Ann Robinson’s research reviews — 1 June 2022

Ann Robinson NHS GP and health writer and broadcaster

Digging in the wardrobe: a new look for metformin?

Repurposing drugs is a bit like digging out an old jacket from your wardrobe and finding that it looks good with a new pair of trousers; it’s trustworthy, cheap, and offers a novel solution. And so to metformin, the carthorse of diabetes treatment that has reportedly been associated with potential benefits in breast cancer patients in some observational studies. In women with diabetes and breast cancer, the question is whether metformin has a direct antitumour effect in addition to its effectiveness in controlling diabetes. If so, then metformin would also be expected to improve survival in non-diabetic women with breast cancer.

However, this useful randomised trial of 3649 women with high risk, non-metastatic, operable breast cancer and no diabetes found that treatment with metformin (850 mg twice daily) for five years compared with placebo did not significantly increase the interval free of invasive disease or overall survival. Analysing the results by hormone receptor status of the cancer did not alter the lack of effect.

JAMA doi:10.1001/jama.2022.6147

Carotid stenosis: surgery or drugs?

Since the publication of several randomised trials in 1995 and 2010, optimal treatment for carotid stenosis has involved surgical intervention in most cases. But medical treatment has improved since then, so which would you opt for now? In this retrospective study of a diverse cohort of nearly 95 000 patients with asymptomatic severe carotid stenosis who didn’t have surgery, the rate of ipsilateral carotid-related acute ischaemic stroke was 4.7% over five years, which is lower than historical reports and likely to be more accurate thanks to the robust study design. More information is still needed; this trial couldn’t assess the quality of imaging data, use of over-the-counter-aspirin, or incidence of transient ischaemic attacks. But it’s useful to know the risk of stroke if you choose modern medical management over surgical intervention, which is likely to become increasingly reserved for a highly selected group.

JAMA doi:10.1001/jama.2022.4835

Tranexamic acid: a finger in the dam?

There’s a worldwide shortage of blood for transfusions, 40% of which are needed after surgical bleeding. Could giving the antifibrinolytic drug tranexamic acid to all patients at risk of perioperative bleeding and cardiovascular complications, help to reduce that need? This international, randomised trial of 9535 patients found fewer significant bleeds (a composite outcome of life threatening, major, or critical organ bleeding at 30 days) in those given a 1 g intravenous bolus of tranexamic acid at the start and end of non-cardiac surgery compared with placebo (9.1% v 11.7%).

I’m always surprised that tranexamic acid doesn’t seem to increase the risk of thrombosis, given that its job is to enhance clotting, but its good safety profile was borne out in this study, with no significant increase (though inferiority not established) in a composite cardiovascular outcome at 30 days (14.2% v 13.9%). It was a shame that financial pressures and covid-19 contributed to the trial being stopped early, although the researchers still recruited 95% of the planned sample size and didn’t know the trial results when the decision to wind up early was made.


Hard day’s night?

A tired surgeon is a worrying prospect, but any association between fatigue and patient outcomes has been hard to study reliably. This important cross-sectional study of outcomes of nearly half a million daytime operations across 50 hospitals in the US and Netherlands found that there was no significant association between surgeons who had operated the previous night and those that hadn’t in terms of the incidence of in-hospital death or major complications such as sepsis, pneumonia, myocardial infarction, thrombosis, or stroke (5.89% v 5.87% after adjusting for confounders). This lack of association held true overall and for those patients at highest risk of death or major surgical complications. The results are certainly reassuring, but intuitively I’d rather be operated on by someone who has had a good night’s sleep rather than one who’s been working all night.


Crohn’s news

There’s encouraging news for people with moderate to severely active Crohn’s disease from two randomised trials which showed that risankizumab, a novel humanised monoclonal antibody targeting interleukin 23A, was well tolerated and effective in inducing and maintaining remission. D’Haens and colleagues reported results of two phase 3 trial induction studies (ADVANCE and MOTIVATE), which found 600 mg and 1200 mg doses of intravenous risankizumab achieved early symptom control by week 4 and endoscopic improvement at week 12 compared with placebo in patients who had never had or had failed to respond to biologic therapy in the past. No new safety concerns identified. Ferrante and colleagues reported similarly positive results from the FORTIFY phase 3 trials using subcutaneous risankizumab for a year while withdrawing other maintenance drugs in those who
responded to 12 weeks of intravenous risankizumab. The co-primary endpoints of clinical remission and robust evidence of endoscopic response made the results more compelling. Currently, risankizumab is used to treat psoriasis and seems to be more effective than its rival, ustekinumab. A trial is under way to compare the two drugs in the treatment of Crohn’s disease.

*Lancet* doi:10.1016/S0140-6736(22)00467-6, doi:10.1016/S0140-6736(22)00466-4

Competing interests: None declared

Provenance and peer review: Not commissioned; not peer reviewed