Supplementary Data

Supplementary data tables.docx
- Supplementary Tables S1-S11
- Supplementary Figure Legends S1-S5

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- Supplementary Figure S1

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Supplementary Table S1. Checklist summarizing compliance with PRISMA guidelines.

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4-5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4-5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	N/A
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	6 (Supplementary Table S2)
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	N/A
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	7

Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	N/A

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	N/A
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Supplementary Figure S1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Supplementary Table S3-4
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	N/A
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	N/A
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	N/A
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	12-17
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	15-16
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	12-17
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	3

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

Supplementary Table S2. Detailed search strategy according to database.

#1. Initial Search (2 May 2021)

PubMed Search Strategy (450 hits)

Years/Issue Searched: 2019 to 2021
Search date: 2 May 2021
("COVID-19" OR "SARS-CoV-2" OR coronavirus OR 2019-nCoV OR "wuhan coronavirus" OR "covid 2019") AND ("2019-ncov vaccine" OR "sars-cov-2 vaccine" OR "covid 19 vaccine" OR "covid-19 vaccine" OR "covid19 vaccine" OR "human coronavirus 2019 vaccine" OR "sars coronavirus 2 vaccine" OR "wuhan coronavirus vaccine") AND ("thrombosis" OR thrombosis OR "rethrombosis" OR "sclerothrombosis" OR "thrombo-obliterative disease" OR "thrombo occlusive" OR "thrombo obliterative" OR thrombotic) Filters: English, from 2019 – 2021

Embase Search Strategy (31 hits)

#1. 'severe acute respiratory syndrome'/exp
#2. 'severe acute respiratory syndrome'
#3. 'coronavirus disease 2019'/exp
#4. 'covid-19' OR 'sars-cov-2' OR coronavirus OR '2019-ncov' OR (novel AND cov) OR (wuhan AND virus) OR 'wuhan coronavirus' OR 'covid 2019'
#5. 'sars-cov-2 vaccine'/exp OR '2019-ncov vaccine' OR 'covid 19 vaccine' OR 'covid-19 vaccine' OR 'covid19 vaccine'
#6. 'human coronavirus 2019 vaccine' OR 'sars coronavirus 2 vaccine' OR 'wuhan coronavirus vaccine'
#7. 'thrombosis'/exp OR 'acute thrombosis' OR 'thrombosis' OR 'thrombotic disease' OR 'thrombotic disorder'
#8. 'thrombo-obliterative disease' OR 'thrombo-occlusive disease'
#9. (#1 OR #2 OR #3 OR #4) AND (#5 OR #6) AND (#7 OR #8) AND [english]/lim AND [2019-2021]/py

Scopus Search Strategy (446 hits)

Years/Issue Searched: 2019 to 2021
Search date: 2 May 2021
("COVID-19" OR "SARS-CoV-2" OR coronavirus OR 2019-nCoV OR "wuhan coronavirus" OR "covid 2019") AND ("2019-ncov vaccine" OR "sars-cov-2 vaccine" OR "covid 19 vaccine" OR "covid-19 vaccine" OR "covid19 vaccine" OR "human coronavirus 2019 vaccine" OR "sars coronavirus 2 vaccine" OR "wuhan coronavirus vaccine") AND ("thrombosis" OR thrombosis OR "rethrombosis" OR "sclerothrombosis" OR "thrombo-obliterative disease" OR "thrombo occlusive" OR "thrombo obliterative" OR thrombotic)

Web of science Search Strategy (1 hit)

#1. TS="severe acute respiratory syndrome"
#2. TS="severe acute respiratory syndrome"
#3. TS="coronavirus disease 2019"
#4. TS=("covid-19" OR "sars-cov-2" OR coronavirus OR "2019-ncov" OR "wuhan coronavirus" OR "covid 2019")
#5. TS=("sars-cov-2 vaccine" OR "2019-ncov vaccine" OR "covid 19 vaccine" OR "covid-19 vaccine" OR "covid19 vaccine")
#6. TS=("thrombosis" OR "acute thrombosis" OR "thrombotic disease*" OR "thrombotic disorder*")
#7. TS=("thrombo-obliterative disease*" OR "thrombo-occlusive disease*")
#8. (#1 OR #2 OR #3 OR #4) AND #5 AND (#6 OR #7)

#2. Database Update (24 June 2021)

PubMed Search Strategy (593 hits)

Years/Issue Searched: 2019 to 2021
Search date: 24 June 2021
("2019-ncov vaccine" OR "sars-cov-2 vaccine" OR "covid 19 vaccine" OR "covid-19 vaccine" OR "covid19 vaccine" OR "human coronavirus 2019 vaccine" OR "sars coronavirus 2 vaccine" OR "wuhan coronavirus vaccine" OR "ChAdOx1 nCoV-19" OR "AZD1222" OR "Oxford–AstraZeneca" OR "AstraZeneca" OR "Ad26.COV2.S" OR "vaccine-induced" OR "vaccine induced" OR "vaccine immune" OR "vaccine-induced immune") AND ("thrombosis" OR "rethrombosis" OR "sclerothrombosis" OR "thrombo-obliterative disease" OR "thrombo occlusive" OR "thrombo obliterative" OR "thrombotic" OR "thrombocytopenia" OR "immune thrombosis" OR "induced thrombosis" OR "thrombotic thrombocytopenia" OR "thrombotic thrombocytopenia syndrome") Filters: English, from 2019 – 2021

Embase Search Strategy (377 hits)

