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of rapid waning of post-booster immunogenicity and immune escape of new variants of concern. Heterologous boosters with next-generation vaccines, such as multivalent vaccines (vaccines providing protection against different variants simultaneously), universal coronavirus vaccines, vaccines eliciting stronger T-cell responses, or mucosal vaccines (either intranasal or oral), are among the future options for COVID-19 vaccination. However, while awaiting these next-generation vaccines, booster immunisations are crucial to restore vaccine effectiveness against severe outcomes in clinically vulnerable populations. The results of this trial are important to help policy makers to determine who benefits most from booster dosing and when booster dosing should be implemented. The question of whether benefit can be gained with longer delays between boosters remains unanswered.

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- 1 Ferdinand JM, Rao S, Dixon BE, et al. Waning 2-dose and 3-dose effectiveness of mRNA vaccines against COVID-19-associated emergency department and urgent care encounters and hospitalizations among adults during periods of delta and omicron variant predominance—VISION Network, 10 states, August 2021–January 2022. *MMWR Morb Mortal Wkly Rep* 2022; **71**: 255–63.
- 2 Bar-On YM, Goldberg Y, Mandel M, et al. Protection by a fourth dose of BNT162b2 against omicron in Israel. *N Engl J Med* 2022; published online April 5. <https://doi.org/10.1056/NEJMoa2201570>.
- 3 Magen O, Waxman JG, Makov-Assif M, et al. Fourth dose of BNT162b2 mRNA COVID-19 vaccine in a nationwide setting. *N Engl J Med* 2022; published online April 13. <https://doi.org/10.1056/NEJMoa2201688>.
- 4 Regev-Yochay G, Gonen T, Gilboa M, et al. Efficacy of a fourth dose of COVID-19 mRNA vaccine against omicron. *N Engl J Med* 2022; **386**: 1377–80.
- 5 Munro APS, Feng S, Janani L, et al. Safety, immunogenicity, and reactogenicity of BNT162b2 and mRNA-1273 COVID-19 vaccines given as fourth-dose boosters following two doses of ChAdOx1 nCoV-19 or BNT162b2 and a third dose of BNT162b2 (COV-BOOST): a multicentre, blinded, phase 2, randomised trial. *Lancet Infect Dis* 2022; published online May 9. [https://doi.org/10.1016/S1473-3099\(22\)00271-7](https://doi.org/10.1016/S1473-3099(22)00271-7).

## Risk of arterial and venous thromboses after COVID-19



Infection can trigger thrombotic events. After respiratory and other infections, people have a 3–6-fold increased risk of arterial thrombosis, such as myocardial infarction and ischaemic stroke, and a 2–3-fold increased risk of venous thromboses, such as deep vein thrombosis of the legs and pulmonary embolism.<sup>1,2</sup> The risk declines in the weeks after infection, although a higher risk can persist for a year or longer, particularly for venous thromboses.<sup>2</sup>

People with severe COVID-19 have a high risk of symptomatic and asymptomatic pulmonary emboli during their hospital stay.<sup>3</sup> However, the longer-term risks of thrombotic events after mild COVID-19 are less clear, and a better understanding of the future risk of heart attack and stroke is a priority for people affected by COVID-19.<sup>4</sup>

In *The Lancet Infectious Diseases*, Edward Burn and colleagues<sup>5</sup> report the 90-day cumulative incidences of venous or arterial thromboembolism and death after a COVID-19 diagnosis in primary care datasets from five countries: the Netherlands, Italy, Spain, the UK, and Germany. The study showed substantial

variation in the 90-day cumulative incidence following COVID-19 diagnosis between the different countries: for venous thromboses from two per 1000 in the Netherlands to eight per 1000 in Spain; and for arterial thromboembolism from one per 1000 in the UK to eight per 1000 in Spain. The incidence of venous and arterial events was higher in older people, and the risk of death after venous and arterial events was higher in people who had been diagnosed with or tested positive for COVID-19 than in people without COVID-19. In other studies, the cumulative excess risks up to 49 weeks after a COVID-19 diagnosis or positive test in linked primary and secondary care databases in England were 25 per 1000 for arterial and six per 1000 for venous thromboses,<sup>6</sup> and the cumulative risk of venous events in Sweden up to 30 days after a COVID-19 diagnosis or positive test was about two per 1000.<sup>7</sup>

The wide variation in the incidence across countries highlights the challenges in combining estimates from different health-care systems and with different public health policies. Each primary care system has different coding practices, populations, and linked

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See [Articles](#) page 1142

datasets to ascertain risk. Although the authors made considerable efforts to analyse their data to a common data model, linkage to hospital records (and hence the completeness of ascertainment of thrombotic events) varied between primary care systems, and different workloads and patterns of use of primary health care might affect coding. The different timing of vaccination programmes between countries could have led to different secular changes in the incidence and severity of COVID-19 and its consequences. However, multicountry studies such as this are crucial for helping to build an evidence basis for decisions about prioritising public health.

