

All you need to read in the other general medical journals  
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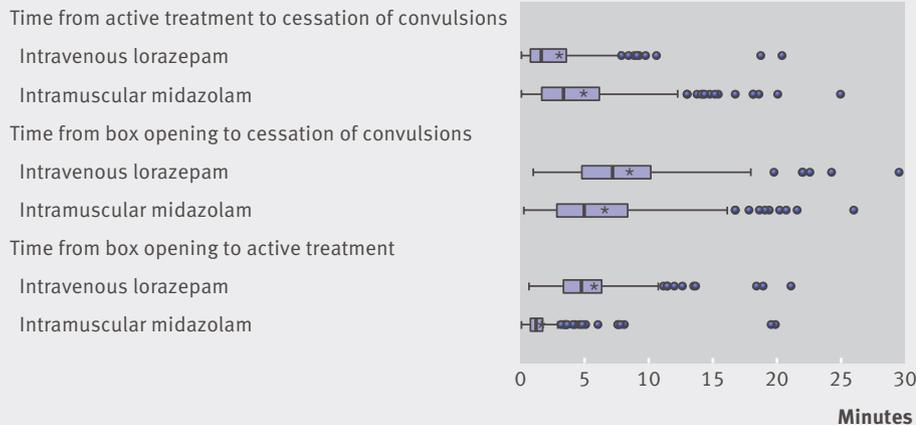


**Fans of Sherlock Holmes will remember the passage in *The Dying Detective* where Holmes fakes delirium and attacks his dear friend Watson for being an ignorant general practitioner . . .**

Richard Lehman's blog at [www.bmj.com/blogs](http://www.bmj.com/blogs)

## Paramedics: intramuscular midazolam is a good choice for status epilepticus

### Time to active treatment and time to cessation of convulsions



Asterisks indicate means, boxes interquartile ranges, bold vertical lines within boxes medians, I bars 1.5 times the interquartile range, and circles outliers

Adapted from *N Engl J Med* 2012;366:591-600

Status epilepticus is defined as prolonged or repetitive seizures without recovery between episodes. About one in five patients who experience this condition die and a quarter of those who survive have reduced functional ability. Early termination of seizures with benzodiazepines improves outcomes. For practical reasons, paramedics often exchange intravenous lorazepam—the preferred treatment in hospital—for intramuscular midazolam, with insufficient evidence to support this practice.

A trial recruited 1023 children and adults who had been convulsing for at least five minutes and were still doing so when the ambulance arrived. Paramedics gave either midazolam via an intramuscular autoinjector or lorazepam as an intravenous infusion. A 10% margin was preset for non-inferiority of midazolam against lorazepam.

This goal was well exceeded. On reaching hospital, 73.4% (329/448) of participants given midazolam intramuscularly had stopped convulsing, compared with 63.4% (282/445) of those given lorazepam intravenously (difference 10%, 95% CI 4.0% to 16.1%;  $P < 0.001$  for both non-inferiority and superiority).

In participants who reached hospital seizure-free, intramuscular treatment was quicker to administer but took longer once administered to take effect (median times 1.2 and 3.3 minutes, respectively) compared with intravenous treatment (4.8 and 1.6 minutes, respectively). The need for endotracheal intubation was compara-

ble between the groups (14.1% with midazolam v 14.4% with lorazepam), as was recurrence of seizures (11.4% v 10.6%).

Intramuscular autoinjectors for midazolam should soon become widely available says an editorial (p 659). Promising alternative routes of administration, such as nasal or buccal routes, which could be introduced as home treatment, also need to be studied.

*N Engl J Med* 2012;366:591-600

### Paricalcitol should not be given to people with chronic kidney disease

Chronic kidney disease is often associated with a deficit in vitamin D owing to impaired activity of a kidney enzyme that converts a precursor molecule to the active compound. Altered vitamin D metabolism leads to overactivity of the parathyroid glands, as well as worsened heart outcomes. Observational evidence suggests that treatment with vitamin D might help by improving the heart's structure and function.

This wasn't confirmed in a trial of 227 patients with chronic kidney disease who were randomised to 2 µg/d oral paricalcitol, an active vitamin D compound, or placebo. All participants had an estimated glomerular filtration rate of 15-60 mL/min/1.73 m<sup>2</sup> and mild to moderate hypertrophy of the left ventricle but preserved ejection fraction.

