

A systematic review of vaccine-induced immune thrombosis and thrombocytopenia triggered by non-adenoviral vector vaccination: ultra-rare or non-existent?

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Supplemental materials

Supplemental Table 1. Search terms.

Adenovirus-associated thrombocytopenia
Anti-PF4 immunothrombosis
Autoimmune anti-PF4 disorder
Heparin-induced thrombocytopaenia
Heparin-induced thrombocytopaenia like
Heparin-induced thrombocytopenia
Heparin-induced thrombocytopenia like
HIT
HIT-like
MGTS
Monoclonal gammopathy of thrombotic significance
Platelet activating anti-PF4 antibodies
Thrombocytopaenia with thrombosis
Thrombocytopenia with thrombosis
Thrombotic thrombocytopaenia
Thrombotic thrombocytopaenic syndrome
Thrombotic thrombocytopenia
Thrombotic thrombocytopenic syndrome
TTS
Vaccine-induced immune thrombotic thrombocytopenia-like
Vaccine-induced thrombosis with thrombocytopaenia
Vaccine-induced thrombosis with thrombocytopenia
Vaccine-induced thrombotic thrombocytopaenia
Vaccine-induced thrombotic thrombocytopenia
VITT
VITT-like

Supplemental Table 2: Criteria for classification of probability of vaccine induced thrombosis with thrombocytopenia (VITT), and TTS (thrombosis with thrombocytopenia syndrome). Criteria for Brighton TTS and VITT case definitions: (1) Thrombocytopenia: platelet count $<150 \times 10^9/L$, or below local laboratory lower limit for normal, or $\geq 50\%$ decrease from a previously documented count. (2) D-dimer >4000 ng/mL (fibrinogen equivalent units). (3) Acute or newly diagnosed thrombosis/ thromboembolism: Thrombotic event confirmed by pathology, imaging or surgical procedure, or severe, persistent headache with onset from 5-30 days after vaccination (for Brighton TTS case definition, this has to be accompanied with an elevated D-dimer >4000 ng/mL). (4) Characteristic interval from vaccination to onset: day 4 to day 30 after vaccination, or day 4 to day 42 after vaccination if the thrombotic event is an isolated DVT/ PE. (5) Anti-PF4 antibody: Positive anti-PF4 antibody ELISA test or Positive functional assay for PF4-dependent antibodies. COVID-19: coronavirus disease 2019; DVT: deep vein thrombosis; ELISA: enzyme-linked immunosorbent assay; FEU: fibrinogen equivalent units; PE: pulmonary embolism; PF4: platelet factor 4; TTS: thrombosis with thrombocytopenia syndrome; VITT: vaccine-induced immune thrombotic thrombocytopenia.

	Brighton TTS case definition ¹	Brighton VITT case definition ¹	UK Expert Haematology Panel case definition ²
Definite	Fulfil VITT criteria number 1, 3 and 4 AND A more plausible alternative explanation for illness not found	Fulfil all five VITT criteria OR A positive functional assay for PF4 dependent antibodies, and fulfils three out of the four remaining VITT criteria	Fulfil all five criteria: 1. Onset of symptoms 5-30 days post COVID-19 vaccine 2. Presence of thrombosis 3. Platelet count $<150 \times 10^9/L$ 4. D-dimer >4000 mcg/L Positive anti-PF4 antibody ELISA assay
Probable	Fulfil VITT criteria number 1 and 4 AND Clinical presentation that is consistent with acute or new onset thrombosis or thrombocytopenia syndrome AND A more plausible alternative explanation for illness not found	A positive PF4 antibody ELISA assay without a functional assay result for PF4 dependent antibodies AND Fulfil three of the remaining four VITT criteria AND A more plausible alternative explanation for illness not found	Fulfil four criteria from 'Definite', one of which must be criterion number 4 OR Fulfil all criteria except criterion number 4 (D-dimer is unknown or 2000-2000 FEU)

Possible NA	Fulfil three VITT criteria AND A more plausible alternative explanation for illness not found	Doesn't fulfil criterion number 4 (D-dimer is unknown or 2000-400 FEU) and one other criterion OR Fulfil three criteria, one of which must be criterion number 4
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Supplemental Table 3: Detailed information on included cases. APTT: activated partial thromboplastin time; CLIA: chemiluminescent immunoassay; COVID-19: coronavirus disease 2019; CVST: cerebral venous sinus thrombosis; DVT: deep vein thrombosis; ELISA: enzyme-linked immunosorbent assay; F: female; Hb: haemoglobin; HIPA: heparin-induced platelet aggregation; HPV: human papillomavirus; ICH: intracranial hemorrhage; INR: international normalised ratio; ITP: immune thrombocytopenic purpura; IVIG: intravenous immunoglobulin; LMWH: low molecular weight heparin; LTA: light transmission aggregometry; M: male; NSTEMI: non ST-elevation myocardial infarction; OD: optical density; PE: pulmonary embolism; PT: prothrombin time; SRA: serotonin release assay; STEMI: ST-elevation myocardial infarction; TIA: transient ischaemic attack; TTS: thrombosis with thrombocytopenia syndrome; UFH: unfractionated heparin; VITT: vaccine-induced immune thrombosis with thrombocytopenia; VKA: vitamin K antagonist; VTE: venous thromboembolism; WCC: white cell count.

