

General Medicine

Over-prescription of short-acting b2 agonists is associated with poor asthma outcomes in an African cohort.

Management of asthma is challenging, especially in settings with fragile health systems like Sub-Saharan Africa. Data on the extent of short-acting b2 agonist (SABA) use and outcomes are lacking. Researchers, through a cohort involving 3 African countries, sought to answer this question. Data of 1778 patients (>12 years old) were analyzed for associations between SABA prescriptions and outcomes. Overall, 46.5% of patients had been prescribed \geq 3 canisters in the preceding 1 year (over-prescription), while 26.2% were prescribed \geq 10 canisters. SABAs were purchased over-the-counter by 32.6% and the majority of these (79.3%) had received SABA prescriptions. Higher SABA prescriptions were associated with increased rates of severe exacerbations. Researchers concluded that SABA overuse is common and is associated with poor outcomes and recommended clinical practice be aligned with current treatment guidelines.

Adel Khattab, Ashraf Madkour, et al. Overprescription of short-acting β_2 -agonists is associated with poor asthma outcomes: results from the African cohort of the SABINA III study, *Current Medical Research and Opinion*, DOI:10.1080/03007995.2022.2100649

Acetazolamide in acute decompensated heart failure with volume overload.

It is unknown if Acetazolamide a carbonic anhydrase inhibitor could improve the efficiency of loop diuretics in acute decompensated heart failure (ADHF) with fluid overload. In this study, a total of 519 patients were randomized to either receive intravenous acetazolamide (500mg once daily) or a placebo added to standardized loop diuretics. The main outcome measure was successful decongestion and the secondary outcome was death or re-hospitalization for heart failure during 3 months of follow-up. The primary outcome occurred in 42.2% in the acetazolamide group, and 30.5% in the placebo group. Acetazolamide treatment was also associated with higher cumulative urine output. Adverse events were similar in the two groups. Researchers concluded that the addition of acetazolamide to loop diuretic therapy in ADHF resulted in better decongestion.

Mullens W, Dauw J, et al. Acetazolamide in Acute Decompensated Heart Failure with Volume Overload. *N Engl J Med*. 2022

Sep 29;387(13):1185-1195. doi: 10.1056/NEJMoa2203094. Epub 2022 Aug 27. PMID: 36027559.

Long-term outcomes among men undergoing active surveillance for prostate cancer in Sweden.

Active surveillance entails conversion to active treatment if disease progression occurs. Its long-term outcomes among men with prostate cancer are not known. In this Swedish cohort, data of over 23655 men diagnosed with prostate cancer and managed with deferred treatment was used to estimate treatment trajectories. Outcome measures included death from prostate cancer or other causes, as well as the proportion of time without active treatment as assessed until death or age 85. The proportion of men diagnosed at 55 years and died of prostate cancer before 85 years was notably higher compared to those diagnosed at 70 years across all prostate cancer risk groups, but especially in the intermediate-risk group. The researchers concluded that active surveillance may be a safe strategy among older men (>65 years) with low-risk prostate cancer.

Ventimiglia E, Bill-Axelsson A, et al. Long-term Outcomes Among Men Undergoing Active Surveillance for Prostate Cancer in Sweden. *JAMA Netw Open*. 2022 Sep 15;5(9):e2231015. doi: 10.1001/jamanetworkopen.2022.31015. PMID: 36103180; PMCID: PMC9475386.

Patterns of retention in hypertension care in primary care settings in Nigeria

Hypertension is a major global public health concern with low- and middle-income countries shouldering almost two-thirds of this burden. Retention in care is essential for hypertension control, yet rates continue to be less than 50% in most limited resource settings. In this cohort study in Nigeria, researchers sought to describe characteristics and patterns of retention in hypertension care programs. The outcome measure was a 3-month rolling average 37-day retention rate. A total of 10686 adult patients in 60 primary health care centers were included in the analysis. The retention rate was found to be 41%; higher among older patients who were female, had a higher body mass index, and had received hypertension treatment at the registration visit. The researchers noted that retention was suboptimal and identified factors that may inform strategies to improve retention.

Ye J, Orji IA, et al. Characteristics and Patterns of Retention in Hypertension Care in Primary Care Settings From the Hypertension Treatment in Nigeria Program. *JAMA Netw Open*. 2022 Sep 15;5(9):e2230025. doi: 10.1001/jamanetworkopen.2022.30025. PMID: 36066896; PMCID: PMC9449788.

