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² The BMJ

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Tom Nolan's research reviews—19 November 2021

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No surprises for Pfizer

The phase II/III double-blind randomised controlled trial of Pfizer's BNT162b2 vaccine in 5-11 year olds has been published in *NEJM*.¹ It contains another classic covid incidence-versus-time graph, where the placebo arm ascends like an alpine pass and the BNT162b2 arm has the gentle ascent of a stroll in Norfolk. The authors report a vaccine efficacy of 90.7% for preventing symptomatic covid-19, when two 10 µg vaccine doses were administered 21 days apart. Over the median 2.3 month follow-up period, no serious adverse events related to the vaccine were observed among the 1450 vaccinated children, and no cases of myocarditis—although the study wasn't powered to detect potential rare side effects. On 29 October, the vaccine received emergency use authorisation from the Food and Drug Administration (FDA) to be administered to 5-11 year olds based on these findings.

All that coughs isn't covid

Our brains naturally seek out explanations for our symptoms, often reaching for those that are most readily available (hence "All that wheezes isn't asthma"—a mandatory line in any talk about asthma). Unsurprising then that persistent symptoms such as fatigue, chest pain, or cough can be associated with believing that you have had covid-19, even if serology suggests (but by no means confirms) otherwise. These were the findings of a cross sectional analysis of data from two large surveys in France, where 26 823 participants also had a serology test for antibodies to SARS-CoV-2 (between May and November 2020).² With the exception of anosmia, positive serology wasn't associated with persistent symptoms, possibly due to a high false positive rate of the test at a time when covid prevalence was low. But that hasn't stopped the predictable online reaction citing this as evidence that long covid doesn't exist.

The stress of public speaking

If, like me, you need some validation about your fear of public speaking, you'll be pleased to hear that it's being used by academics to provoke mental stress-induced ischaemia. There are some striking findings in this pooled analysis of two prospective cohort studies that included 918 participants with stable coronary heart disease: the 16% who had mental stress-induced ischaemia had a rate of cardiovascular death or first or recurrent non-fatal myocardial infarction of 6.9 per 100 patient-years, compared with a rate of only 2.6 per 100 patient-years in the patients without mental stress-induced ischaemia.³ I guess it wasn't the public speaking test itself that carries the risk, but I'm not going to let that stop me using it as an excuse to get out of giving any talks.

Being depressed in lockdown

When the waves of covid-19 hospital admissions and lockdowns hit, I didn't know many people whose scores on a PHQ-9 or GAD-7 questionnaire wouldn't have been higher than before the pandemic. Feeling down and anxious felt like an appropriate response to what was going on, just like trawling the net for covid-19 preprints and refreshing the Johns Hopkins coronavirus map 10 times a day. A systematic review and meta-analysis in the *Lancet* mainly included studies that used symptom scales (such as PHQ-9 and GAD-7) to estimate the impact of covid-19 on the global prevalence of depressive and anxiety disorders in 2020.⁴ But were these tests valid in such exceptional circumstances? The authors recognise that assuming they were is one weakness in the study design, but one that they were not able to test or adjust for. They estimated that depression and anxiety disorders had both increased by over 25% thanks to the pandemic, with an additional 53.2 million cases of major depressive disorder globally and an additional 76.2 million cases of anxiety disorders. Females were affected more than males, and younger age groups more than older.

No paradigm shift for myocardial infarction

Sacubitril with valsartan is recommended by NICE as an option for treating symptomatic chronic heart failure. The original PARADIGM-HF trial reported an impressive reduction in risk of hospital admission and death from cardiovascular causes for sacubitril-valsartan versus enalapril, but the study population (mostly men, relatively young, and almost all already taking an ACE inhibitor) didn't reflect typical clinical practice, and a 2016 NICE technology appraisal did not recommend it as a first line treatment.

This latest study, PARADIGM-MI, randomised 5661 patients with myocardial infarction complicated by a reduced left ventricular ejection fraction and/or pulmonary congestion to receive either sacubitril-valsartan (97 mg sacubitril with 103 mg valsartan twice daily) or ramipril (5 mg twice daily) in addition to recommended therapy.⁵ It found no significant difference between the two treatments in death from cardiovascular disease or incidence of heart failure. Hypotension occurred more in participants taking sacubitril-valsartan, but cough was less common. Around 40% of participants in both arms had a serious adverse event.

Competing interests: none declared

Provenance and peer review: commissioned, not peer reviewed

¹ Walter EB, Talaat KR, Sabharwal C, et al. C4591007 Clinical Trial Group. Evaluation of the BNT162b2 Covid-19 Vaccine in Children 5 to 11 Years of Age. *N Engl J Med* 2021. doi: 10.1056/NEJMoa2116298. PMID: 34752019

- 2 Matta J, Wiernik E, Robineau O, et al Santé, Pratiques, Relations et Inégalités Sociales en Population Générale Pendant la Crise COVID-19—Sérologie (SAPRIS-SERO) Study Group. Association of Self-reported COVID-19 Infection and SARS-CoV-2 Serology Test Results With Persistent Physical Symptoms Among French Adults During the COVID-19 Pandemic. *JAMA Intern Med* 2021. doi: 10.1001/jamainternmed.2021.6454. pmid: 34747982
- 3 Vaccarino V, Almuwaqqat Z, Kim JH, et al. Association of Mental Stress-Induced Myocardial Ischemia With Cardiovascular Events in Patients With Coronary Heart Disease. *JAMA* 2021;326:1818-28. doi: 10.1001/jama.2021.17649. pmid: 34751708
- 4 COVID-19 Mental Disorders Collaborators. Global prevalence and burden of depressive and anxiety disorders in 204 countries and territories in 2020 due to the COVID-19 pandemic. *Lancet* 2021;398:1700-12. doi: 10.1016/S0140-6736(21)02143-7. pmid: 34634250
- 5 Pfeffer MA, Claggett B, Lewis EF, et al PARADISE-MI Investigators and Committees. Angiotensin Receptor-Neprilysin Inhibition in Acute Myocardial Infarction. *N Engl J Med* 2021;385:1845-55. doi: 10.1056/NEJMoa2104508. pmid: 34758252