



The BMJ, London

Cite this as: *BMJ* 2022;379:o2804<http://dx.doi.org/10.1136/bmj.o2804>

Published: 24 November 2022

Tom Nolan's research reviews—24 November 2022

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New hope for lipid profile chat

Looking for something new to spice up those cholesterol consultations? Lipoprotein(a) might be just what you're looking for. It's thought to be a marker of cardiovascular disease and therefore a candidate for new preventive treatments. A phase 2, dose-finding trial examined the effect of olpasiran (which reduces lipoprotein(a) synthesis in the liver) on lipoprotein(a) levels. This small study, which recruited 281 people with established atherosclerotic cardiovascular disease and high lipoprotein(a) levels, did indeed find a dose dependent reduction in lipoprotein(a) levels in those who received olpasiran. But it's early days: will this reduction translate into clinically meaningful endpoints? Until then, it's back to the familiar "good and bad cholesterol" and "let's take a look at your overall risk" chat.

N Engl J Med doi:10.1056/NEJMoa2211023

Match of the day

The *New England Journal of Medicine* gets into the football World Cup spirit with some research from Qatar. Like the world cup, this cohort study examining the effects of covid vaccination in children involved a lot of matches: matching unvaccinated and vaccinated children and waiting to see which of the matched pair scores the own goal of getting covid. It found that vaccination was associated with modest, rapidly waning protection from the omicron variant in 5-11 year olds, with only 2.1% of the vaccinated children in this age group getting covid in the 110 day follow-up period, compared with 2.4% of unvaccinated controls. There was a larger reduction in covid rates in adolescents, who received a higher 30 µg dose of the BNT162b2 vaccine—but the benefits of vaccination in a pre-omicron cohort were much greater, estimated at 95%, compared with 30% in the omicron era.

N Engl J Med doi:10.1056/NEJMoa2210058

Ankle replacement or arthrodesis?

It must be strange being a participant of the TARVA trial, where the decision to have either a total ankle replacement or arthrodesis was made by a sophisticated computer version of the toss of a coin. It's no wonder that, of the 933 people with end stage ankle osteoarthritis who were eligible for the study across 17 sites in the UK, only 303 agreed to take part. A year after surgery, both groups of patients showed a considerable improvement in the primary endpoint for the study—a Manchester-Oxford Foot Questionnaire walking/standing domain score—but there was no significant difference in these scores between the two groups.

Ann Intern Med doi:10.7326/M22-2058

What goes up must come down

Using 11 variables commonly available in patient records, such as body mass index and blood pressure, researchers were able to create a prediction score that would identify people at greater risk of having an ascending aortic aneurysm. Their model had a number needed to screen somewhere between 1.8 and 22.8, depending on which cohort it was tested against and the sensitivity threshold. But how many of those diagnosed would actually benefit? A cut-off of 4 cm was chosen as the lower bound of moderate ascending aortic dilatation because it had been used in other studies. However, surgery isn't indicated unless aneurysms are much bigger (>5.5 cm according to European Society of Cardiology guidelines, with some exceptions such as Marfan syndrome and rapid growth), and there is no effective medical treatment to slow progression—or, as the authors put it, "evidence for effectiveness [of medical treatment] in nonsyndromic aneurysm remains understudied."

JAMA doi:10.1001/jama.2022.19701

Monoclonal antibodies for malaria prevention

Could monoclonal antibodies be effective in preventing malaria? Results from a phase 2 study of CIS43LS, a monoclonal antibody against the sporozoites of *Plasmodium falciparum*, show some promise, but there may still be a long way to go. Laboratory diagnosed *P falciparum* infection was used to determine efficacy among the 330 people enrolled onto the study in Mali—episodes of clinical malaria were not recorded. The higher of the two doses studied had an efficacy of 88% at six months compared with placebo. Further studies will tell us how this translates into prevention of clinical malaria, but the need for a 30 minute intravenous infusion may limit its potential to be rolled out for widespread use.

N Engl J Med doi:10.1056/NEJMoa2206966

Competing interests: None declared.

Provenance and peer review: Not commissioned, not peer reviewed.