#1. 'sars-cov-2 vaccine'/exp OR '2019-ncov vaccine' OR 'covid 19 vaccine' OR 'covid-19 vaccine' OR 'covid19 vaccine'
#2. 'human coronavirus 2019 vaccine' OR 'sars coronavirus 2 vaccine' OR 'wuhan coronavirus vaccine'
#3. 'ChAdOx1 nCoV-19' OR 'AZD1222' OR 'Oxford–AstraZeneca' OR 'AstraZeneca' OR 'Ad26.COV2.S'
#4. 'vaccine-induce' OR 'vaccine induced' OR 'vaccine immune' OR 'vaccine-induced immune'
#5. 'thrombosis'/exp OR 'acute thrombosis' OR 'thrombosis' OR 'thrombotic disease' OR 'thrombotic disorder' OR 'rethrombosis' OR 'sclerothrombosis' OR 'thrombocytopenia'
#6. 'thrombo-obliterative disease' OR 'thrombo occlusive' OR 'thrombo obliterative'
#7. 'immune thrombosis' OR 'induced thrombosis' OR 'thrombotic thrombocytopenia' OR 'thrombotic thrombocytopenia syndrome'
#8. (#1 OR #2 OR #3 OR #4) AND (#5 OR #6 OR #7) AND [english]/lim AND [2019-2021]/py

Scopus Search Strategy (1418 hits)

Years/Issue Searched: 2019 to 2021
Search date: 24 June 2021
("2019-ncov vaccine" OR "sars-cov-2 vaccine" OR "covid 19 vaccine" OR "covid-19 vaccine" OR "covid19 vaccine" OR "human coronavirus 2019 vaccine" OR "sars coronavirus 2 vaccine" OR "wuhan coronavirus vaccine" OR "ChAdOx1 nCoV-19" OR "AZD1222" OR "Oxford–AstraZeneca" OR "AstraZeneca" OR "Ad26.COV2.S" OR "vaccine-induced" OR "vaccine induced" OR "vaccine immune" OR "vaccine-induced immune") AND ("thrombosis" OR "rethrombosis" OR "sclerothrombosis" OR "thrombo-obliterative disease" OR "thrombo occlusive" OR "thrombo obliterative" OR "thrombotic" OR "thrombocytopenia" OR "immune thrombosis" OR "induced thrombosis" OR "thrombotic thrombocytopenia" OR "thrombotic thrombocytopenia syndrome") AND (LIMT-TO (PUBYEAR,2021) OR LIMT-TO (PUBYEAR,2020) OR LIMT-TO (PUBYEAR,2019)) AND (LIMIT-TO (LANGUAGE, "English"))

Web of science Search Strategy (57 hits)

#1. TS=("sars-cov-2 vaccine" OR "2019-ncov vaccine" OR "covid 19 vaccine" OR "covid-19 vaccine" OR "covid19 vaccine")"
#2. TS=("human coronavirus 2019 vaccine" OR "sars coronavirus 2 vaccine" OR "wuhan coronavirus vaccine")
#3. TS=("ChAdOx1 nCoV-19" OR "AZD1222" OR "Oxford–AstraZeneca" OR "AstraZeneca" OR "Ad26.COV2.S")
#4. TS=("vaccine-induce" OR "vaccine induced" OR "vaccine immune" OR "vaccine-induced immune") #5. TS=("sars-cov-2 vaccine" OR "2019-ncov vaccine" OR "covid 19 vaccine" OR "covid-19 vaccine" OR "covid19 vaccine")
#5. TS=("thrombosis" OR "acute thrombosis" OR "thrombosis" OR "thrombotic disease" OR "thrombotic disorder" OR "rethrombosis" OR "sclerothrombosis" OR "thrombocytopenia")
#6. TS=("thrombo-obliterative disease" OR "thrombo occlusive" OR "thrombo obliterative")
#7. TS=("immune thrombosis" OR "induced thrombosis" OR "thrombotic thrombocytopenia" OR "thrombotic thrombocytopenia syndrome")
#8. (#1 OR #2 OR #3 OR #4) AND (#5 OR #6 OR #7)

Supplementary Table S3. Characteristics of included studies.

Authors	Number of cases	Vaccine type	Country	Day of symptom onset	Dose	Mortality	Thrombosis/hemorrhage
Schultz et al. [10]	5	ChAdOx1 nCoV-19	Norway	~10 days	First dose	60% (3/5)	5 CVT, 1 SVT
Scully et al. [11]	23	ChAdOx1 nCoV-19	United Kingdom	6-24 days	First dose	30% (7/23)	14 CVT, 4 PE, 1 DVT, 2 SVT
Greinacher et al. [12]	11	ChAdOx1 nCoV-19	Germany, Austria	5-16 days	First dose	54.5% (6/11)	9 CVT, 3 SVT, 3 PE, 4 Other
Franchini et al. [13]	1	ChAdOx1 nCoV-19	Italy	11 days	First dose	100% (1/1)	CVT, ICH
Mehta et al. [14]	2	ChAdOx1 nCoV-19	United Kingdom	6-9 days	First dose	100% (2/2)	2 CVT
Thaler et al. [15]	1	ChAdOx1 nCoV-19	Austria	8 days	First dose	0% (0/1)	Isolated thrombocytopenia
Tiede et al. [16]	5	ChAdOx1 nCoV-19	Germany	5-11 days	First dose	0% (0/5)	1 CVT, 2 arterial infarction, 1 TIA, 1 SVT
Hocking et al. [28]	1	ChAdOx1 nCoV-19	Australia	8 days	First dose	0% (0/1)	SVT, Bowel, aortoiliac thrombosis
Turi et al. [29]	1	ChAdOx1 nCoV-19	Italy	6 days	First dose	0% (0/1)	PE, SVT
Bersinger et al. [30]	1	ChAdOx1 nCoV-19	France	9 days	First dose	0% (0/1)	CVT, PE, SVT, aortoiliac thrombosis, IJVT
Jones et al. [31]	1	ChAdOx1 nCoV-19	Canada	20 days	First dose	0% (0/1)	SVT, aortoiliac thrombosis
Al-Mayhani et al. [32]	3	ChAdOx1 nCoV-19	United Kingdom	6-21 days	First dose	33.3% (1/3)	1 CVT, 2 MCA, 2 SVT, 1 PE
Wolf et al. [33]	3	ChAdOx1 nCoV-19	Germany	4-7 days	First dose	0% (0/3)	3 CVT
Aladdin et al. [34]	1	ChAdOx1 nCoV-19	Saudi Arabia	14 days	First dose	100% (1/1)	CVT, Bowel, SVT
Suresh et al. [35]	1	ChAdOx1 nCoV-19	United Kingdom	2 days	First dose	100% (1/1)	CVT
Guetl et al. [36]	1	ChAdOx1 nCoV-19	Austria	10 days	First dose	0% (0/1)	CVT, lung thrombosis, 4 Other
Muster et al. [37]	1	ChAdOx1 nCoV-19	Austria	11 days	First dose	0% (0/1)	PE, aortoiliac thrombosis, IJVT
Xie et al. [38]	1	ChAdOx1 nCoV-19	United Kingdom	7 days	First dose	0% (0/1)	SVT, PE, intraventricular thrombosis
Blauenfeldt et al. [39]	1	ChAdOx1 nCoV-19	Denmark	7 days	First dose	100% (1/1)	CVT

