

The Comparative Risk of Thrombosis with Thrombocytopenia Associated with Different COVID-19 Vaccines

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6 Dec 2022
OHDSI Community call

Disclosures

- This study was funded by the European Medicines Agency (EMA).
- The views expressed in this article are the personal views of the authors, and may not be understood or quoted as being made on behalf of or reflecting the position of the EMA or one of its committees or working parties.
- The funder had no role in considering the study design or in the collection, analysis, interpretation of data, writing of the report, or decision to submit the article for publication.

Back to early 2021: Safety concerns on thrombocytopenia and thromboembolism after adenovirus-based COVID-19 vaccines

Article | [Open Access](#) | Published: 09 June 2021

First-dose ChAdOx1 and BNT162b2 COVID-19 vaccines and thrombocytopenic, thromboembolic and hemorrhagic events in Scotland

[C. R. Simpson](#), [T. Shi](#), ... [A. Sheikh](#)  

[Nature Medicine](#) 27, 1290–1297 (2021) | [C](#)

ORIGINAL ARTICLE

Thrombotic Thrombocytopenia after ChAdOx1 nCoV-19 Vaccination

[Simpson, C.R.](#), M.D., Theodore E. Warkentin, M.D., Karin Weisser, Ph.D., .D., and Sabine Eichinger, M.D.

Research

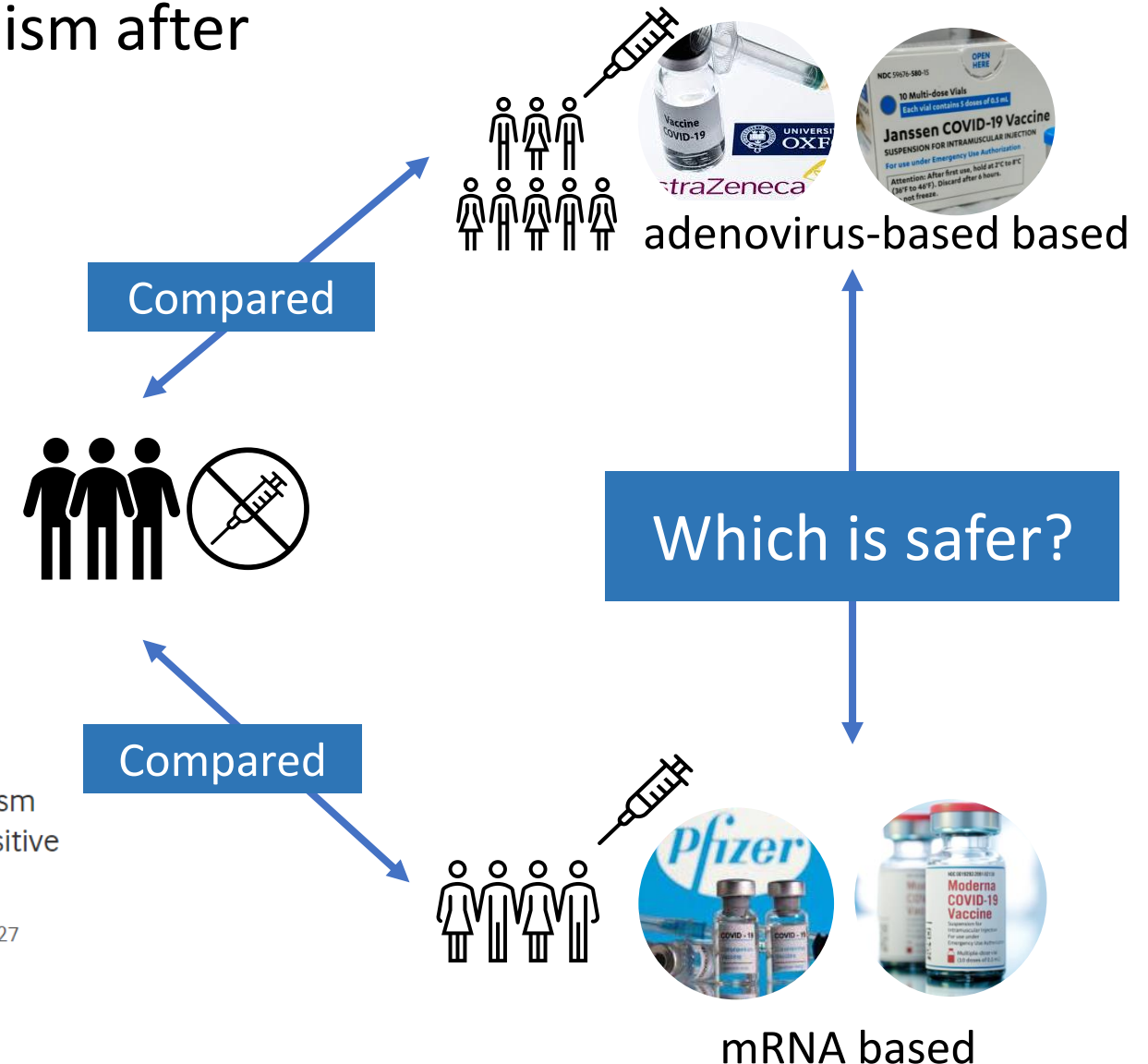
Arterial events, venous thromboembolism, thrombocytopenia, and bleeding after vaccination with Oxford-AstraZeneca ChAdOx1-S in Denmark and Norway: population based cohort study

