Tom Nolan’s research reviews—30 November 2023

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Clinical benefits from new drugs
Prescrire is a French independent non-profit organisation that offers healthcare professionals information on the clinical benefits—or otherwise—of medicines and diagnostic strategies. It rates new medicines on a seven point scale from “bravo” to “judgement reserved,” via “possibly helpful,” “nothing new,” and “not acceptable.” A cross sectional study of 632 medicines entering the French market between 2008 and 2018 looked at the clinical benefit of each medicine according to Prescrire (and the Haute Autorité de Santé (HAS), which has a similar but less interesting 6 point scale). Of the new drugs, 73% originated in the commercial sector, and 27% came from an academic setting or in collaboration with commercial enterprises. Most of the medicines were judged as having no added clinical benefit, but a greater proportion of those developed in academia were likely to have some added benefit, according to Prescrire, than those from the commercial sector (57 (34%) v 98 (21%) respectively, P=0.001). Bravo academics.


You say NOAC, I say DOAC
When oral anticoagulants such as edoxaban hit the scene, they really seemed worthy of the “N for Novel” of the acronym of the new drug class NOAC. An oral anticoagulant that didn’t need INR monitoring really was a welcome novelty (bravo, as Prescrire might say). After the novelty wore off, we switched to DOAC: “D for Direct,” as in direct factor Xa inhibitors (and the added subliminal benefit of the acronym shouting “DO” instead of “NO”). A new study in JAMA Internal Medicine prefers NOAC, with N now standing for non-vitamin K antagonist.

Nomenclature issues aside, most guidelines currently say to withhold intravenous thrombolyis in people who have recently taken a NOAC/DOAC. The cohort study set in Taiwan looked at whether people who had taken a NOAC within the two days before being treated with intravenous alteplase for an acute ischaemic stroke were more likely to have an intracranial haemorrhage than people not taking a NOAC. It found no increase in risk of intracranial haemorrhage in the 19 people (1.2%) taking a NOAC, but prospective studies are needed before more certain conclusions can be reached.


Under my umbrella
Get your brolly out, it’s raining clinical trials of dietary interventions for type 2 diabetes. An umbrella review found 88 eligible systematic reviews and meta-analyses of randomised controlled trials of the effects of dietary factors in type 2 diabetes from a literature search that yielded 25 221 publications. It found that liquid meal replacement as part of a weight loss diet can reduce body weight and improve cardiometabolic health, and a Mediterranean, low carbohydrate (<26% total energy), or high protein diet is good for cardiometabolic health. The clinical significance of these is debatable though: liquid meal replacement was found to reduce body weight by only 2.4 kg by at least 12 weeks. With NovoNordisk enjoying the pot of gold that is semaglutide, will the sun ever come out in the world of dietary interventions to reveal a rainbow leading to similar treasures?

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Deep learning and pancreatic cancer screening
Pancreatic ductal adenocarcinoma (PDAC) has one of the worse prognoses of all malignancies. Yet, with it being relatively rare, “effective screening in the general population requires high sensitivity and exceptionally high specificity to mitigate the risk of over-diagnosis” say researchers investigating population based screening with non-contrast computed tomography and deep learning. Despite this challenge, they confidently conclude that Pancreatic Cancer Detection with AI (PANDA) has “the ability to detect and diagnose PDAC...with high accuracy and can be readily utilised for opportunistic screening in large scale populations.”

There’s a lot to unpick from this research, but I’m not sure everyone will agree with their claim. In their real world evaluation of 16420 scans, they found 26 pancreatic lesions not already detected by standard care, one of which was a PDAC. PANDA came up with a false positive 76 times, although 70 of these were ruled out easily by a radiologist review.

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Scratching the surface of urticaria studies
You wait all year for a major randomised control trial of a treatment for chronic spontaneous urticaria and then three come along at once. Last week, we saw acupuncture fail to make a clinically important difference in symptom scores; this week, we have two phase 3 trials of ligelizumab published together (you can’t get FDA approval with just one RCT). The improvements in symptoms after 12 weeks of treatment according to the Urticaria Activity Score 7 (UAS7) from ligelizumab was greater than we saw from acupuncture, but in only one of the two trials was this above the minimal clinically important difference—reported as 9.5-10.5 elsewhere, but not mentioned in this study.
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