

### Population-level impacts of improved uptake of SGLT2 inhibitors in patients with chronic kidney disease

Sodium-glucose cotransporter-2 (SGLT2) inhibitors substantially reduce the risk of cardiorenal events, and thus are recommended in chronic kidney disease (CKD). Their population-level impact is however not well evidenced. Researchers in Australia in this observational study identified patients that would have met the inclusion criteria of key SGLT2 inhibitor trials and estimated the number of preventable events. Primary outcomes included cardiorenal events and kidney failure. The researchers found that of the total 230,246 patients with CKD, 44.2% would have met the criteria for an SGLT2 inhibitor. Baseline use was 4.1%. Optimal (75%) uptake of SGLT2 inhibitor could reduce cardiorenal and kidney failure events annually in Australia by 3644 and 1312 respectively. They thus concluded that strategies to increase SGLT2 inhibitors' uptake are critical to realizing their population-level benefits.

#### Reference

Neuen, B. L., et al. (2023). Estimating the population-level impacts of improved uptake of SGLT2 inhibitors in patients with chronic kidney disease: a cross-sectional observational study using routinely collected Australian primary care data. *The Lancet Regional Health – Western Pacific*, 43, 100988.

### Rosuvastatin versus Atorvastatin treatment in adults with coronary artery disease

Statins are a mainstay in patients with coronary artery disease (CAD). Whether the efficacy and safety differ with potency isn't well known. Researchers conducted a secondary analysis of the LODESTAR trial, and randomized 4400 patients to either receive rosuvastatin (n=2204) or atorvastatin (n=2196). The primary outcome was a three-year composite of all-cause death, myocardial infarction, stroke, or any coronary revascularization, with secondary outcomes being new-onset diabetes, etc. The researchers found no difference in the primary outcome between rosuvastatin and atorvastatin arms i.e., 8.7% versus 8.2% respectively. They however noted lower low-density lipoprotein cholesterol in the rosuvastatin group at the expense of higher risk of new-onset diabetes and cataract surgery. The researchers thus concluded that both statins had similar efficacy, but rosuvastatin raised some safety concerns whose mechanisms need investigation.

#### Reference

HLee, Y. J., et al. (2023). Rosuvastatin versus atorvastatin treatment in adults with coronary artery disease: secondary analysis of the randomized LODESTAR trial. *BMJ*, 383, e075837. <https://doi.org/10.1136/BMJ-2023-075837>

### Early versus delayed antihypertensive treatment in patients with acute ischaemic stroke

After an acute ischaemic stroke, it's still unclear whether early or late antihypertensive treatment is better for long-term outcomes. Researchers in this trial enrolled 4810 patients with acute ischemic stroke within 24-48 hours of symptom onset and elevated blood pressure and randomized them into early (within 24 hours) or late (on day 8) arms. The primary outcome was a composite

of functional dependency or death at 90 days. The researchers found that at day 7, more people in the early treatment arm had a blood pressure less than 140/90 mm Hg i.e. 54.6% versus 22.4% respectively. There was a trend towards increased odds of primary outcome in the early treatment arm, though not statistically significant (odds ratio 1.18, p=0.008). They thus concluded that early antihypertensive treatment didn't reduce death or dependency at 3 months.

#### Reference

Liu, L., et al. (2023). Early versus delayed antihypertensive treatment in patients with acute ischaemic stroke: multicentre, open-label, randomized, controlled trial. *BMJ*, 383. <https://doi.org/10.1136/BMJ-2023-076448>

### Daily low-dose aspirin and incident type 2 diabetes in community-dwelling healthy older adults

Inflammation is implicated in the pathogenesis of diabetes. Whether aspirin could reduce the incidence of type 2 diabetes isn't well known. Researchers, through this posthoc analysis of the ASPREE study randomized a total of 16,209 older patients without diabetes at baseline to either oral 100 mg daily enteric-coated aspirin or placebo. The primary outcome was incident diabetes. Over a median follow-up of 4-7 years, the aspirin group had a 15% risk reduction in incident diabetes (hazard ratio 0.85, p=0.013) and a slower rate of increase in fasting plasma glucose concentration, at the expense of increased major bleeding risk. The researchers recommended further studies to confirm this observed benefit of aspirin and a detailed assessment of its safety.