Effect of digital health technology versus standard directly observed therapy on tuberculosis care.

Despite anti-tuberculous treatment being efficacious, the cost involved to achieve optimal adherence is high. Little is known about the effect of a digital medication event reminder and monitor (MERM) compared to the standard on the quality of life and costs to patients. Researchers in Ethiopia, randomized a total of 114 patients with susceptible TB to either MERM-observed therapy or standard directly observed therapy for 2 months. Standard tools were used to assess health-related quality of life (HRQoL) and catastrophic costs. The study found HRQoL to be significantly higher in the intervention arm, and costs lower compared to the standard of care. The researchers concluded that digital health technologies have the potential to overcome structural barriers to anti-TB therapy.

Manyazewal T, Woldeamanuel Y, et al. Effect of Digital Medication Event Reminder and Monitor-Observed Therapy vs Standard Directly Observed Therapy on Health-Related Quality of Life and Catastrophic Costs in Patients With Tuberculosis: A Secondary Analysis of a Randomized Clinical Trial. *JAMA Netw Open*. 2022 Sep 15;5(9):e2230509. doi: 10.1001/jamanetworkopen.2022.30509. PMID: 36107429; PMCID: PMC9478770.

The role of follow-up blood cultures among patients with gram-negative bloodstream infections.

In patients with gram-negative bloodstream infections, it is unclear if obtaining follow-up blood cultures (FUBCs) affects patient mortality. Researchers conducted a systematic review and meta-analysis of both scholarly and gray literature that included 5 observational studies and 4378 patients in the primary analysis. The primary outcome was mortality before hospital discharge or up to 30 days from index blood culture. The researchers found that obtaining FUBCs

was associated with decreased mortality. Additionally, positive FUBCs were associated with increased mortality compared to negative FUBCs. The research findings hence supported the use of FUBCs in patients with gram-negative bloodstream infections, but researchers noted the need for more studies to identify patient subgroups that do not require FUBCs.

Thaden JT, Cantrell S, et al. Association of Follow-up Blood Cultures With Mortality in Patients With Gram-Negative Bloodstream Infections: A Systematic Review and Meta-analysis. *JAMA Netw Open.* 2022 Sep 1;5(9):e2232576. doi: 10.1001/jamanetworkopen.2022.32576. PMID: 36136334.

Glycemia reduction Type 2 diabetes

A glycated hemoglobin (HBA1C) level below 7.0% is recommended in type 2 diabetes mellitus (T2DM). This is often achieved with metformin and a second medication added as needed. Studies to compare the effectiveness of these second-line therapies are lacking. Researchers in this study compared four common glucose-lowering drugs: insulin glargine, glimepiride, liraglutide, and sitagliptin in participants with T2DM, receiving metformin with an HBA1C of 6.8 to 8.5%. The outcome measure was an HBA1C of 7.0% or higher. Of 5047 participants followed for 5 years, the cumulative incidence of the outcome was similar and lower with insulin glargine and liraglutide as compared to glimepiride or sitagliptin. The researchers noted that all drugs decreased HBA1C but insulin glargine and liraglutide were better at achieving and maintaining target HBA1C levels.

GRADE Study Research Group, Nathan DM, et al. Glycemia Reduction in Type 2 Diabetes - Glycemic Outcomes. *N Engl J Med.* 2022 Sep 22;387(12):1063-1074. doi: 10.1056/NEJMoa2200433. PMID: 36129996.

Statin therapy on cardiovascular and limb outcomes in end-stage renal patients with peripheral artery disease receiving maintenance dialysis.

Whether statin use in patients with end-stage renal disease (ESRD) and peripheral artery disease (PAD) on dialysis is beneficial remains uncertain. Researchers, through a retrospective cohort study conducted in Taiwan analyzed data of 20731 patients with ESRD receiving dialysis and diagnosed with PAD. The major outcome measure was all-cause death, as well as cardiovascular and adverse limb events. A total of 10767 patients met the study criteria. The researchers found all-cause death and cardiovascular risk to be significantly lower in the statin group at 3 years of follow-up i.e 611 versus 685 patients. Adverse limb outcomes were also lower in the statin group compared to the non-statin

group. The study suggested that statins are beneficial in cardiovascular and limb protection in this patient group. Lo HY, Lin YS, et al. Association of Statin Therapy With Major Adverse Cardiovascular and Limb Outcomes in Patients With End-stage Kidney Disease and Peripheral Artery Disease Receiving Maintenance Dialysis. *JAMA Netw Open.* 2022 Sep 1;5(9):e2229706. doi: 10.1001/jamanetworkopen.2022.29706. PMID: 36048442; PMCID: PMC9437764.