The prevention of arterial or venous thromboses through vaccination against common infections, or other population-level approaches, is appealing. Influenza vaccination reduces the relative risk of major cardiovascular events by about a third, from a meta-analysis of randomised controlled trials, and observational data suggest that COVID-19 vaccination has a similar protective effect in older people, although is subject to biases and residual confounding.<sup>8</sup> Results of further studies in high-risk individuals are awaited.<sup>9</sup> Although acute antithrombotic therapy might reduce the short-term risk of venous thromboses (with an increased risk of haemorrhage) after infection with SARS-CoV-2, aspirin does not seem to be of overall benefit.<sup>10</sup> New trials of aspirin use could answer this question definitively for non-COVID-19 infections such as pneumonia.

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- 1 Smeeth L, Thomas SL, Hall AJ, Hubbard R, Farrington P, Vallance P. Risk of myocardial infarction and stroke after acute infection or vaccination. *N Engl J Med* 2004; **351**: 2611-18.
- 2 Clayton TC, Gaskin M, Meade TW. Recent respiratory infection and risk of venous thromboembolism: case-control study through a general practice database. *Int J Epidemiol* 2011; **40**: 819-27.
- 3 Desai R, Gandhi Z, Singh S, et al. Prevalence of pulmonary embolism in COVID-19: a pooled analysis. *SN Compr Clin Med* 2020; **2**: 2722-25.
- 4 Houchen-Wolloff L, Poinasamy K, Holmes K, et al. Joint patient and clinician priority setting to identify 10 key research questions regarding the long-term sequelae of COVID-19. *Thorax* 2022; published online March 30. <https://doi.org/10.1136/thoraxjnl-2021-218582>.
- 5 Burn E, Duarte-Salles T, Fernandez-Bertolin S, et al. Venous or arterial thrombosis and deaths among COVID-19 cases: a European network cohort study. *Lancet Infect Dis* 2022; published online May 13. [https://doi.org/10.1016/S1473-3099\(22\)00223-7](https://doi.org/10.1016/S1473-3099(22)00223-7).
- 6 Knight R, Walker V, Ip S, et al. Association of COVID-19 with arterial and venous vascular diseases: a population-wide cohort study of 48 million adults in England and Wales. *medRxiv* 2021; published online Nov 24. <https://doi.org/10.1101/2021.11.22.21266512> (preprint).
- 7 Katsoularis I, Fonseca-Rodriguez O, Farrington P, et al. Risks of deep vein thrombosis, pulmonary embolism, and bleeding after COVID-19: nationwide self-controlled cases series and matched cohort study. *BMJ* 2022; **377**: e069590.
- 8 Whiteley WN, Ip S, Cooper JA, et al. Association of COVID-19 vaccines ChAdOx1 and BNT162b2 with major venous, arterial, or thrombocytopenic events: a population-based cohort study of 46 million adults in England. *PLoS Med* 2022; **19**: e1003926.
- 9 Loeb M, Dokainish H, Dans A, et al. Randomized controlled trial of influenza vaccine in patients with heart failure to reduce adverse vascular events (IVVE): rationale and design. *Am Heart J* 2019; **212**: 36-44.
- 10 Abani O, Abbas A, Abbas F, et al. Aspirin in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. *Lancet* 2022; **399**: 143-51.

For more on trials of aspirin use to prevent cardiovascular events following pneumonia see <https://fundingawards.nihr.ac.uk/award/NIHR132968>



## The state of tuberculosis in South Africa: what does the first national tuberculosis prevalence survey teach us?

South Africa is among WHO's list of 30 high-burden tuberculosis countries and has one of the highest incidence rates of notified tuberculosis in the world.<sup>1</sup> In *The Lancet Infectious Diseases*, Sizulu Moyo and colleagues<sup>2</sup> report their findings from the first national tuberculosis prevalence survey in South Africa, which is a very important study that provides improved understanding of the true extent of tuberculosis and helps to identify groups who might be underserved by health services and where tuberculosis might be undiagnosed. Tuberculosis prevalence surveys are

massive endeavours; this survey included more than 35 000 participants across all nine provinces of South Africa, all of whom were screened using a symptom questionnaire and chest X-rays, and more than 9000 were eligible to provide sputum samples for Xpert MTB/RIF Ultra assay testing and mycobacterial culture. Although diagnosis of tuberculosis has improved in recent years it is still fraught with challenges. This survey, like many before it, has shown the inadequacy of using symptom screening to identify people living in the community who have culturable *Mycobacterium*

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See [Articles](#) page 1172