### BMJ

**Long term tapering versus standard prednisolone treatment for first episode of childhood nephrotic syndrome: phase III randomised controlled trial and economic evaluation**

**Conclusions** Clinical outcomes did not improve when the initial course of prednisolone treatment was extended from eight to 16 weeks in UK children with steroid sensitive nephrotic syndrome. However, evidence was found of a short term health economic benefit through reduced resource use and increased quality of life.

**Understanding the consequences of education inequality on cardiovascular disease: mendelian randomisation study**

**Conclusions** BMI, systolic blood pressure, and smoking behaviour mediate a substantial proportion of the protective effect of education on the risk of cardiovascular outcomes and intervening on these would lead to reductions in cases of cardiovascular disease attributable to lower levels of education. However, more than half of the protective effect of education remains unexplained and requires further investigation.

**Determinants of the decline in mortality from acute stroke in England: linked national database study of 795,869 adults**

**Conclusions** Declines in case fatality, probably driven by improvements in stroke care, contributed more than declines in event rates to the overall reduction in stroke mortality. Mortality reduction in men and women younger than 55 was solely a result of a decrease in case fatality, whereas stroke event rates increased in the age group 35 to 54 years. The increase in stroke event rates in young adults is a concern. This suggests that stroke prevention needs to be strengthened to reduce the occurrence of stroke in people younger than 55 years.

### JAMA

**Effect of Laparoscopic vs Open Distal Gastrectomy on 3-Year Disease-Free Survival in Patients With Locally Advanced Gastric Cancer The CLASS-01 Randomized Clinical Trial**

**Conclusions** Among patients with a preoperative clinical stage indicating locally advanced gastric cancer, laparoscopic distal gastrectomy, compared with open distal gastrectomy, did not result in inferior disease-free survival at 3 years.

**Effect of a Recombinant Human Soluble Thrombomodulin on Mortality in Patients With Sepsis-Associated Coagulopathy The SCARLET Randomized Clinical Trial**

**Conclusions** Among patients with sepsis-associated coagulopathy, administration of a human recombinant thrombomodulin, compared with placebo, did not significantly reduce 28-day all-cause mortality.

**Derivation, Validation, and Potential Treatment Implications of Novel Clinical Phenotypes for Sepsis**

**Conclusions** In this retrospective analysis of data sets from patients with sepsis, 4 clinical phenotypes were identified that correlated with host-response patterns and clinical outcomes, and simulations suggested these phenotypes may help in understanding heterogeneity of treatment effects. Further research is needed to determine the utility of these phenotypes in clinical care and for informing trial design and interpretation.

**Effect of Initial Management With Aflibercept vs Laser Photocoagulation vs Observation on Vision Loss Among Patients With Diabetic Macular Edema Involving the Center of the Macula and Good Visual Acuity A Randomized Clinical Trial**

**Conclusions** Among eyes with CI-DME and good visual acuity, there was no significant difference in vision loss at 2 years whether eyes were initially managed with aflibercept or with laser photocoagulation or observation and given aflibercept only if visual acuity worsened. Observation without treatment unless visual acuity worsens may be a reasonable strategy for CI-DME.
THE LANCET

An injectable implant to stimulate the sphenopalatine ganglion for treatment of acute ischaemic stroke up to 24 h from onset (ImpACT-24B): an international, randomised, double-blind, sham-controlled, pivotal trial

Interpretation Sphenopalatine ganglion stimulation is safe for patients with acute ischaemic stroke 8–24 h after onset, who are ineligible for thrombolytic therapy. Although not reaching significance, the trial’s results support that, among patients with imaging evidence of cortical involvement at presentation, sphenopalatine ganglion stimulation is likely to improve functional outcome.

Upadacitinib as monotherapy in patients with active rheumatoid arthritis and inadequate response to methotrexate (SELECT-MONOTHERAPY): a randomised, placebo-controlled, double-blind phase 3 study

Interpretation Upadacitinib monotherapy showed statistically significant improvements in clinical and functional outcomes versus continuing methotrexate in this methotrexate inadequate-responder population. Safety observations were similar to those in previous upadacitinib rheumatoid arthritis studies.

Effects of antiplatelet therapy after stroke due to intracerebral haemorrhage (RESTART): a randomised, open-label trial

Interpretation These results exclude all but a very modest increase in the risk of recurrent intracerebral haemorrhage with antiplatelet therapy for patients on antithrombotic therapy for the prevention of occlusive vascular disease when they developed intracerebral haemorrhage. The risk of recurrent intracerebral haemorrhage is probably too small to exceed the established benefits of antiplatelet therapy for secondary prevention.

Extending thrombolysis to 4.5–9 h and wake-up stroke using perfusion imaging: a systematic review and meta-analysis of individual patient data

Interpretation Patients with ischaemic stroke 4.5–9 h from stroke onset or wake-up stroke with salvageable brain tissue who were treated with alteplase achieved better functional outcomes than did patients given placebo. The rate of symptomatic intracerebral haemorrhage was higher with alteplase, but this increase did not negate the overall net benefit of thrombolysis.

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The NEW ENGLAND JOURNAL of MEDICINE

Controlled Trial of Budesonide–Formoterol as Needed for Mild Asthma

Conclusions In an open-label trial involving adults with mild asthma, budesonide–formoterol used as needed was superior to albuterol used as needed for the prevention of asthma exacerbations. (Funded by AstraZeneca and the Health Research Council of New Zealand; Novel START Australian New Zealand Clinical Trials Registry number, ACTRN1261500099538)

Early Neuromuscular Blockade in the Acute Respiratory Distress Syndrome

Conclusions Among patients with moderate-to-severe ARDS who were treated with a strategy involving a high PEEP, there was no significant difference in mortality at 90 days between patients who received an early and continuous cisatracurium infusion and those who were treated with a usual-care approach with lighter sedation targets. (Funded by the National Heart, Lung, and Blood Institute; ROSE ClinicalTrials.gov number, NCT02509078)

Mometasone or Tiotropium in Mild Asthma with a Low Sputum Eosinophil Level

Conclusions The majority of patients with mild, persistent asthma had a low sputum eosinophil level and had no significant difference in their response to either mometasone or tiotropium as compared with placebo. These data provide equipoise for a clinically directive trial to compare an inhaled glucocorticoid with other treatments in patients with a low eosinophil level. (Funded by the National Heart, Lung, and Blood Institute; SIENA ClinicalTrials.gov number, NCT02066298)

Nasal High-Flow Therapy for Newborn Infants in Special Care Nurseries

Conclusions Nasal high-flow therapy was not shown to be noninferior to CPAP and resulted in a significantly higher incidence of treatment failure than CPAP when used in nontertiary special care nurseries as early respiratory support for newborn infants with respiratory distress. (Funded by the Australian National Health and Medical Research Council and Monash University; HUNTER Australian New Zealand Clinical Trials Registry number, ACTRN12614001203640.)

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