or discharge would affect outcomes. A new study in Canada employed a stepped-wedge cluster-randomized approach involving 10 hospitals to compare usual care to intervention (a point-of-care algorithm to stratify patients according to the risk of death). In the intervention, low-risk patients were discharged early while high-risk patients were admitted. The primary outcome was a composite of all-cause death or cardiovascular-related hospitalization within 30 days after presentation. Researchers found that the primary outcome occurred less during the intervention than in the control phase (12.1% versus 14.5%). They hence concluded that the use of a hospital-based decision-support strategy lowers the risk of death or hospitalization compared to usual care.

Reference

Lee, D.S. et al. (2023) 'Trial of an Intervention to Improve Acute Heart Failure Outcomes', *New England Journal of Medicine*, 388(1), pp. 22–32. Available at: <https://doi.org/10.1056/NEJMOA2211680>

Empagliflozin in Patients with Chronic Kidney Disease

There has been much excitement about sodium-glucose co-transporters (SGLTs) including empagliflozin in the management of diabetes and heart failure. Its role in chronic kidney disease (CKD) is, however, uncertain. Researchers in this trial enrolled 6609 CKD patients (54.0% of whom had diabetes), with estimated glomerular-filtration-rate (eGFR) of 20 to <45 or eGFR 40 to <90 ml/min per 1.73m² with a urinary albumin-to-creatinine ratio \geq 200mg/g. They were randomized to receive empagliflozin 10mg or placebo. The outcome measure was kidney disease progression or death from cardiovascular causes. During a median follow-up of 2 years, the outcome occurred in fewer patients in the empagliflozin group (13.1%) than in the placebo (16.9%) as with the rate of hospitalization. The authors thus concluded that in CKD patients at risk of progression, empagliflozin lowers progression risk more than placebo.

Reference

Empagliflozin in Patients with Chronic Kidney Disease (2023) *New England Journal of Medicine*, 388(2), pp. 117–127. Available at: <https://doi.org/10.1056/NEJMOA2204233>

Risk Factors and Outcomes of Sepsis-Associated Acute Kidney Injury in Intensive Care Units in Johannesburg, South Africa

Although acute kidney injury is an important cause of morbidity and mortality among patients admitted to the intensive care unit (ICU) with sepsis, there is paucity of information on predictors and outcomes of sepsis-associated acute kidney injury (SA-AKI) among patients admitted to ICUs in sub-Saharan Africa. Researchers studied the rate of SA-AKI, factors associated with its onset and predictors of mortality at 90days among sepsis patients admitted to the ICUs at two teaching hospitals in South Africa. Of 327 patients prospectively observed, 185 (56.6%) developed SA-AKI. Common comorbidities included HIV/AIDS (19.3%), hypertension (14.2%) and diabetes mellitus (10.1%). Older men with cardiovascular disease, malignancies, hypotension and a low serum albumin level were more likely to develop SA-AKI. At

multivariate analysis, predictors of SA-AKI were age \geq 55 years (odds ratio (OR) 2.43; 95% CI 1.27 - 4.65), inotropic support (OR 3.61; 95% CI 2.18 - 5.96) and a low serum albumin level (OR 2.93; 95% CI 1.40 - 6.13). SA-AKI and the need for inotropic support were associated with 1.9-fold and 1.7-fold increase in mortality at 90 days after ICU admission, respectively.

Reference

Mweene MD, Richards GA, et. al. Risk factors and outcomes of sepsis-associated acute kidney injury in intensive care units in Johannesburg, South Africa. *S Afr Med J*. 2022 Dec 1;112(12):919-923. doi: 10.7196/SAMJ.2022.v112i12.16410. PMID: 36472316.

Prevalence and Predictors of Peripheral Artery Disease among Hypertensive Patients in a Tertiary Hospital in North-Central Nigeria

Peripheral artery disease (PAD) is associated with a high cardiovascular morbidity and mortality. Even though hypertension is a known risk factor for PAD, the burden and predictors of PAD among patients attending hypertension clinics in Africa is not well studied. Researchers, through a hospital-based cross sectional study at a teaching hospital in Nigeria, compared 150 hypertensive patients and 150 normotensive patients. They found a prevalence of peripheral artery disease among the hypertensive patients and normotensive patients of 20% and 3.3% respectively. The patient's age, duration of hypertension, abnormal body mass index, low-density lipoprotein cholesterol and total cholesterol were important predictors of PAD. They concluded that PAD was a common complication among the hypertensive patients studied. The highlighted predictors could be important factors in prioritizing patients for screening in a busy hypertension clinic.