Apparent insulin deficiency among adults with new-onset Type 2 Diabetes in Uganda

It is important to identify insulin deficiency among adults with new onset type 2 diabetes mellitus (T2DM) so insulin therapy is initiated early. Researchers in Uganda assessed for the prevalence of insulin deficiency among 494 adults with new onset T2DM who presented to seven tertiary hospitals. Insulin deficiency was defined by a fasting C-peptide concentration of <0.76ng/ml. Insulin deficiency was found in 21% and was more likely among patients with a lower BMI, fewer indicators of adiposity and higher HBA1C. The researchers concluded that insulin deficiency was prevalent in the studied population and recommended targeted testing and initiation of insulin replacement therapy.

Kibirige D, Sekitoleko I, et al. Apparent Insulin Deficiency in an Adult African Population With New-Onset Type 2 Diabetes. *Front. Clin. Diabetes Healthc.* 3:944483. doi: 10.3389/fcdhc.2022.944483

Lifestyle and Preventive Medicine

Ultra-processed food consumption with colorectal cancer risk among men and women.

Colorectal cancer is the second leading cause of death from cancer worldwide. Ultra-processed food consumption is associated with several chronic diseases. Its association with colorectal cancer is unclear. Researchers through three large US cohorts estimated this association. The study estimated that 3216 cases of colorectal cancer were documented during the 24-28 years of follow-up. Men in the highest fifth of ultra-processed food consumption had a 29% higher risk of developing colorectal cancer compared to their lower fifth counterparts, an association limited to distal colon cancer. Among women, ready-to-eat/heat-mixed dishes were associated with increased risk, while dairy-based products were negatively associated with colorectal cancer risk. The researchers recommended further studies to understand the attributes of ultra-processed foods that contribute to

carcinogenesis.

Wang L, Du M, Wang K, Khandpur N, Rossato S L, Drouin-Chartier J et al. Association of ultra-processed food consumption with colorectal cancer risk among men and women: results from three prospective US cohort studies *BMJ* 2022; 378 :e068921 doi:10.1136/bmj-2021-068921

Polypill strategy in secondary cardiovascular prevention.

A polypill composed of key medications (aspirin, angiotensin-converting enzyme inhibitor, and statin) known to improve outcomes has been suggested as a strategy for secondary prevention of cardiovascular events following myocardial infarction (MI). Researchers, through this study, sought to determine if this strategy was superior to usual care. A total of 2499 patients with MI within the previous 6 months were randomized to either the polypill strategy or usual care. The outcome measure was a composite of cardiovascular death, nonfatal MI, or nonfatal ischemic stroke. The outcome occurred at a significantly higher rate in the usual care arm (12.7%) compared to the polypill arm (9.5%). Additionally, medication adherence was better in the latter. The researchers concluded that the polypill strategy reduced major cardiovascular events more than usual care.

Castellano JM, Pocock SJ, et al. Polypill Strategy in Secondary Cardiovascular Prevention. *N Engl J Med.* 2022 Sep 15;387(11):967-977. doi: 10.1056/NEJMoa2208275. Epub 2022 Aug 26. PMID: 36018037.

A healthy lifestyle is positively associated with mental health and well-being and core markers in aging

The association between lifestyle and health outcomes has been well investigated; studies have however evaluated individual health behaviors (unlike multiple behaviors) and the biological mechanisms explaining the association is unclear. This study included a total of 6054 adults from the 2018 Belgian Health Interview Survey and evaluated the association between lifestyle and mental health, and its effect on core markers of aging: telomere length (TL) and mitochondrial DNA content (mtDNAC). A validated lifestyle score integrating different behaviors (diet, physical activity, smoking status, alcohol consumption and BMI) was used. The study found that a one-point increment in the lifestyle score was associated with lower odds for mental health outcomes, a 1.74% longer TL, and a 4.07% higher mtDNAC. The researchers hence indicated that living a healthy lifestyle leads to favorable biological aging.

