COVID-19, not vaccination, presents biggest blood clot risks: study

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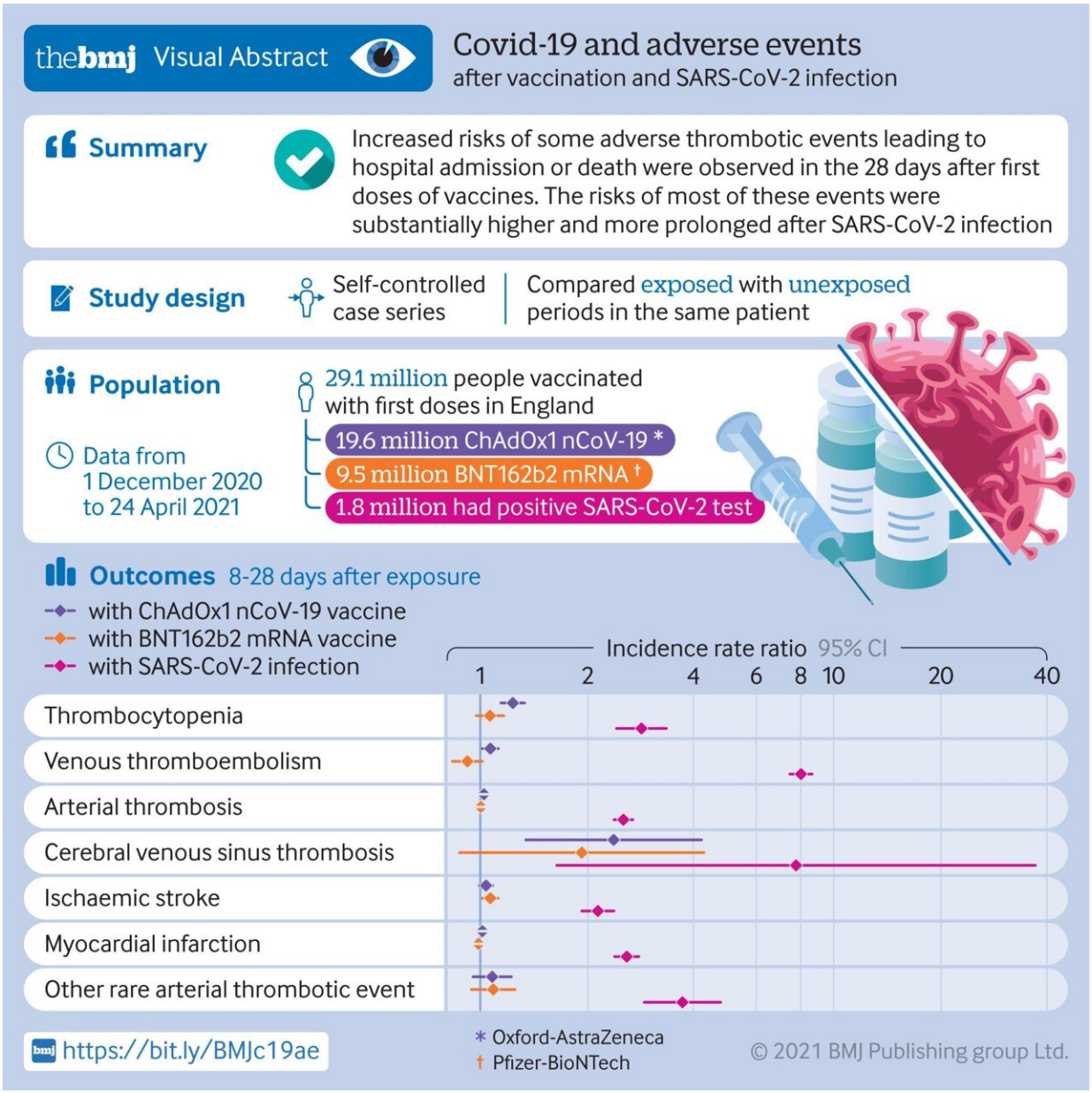

Graphical abstract. Credit: DOI: 10.1136/bmj.n1931

Researchers from the University of Oxford have today announced the results of a study into thrombocytopenia (a condition with low platelet counts) and thromboembolic events (blood clots) following vaccination for COVID-19, some of the same events which have led to restricted use of the Oxford-AstraZeneca vaccine in a number of countries.