[BMJ](#) 2021 ; 373 doi: <https://doi.org/10.1136/bmj.n1114> (Published 05 May 2021)
Thrombocytopenia and thromboembolism after COVID-19 vaccination and SARS-CoV-2 positive testing: self-controlled case series study

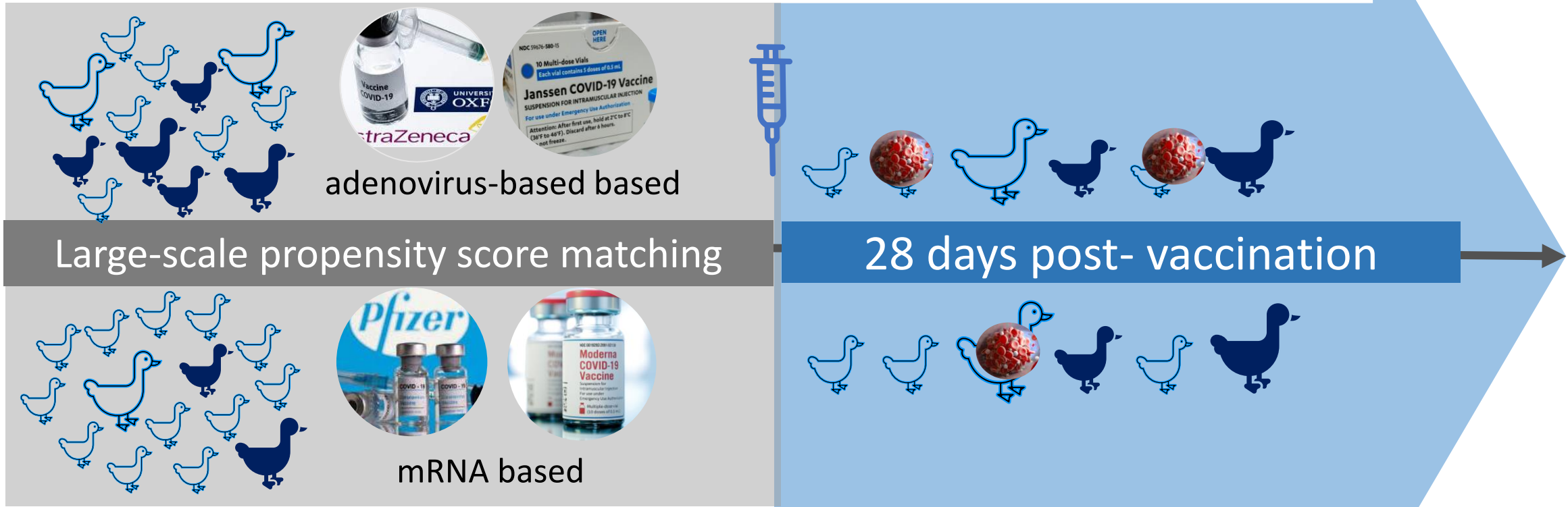
[BMJ](#) 2021 ; 374 doi: <https://doi.org/10.1136/bmj.n1931> (Published 27 August 2021)