Hautekiet P, Saenen ND, et al. A healthy lifestyle is positively associated with mental

health and well-being and core markers in ageing. *BMC Med.* 2022 Sep 29;20(1):328. doi: 10.1186/s12916-022-02524-9. PMID: 36171556; PMCID: PMC9520873.

Artificial sweeteners and the risk of cardiovascular diseases.

The harmful effects of added sugars to processed foods and beverages on health outcomes have been well investigated. Artificial sweeteners emerged as an alternative to these, but their association with cardiovascular outcomes isn't well understood. Researchers through this large population-based prospective study in France evaluated the association between artificial sweeteners and cardiovascular disease risk. The study found that artificial sweetener intake was associated with increased risk of cardiovascular diseases, and more especially with cerebrovascular disease risk (incidence rates of 195 and 150 per 100,000 person-years in higher- and non-consumers respectively). The researchers hence suggested a potential direct association between higher artificial sweetener consumption and increased cardiovascular risk, and recommend that artificial sweeteners should not be considered a healthy alternative to sugar.

BMJ 2022;378:e071204 <http://dx.doi.org/10.1136/bmj-2022-071204>

Childhood obesity and adult-onset chronic kidney disease

Chronic kidney disease (CKD) is rising worldwide, with an increase in the prevalence of risk factors. Childhood obesity is associated with impaired kidney function, but its impact on the subsequent development of CKD is unclear. Researchers in Denmark, through a population-based cohort, investigated if childhood body mass index (BMI) was associated with adult-onset CKD. A total of 151,506 boys and 148,590 girls born between 1930 to 1987 with weight and height information at age 6 to 15 years were included. Outcome data on CKD and End-stage renal disease (ESRD) was drawn from national health registers. The researchers found the rates of CKD and ESRD significantly increased with higher child BMI trajectories, compared with lower ones. The findings suggested that the high prevalence of childhood obesity may contribute to the future burden of CKD.

Aarestrup J, Blond K, et al. Childhood body mass index trajectories and associations with adult-onset chronic kidney disease in Denmark: A population-based cohort study. *PLoS Med.* 2022 Sep 21;19(9):e1004098. doi: 10.1371/journal.pmed.1004098. PMID: 36129893; PMCID: PMC9491561.

Supplemental Vitamin D and incident fractures in midlife and older adults

Vitamin D supplements are widely recommended for bone health but whether their use can prevent fractures is not known. Researchers through a controlled trial investigated whether supplemental vitamin D would result in a lower risk of fractures than placebo in midlife and older adults not selected for vitamin deficiency, low bone mass, or osteoporosis. The outcome measure was incident total non-vertebral and hip fractures. Of the 25871 participants, 1991 incident fractures were confirmed during a median follow-up period of 5.3 years. There was no significant difference in total number of fractures in the two groups. The treatment effect was also not modified by baseline characteristics. The researchers concluded that vitamin D supplementation did not significantly lower the risk of fractures in midlife and older adults.

LeBoff MS, Chou SH, et al. Supplemental Vitamin D and Incident Fractures in Midlife and Older Adults. *N Engl J Med.* 2022 Jul 28;387(4):299-309. doi: 10.1056/NEJMoa2202106. PMID: 35939577.

Maternal-child health

Optimal Timing of Labor Induction after Pre-labor Rupture of Membranes at Term

Although early labor induction following pre-labour rupture of membranes (PROM) is beneficial for pregnancy outcomes, it is unclear what the optimal timing of labor induction should be. Researchers conducted a secondary analysis of a large randomized trial, comparing outcomes at 1-hour time intervals for participants who had labor induced and those managed expectantly within 36 hours following PROM. The neonatal outcome was neonatal infection or admission while the maternal outcome was a maternal infection or caesarean delivery. Among the 4742 subjects included in the analysis, researchers found the rate of neonatal and maternal outcomes increased with time following PROM and were lower in those induced compared to those managed expectantly. Findings suggested immediate labor induction as an optimal strategy following PROM.

Melamed N, Berghella V, et al. Optimal timing of labor induction after prelabor rupture of membranes at term: a secondary analysis of the TERMPROM study. *Am J Obstet Gynecol.* 2022 Sep 15;S0002-9378(22)00742-6. doi: 10.1016/j.ajog.2022.09.018. Epub ahead of print. PMID: 36116523.