#### Reference

Zoungas, S., et al. (2023). Daily low-dose aspirin and incident type 2 diabetes in community-dwelling healthy older adults: a posthoc analysis of efficacy and safety in the ASPREE randomized placebo-controlled trial. *The Lancet Diabetes & Endocrinology*, 0(0). [https://doi.org/10.1016/S2213-8587\(23\)00327-3](https://doi.org/10.1016/S2213-8587(23)00327-3)

### Global Effect of Modifiable Risk Factors on Cardiovascular Disease and Mortality

Five modifiable risk factors (body mass index, systolic blood pressure, non-high-density lipoprotein cholesterol, current smoking, and diabetes) are associated with cardiovascular events. Individual-level data to evaluate regional and sex-specific prevalence of these factors and outcomes is lacking. Researchers pooled data from a Global Cardiovascular Risk Consortium and examined associations between risk and incident cardiovascular disease (CVD) and death from any cause. The researchers found that in more than 1.5 million participants involved, for all risk factors combined, the population-attributable fraction of the 10-year incidence of CVD was 57.2% among women versus 52.6% among men, with mortalities of 22.2% and 19.1% respectively. The researchers concluded that more than half and one-fifth of incident CVD and deaths respectively may be attributable to the five modifiable risk factors.

#### Reference

Magnussen, C., et al. (2023). Global Effect of Modifiable Risk Factors on Cardiovascular Disease and Mortality. *New England Journal of Medicine*, 389(14), 1273–1285

### Apixaban for Stroke Prevention in Subclinical Atrial Fibrillation

Subclinical atrial fibrillation (AF) is short-lasting and asymptomatic but is associated with a 2.5 times increased risk of stroke. The role of oral anticoagulation is however unclear. In this double-blind randomized controlled trial, a total of 4012 patients with subclinical AF were randomized to receive apixaban 5mg twice daily (or 2.5mg twice daily as indicated), or aspirin at 81 mg daily. The primary endpoint was stroke or systemic embolism, while the safety endpoint was major bleeding. The researchers found that the primary outcome occurred less in the apixaban group (55 patients) than the aspirin group (86 patients) (hazard ratio, 0.63;  $P=0.007$ ), but with a higher risk of major bleeding; 1.71% versus 0.94% per patient-year respectively. The authors thus recommended a benefit-risk assessment in the treatment of subclinical AF with anticoagulation.

#### Reference

Healey, J. S., et al. (2023). Apixaban for Stroke Prevention in Subclinical Atrial Fibrillation. <https://doi.org/10.1056/NEJMoa2310234>.

### Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes

Semaglutide, a glucagon-like peptide-1 receptor agonist reduces the risk of adverse cardiovascular events in diabetes. Whether it can reduce cardiovascular risk in overweight and obese patients without diabetes is unclear. In this randomized placebo-controlled trial, 17,604 adult patients  $\geq 45$  years with a body mass index  $\geq 27$  but no diabetes history were enrolled and randomized in a 1:1 to receive 2.4 mg once-weekly semaglutide or placebo. The primary outcome was a composite of death from cardiovascular causes, nonfatal myocardial infarction, or stroke. After a mean follow-up of  $39.8 \pm 9.4$  months, the primary outcome occurred less in the semaglutide group compared to placebo i.e. 6.5% versus 8.0% (hazard ratio, 0.80,  $P < 0.001$ ). The researchers concluded that semaglutide is superior to placebo in reducing cardiovascular events in non-diabetic overweight patients.

#### Reference

Lincoff, A. M., et al. (2023). Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes. *New England Journal of Medicine*.