Writing in the *British Medical Journal* (*BMJ*), they detail the findings from over 29 million people vaccinated with first doses of either the ChAdOx1 nCov-19 "Oxford-AstraZeneca" vaccine or the BNT162b2 mRNA "Pfizer-BioNTech' vaccine. They conclude that with both of these vaccines, for short time intervals following the first dose, there are increased risks of some hematological and vascular adverse events leading to hospitalization or death.

Julia Hippisley-Cox, Professor of Clinical Epidemiology and General Practice at the University of Oxford, lead author of the paper, said:

"People should be aware of these increased risks after COVID-19 vaccination and seek medical attention promptly if they develop symptoms, but also be aware that the risks are considerably higher and over longer periods of time if they become infected with SARS-CoV-2."

The authors further note that the risk of these adverse events is substantially higher and for a longer period of time, following infection from the SARS-CoV-2 "coronavirus" than after either vaccine.

All of the coronavirus vaccines currently in use have been tested in randomized clinical trials, which are unlikely to be large enough to detect very rare adverse events. When rare events are uncovered, then

regulators perform a risk-benefit analysis of the medicine; to compare the risks of the adverse events if vaccinated versus the benefits of avoidance of the disease—in this case, COVID-19.

In this paper, the team of authors from the University of Oxford, University of Leicester, Guys and St Thomas' NHS Foundation Trust, the Intensive Care National Audit & Research Centre, the London School of Hygiene and Tropical Medicine, the University of Cambridge, the University of Edinburgh and the University of Nottingham, compared rates of adverse events after vaccination with Pfizer-BioNTech and Oxford-AstraZeneca vaccines with rates of the same events after a positive SARS-CoV-2 test result.

For this, they used routinely collected electronic health records to evaluate the short-term risks (within 28 days) of hospital admission with thrombocytopenia, venous thromboembolism (VTE) and arterial thromboembolism (ATE), using data collected from across England between December 1, 2020 and April 24, 2021. Other outcomes studied were cerebral venous sinus thrombosis (CVST), ischemic stroke, myocardial infarction and other rare arterial thrombotic events.

Prof. Hippisley-Cox added:

"This research is important as many other studies, while useful, have been limited by small numbers and potential biases. Electronic healthcare records, which contain detailed recording of vaccinations, infections, outcomes and confounders, have provided us with a rich source of data with which to perform a robust evaluation of these vaccines, and compare to risks associated with COVID-19 infection."

The authors detail the following limitations to their study:

- restricting the analysis to first vaccine dose only

- a short vaccination exposure window
- the lack of formal adjudication of routinely acquired outcomes, and the potential for misclassification of outcomes or exposures
- admissions where patients were still in hospital by the study end date being excluded.

However, they believe that any bias, if present, is likely to not change with respect to each vaccine and so the comparisons between vaccines are unlikely to be affected.

Andrew Morris, Director, Health Data Research UK and Lead, Data and Connectivity National Core Study:

"Congratulations to the team at Oxford who have worked with colleagues across the UK on this important research. This is truly health data science in action—the use of secure, large scale, linked datasets to develop real-world insights on the safety of COVID-19 vaccines. The analyses in this paper are a vital addition to all of the work enabled by HDR UK to enhance our understanding of the virus, and a key output from the Data and Connectivity National Core Study."

Aziz Sheikh, Professor of Primary Care Research & Development and Director of the Usher Institute at The University of Edinburgh and a co-author of the paper, said:

"This enormous study, using data on over 29 million vaccinated people, has shown that there is a very small risk of clotting and other blood disorders following first dose COVID-19 vaccination. Though serious, the risk of these same outcomes is much higher following SARS-CoV-2 infection.

"On balance, this analysis therefore clearly underscores the importance of getting vaccinated to reduce the risk of these clotting and bleeding

outcomes in individuals, and because of the substantial public health benefit that COVID-19 vaccinations offer."

More information: Julia Hippisley-Cox et al, Risk of thrombocytopenia and thromboembolism after covid-19 vaccination and SARS-CoV-2 positive testing: self-controlled case series study, *BMJ* (2021). DOI: 10.1136/bmj.n1931

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