CVT: cerebral venous thrombosis, SVT: splanchnic vein thrombosis, PE: pulmonary embolism, TIA: transient ischemic attack

Supplementary Table S4. Main characteristics and findings of the published cases.

Authors	Number of cases	Vaccine type	Date of report	Findings
Franchini et al. [13]	1	ChAdOx1 nCoV-19	April 8, 2021	A previously healthy 50-year-old Caucasian male presented with fatal intracerebral hemorrhage and central venous sinus thrombosis 11 days after the first dose of vaccination.
Greinacher et al. [12]	11	ChAdOx1 nCoV-19	April 9, 2021	11 patients at 22-49 years of age (81% female) presented with severe thrombotic events such as cerebral venous thrombosis, splanchnic vein thrombosis, or pulmonary embolism 5-16 days after the first dose of vaccination. 6 patients (54.5%) died.
Schultz et al. [10]	5	ChAdOx1 nCoV-19	April 9, 2021	Five healthcare workers at 32-54 years of age (80% female) without preexisting prothrombotic conditions presented with cerebral venous thrombosis and severe thrombocytopenia.
Scully et al. [11]	23	ChAdOx1 nCoV-19	April 16, 2021	23 patients without previous thrombotic tendency (median age 46, 61% female) presented with thrombosis (22/23) or hemorrhage (1/23) 6-24 days after the first dose of vaccination. 7 patients (30%) died.
Mehta et al. [14]	2	ChAdOx1 nCoV-19	April 20, 2021	A 32-year-old previously healthy male and a 25-year-old male with a history of primary sclerosing cholangitis and migraines presented with fatal cerebral vein thrombosis and

				intracerebral and subarachnoid hemorrhages, each 9 days and 6 days after receiving the first dose of vaccination, respectively.
Thaler et al. [15]	1	ChAdOx1 nCoV-19	April 20, 2021	A healthy 62-year-old female presented with atraumatic hematoma, petechiae, and gum bleeding 8 days after the first dose of vaccination and was successfully treated and discharged.
Tiede et al. [16]	5	ChAdOx1 nCoV-19	April 28, 2021	Five women 41-67 years of age presented 5 to 11 days after receiving the first dose of vaccination, each with CVST, cortical emboli, transient ischemic attack, splanchnic vein thrombosis, and arterial cerebral thrombosis.
Hocking et al. [28]	1	ChAdOx1 nCoV-19	June 11, 2021	A previously well 44-year-old male presented with fevers, fatigue, and head “fogginess” with abdominal discomfort and increased bowel frequency 8 days after the first dose of vaccination.
Turi et al. [29]	1	ChAdOx1 nCoV-19	May 21, 2021	A previously healthy 57-year-old female presented with fever, arthromyalgia and headache 6 days after the first dose of vaccination.
Bersinger et al. [30]	1	ChAdOx1 nCoV-19	June 1, 2021	A 21-year-old female presented with massive thrombosis in the deep and superficial cerebral veins together with seizures, neurologic focal deficit, and thrombocytopenia after 9 days of the first dose of vaccination.
Jones et al. [31]	1	ChAdOx1 nCoV-19	May 14, 2021	A 63-year-old male presented painful left leg, new onset of paresthesia of the left leg and foot, and severe shortness of breath after 20 days of the first dose of vaccination.
Al-Mayhani et al. [32]	3	ChAdOx1 nCoV-19	May 25, 2021	3 patients at 35-43 years of age (33.3% male) presented with ischemic stroke after the first dose of vaccination, 1 patient (33.3%) died.
Wolf et al. [33]	3	ChAdOx1 nCoV-19	April 9, 2021	3 patients at 22-46 years of age female presented with headaches, hemianopia, and hemiparesis respectively after the first dose of vaccination.
Aladdin et al. [34]	1	ChAdOx1 nCoV-19	June 2, 2021	A previously healthy 36-year-old female presented with fever, headache, vomiting, and convulsion 14 days after the first dose of vaccination.
Suresh et al. [35]	1	ChAdOx1 nCoV-19	June 16, 2021	A previously healthy 27-year-old male presented with headache, visual disturbance and vomiting 2 days after the first dose of vaccination.
Guetl et al. [36]	1	ChAdOx1 nCoV-19	June 11, 2021	A previously healthy 50-year-old female presented with back pain 10 days after the first dose of vaccination.
Muster et al. [37]	1	ChAdOx1 nCoV-19	April 14, 2021	A previously healthy 51-year-old female presented with fatigue, cough and dyspnea 11 days after the first dose of vaccination.
Xie et al. [38]	1	ChAdOx1 nCoV-19	May 5, 2021	A previously healthy 23-year-old female presented with cough and dyspnea 7 days after the first dose of vaccination.
Blauenfeldt et al. [39]	1	ChAdOx1 nCoV-19	April 14, 2021	A 60-year-old female presented with visual disturbance, abdominal pain and hemiplegia 7 days after the first dose of vaccination.