### Adjunctive Dexamethasone for Tuberculous Meningitis in HIV-Positive Adults

Tuberculous meningitis (TBM), common in HIV-positive patients is associated with significant mortality despite antituberculous chemotherapy. Adjunctive glucocorticoids are often used in TBM but their efficacy and safety are unclear. Researchers in this study randomized 520 patients with TBM to either receive dexamethasone or placebo, with duration of therapy based on grade of disease. The primary outcome was death from any cause during 12 months. The researchers found no significant difference in the percentage of participants who died between the dexamethasone group (44.1%) and the placebo group (49.0%). They thus concluded that among adults with HIV-associated TBM, the addition of dexamethasone to antituberculosis chemotherapy and antiretroviral therapy did not reduce

mortality during 12 months of follow-up.

#### Reference

Donovan, J., et al. (2023). Adjunctive Dexamethasone for Tuberculous Meningitis in HIV-Positive Adults. *New England Journal of Medicine*, 389(15), 1357–1367.

### Foot-at-Risk among adult outpatients with diabetes mellitus in Nigeria

The prevalence of diabetes mellitus is rising globally and so are its complications. Diabetic foot complications are common, and costly and mandate aggressive prevention. A cross-sectional study in Nigeria screened 299 outpatients with diabetes (of at least 6 months duration) with Comprehensive Foot Examination and Risk Assessment tool to identify foot-at-risk categories. The researchers found a high foot-at-risk prevalence of 64.9%, with 35.1% of these in Category 0, 37.8% in Category 1, 16.1% in Category 2, and 11.0% in Category 3. Factors found to be associated with increased risk of diabetic foot included increasing age, christianity, lower level of education, smoking, and poor glycemic control. The researchers concluded that there's a high prevalence of foot-at-risk and recommended foot screening and health education intensification to prevent adversities.

#### Reference

Idowu, A. E., et al. (2023). Foot-at-Risk among adult outpatients with diabetes mellitus in Bowen University Teaching Hospital, Ogbomosho, Nigeria. *PAMJ*. 2023; 46:106, 46(106).

## MCH

### Untreated cervical intraepithelial neoplasia grade 2 and subsequent risk of cervical cancer

Researchers in this study described the long-term risk of cervical cancer in women undergoing active surveillance compared to those immediately treated for cervical intraepithelial neoplasia grade 2 (CIN2). This was a nationwide historical cohort study that included 27,524 women with CIN2, of whom 12,483 (45%) had active surveillance and 15,041 (55%) had immediate large loop excision of the transformation zone (LLETZ). The cumulative risk of cervical cancer was comparable between groups during 2 years of follow-up, where it increased after 20 years in the active surveillance arm reaching 2.65% while it remained stable at 0.76% in the LLETZ group. They thus concluded that undergoing surveillance for CIN2 was associated with increased long-term risk of cervical cancer, and underscored the role of continued follow-up in those having active surveillance.

#### Reference

Lykke, K. D., et al. (2023). Untreated cervical intraepithelial neoplasia grade 2 and subsequent risk of cervical cancer: population-based cohort study. *BMJ*, 383, e075925. <https://doi.org/10.1136/BMJ-2023-075925>

### Early Metformin in Gestational Diabetes

Gestational diabetes is a common pregnancy complication whose optimal treatment remains unclear. Whether early initiation of metformin could reduce

insulin initiation or improve fasting hyperglycemia at gestation weeks 32 or 38 isn't known. A total of 510 individuals (535 pregnancies) were randomized (1:1) to either receive metformin (maximum dose 2500 mg) or placebo. The primary endpoint was a composite of insulin initiation or fasting glucose level  $\geq 5.1$  mmol/L at gestation weeks 32 or 38. The researchers found no significant difference between the primary outcome but 3 secondary outcome measures favored metformin i.e., time to insulin initiation, self-reported capillary glycemic control, and gestational weight gain. Smaller neonates were seen in the metformin group. The authors recommended that the significant secondary outcomes merit further investigation in larger studies.