ORIGINAL ARTICLE BRIEF REPORT

Thrombosis and Thrombocytopenia after ChAdOx1 nCoV-19 Vaccination

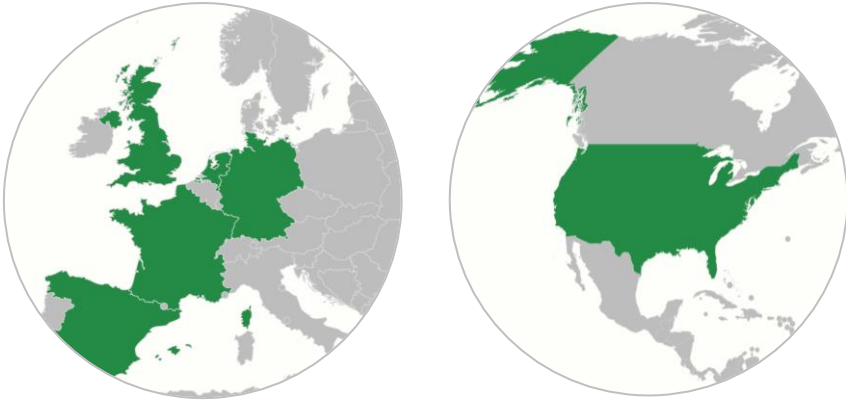


- Multinational network cohort study

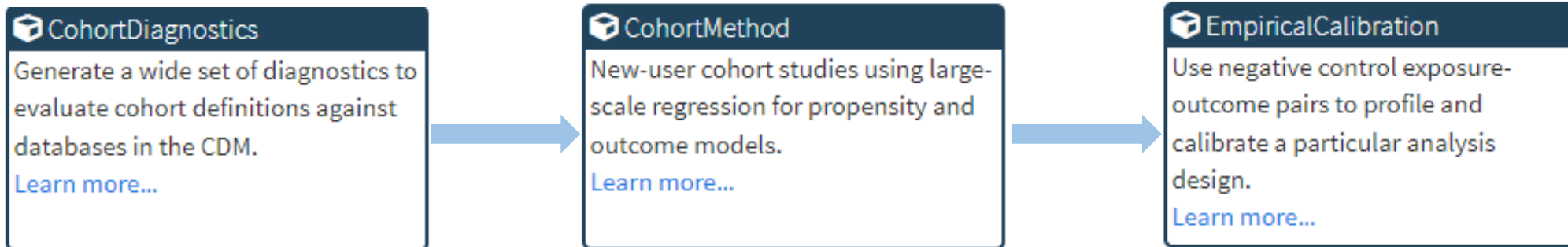


Outcomes:

- Thrombosis with thrombocytopenia syndrome (TTS)
- Thromboembolic events (TE)







- 5 European, 2 US databases in OMOP CDM



- Vaccine cohorts
- Outcome cohorts

- Propensity score
- Outcome model

		First-dose	Second-dose
	ChAdOx1	3,986,974	1,280,777
	Ad26.COV2.S	1,122,012	
	BNT162b2	10,828,104	6,465,703
	mRNA-1273	4,580,757	2,996,711



