



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

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



Lancet Infect Dis 2022

Published Online  
May 13, 2022  
[https://doi.org/10.1016/S1473-3099\(22\)00314-0](https://doi.org/10.1016/S1473-3099(22)00314-0)

See Online/Articles  
[https://doi.org/10.1016/S1473-3099\(22\)00223-7](https://doi.org/10.1016/S1473-3099(22)00223-7)

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 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.

WW is supported by the Chief Scientist's Office, the Stroke Association, and the Alzheimer's Society; sits on data monitoring committees for academic trials (TEMPO-2, PROTECT-U, and CATIS-ICAD); and is an expert witness to UK courts. AW declares no competing interests.

\*William Whiteley, Angela Wood  
[william.whiteley@ed.ac.uk](mailto:william.whiteley@ed.ac.uk)

Centre for Clinical Brain Sciences, University of Edinburgh, Edinburgh EH16 4SB, UK (WW); MRC Population Health Research Unit, University of Oxford, Oxford, UK (WW); Department of Public Health and Primary Care, University of Cambridge, Cambridge, UK (AW)

- 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>.

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

- 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-Rodríguez 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.