**Reference**

Dunne, F., et al. (2023). Early Metformin in Gestational Diabetes: A Randomized Clinical Trial. *JAMA*, 330(16), 1547–1556. <https://doi.org/10.1001/JAMA.2023.19869>

**Delayed umbilical cord clamping compared with umbilical cord milking and immediate clamping at preterm birth**

Delayed umbilical cord clamping improves infant survival among those born preterm, however, the optimal duration of deferral remains unclear. Researchers conducted a systematic review and meta-analysis involving 47 trials with 6094 participants, and interventions were grouped into immediate clamping, short deferral ( $\geq 15$  s to  $< 45$  s), medium deferral ( $\geq 45$  s to  $< 120$  s), long deferral ( $\geq 120$  s), and intact cord milking. The primary outcome was death before hospital discharge. In this low heterogeneity and fairly consistent data, long deferral reduced death before discharge the most compared with immediate clamping (odds ratio 0.31). The researchers thus confirmed that delayed umbilical clamping reduced the odds of death before discharge in preterm infants and that this should inform future guidelines and practice.

**Reference**

Seidler, A. L., et al. (2023). Short, medium, and long deferral of umbilical cord clamping compared with umbilical cord milking and immediate clamping at preterm birth: a systematic review and network meta-analysis with individual participant data. *Lancet* (London, England), 402(10418). [https://doi.org/10.1016/S0140-6736\(23\)02469-8](https://doi.org/10.1016/S0140-6736(23)02469-8)

**Intrapartum epidural analgesia associated with higher rate of emergency delivery for presumed fetal compromise**

In this study, researchers investigated if epidural analgesia (EDA) compared to alternative or no analgesia affected the rate of emergency delivery for presumed fetal compromise. In this Dutch study involving 629,951 pregnancies delivered at 36–42 weeks of gestation; 120,426 received EDA, compared to 86,957 that received alternative analgesia and 422,568 that received no analgesia. The primary outcome was emergency delivery for presumed fetal compromise. The researchers found that among EDA recipients 13.2% got primary outcome compared to 4.1% who had no analgesia (relative risk 3.23), and 7.0% who received alternative analgesia (relative risk 1.72). Upon stratification by parity,

emergency delivery fell with increasing birth weight. The authors thus concluded that in pregnancies with a high background risk of fetal compromise, alternative analgesia may be preferable to EDA.

**Reference**

Damhuis, S. E., et al. (2023). Effect of intrapartum epidural analgesia on rate of emergency delivery for presumed fetal compromise: nationwide registry-based cohort study. *Ultrasound in Obstetrics & Gynecology: The Official Journal of the International Society of Ultrasound in Obstetrics and Gynecology*, 62(5), 668–674. <https://doi.org/10.1002/UOG.26309>

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*General Surgery*

**Breast-conserving surgery versus modified radical mastectomy for early breast cancer**

Breast-conserving surgery followed by radiotherapy (BCT) and modified radical mastectomy (MRM) in the treatment of early breast cancer (EBC) have comparable clinical outcomes. Whether quality of life (QOL) varies by treatment approach in our setting isn't known. Researchers in this study enrolled 81 female patients with EBC who underwent BCT (42) or MRM (39) and invited them to fill out the European Organization for the Treatment and Research of Cancer Quality of Life Questionnaire. Scores on QOL were obtained and associated factors were also assessed. BCT patients at 1 year had better QOL than MRM patients ( $p=0.0149$ ). QOL was also associated with duration from the time of surgery, level of education, and diabetes mellitus. The researchers concluded that BCT was better at QOL than MRM.

**Reference**

Andrew, S., et al. (2023). Quality of life of patients one year after breast-conserving surgery versus modified radical mastectomy for early breast cancer: a Kenya tertiary hospital five-year review. *PAMJ*. 2023; 46:69, 46(69). <https://doi.org/10.11604/PAMJ.2023.46.69.39151>

## Critical Care Medicine

### Conservative management versus laparoscopic cholecystectomy in uncomplicated symptomatic gallstone disease

The clinical and cost-effectiveness of either conservative management or laparoscopic cholecystectomy in uncomplicated symptomatic gallstone disease isn't clear. Researchers in this study enrolled 434 adults with uncomplicated symptomatic gallstone disease and randomly assigned (1:1) them to either receive conservative management or laparoscopic cholecystectomy. The primary endpoint was quality of life over 18 months, and secondary endpoints included costs, among others. By 18 months, one-quarter of participants in the conservative arm compared to two-thirds of patients in the cholecystectomy had received surgery. The QOL (assessed by short form-36 norm-based bodily pain score) didn't differ between groups ( $p=1.00$ ), but the conservative approach was less costly (mean difference  $-\pounds 1033$ ). The researchers concluded that laparoscopic surgery was not more effective, and a conservative approach may be more cost-effective.