Parathyroid hormones were reduced to normal concentrations in the active treatment group by week 4. However, 48 months into the trial, neither changes in the mass of the left ventricle nor any of the tested measures of heart function differed between the groups. In fact, kidney function deteriorated more with paricalcitol, with more patients needing to start long term dialysis (6 v 1 with placebo).

Nevertheless, there were fewer admissions to hospital for cardiovascular disease in the paricalcitol group (1 v 8 in the placebo group). The editorialists (p 722) discuss why this finding should be interpreted with caution. A previous meta-analysis of trials found no benefit for vitamin D in chronic kidney disease on the risk of death, bone pain, vascular calcification, or parathyroidectomy.

*JAMA* 2012;307:674-84

### No support for amoxicillin in uncomplicated acute rhinosinusitis

A multicentre trial recruited 166 adults with moderate to severe acute bacterial rhinosinusitis. At enrolment, all participants had maxillary pain or tenderness as well as purulent nasal secretion that had lasted seven to 28 days. All were given a week's supply of symptomatic treatment and were randomised to 1500 mg/d of amoxicillin or placebo over 10 days.

At day 3, no difference in outcomes was seen between people who received amoxicillin and those who received placebo. Outcomes included disease specific quality of life, changes in symptoms, days missed from work or unable to perform usual activities, rates of relapse and recurrence by 28 days, additional use of healthcare, satisfaction with treatment, and adverse events.

The same was true for day 10. Some support for amoxicillin was seen at day 7, when 74% of those allocated to amoxicillin reported improvement in the symptoms, compared with 56% of those who received placebo. The number needed to treat was six. Symptoms that bothered people most, such as runny nose and cough, persisted for at least 10 days in most patients.

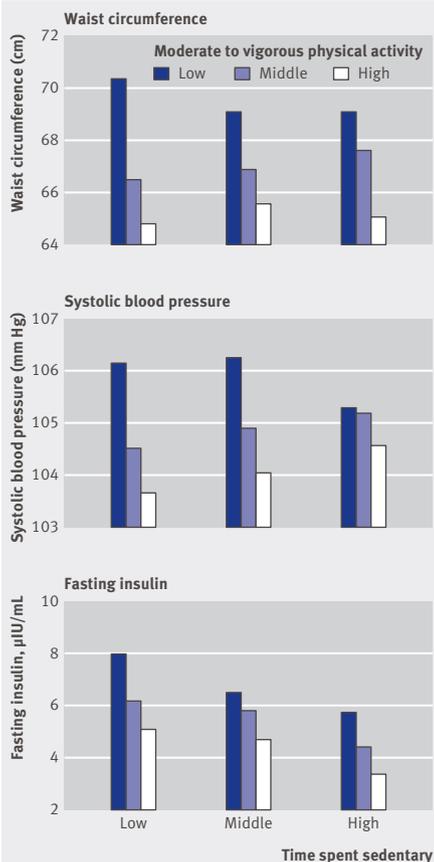
Overall, say the authors, the study supports recommendations from recent guidelines that routine treatment with antibiotics should be avoided in patients with uncomplicated acute rhinosinusitis.

*JAMA* 2012;307:685-92

## Physical activity improves children's cardiometabolic health regardless of sedentary time

Both lack of physical activity and sedentary behaviour have been linked with cardiovascular disease and cardiometabolic risk factors such as waist circumference, blood pressure, insulin, and blood lipids. Most studies have focused on either physical activity or sedentary time alone, although only weak to moderate associations have been shown between the two. Few studies have included both measures, and those that have suggest that, in adults, both physical activity and sedentary time are independent predictors of cardiometabolic health.

### Effect of sedentary time and physical activity on risk factors



Adapted from *JAMA* 2012;307:704-12

This didn't seem to hold true for children though in a meta-analysis of 14 observational studies that used accelerometry in nearly 21 000 children aged 4-18 years. Although time spent in moderate to vigorous physical activity was linked with all studied cardiometabolic risk factors, sedentary time was linked with none. Analyses were adjusted for most potential confounders but not participants' diet or genetic profile.

In combined analyses, those who spent more time in moderate to vigorous physical activity had better cardiometabolic outcomes across thirds of sedentary time. Nonetheless, the benefits of physical activity were higher in those with less sedentary behaviour. A prospective analysis showed no association between physical activity or sedentary time and waist circumference, but waist circumference at baseline predicted sedentary time, supporting the view that causality goes both ways.