Meta-analysed results across databases

Findings



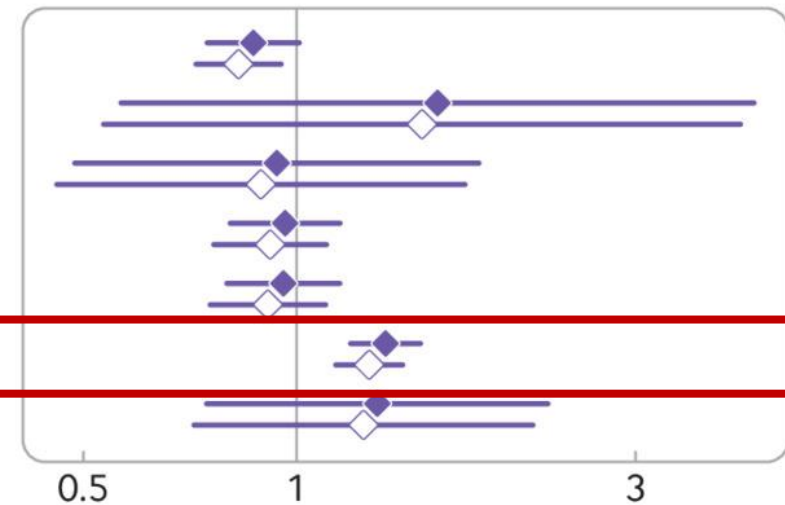
Outcome

Calibrated incidence
rate ratio (95% CI)

Calibrated incidence
rate ratio (95% CI)

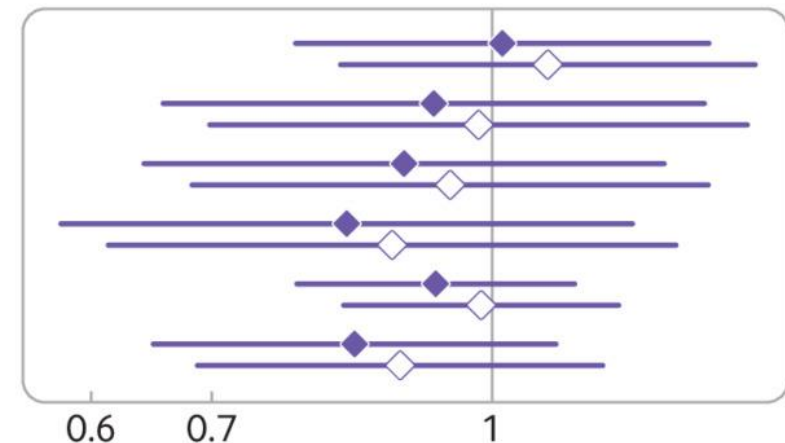
ChAdOx1-S first dose v BNT162b2 first dose

Arterial thromboembolism	0.87 (0.75 to 1.01)
Deep vein thrombosis	1.58 (0.56 to 4.42)
Ischemic stroke	0.94 (0.48 to 1.81)
Myocardial infarction	0.96 (0.8 to 1.15)
Pulmonary embolism	0.96 (0.79 to 1.15)
Thrombocytopenia	1.33 (1.18 to 1.5)
Venous thromboembolism	1.3 (0.75 to 2.26)



ChAdOx1-S second dose v BNT162b2 second dose

Arterial thromboembolism	1.01 (0.78 to 1.32)
Deep vein thrombosis	0.93 (0.66 to 1.31)
Myocardial infarction	0.89 (0.64 to 1.25)
Pulmonary embolism	0.83 (0.58 to 1.2)
Thrombocytopenia	0.93 (0.78 to 1.11)
Venous thromboembolism	0.84 (0.65 to 1.09)