#### Reference

Ahmed, I., et al. (2023). Effectiveness of conservative management versus laparoscopic cholecystectomy in the prevention of recurrent symptoms and complications in adults with uncomplicated symptomatic gallstone disease (C-GALL trial): pragmatic, multicentre randomized controlled trial. *BMJ*, 383, e075383. <https://doi.org/10.1136/BMJ-2023-075383>

### Role of preoperative in-hospital delay on appendiceal perforation while awaiting appendicectomy

Appendicectomy is the standard treatment of appendicitis. Consensus on the surgical urgency for acute uncomplicated appendicitis is inexistent. Researchers in this study that was conducted in Finland and Norway randomized 1822 patients with acute uncomplicated appendicitis to either appendicectomy scheduled within 8 h ( $n=914$ ) or 24 h ( $n=908$ ). In the intention-to-treat analysis, appendiceal perforation rate was similar between groups (absolute risk difference of 0.6%), with no significant differences in complication rates in 30 days i.e. 7% versus 6% in the  $< 8h$  and  $< 24h$  groups respectively. The researchers concluded that scheduling appendicectomy within 24 hours doesn't increase perforation risk and suggested that this information can be used to allocate operating room resources, for instance postponing night-time appendicectomy to daytime.

#### Reference

Jalava, K., et al. (2023). Role of preoperative in-hospital delay on appendiceal perforation while awaiting appendicectomy (PERFECT): a Nordic, pragmatic, open-label, multicentre, non-inferiority, randomized controlled trial. *Lancet* (London, England), 402(10412), 1552–1561. [https://doi.org/10.1016/S0140-6736\(23\)01311-9](https://doi.org/10.1016/S0140-6736(23)01311-9)

### Noninvasive Airway Management of Comatose Patients With Acute Poisoning

Intubation is recommended for comatose patients and those with severe brain injury. Its role in patients with reduced levels of consciousness from acute poisoning is however not known. Researchers in France enrolled 225 comatose patients with suspected acute poisoning, randomized to conservative airway strategy of withholding intubation or routine practice. The primary outcome was a composite of hospital death, length of ICU stay, and length of hospital stay, with secondary endpoints of adversities from intubation or pneumonia within 48 hours. The study found clinical benefit for the primary outcome in the intervention group with a win ratio of 1.85. A similar benefit was noted with intubation adversities and pneumonia occurrence. Among comatose patients with suspected acute poisoning, withholding intubation showed clinical benefits.

#### Reference

Freund, Y., et al. (2023). Effect of Noninvasive Airway Management of Comatose Patients With Acute Poisoning: A Randomized Clinical Trial. *JAMA*, 330(23). <https://doi.org/10.1001/JAMA.2023.24391>

### Noninvasive respiratory support after extubation on postoperative pulmonary complications in obese patients.

Obesity is associated with an increased risk of sleep-disordered breathing and postoperative pulmonary complications (PPCs). Postoperative noninvasive respiratory support (NRS) in this population remains controversial. In this systematic review and meta-analysis, 20 clinical trials involving 1184 obese patients were included, in which one of the four techniques of NRS: continuous positive airway pressure (CPAP), bi-level positive airway pressure (BiPAP), a high-flow nasal cannula (HFNC), or conventional oxygen therapy (COT) were performed after general anesthesia. The primary outcome was the incidence of PPCs while the secondary outcomes were the incidence of oxygen treatment failure and length of hospital stay, among others. Among all, HFNC ranked first under the cumulative ranking curve. The authors concluded that HFNC seemed to be the optimal choice for obese patients.

#### Reference

Li, R., et al. (2023). Effect of noninvasive respiratory support after extubation on postoperative pulmonary complications in obese patients: A systematic review and network meta-analysis. *Journal of Clinical Anesthesia*, 91. <https://doi.org/10.1016/J.JCLINANE.2023.111280>