Supplementary Table S5. Clinical presentation of patients with VITT after ChAdOx1 nCoV-19 vaccination according to outcome.

Clinical presentation	Total patients (n=64*)	Survivors (n=40)	Non-survivors (n=23)	P - value
	Number of patients (%)	Number of patients (%)	Number of patients (%)	
Systemic	15/30 (50.0%)	9/20 (45.0%)	6/10 (60.0%)	0.700
Fever	7/30 (23.3%)	5/20 (25.0%)	2/10 (20.0%)	1.000
Fatigue	3/30 (10.0%)	3/20 (15.0%)	0/10 (0.0%)	0.532
Reduced consciousness/drowsiness	5/30 (16.7%)	2/20 (10.0%)	3/10 (30.0%)	0.300
Hypertension	1/30 (3.3%)	1/20 (5.0%)	0/10 (0.0%)	1.000
Myalgia	2/30 (6.7%)	1/20 (5.0%)	1/10 (10.0%)	1.000
Neurologic	26/30 (86.7%)	16/20 (80.0%)	10/10 (100.0%)	0.272
Headache	22/30 (73.3%)	13/20 (65.0%)	9/10 (90.0%)	0.210
Visual disturbance	8/30 (26.7%)	3/20 (15.0%)	5/10 (50.0%)	0.078
Hemiplegia	3/30 (10.0%)	2/20 (10.0%)	1/10 (10.0%)	1.000
Hemiparesis	9/30 (30.0%)	4/20 (16.7%)	5/10 (50.0%)	0.115
Hemisensory loss	1/30 (3.3%)	0/20 (0.0%)	1/10 (10.0%)	0.333
Dizziness	4/30 (13.3%)	4/20 (20.0%)	0/10 (0.0%)	0.272
Conjugate gaze palsy	1/42 (2.4%)	1/20 (5.0%)	1/10 (10.0%)	1.000
Seizure	4/30 (13.3%)	2/20 (10.0%)	2/10 (20.0%)	0.584
Dysarthria	1/30 (3.3%)	1/20 (5.0%)	0/10 (0.0%)	1.000
Dysphasia	5/30 (16.7%)	5/20 (25.0%)	0/10 (0.0%)	0.140
Fogginess	1/30 (3.3%)	1/20 (5.0%)	0/10 (0.0%)	1.000
Convulsion	1/30 (3.3%)	0/20 (0.0%)	1/10 (10.0%)	0.333
Bleeding	3/30 (10.0%)	1/20 (5.0%)	2/10 (20.0%)	0.251
Petechial rash	1/30 (3.3%)	0/20 (0.0%)	1/10 (10.0%)	0.333
Hematoma	2/30 (6.7%)	1/20 (5.0%)	1/10 (10.0%)	1.000
Gum bleeds	2/30 (6.7%)	1/20 (5.0%)	1/10 (10.0%)	1.000
Gastrointestinal	7/30 (23.3%)	3/20 (15.0%)	4/10 (40.0%)	0.181
Vomiting	3/30 (10.0%)	0/20 (0.0%)	3/10 (30.0%)	**0.030**
Abdominal pain	4/30 (13.3%)	3/20 (15.0%)	1/10 (10.0%)	1.000
Cardiopulmonary	4/30 (13.3%)	4/20 (20.0%)	0/10 (0.0%)	0.272
Dyspnea	3/30 (10.0%)	3/20 (15.0%)	0/10 (0.0%)	0.532
Chest pain	2/30 (6.7%)	2/20 (10.0%)	0/10 (0.0%)	0.540
Cough	2/30 (6.7%)	2/20 (10.0%)	0/10 (0.0%)	0.540
MSK	3/30 (10.0%)	3/20 (15.0%)	0/10 (0.0%)	0.532
Arthralgia	1/30 (3.3%)	1/20 (5.0%)	0/10 (0.0%)	1.000
Back pain	2/30 (6.7%)	2/20 (10.0%)	0/10 (0.0%)	0.540

*One patient had an unknown outcome.

Supplementary Table S6. Correlation among key clinical characteristics and laboratory finding of patents with COVID-19 vaccination.