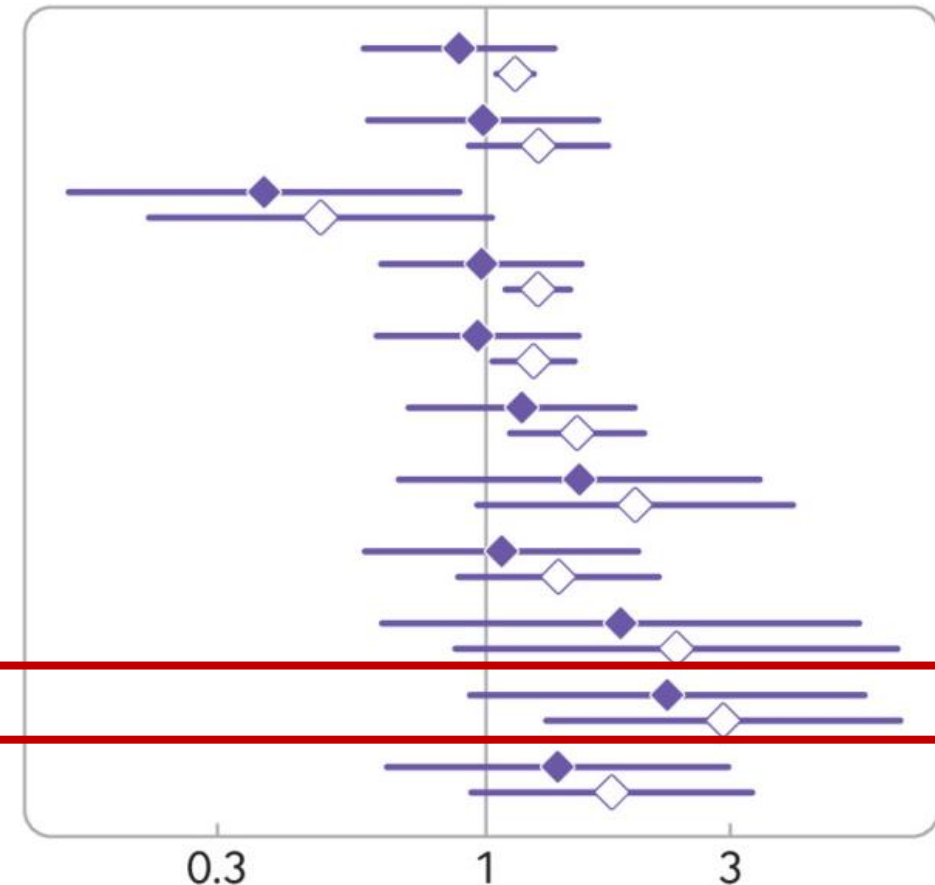
Meta-analysed results across databases

Findings

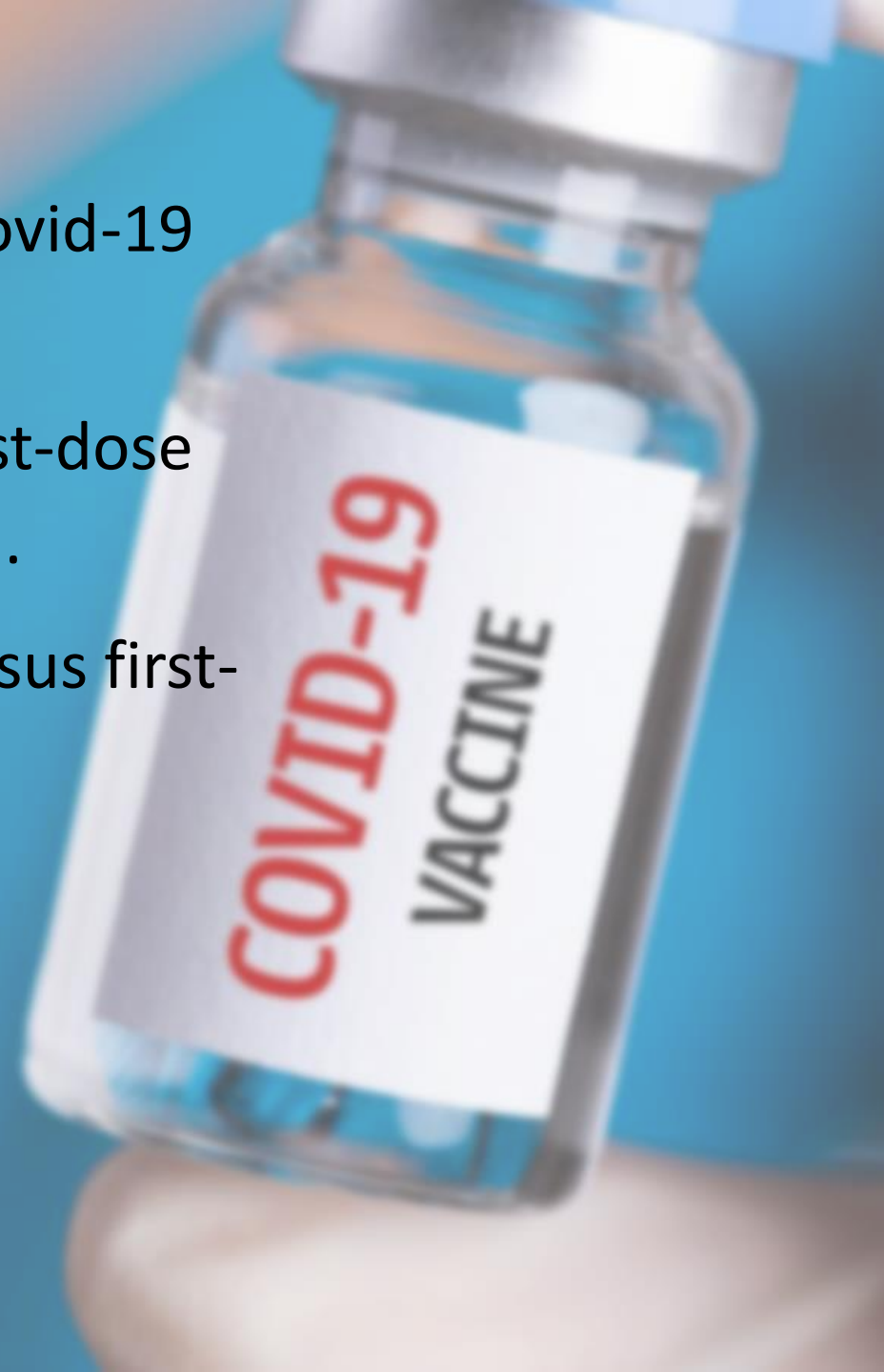


Ad26.COVS.S v BNT162b2 first dose

Arterial thromboembolism	0.89 (0.58 to 1.37)
Deep vein thrombosis	0.99 (0.58 to 1.67)
Intestinal infarction	0.37 (0.15 to 0.89)
Ischemic stroke	0.99 (0.63 to 1.55)
Myocardial infarction	0.97 (0.61 to 1.53)
Pulmonary embolism	1.17 (0.7 to 1.97)
Splanchnic and visceral thrombosis	1.52 (0.67 to 3.47)
Thrombocytopenia	1.08 (0.58 to 1.99)
TTS Deep vein thrombosis	1.83 (0.62 to 5.38)
TTS Venous thromboembolism	2.26 (0.93 to 5.52)
Venous thromboembolism	1.38 (0.64 to 2.99)



- Multinational analysis of comparative safety of covid-19 vaccines.
- 30% increased risk of thrombocytopenia after first-dose ChAdOx1 versus first-dose BNT162b2 vaccination.
- Potential double risk of TTS-VTE with Janssen versus first-dose BNT162b2 vaccine recipients.
- Inform future immunization program




Research

Comparative risk of thrombosis with thrombocytopenia syndrome or thromboembolic events associated with different covid-19 vaccines: international network cohort study from five European countries and the US

BMJ 2022 ; 379 doi: <https://doi.org/10.1136/bmj-2022-071594> (Published 26 October 2022)

Cite this as: BMJ 2022;379:e071594

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<https://www.bmj.com/content/379/bmj-2022-071594>

Acknowledgements

Professor Daniel Prieto-Alhambra
Dr. Edward Burn
Dr. Victoria Strauss
Dr. Talita Duarte-Salles
Can Yin
Dr. Christian Reich
Dr. Antonella Delmestri
Professor Katia Verhamme
Professor Peter Rijnbeek
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EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH



Descriptions of medical records databases used in study

Database full (short) names	Country	Active size of database (by mid-2021; No of people)	Latest data available time	Key data available				
				Covid-19 vaccines	Hospital treatments	Hospital outcomes	Outpatient treatments	Platelet counts
Clinical Practice Research Datalink Aurum (UK CPRD)	UK	13m	May 2021	Complete	No	Incomplete	Yes	Yes
Information System for Research in Primary Care with minimum basic set of hospital discharge data (CMBD-HA; Spain SIDIAP)	Spain	6m	June 2021	Complete	No	Linked	Yes	Yes
Integrated Primary Care Information (Netherlands IPCI)	The Netherlands	2m	June 2021	Incomplete	No	Incomplete	Yes	Yes
IQVIA Longitudinal Patient Data France (France LPD)	France	2.3m	September 2021	Incomplete	No	Incomplete	Yes	Yes
IQVIA Disease Analyser Germany (Germany DA)	Germany	8.5m	August 2021	Incomplete	No	Incomplete	Yes	Yes
Medical and Institutional Claims (US Open Claims)	US	187m	September 2021	Incomplete	Incomplete	Incomplete	Yes	Yes
Charge Data Master (US Hospital CDM)	US	30m	July 2021	Incomplete	Yes	Yes	Incomplete	Incomplete

DATABASE	DIAGNOSTIC		1 st dose ChAdOx1 vs BNT162b2	1 st dose ChAdOx1 vs mRNA-1273	2 nd dose ChAdOx1 vs BNT162b2	2 nd dose ChAdOx1 vs mRNA-1273	Ad26.COV2.S vs BNT162b2	Ad26.COV2.S vs mRNA-1273
UK CPRD								
	Covariate balance	SMD<0.1 for all	✓	n/a	✓	n/a	n/a	n/a
	Power	MDRR<5 for 1+ outcomes	10	n/a	9	n/a	n/a	n/a
	Systematic error	<20% associated w exposure	98.0%	n/a	94.4%	n/a	n/a	n/a
Spain SIDIAP								
	Covariate balance	SMD<0.1 for all	x	x	x	x	✓	n/a
	Power	4<5 for 1+ outcomes					8	n/a
	Systematic error	<20% associated w exposure					96.4%	n/a
GERMANY DA								
	Covariate balance	SMD<0.1 for all	✓	x	✓	x	✓	n/a
	Power	MDRR<5 for 1+ outcomes	7	0	0	0	1	n/a
	Systematic error	<20% associated w exposure	84.2%		\$		70.0%	n/a
FRANCE LPD								
	Covariate balance	SMD<0.1 for all	✓	✓	x	x	n/a	n/a
	Power	MDRR<5 for 1+ outcomes	0	0	0	0	n/a	n/a
	Systematic error	<20% associated w exposure	83.3%	\$			n/a	n/a
Netherlands IPCI								
	Covariate balance	SMD<0.1 for all	✓	n/a	✓	n/a	✓	✓
	Power	MDRR<5 for 1+ outcomes	3	n/a	0	n/a	0	0
	Systematic error	<20% associated w exposure	\$	n/a	\$	n/a	\$	\$
IQVIA US OpenClaims								
	Covariate balance	SMD<0.1 for all	n/a	n/a	n/a	n/a	✓	✓
	Power	MDRR<5 for 1+ outcomes	n/a	n/a	n/a	n/a	12	13
	Systematic error	<20% associated w exposure	n/a	n/a	n/a	n/a	72.2%	67.9%
IQVIA US HOSPITAL CDM								
	Covariate balance	SMD<0.1 for all	n/a	n/a	n/a	n/a	x	x
	Power	MDRR<5 for 1+ outcomes	n/a	n/a	n/a	n/a	0	0
	Systematic error	<20% associated w exposure	n/a	n/a	n/a	n/a		