Reference

A. I. Yusuf, O. M. Akinlade. et. al, Prevalence and predictors of peripheral artery disease among hypertensive patients in a tertiary hospital in north - central Nigeria <https://www.ajol.info/index.php/eamj/article/view/242640>

MCH

Higher Incidence of Preeclampsia in In-Vitro Fertilization after few Sperm Exposures.

The prevalence of preeclampsia in the setting of assisted reproductive technology (ART) after various cycles of sperm donation are uncertain. Researchers in this retrospective study compared the prevalence of preeclampsia amongst 228 participants who conceived via ART from the same sperm donor after 0-1 cycles compared to those who conceived after 2 or more cycles. The researchers found that preeclampsia occurred more in the group conceiving after one cycle (8.2%) compared to those conceiving after 2 or more cycles (1.7%). There was also no difference in preeclampsia prevalence between those conceiving after 2 or more cycles by ART and individuals conceiving spontaneously. The authors concluded that there is a correlation between pre-eclampsia when conception follows fewer sperm exposures.

Reference

Hendin, N. et al. (2023) 'Higher incidence of preeclampsia among participants undergoing in-vitro fertilization after fewer sperm exposures', *European Journal of Obstetrics and Gynecology and Reproductive Biology*, 0(0). Available at: <https://doi.org/10.1016/J.EJOGRB.2023.03.028>.

Factors Associated with Positive Blood Cultures in Neonatal Sepsis in an African Neonatal Unit.

Neonatal sepsis is still an important cause of morbidity and mortality in low-income countries. This retrospective study conducted in Kenya used data from neonates admitted at a neonatal care unit over 7 years. All neonates fitting the WHO criteria of sepsis were enrolled. The researchers found that positive blood cultures in neonatal sepsis were associated with place of birth, maternal level of education, maternal vaginal discharge, birth weight less than 2500 grams, presence of severe abdominal distension, inability to breastfeed, tachypnea, and severe chest wall in-drawing. The authors concluded that positive blood cultures were associated with early onset neonatal sepsis and higher mortality and that knowledge of ante- and peripartum factors help in averting neonatal morbidity and mortality.

Reference

Murila, F. et al. (2023) 'A retrospective study on the factors associated with positive blood cultures in neonates with neonatal sepsis at mater hospital newborn unit', *East African Medical Journal*, 100(1), pp. 5500-5509

Malaria Prevention Regimens and Pregnancy Outcomes in East Africa

Intermittent preventive therapy of malaria in pregnancy with sulfadoxine-pyrimethamine (SP) is important for reducing malaria-associated adverse birth outcomes. Dihydroartemisinin-piperazine (DP) could be important in the setting of SP resistance. Researchers through this trial conducted in East Africa involved over 4700 pregnant women without HIV. These were randomized to either receive SP only, DP only, or DP with azithromycin. The researchers found that DP resulted in a 41 percent reduction in clinical malaria but a higher composite rate of adverse pregnancy outcomes (low birth weight, small for gestational age, preterm birth, death). The authors concluded that despite DP having superior antimalarial effects, SP may have other benefits on pregnancy outcomes, and recommended more research into malaria prevention in the setting of SP resistance.

Reference

Lingani, M. et al. (2023) 'Effects of maternal antenatal treatment with two doses of azithromycin added to monthly sulfadoxine-pyrimethamine for the prevention of low birth weight in Burkina Faso: an open-label randomized controlled trial', *Malaria Journal*, 22(1), pp. 1-9

Cerebral Palsy and Maternal Injury During Pregnancy

Maternal unintentional injury during pregnancy has been shown to have negative impacts on the mother and fetus, but its long-term effects on children's neurodevelopment in unknown. Researchers in Canada through a population-based, longitudinal cohort study with data from over 2,110,177 children examined the association

between maternal unintentional injury and cerebral palsy (CP) in the offspring. The authors found maternal unintentional injury had a modest increase in the risk of CP, compared with those unexposed, with mean incidence rates of 4.36 and 2.93 per 10 000 child-years respectively. An even higher risk was noted for severe injuries resulting in hospitalization and delivery within one week of the injury. The authors hence recommended a need for emphasis on safety during pregnancy and early assessment of children exposed to maternal injury.