	Fibrino ɣ	Age	Platelet σ	D-dimer ħ	PT INR	PTT sec	Time ‡	Hemorr ε	Thromb⁂	PF4 OD†	"4 T" score	FAPIC
Fibrinogen ɣ	1.000	0.087	**0.443****	-0.156	**-0.547****	-0.304	-0.275	-0.092	-0.058	-0.312	0.000	**-0.697****
		0.570	0.001	0.313	0.003	0.148	0.053	0.524	0.687	0.100	0.999	0.000
Age	0.087	1.000	**-0.277***	**0.284***	-0.015	0.304	0.016	0.052	0.007	-0.129	0.075	**-0.309***
	0.570		0.045	0.048	0.945	0.193	0.906	0.710	0.963	0.539	0.591	0.041
Platelet σ	**0.443****	**-0.277***	1.000	**-0.386****	-0.054	-0.319	-0.201	-0.032	-0.112	-0.212	-0.015	**-0.534****
	0.001	0.045		0.004	0.779	0.121	0.116	0.806	0.384	0.253	0.909	0.000
D-dimer ħ	-0.156	**0.284***	-.386**	1.000	0.173	0.399	0.209	0.078	0.167	0.200	0.171	0.110
	0.313	0.048	0.004		0.399	0.059	0.127	0.571	0.222	0.327	0.212	0.482
PT INR	**-0.547****	-0.015	-0.054	0.173	1.000	**0.697****	0.252	-0.191	0.003	0.284	-0.259	0.032
	0.003	0.945	0.779	0.399		0.003	0.179	0.313	0.986	0.269	0.167	0.873
PTT sec	-0.304	0.304	-0.319	0.399	**0.697****	1.000	0.159	-0.243	**0.410***	0.172	-0.180	0.003
	0.148	0.193	0.121	0.059	0.003		0.438	0.232	0.038	0.541	0.379	0.989
Time ‡	-0.275	0.016	-0.201	0.209	0.252	0.159	1.000	-0.024	0.002	-0.004	**-0.302***	0.074
	0.053	0.906	0.116	0.127	0.179	0.438		0.853	0.988	0.983	0.015	0.615
Hemorrhage ε	-0.092	0.052	-0.032	0.078	-0.191	-0.243	-0.024	1.000	-0.089	-0.236	0.214	**0.386****
	0.524	0.710	0.806	0.571	0.313	0.232	0.853		0.487	0.186	0.089	0.006
Thrombosis⁂	-0.058	0.007	-0.112	0.167	0.003	**0.410***	0.002	-0.089	1.000	-0.285	0.126	0.102
	0.687	0.963	0.384	0.222	0.986	0.038	0.988	0.487		0.108	0.322	0.487
PF4 OD†	-0.312	-0.129	-0.212	0.200	0.284	0.172	-0.004	-0.236	-0.285	1.000	-0.107	0.198
	0.100	0.539	0.253	0.327	0.269	0.541	0.983	0.186	0.108		0.554	0.312
"4 T" score	0.000	0.075	-0.015	0.171	-0.259	-0.180	**-0.302***	0.214	0.126	-0.107	1.000	0.160
	0.999	0.591	0.909	0.212	0.167	0.379	0.015	0.089	0.322	0.554		0.271
FAPIC	**-0.697****	**-0.309***	**-0.534****	0.110	0.032	0.003	0.074	**0.386****	0.102	0.198	0.160	1.000
	0.000	0.041	0.000	0.482	0.873	0.989	0.615	0.006	0.487	0.312	0.271	

Spearman correlation. ** Correlation is significant at the 0.01 level (2-tailed); * Correlation is significant at the 0.05 level (2-tailed).

‡ Time to admission/symptom onset after vaccination Clinical presentations per patient ε Presence of hemorrhage σ Platelet count (cells/mm^3) ɣ Fibrinogen (mg/dL) ħ D-dimer (mg/L, FEU) †PF4/heparin enzyme-linked immunosorbent assay for Heparin-induced thrombocytopenia ⁂ Number of thromboses

Supplementary Table S7. Comparison of predictors in patients with VITT after ChAdOx1 nCoV-19 vaccination according to treatments.