Public health efforts should focus primarily on improving children's levels of physical activity, but reducing sedentary behaviour may still be an important goal too. The study measured sedentary behaviour only, not TV viewing, which is often coupled with consumption of snacks and fizzy drinks as well as exposure to adverts, which are thought to have an adverse effect on cardiometabolic health in their own right.

*JAMA* 2012;307:704-12

## Deciding on heparin for people on chemotherapy

Semuloparin, an ultra low molecular weight heparin, was tested in a manufacturer funded and analysed trial for prevention of venous thromboembolism. Participants were more than 3200 patients with cancer who were undergoing chemotherapy—an increasingly recognised risk factor for thrombosis—for metastases or locally advanced solid tumours. Semuloparin was given subcutaneously at a dose of 20 mg a day, for a median of 3.5 months.

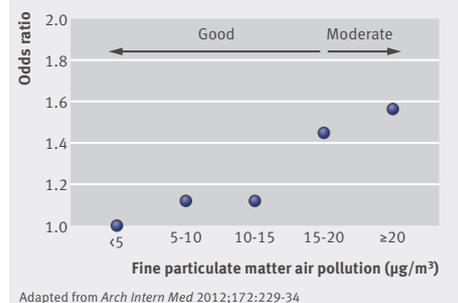
The drug did lower the risk of clotting events compared with placebo (1.2% (20/1608) v 3.4% (55/1604); hazard ratio 0.36, 95% CI 0.21 to 0.60). However, it did not affect mortality, and rates of bleeding were comparable between the groups (for major bleeding this was 1.2% (19/1589) with semuloparin v 1.1% (18/1583) with placebo). The effects did not vary with the site or stage of cancer.

The trial recruited more patients than were included in the editorialists' systematic review on the topic published last year (p 661). When updated with the findings of the current study and another smaller trial published in the meantime, the systematic review—briefly presented as part of the editorial—indicates that heparin might also confer a survival benefit, although the confidence intervals are wide. If 1000 people on chemotherapy were given prophylactic heparin for a year, 30 (95% CI 0 to 60) deaths would be averted, 20 (9 to 27) cases of venous thromboembolism would be averted, and one patient (5 fewer to 9 more) would have a major bleeding complication.

*N Engl J Med* 2012;366:601-9

## Air pollution can trigger myocardial infarction and stroke and speed up cognitive decline

### Level of air pollution and odds of ischaemic stroke



Adapted from *Arch Intern Med* 2012;172:229-34

A meta-analysis of 34 studies found that all studied air pollutants except ozone were associated with increased risk of myocardial infarction within a week of exposure. An increase of 1 mg/ $\text{m}^3$  in the air concentration of carbon monoxide, for example, increased the risk of infarction 1.048-fold. An increase of 10  $\mu\text{g}/\text{m}^3$  in fine particulate matter (particles smaller than 2.5  $\mu\text{m}$  in diameter) increased the risk 1.025-fold. Excess risks were similarly small for all examined pollutants, but because of the large number of people exposed, population attributable fractions have been estimated between 0.6% and 4.5% for individual pollutants.

Another study found that, among 1705 people admitted to hospital for ischaemic stroke in the Boston area, the odds of stroke were increased by 34% after a day's exposure to concentrations of fine particulate matter classified by authorities as "moderate" compared with that classified as "good." The risk of stroke was increased most in the 12-14 hours after exposure to higher concentrations of fine particulate matter. The associations were strongest for air pollutants related to traffic. More restrictive regulations are needed if risk is to be lowered in susceptible people (editorial, p 235).

Finally, the Nurses' Health Study provided for the first time longitudinal data on the link between air pollution and cognition. The study looked at nearly 20 000 women aged 70-81 years at baseline and followed up for a mean of four years. Exposure to higher concentrations of both coarse and fine particulate matter was associated with a faster cognitive decline. A 10  $\mu\text{g}/\text{m}^3$  increment in long term exposure to particulate matter was equivalent to ageing by two years. The authors stressed that these are typical exposure levels for many people in the US.

*JAMA* 2012;307:713-21, *Arch Intern Med* 2012;172:229-34, 219-27

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