Reference

Ahmed, A. et al. (2023) 'In Utero Exposure to Maternal Injury and the Associated Risk of Cerebral Palsy', *JAMA Pediatrics*, 177(1), pp. 53-61.

What are the Outcomes of Maximum Oxytocin Dosing in Labor?

There is lack of evidence for a safety threshold of oxytocin dose rate. Many labor and delivery units limit the maximum oxytocin infusion dose to no more than 40 milliunits per minute during labor with a live fetus in the third trimester. In this trial doses as high as 90 milliunits per minute were used without adverse maternal or fetal effects. Based on this and previous data of the variability in uterine response to the medication, the authors recommended titration of oxytocin dose according to the oxytocin responsiveness of the individual patient, this being based on their contraction and fetal heart rate patterns, without regard to an arbitrary maximum dose.

Reference

Son, M. et al. (2023) 'Maximum Dose Rate of Intrapartum Oxytocin Infusion and Associated Obstetric and Perinatal Outcomes', *Obstetrics & Gynecology*, 141(2), pp. 379-386. Available at: <https://doi.org/10.1097>

Tamoxifen Treatment in Premenopausal Women with Breast Cancer

Tamoxifen, a selective estrogen-receptor modulator, is used as adjuvant therapy in some patients with hormone-sensitive breast cancer or at increased risk for breast cancer. It's however, associated with an increased risk for uterine pathology. Researchers in Korea, through a large retrospective study followed up over 78,000 premenopausal patients (mean age 42 years) with breast cancer for an average of six years. Those treated with versus without tamoxifen had higher rates of uterine disease (32 versus 7 per 1000 person-years), including (in descending order of frequency) endometrial polyps, endometrial hyperplasia, endometrial cancer, and other uterine cancers (rare). The authors recommended a discussion of these risks with all patients being counseled about the use of tamoxifen.

Reference

Ryu, K.J. et al. (2022) Risk of Endometrial Polyps, Hyperplasia, Carcinoma, and Uterine Cancer After Tamoxifen Treatment in Premenopausal Women With Breast Cancer', *JAMA Network Open*, 5(11), p. E2243951. Available at: <https://doi.org/10.1001>

Azithromycin in the Prevention of Sepsis or Death in Planned Vaginal Deliveries.

Azithromycin is known to reduce maternal infection in women with unplanned cesarean delivery. Whether its intrapartum use in planned vaginal deliveries would reduce maternal and neonatal sepsis or death is

uncertain. Researchers in this trial randomized 29,278 women at ≥ 28 weeks of gestation planning a vaginal delivery to receive a 2g dose of azithromycin or placebo. The primary outcomes were composites of maternal sepsis or death and stillbirth, and neonatal sepsis or death. Researchers found that maternal sepsis or death was lower in the azithromycin group compared to placebo, but with no differences in fetal and neonatal outcomes. The authors concluded that a single oral dose of azithromycin in women planning vaginal delivery reduced the risk of maternal sepsis and death more than a placebo with little effect on neonatal outcomes.

Reference

Tita, A.T.N., et al. (2023) 'Azithromycin to Prevent Sepsis or Death in Women Planning a Vaginal Birth.', *The New England journal of medicine* [Preprint]. Available at: <https://doi.org/10.1056/NEJMOA2212111>

Expectant Management or Early Ibuprofen in Patent Ductus Arteriosus

Cyclooxygenase inhibitors have traditionally been used in infants with patent ductus arteriosus (PDA) to induce closure but we're not certain of their benefit. Expectant management is being recommended but evidence to support it is lacking. Researchers through this non-inferiority randomized control trial compared expectant management to early ibuprofen use. A total of 273 extremely preterm infants with echocardiographically-confirmed PDA underwent randomization to either expectant management or ibuprofen use. The primary outcome measure was a composite of necrotizing enterocolitis, bronchopulmonary dysplasia, or death at 36 weeks postmenstrual age. Overall the outcome occurred in 46.3% of the expectant group, and 63.5% in the early ibuprofen group meeting the study's criteria for non-inferiority. The researchers hence concluded that expectant management was non-inferior to early ibuprofen in regard to the above outcomes.