Variables	Total patients			Treatment			No treatment		
	Treatment	No treatment	P v	Survivors	Non-survivors	P v	Survivors	Non-survivors	P v
Non-heparin anticoagulants									
Fibrinogen < 150mg/dL	2/8 (25.0%)	11/19 (57.9%)	0.209	2/7 (28.6%)	0/1 (0.0%)	1.000	2/8 (25.0%)	9/11 (81.8%)	**0.024**
Age ≤ 60 years	10/14 (71.4%)	25/27 (92.6%)	0.157	9/13 (69.2%)	1/1 (100.0%)	1.000	9/11 (81.8%)	15/15 (100.0%)	0.169
Platelet < 25×10^3/μL	1/14 (7.1%)	13/26 (50.0%)	0.013	1/13 (7.7%)	0/1 (0.0%)	1.000	3/11 (27.3%)	10/14 (71.4%)	**0.047**
ICH (intracerebral hemorrhage)	2/14 (14.3%)	7/27 (25.9%)	0.692	2/13 (15.4%)	0/1 (0.0%)	1.000	2/11 (18.2%)	5/15 (33.3%)	0.658
CVT (cerebral venous thrombosis)	5/14 (35.7%)	20/27 (74.1%)	**0.023**	4/13 (30.8%)	1/1 (100.0%)	0.357	6/11 (54.5%)	13/15 (86.7%)	0.095
FAPIC score	1.50 (0.25, 2.00)	3.00 (2.00, 4.00)	**0.006**	1.00 (0.00, 2.00)	2.00	0.500	2.00 (1.00, 2.75)	4.00 (3.00, 5.00)	**0.002**
Direct thrombin inhibitor									
Fibrinogen < 150mg/dL	2/5 (40.0%0	11/22 (50.0%)	1.000	2/6 (33.3%)	-	-	2/9 (22.2%)	9/12 (75.0%)	**0.030**
Age ≤ 60 years	3/6 (50.0%)	32/35 (91.4%)	**0.031**	4/7 (57.1%)	-	-	14/17 (82.4%)	16/16 (100.0%)	0.227
Platelet < 25×10^3/μL	1/6 (16.7%)	13/34 (38.2%)	0.399	1/7 (14.3%)	-	-	3/17 (17.6%)	10/15 (66.7%)	**0.010**
ICH (intracerebral hemorrhage)	1/6 (16.7%)	8/35 (22.9%)	1.000	1/7 (14.3%)	-	-	3/17 (17.6%)	5/16 (31.3%)	0.438
CVT (cerebral venous thrombosis)	1/6 (16.7%)	24/35 (68.6%)	**0.026**	1/7 (14.3%)	-	-	9/17 (52.9%)	14/16 (87.5%)	0.057
FAPIC score	1.50 (0.75, 4.00)	3.00 (2.00, 4.00)	**0.046**	1.50 (0.75, 2.25)	-	-	2.00 (1.00, 2.50)	4.00 (3.00, 4.75)	**0.002**
Platelet transfusion									
Fibrinogen < 150mg/dL	4/7 (57.1%)	9/20 (45.0%)	0.678	0/1 (0.0%)	4/6 (66.7%)	0.429	4/14 (28.6%)	5/6 (83.3%)	**0.050**
Age ≤ 60 years	8/8 (100%)	27/33 (81.8%)	0.323	2/2 (100.0%)	6/6 (100.0%)	-	16/22 (72.7%)	10/10 (100.0%)	0.142
Platelet < 25×10^3/μL	6/8 (75.0%)	8/32 (25.0%)	**0.014**	1/2 (50.0%)	5/6 (83.3%)	0.464	3/22 (13.6%)	5/9 (55.6)	**0.027**
ICH (intracerebral hemorrhage)	4/8 50.0%)	5/33 (15.2%)	0.054	0/2 (0.0%)	4/6 (66.7%)	0.429	4/22 (18.2%)	1/10 (10.0%)	1.000
CVT (cerebral venous thrombosis)	6/8 (75.0%)	19/33 (57.6%)	0.448	0/2 (0.0%)	6/6 (100.0%)	**0.036**	10/22 (45.5%)	8/10 (80.0%)	0.124
FAPIC score	4.00 (2.00, 5.00)	2.00 (1.00, 3.00)	**0.006**	2.00 (1.00, 2.50)	4.00 (3.00, 4.75)	0.286	1.50 (1.00, 2.25)	3.50 (2.75, 4.00)	**0.007**
Neurosurgery									
Fibrinogen < 150mg/dL	3/7 (42.9%)	10/20 (50.0%)	1.000	0/1 (0.0%)	3/6 (50.0%)	1.000	4/14 (28.6%)	6/6 (100.0%)	**0.011**
Age ≤ 60 years	8/8 (100.0%)	27/33 (81.8%)	0.323	1/1 (100.0%)	7/7 (100.0%)	-	17/23 (73.9%)	9/9 (100.0%)	0.150
Platelet < 25×10^3/μL	4/8 (50.0%)	10/32 (31.3%)	0.416	0/1 (0.0%)	4/7 (57.1%)	1.000	4/23 (17.4%)	6/8 (75.0%)	**0.006**
ICH (intracerebral hemorrhage)	5/8 (62.5%)	4/33 (12.1%)	**0.007**	1/1 (100.0%)	4/7 (57.1%)	1.000	3/23 (13.0%)	1/9 (11.1%)	1.000
CVT (cerebral venous thrombosis)	7/8 (87.5%)	18/33 (54.5%)	0.120	1/1 (100.0%)	6/7 (85.7%)	1.000	9/23 (39.1%)	8/9 (88.9%)	**0.018**
FAPIC score	4.00 (2.00, 5.00)	2.00 (1.00, 3.75)	**0.024**	3.00	4.50 (2.00, 5.00)	0.857	1.50 (1.00, 2.00)	4.00 (3.00, 4.00)	**0.001**

Supplementary Table S8. Predictors of survival in patients with VITT after ChAdOx1 nCoV-19 vaccination.

Variables	Fisher's exact test			Logistic regression analysis		
	Survivors	Non-survivors	P value	Odds ratio	95% CI	P value
Fibrinogen < 150mg/dL	11/31 (35.5%)	15/19 (78.9%)	**0.004**	6.818	(1.811, 25.672)	**0.005**
Age ≤ 60 years	30/40 (75.0%)	23/23 (100.0%)	**0.010**	-	-	-
Platelet < 25×10^3/μL	9/39 (23.1%)	13/22 (60.9%)	**0.007**	4.815	(1.555, 14.907)	**0.006**
ICH (intracerebral hemorrhage)	4/40 (10.0%)	8/23 (34.8%)	**0.022**	4.800	(1.253, 18.384)	**0.022**
CVT (cerebral venous thrombosis)	19/40 (47.5%)	18/23 (78.3%)	**0.020**	3.979	(1.236, 12.809)	**0.021**

Supplementary Table S9. Demographic and clinical characteristics of patients with VITT after COVID-19 vaccination according to vaccine type.

