Abstracts

**Low-dose aspirin increases risk of major bleeding, but not in diabetes**

Low-dose aspirin for primary prevention of cardiovascular events is generally considered a bad idea because the risks of bleeding seem to outweigh the benefits. However, things may be different for people with diabetes.

A claims study used data from more than 4 million residents of Perugia, Italy, over a period of six years. Of these, 186 425 people were taking low-dose aspirin. Propensity score matching was used to assign one control, without long-term low-dose aspirin use, to each participant taking aspirin. Propensity scoring took into account several potential confounders, including age, sex, diabetes, previous admission to hospital for cardiovascular disease, and use of various drugs. However, behavioural risk factors such as smoking, poor diet, excess alcohol consumption, obesity, and use of over-the-counter drugs (including aspirin) could not be considered in this study.

Overall, 5.58 (95% CI 5.39 - 5.77) hospital admissions for major bleeding in the gastrointestinal tract or brain occurred per 1 000 person years in users of aspirin; the incidence in non-users was 3.60 (3.48 - 3.72) per 1 000 person years (incidence rate ratio 1.55, 1.48 - 1.63). In other words, for 1 000 people treated over a year, two extra cases of major bleeding will occur – about the number of major cardiovascular events prevented in people with a 10-year risk of 10 - 20%.

In people with diabetes, however, no increased risk was seen (1.09, 0.97 - 1.22);

The risk of admission to hospital for major bleeding was increased by about one-third in all patients with diabetes, irrespective of aspirin use. This could be due to the high platelet reactivity seen in diabetes. The clinical implications that this might have remain to be explored.

Of note, the incidence of major bleeding found in this study is about 5 times higher than that reported in randomised trials.


**CT scans increase risk of cancer in children and adolescents**

Two to three computed tomography (CT) scans of the head may triple children's risk of brain cancer; five to ten such scans may triple the risk of leukaemia.

This was seen in a study of all people under 22 years of age who had a first CT scan within the NHS in England, Wales, or Scotland between 1985 and 2002. Linkage with the central NHS registry provided data for the incidence of cancer in these people over an average of 10 years, and up to 23 years, of follow-up.

During this time, 74 diagnoses of leukaemia and 135 diagnoses of brain cancer were recorded in more than 175 000 participants.

Excess relative risk per mGy was 0.036 (95% CI 0.005 - 0.120) and 0.023 (0.010 - 0.049) for leukaemia and brain tumours, respectively. For every 1 000 head CT scans performed in children under 10 years, one additional case of leukaemia and one additional brain tumour can be expected in the subsequent 10 years.

Up to a half of CT scans are done unnecessarily, writes the commentator. Because we now know that CT confers an increased, albeit small, risk of cancer, good clinical judgement is needed to justify performing each CT scan, using as low a dose as possible.


**Any decrease in serum glucose pays for patients with pre-diabetes**

Observational follow-up of participants in an earlier prevention of diabetes trial showed that those who had at least one normal serum glucose measurement during the trial had half the risk of developing diabetes over the 6-year follow-up compared...
with those who had high serum glucose in all measurements. Two and 3 normal blood glucose measurements conferred a 61% and 67% reduced risk of developing diabetes, respectively.

This finding was irrespective of group assignment in the three-arm trial, which lasted 3 years and tested an intensive lifestyle intervention, metformin, and placebo in the prevention of diabetes in people with high risk at baseline. Only those participants who did not develop diabetes during the trial (72% (1 990/2 761)) were included in the observational study. Serum glucose was measured twice a year.

Unexpectedly, among people without normal glucose measurements, those randomised to a lifestyle intervention had a 30% higher risk of developing diabetes than those who received placebo. It is not clear how to interpret this finding; it could be that people who responded poorly to a lifestyle intervention might have somehow been more susceptible to developing diabetes, or those who responded well to placebo might have been less susceptible.

In any case, the study seems to support early and aggressive lowering of blood glucose in people at high risk of diabetes. The linked comment suggests that future research should explore whether a similar strategy might reduce the risk of complications, such as blindness or vascular disease, in full-blown diabetes.

Drug-resistant tuberculosis is on the rise worldwide, says a linked editorial. If the epidemic is to be contained, diagnosis and treatment need to be improved. Global policies already call for testing microbial resistance in all patients, but most programmes still focus only on patients considered to be at high risk.

New drugs, such as delamanid and bedaquiline, may soon be approved for second-line treatment on the basis of placebo-controlled trials. However, we don't know whether they can be given concurrently or how best to incorporate them into existing regimens.


One in 10 tuberculosis cases in China is multidrug resistant
About a million new cases of tuberculosis are detected in China each year. A nationally representative survey of about 4 000 people with tuberculosis showed that, in 2007, one- third of new cases as well as more than a half of previously treated cases had tuberculosis resistant to at least one of the first-line drugs – isoniazid, rifampicin, ethambutol, and streptomycin. One in 10 people had multidrug-resistant tuberculosis – where the organism is resistant to at least isoniazid and rifampicin – and 1 in 120 was also resistant to second-line drugs ofloxacin and kanamycin. In most cases, the organism was already resistant at the point of infection.

Drug-resistant tuberculosis has been well established in studies of brain disease, ‘says Beth Stevens of Boston Children’s Hospital. ‘But now, even without damage, we’ve found them to respond to subtle changes in synaptic function.’ Stevens and her colleagues manipulated mice to make one eye more active than the other, creating a disparity in activity between the two neural circuits linking the eyes to the brain. With the help of dyes to distinguish the signals from the left and right eyes, they saw in postmortems that microglia had preferentially pruned the connections, or synapses, from circuits serving the underactive eye. Synapses were marked out for destruction through labelling with an immune chemical called C3.

‘We think C3 is an “eat me” signal,’ says Stevens.

Finding out why some synapses but not others are earmarked for elimination could point to ways of preventing degenerative brain diseases.

‘Early synapse loss is a feature of many neurodegenerative diseases,’ says Stevens. ‘So there’s lots of excitement about finding out what the trigger is.’

‘Microglia were considered to be just garbage collectors,’ says Francesca Peri of the European Molecular Biology Laboratory in Heidelberg, Germany. ‘They are turning out to be far more interesting – but before we can understand their role in disease, we need to understand what these cells do normally.’

New Scientist, 1 June 2012.