Reference

Hundscheid, T. et al. (2022) 'Expectant Management or Early Ibuprofen for Patent Ductus Arteriosus', *New England Journal of Medicine* [Preprint]. Available at: <https://doi.org/10.1056>

General Surgery

Surgical Apgar Score as a Predictor of Outcomes in Patients Following Laparotomy at Mulago National Referral Hospital.

Laparotomy is associated with a high risk of postoperative complications and mortality. Stratifying patients by their risk may improve outcomes. Researchers at Mulago hospital, through a prospective observational study, evaluated the performance of the surgical Apgar score (SAS), a simple and objective bedside tool, in predicting outcomes in 151 patients undergoing laparotomy at the hospital. They classified patients into 3 SAS groups: low (8–10), medium (5–7), and high (0–4). Postoperative in-hospital major complications and mortality rates of 24.2% and 10.6% were recorded, respectively. Patients with a high SAS category were 18.4 times more likely to develop major complications, while those in medium SAS category had 3.9 times risk of dying. The

found a sensitivity and specificity of $SAS \leq 6$ for major complications of 60.5% and 81.14% respectively, and for death at 54.8% and 81.3%, respectively. In conclusion, a SAS of ≤ 6 was associated with increased risk of major complications and/or mortality. SAS was highly specific with a fair discriminatory ability for predicting the risk of developing in-hospital major complications and/or death following laparotomy.

Reference

Onen, B.C., Semulimi, A.W. et al. Surgical Apgar score as a predictor of outcomes in patients following laparotomy at Mulago National Referral Hospital, Uganda: a prospective cohort study. *BMC Surg* 22, 433 (2022). <https://doi.org/10.1186/s12893-022-01883-7>

Breast-Conserving Surgery with or without Irradiation in Early Breast Cancer

Evidence for the omission of radiotherapy following breast conservation surgery in older women with localized breast cancer is lacking. In a new study involving 1326 women ≥ 65 years with receptor-positive, node-negative, T1 or T2 primary breast cancer who underwent breast-conservation surgery and adjuvant endocrine therapy, outcomes were compared in whole breast-irradiation and no irradiation. The primary outcome was local breast cancer recurrence. Distant recurrence, and survival, were also determined. After 10 years, the researchers found that the cumulative incidence of local recurrence of breast cancer was higher in the non-irradiation group than in the irradiation group (9.5 versus 0.9%). No difference in the rate of distant recurrence or survival was noted. The authors concluded that the omission of radiotherapy in this patient group increased the risk of local recurrence but didn't affect survival or distant recurrence as the first event.

Reference

Kunkler, I.H. et al. (2023) 'Breast-Conserving Surgery with or without Irradiation in Early Breast Cancer.', *The New England journal of medicine*, 388(7), pp. 585–594. Available at: <https://doi.org/10.1056/NEJMOA2207586>

Aspirin or Low-Molecular-Weight Heparin for Thromboprophylaxis after a Fracture

Several guidelines recommend low-molecular-weight heparin (LMWH) to prevent thrombosis in patients with fractures. Studies to compare LMWH to aspirin, a cheaper and easy-to-administer option are lacking. Researchers in this large trial involving 12,211 patients with traumatic extremity fractures were randomized to receive thromboprophylaxis with either LMWH 30mg or aspirin 81mg twice daily while in the hospital and continued after discharge as per the hospital protocols. The primary outcome was all-cause mortality at 90 days. The researchers found that the primary outcome occurred in 0.78% of the aspirin group and 0.73% in the LMWH group. Non-fatal pulmonary embolism and bleeding complications were similar in both groups. The authors thus concluded that in patients with fractures, aspirin wasn't inferior to LMWH in preventing death from any cause.

Reference

Aspirin or Low-Molecular-Weight Heparin for Thromboprophylaxis after a Fracture (2023) *New England Journal of Medicine*, 388(3), pp. 203–213. Available at: <https://doi.org/10.1056/NEJMOA2205973>