Laboratory findings	Total (n=82)	ChAdOx1 nCoV-19 / Astra-Zeneca (n=64)	Ad26.COV.2.S / Janssen (n=16)	P - value
	Number of patients (%) / Median [IQR]	Number of patients (%) / Median [IQR]	Number of patients (%) / Median [IQR]	
Demographic information				
Age > 60 years	10/80 (12.5%)	10/64 (15.6%)	0/16 (0.0%)	0.198
Female	51/80 (72.9%)	37/64 (68.5%)	14/16 (87.5%)	0.203
Days to admission*	10.5 (8.0, 14.0)	10.0 (8.0, 12.5)	16.5 (13.0, 18.5)	**<0.001**
Laboratory findings				
Platelets				
Platelet count (cells/mm^3)	32,500.00 (16,000.00, 70,000.00)	35,000.00 (17,000.00, 70,000.00)	20,000.00 (13,000.00, 71,500.00)	0.565
Platelet count < 150 $\times 10^3/\mu L$	78/78 (100/0%)	62/62 (100.0%)	16/16 (100.0%)	-
Platelet count < 25 $\times 10^3/\mu L$	31/78 (39.7%)	22/62 (35.5%)	9/16 (56.2%)	0.158
PT				
PT INR	1.2 (1.1, 1.3)	1.2 (1.1, 1.4)	1.2 (1.1, 1.2)	0.493
PT, abnormal value†	40/57 (70.2%)	31/44 (70.5%)	9/13 (69.2%)	1.000
aPTT				
aPTT sec	29.6 (25.7, 35.0)	29.9 (25.0, 38.7)	29.1 (26.4, 31.2)	0.300
aPTT, abnormal value††	20/57 (35.1%)	16/43 (37.2%)	4/14 (28.6%)	0.749
Fibrinogen				
Fibrinogen (mg/dL)	141.00 (110.00, 240.00)	140.00 (110.00, 260.00)	149.00 (91.00, 222.50)	0.580
Fibrinogen < 200mg/dL	40/65 (63.9%)	30/45 (60.0%)	10/15 (66.7%)	0.766
Fibrinogen < 150mg/dL	35/65 (57.4%)	26/45 (52.0%)	9/15 (60.0%)	0.769
D-dimer				
D-dimer/Upper limit of normal range	45.8 (18.5, 70.4)	62.6 (21.6, 70.4)	21.9 (12.2, 68.9)	0.184
D-dimer, abnormal value (>500mg/L, FEU)	71/71 (100.0%)	55/55 (100.0%)	16/16 (100.0%)	-
Anti-PF4/heparin antibody ELISA ψ				
Anti-PF4/heparin antibody ELISA OD	2.2 (1.4, 2.8)	2.2 (1.2, 2.8)	2.5 (2.1, 2.7)	0.256
Anti-PF4/heparin antibody ELISA positive	61/62 (98.4%)	46/47 (97.9%)	15/15 (100.0%)	1.000
Functional platelet activation assay positive	20/31 (64.5%)	19/21 (90.5%)	1/10 (10.0%)	**<0.001**
Thromboses and Hemorrhages				
Presence of thrombosis	77/80 (96.2%)	61/64 (95.3%)	16/16 (100.0%)	1.000
Presence of CVT	52/80 (65.0%)	38/64 (59.4%)	14/16 (87.5%)	0.098
Presence of hemorrhage	29/80 (36.2%)	21/64 (32.8%)	8/16 (50.0%)	0.245
Presence of ICH	18/80 (22.5%)	12/64 (18.8%)	6/16 (37.5%)	**0.039**

Mortality	28/80 (32.9%)	23/63 (36.5%)	3/16 (18.8%)	0.239

IQR: interquartile range. ELISA: enzyme-linked immunosorbent assay.

† PT (Prothrombin time) / PT sec normal range: 10.0-12.0 sec / PT INR normal range: 0.9-1.1

†† aPTT (activated Partial thromboplastin time) / aPTT sec normal range: 25.0-35.0 sec / aPTT ratio normal range: 0.8-1.2

Supplementary Table S10. Methods of functional platelet activation test utilized in individual studies.

Reference	Method of Functional Platelet Activation Test	Results as reported by original manuscript	Cautionary details that must be considered in interpretation
Scully et al. [11]	Functional HIT assay was performed with HITAlert (Diapharma) by incubating donor platelets with calcium ionophore, physiological concentrations of heparin, patient serum, patient serum with heparin, and patient serum plus excess heparin.	5/7 (71.4%) Positive	In the patient samples, 55% of the platelets were originally activated in the buffer control, whereas the activity was not enhanced with the addition of physiologic doses of heparin (0.3 U/mL), which was only 37%. There was a drastic reduction with excess doses of heparin. These results do not fit the "classic" definition of a positive HIT functional platelet test. The authors have interpreted this as a positive result, even though the platelet activation was evident without the addition of heparin and was not increased with the addition of heparin.
Greinacher et al. [12]	Washed platelets were incubated with buffer, LWMH, or PF4; serum was coincubated with PF4 and platelets to test for reactivity.	9/9 (100.0%) Positive	The results clearly show greatly enhanced activity with the addition of PF4. That said, it is notable that in many patients, platelets were already activated in the buffer control.
Schultz et al. [10]	A heparin-induced multiple-electrode aggregometry on a Multiplate analyzer (Dynabyte Medical) was used to evaluate platelet aggregation in the presence of serum and saline buffer, high concentration of UFH, and low concentration of UFH.	4/5 (80.0%) Positive	As platelets were already activated in the buffer control and the activity was not enhanced with physiologic doses of heparin, these results do not fit the "classic" definition of a positive HIT functional platelet test. The authors have tentatively interpreted that this may be the effect of residual heparin, as 4 out of 5 patients had already administered heparin; however, this is not definite, and these results could have likely come from antibodies that activate platelets independent of heparin.
Jones et al. [31]	Serotonin-release assay with addition of PF4 to patient serum (McMaster University Platelet Immunology Laboratory).	1/1 (100.0%) Positive	From the authors' descriptions, it is stated that a serotonin release assay was performed with the addition of PF4, with positive results confirming the diagnosis of VITT.

Supplementary Table S11. Methods of heparin/PF4 antibody assay utilized in individual studies.