Low-dose aspirin use in pregnancy and the risk of preterm birth

Low-dose aspirin has been shown to reduce

the risk of preterm birth in women at risk of preeclampsia, but its utility in preventing preterm birth in women with a history of preterm birth is not clear. Researchers in Sweden conducted this cohort study and estimated the association between low-dose aspirin use and preterm birth in women with a history of preterm birth in a previous pregnancy. Among the studied 22,127 women, 3057 were prescribed aspirin, and 3703 gave birth prematurely. The study found that low-dose aspirin was associated with a significantly reduced risk for spontaneous preterm births but with no effect on medically indicated preterm birth. The researchers concluded that low-dose aspirin could be effective prophylaxis for recurrent preterm birth.

Kupka E, Hesselman S, et al. Low-dose aspirin use in pregnancy and the risk of preterm birth: a Swedish register-based cohort study. *Am J Obstet Gynecol.* 2022 Sep 9;S0002-9378(22)00728-1. doi: 10.1016/j.ajog.2022.09.006. Epub ahead of print. PMID: 36096185.

Umbilical cord milking in non-vigorous newborns: a cluster-randomized crossover trial

Delayed cord clamping and cord milking are recommended in vigorous newborns. Among the non-vigorous babies, however, the perceived need for immediate resuscitation supersedes that for delayed cord clamping. Researchers hypothesized that umbilical cord milking rather than early cord clamping may be a better alternative in non-vigorous newborns. Through this multi-centric cluster randomized trial, non-vigorous babies at birth were randomized to either umbilical cord milking or early cord clamping. The primary outcome measure was neonatal unit admission. Of 1730 newborns included in the primary analysis, the difference in frequency of neonatal unit admissions between the two groups was not significant. Babies who had their cord milked, however, had higher hemoglobin, received less cardiorespiratory support, and lower incidence of HIE. This first-of-a-kind study suggested that cord milking is feasible, safe, and better than early cord clamping in non-vigorous newborns.

Katheria AC, Clark E, et al. Umbilical cord milking in nonvigorous infants: a cluster-randomized crossover trial. *Am J Obstet Gynecol.* 2022 Aug 13;S0002-9378(22)00649-4. doi: 10.1016/j.ajog.2022.08.015. Epub ahead of print. PMID: 35970202.

Polycystic ovarian syndrome and risk of adverse obstetric outcomes

Polycystic ovarian syndrome (PCOS) is a common yet underdiagnosed endocrine disorder in women. Previous studies have

shown varying obstetric outcomes in this condition. Researchers in England, through a population-based study, compared a cohort of women with PCOS with an age-matched cohort of women without PCOS using data from Clinical Practice Research Datalink and Hospital Episodes Statistic.

The study found maternal PCOS to be associated with preterm birth and assisted (Caesarean section and instrumental) delivery as compared to spontaneous delivery. However, there was no association with low-or high birthweight or still birth. The researchers concluded that maternal PCOS was associated with an increased risk of preterm and cesarean delivery and that low birth weight may likely be from lower gestational age at birth.

Subramanian A, Lee SI, et al. Polycystic ovary syndrome and risk of adverse obstetric

outcomes: a retrospective population-based matched cohort study in England. *BMC Med.* 2022 Aug 30;20(1):298. doi: 10.1186/s12916-022-02473-3. PMID: 36038914; PMCID: PMC9425992.

Blackwater fever and acute kidney injury in children hospitalized with an acute febrile illness in Uganda.

Acute kidney injury (AKI) and Blackwater fever (BWF) are related yet distinct renal complications of acute febrile illness (AFI) in East Africa. Researchers, through a cohort study conducted in Eastern Uganda, sought to evaluate the association between AKI and BWF in children with AFI, as well as with mortality and host response biomarkers. A total of 999 children with AFI were evaluated. At enrollment, 8.2% of children had BWF, 49.5% had AKI and

11.1% had severe AKI. A history of BWF was independently associated with 2.18-fold increased odds of AKI. Severe AKI, not BWF was associated with an increased risk of in-hospital death. The researchers noted that BWF was associated with severe AKI hence a need for improved access to AKI diagnostics and early institution of kidney-protective measures to avert mortality.

Conroy AL, Hawkes MT, et al. Blackwater fever and acute kidney injury in children hospitalized with an acute febrile illness: pathophysiology and prognostic significance. *BMC Med.* 2022 Jul 1;20(1):221. doi: 10.1186/s12916-022-02410-4. PMID: 35773743; PMCID: PMC9248152.



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