Reference	Method of heparin/PF4 antibody assay	Positive Results
Greinacher et al. [12]	PF4-heparin ELISA and PF4 ELISA with antibody binding measured by a secondary purified antihuman IgG.	9/9
Schultz et al. [10]	LIFECODES PF4 IgG ELISA (Immucor).	5/5
Scully et al. [11]	Asserachrom HPIA IgG assay and LIFECODES PF4 IgG ELISA (Immucor).	22/23
Tiede et al. [16]	HIT IgG CLIA and ELISA.	0/5 in CLIA 5/5 in ELISA
Franchini et al. [13]	PF4 Enhanced ELISA (Immucor).	1/1
Jones et al. [31]	PF4 ELISA.	1/1
Al-Mayhani et al. [32]	Asserachrom HPIA IgA assay for anti-PF4 antibodies.	3/3
Suresh et al. [35]	PF4 antibody ELISA.	1/1

Supplementary Table S12. Treatment combinations in patients with VITT after ChAdOx1 nCoV-19 vaccination.

Treatment	Total number of patients(n=39)
	Number of patients (%)
Single treatment modality	**6 (15.4%)**
Heparin products only	5 (12.8%)
Non-heparin anticoagulants only	1 (2.6%)
Two treatment modalities	**4 (10.3%)**
Heparin products + Others†	2 (5.1%)
IVIG + Non-heparin anticoagulants	2 (5.1%)
Three treatment modalities	**11 (28.2%)**
Heparin products + IVIG + Steroid	1 (2.6%)
Heparin products + IVIG + Platelet transfusion	1 (2.6%)
Heparin products + IVIG + Surgery	2 (5.1%)
Heparin products + Non-heparin anticoagulants + Steroids	1 (2.6%)
Heparin products + Non-heparin anticoagulants + Surgery	1 (2.6%)
Heparin products + Non-heparin anticoagulants + Others†	1 (2.6%)
Heparin products + Platelet transfusion + Surgery	1 (2.6%)
IVIG + Non-heparin anticoagulants + Steroids	1 (2.6%)
IVIG + Non-heparin anticoagulants + Others†	1 (2.6%)
Platelet transfusion + Surgery + Others†	1 (2.6%)
Four treatment modalities	**9 (23.1%)**
Heparin products + IVIG + Non-heparin anticoagulants + Surgery	1 (2.6%)
Heparin products + IVIG + Platelet transfusion + Steroids	2 (5.1%)
Heparin products + IVIG + Steroids + Others†	2 (5.1%)
Heparin products + Non-heparin anticoagulants + Steroids + Others†	1 (2.6%)
Heparin products + Non-heparin anticoagulants + Surgery + Others†	1 (2.6%)
Heparin products + Platelet transfusion + Steroids + Surgery + Others†	1 (2.6%)
IVIG + Non-heparin anticoagulants + Steroids + Others†	1 (2.6%)
Five treatment modalities	**3 (7.7%)**
Heparin products + IVIG + Non-heparin anticoagulants + Surgery + Surgery	1 (2.6%)
Heparin products + IVIG + Platelet transfusion + Steroids + Surgery	1 (2.6%)
IVIG + Non-heparin anticoagulants + Steroids + Surgery + Others†	1 (2.6%)

† Others contain all treatment except heparin products, IVIG, direct thrombin inhibitor or DOAC, platelet transfusion, steroids, and surgery.

Supplementary Table S13. Thrombosis sites in patients with VITT after ChAdOx1 nCoV-19 vaccination.

Sites of thrombosis	Total number of patients (n=64)
	Number of patients (%)
Single site of thrombosis	**39 (60.9%)**
Brain only	31 (48.4%)
Gastrointestinal system only	2 (3.1%)
Pulmonary system only	4 (6.3%)
Medium to large sized vessels only	1 (1.6%)
Others† only	1 (1.6%)
Two sites of thromboses	**13 (20.3%)**
Brain + Gastrointestinal system	3 (4.7%)
Brain + Medium to large sized vessels	1 (1.6%)
Brain + Others†	3 (4.7%)
Gastrointestinal system + Heart	1 (1.6%)
Gastrointestinal system + Medium to large sized vessels	1 (1.6%)
Gastrointestinal system + Others†	1 (1.6%)
Pulmonary system + Medium to large sized vessels	3 (4.7%)
Three sites of thromboses	**5 (7.8%)**
Brain + Gastrointestinal system + Pulmonary system	2 (3.1%)
Gastrointestinal system + Heart + Pulmonary system	1 (1.6%)
Gastrointestinal system + Pulmonary system + Medium to large sized vessels	1 (1.6%)
Pulmonary system + Medium to large sized vessels + Others†	1 (1.6%)
More than four sites of thromboses	**4 (6.3%)**
Brain + Gastrointestinal system + Pulmonary system + Medium to large sized vessels	3 (4.7%)
Brain + Gastrointestinal system + Heart + Pulmonary system + Medium to large sized vessels + Others†	1 (1.6%)

† Others contain all sites excluding the brain, gastrointestinal system, heart, pulmonary system and medium to large sized vessels.

Supplementary Figure S1. PRISMA flow chart showing the selection process of studies.

Supplementary Figure S2. Adverse clinical characteristics of patients with VITT after ChAdOx1 nCoV-19 vaccination stratified by age.
CVT: cerebral venous thrombosis, ICH: intracerebral hemorrhage.

Supplementary Figure S3. The receiver operating characteristics (ROC) curve and the area under the curve (AUC) of the FAPIC score on an external dataset of patients with VITT after Ad26.COV2.S vaccination.

Supplementary Figure S4. The re-assessed receiver operating characteristics (ROC) curve and the area under the curve (AUC) of the FAPIC score after multiple imputation on (A) the original model, (B) cross-validation, (C) bootstrapping, and (D) external validation on patients with VITT after Ad26.COV2.S vaccination.