Author	Author diagnosis	Age (y), sex	Country	Possible trigger	Days between exposure and presentation	Presenting features	Platelet count: presentation, nadir ($\times 10^9/L$)	Other lab investigations	Diagnosis testing	Treatment and outcome	Outcome	Our diagnosis
Al-Maqbali (2021)³	VITT	59, F	Oman	Pfizer-BioNTech mRNA COVID-19 vaccine (first dose)	7	DVT, PE	182, NA	Hb 150 g/L WCC $6.1 \times 10^9/L$ D-dimer 24000 ng/mL FEU PT 10.8 s APTT 27.3 s Fibrinogen 6.1 g/L	ELISA OD 0.617	LMWH Rvaroxaban	Recovery	Brighton TTS: NA Brighton VITT: Possible UK Expert: Probable
Andraska (2021)⁴	VTE	84, F	USA	Moderna mRNA COVID-19 vaccine (second dose)	3	DVT	144, NA	Hb 127 g/L INR 1.1	NA	Heparin Apixaban	Recovery	Brighton TTS: Definite Brighton VITT: Possible UK Expert: Possible
Chen (2022)⁵	VITT	42, F	Taiwan	Moderna mRNA COVID-19 vaccine (booster dose after two doses of AstraZeneca)	32	CVST, ICH	31, 16	Hb 95 g/L D-dimer >20000 ng/ml FEU	ELISA OD 2.91 Flow cytometry for p-selectin 12.28% baseline to 29.95 with serum + PF4 5ug/ml	Plasma exchange IVIG	Fatal	Brighton TTS: Definite Brighton VITT: Probable UK Expert: Probable
Cheong (2022)⁶	VITT	70, M	Taiwan	Moderna mRNA	35	PE, DVT	Normal	Hb normal	ELISA OD 0.424	LMWH Dabigatran	Recovery	Brighton TTS: did not meet

				COVID-19 vaccine (first dose)				D-dimer 4895 ng/mL Fibrinogen				criteria (no thrombocytopenia) Brighton VITT: Possible UK Expert: Possible
Chittal (2021)⁷	VITT	34, F	USA	Moderna mRNA COVID-19 vaccine (second dose)	3	Petechial rash	65, 29	Hb 135 g/L WCC 4.8×10 ⁹ /L APTT 59.3 s PT 13.2 s	ELISA OD 0.505		Recovery	Brighton TTS: did not meet criteria (no thrombosis) Brighton VITT: did not meet criteria UK Expert: Possible
Devi (2022)⁸	VITT	73, M	Pakistan	Sinopharm COVID-19 vaccine (not known if first or second dose)	14	DVT, PE	78, NA	Hb 130 g/L WBC 16.5×10 ⁹ /L D-dimer >30000 ng/mL FEU PT 14 s APTT 27 s Fibrinogen 1.83 g/L	PF4/heparin gel agglutination assay negative (poorly sensitive for VITT)	Rivaroxaban	Recovery	Brighton TTS: Definite Brighton VITT: Possible UK Expert VITT: Probable
Esefeld (2025)⁹	TTS	57, M	Germany	Moderna mRNA COVID-19 vaccine (second dose)	61	Splanchnic Vein Thrombosis and DVT	54, 29	D-dimer >35200 ng/mL	ELISA negative PS exposure of washed platelets positive	Apixaban LMWH UFH Thrombectomy, IVIG VKA Rituximab	Recovery	Brighton TTS: Definite Brighton VITT: Possible UK Expert VITT: Possible
Esefeld (2025)⁹	TTS	37, M	Germany	Pfizer-BioNTech mRNA COVID-19 vaccine (second dose)	3	Splanchnic Vein Thrombosis, PE, Petechiae	8, 2	D-dimer >12000 ng/mL	ELISA negative PS exposure of washed platelets positive	IVIG Apixaban Thrombolysis Argatroban	Recovery	Brighton TTS: Definite Brighton VITT: Possible UK Expert VITT: Possible
Esefeld (2025)⁹	TTS	71, M	Germany	Pfizer-BioNTech mRNA	6	PE, DVT, Petechiae	NA, 37		ELISA negative			Brighton TTS: Definite

				COVID-19 vaccine (first dose)				PS exposure of washed platelets positive	Brighton VITT: Possible
									UK Expert VITT: Possible
Esefeld (2025)⁹	TTS	59, M	Germany	Pfizer-BioNTech mRNA COVID-19 vaccine (second dose)	>60	DVT, Petechiae	NA, 0	ELISA negative PS exposure of washed platelets positive	Brighton TTS: Definite Brighton VITT: does not meet criteria UK Expert VITT: does not meet criteria
Esefeld (2025)⁹	TTS	58, M	Germany	Pfizer-BioNTech mRNA COVID-19 vaccine (first dose)	5	PE	NA, 79	ELISA negative PS exposure of washed platelets positive	Brighton TTS: Definite Brighton VITT: Possible UK Expert VITT: Possible
Esefeld (2025)⁹	TTS	49, M	Germany	Pfizer-BioNTech mRNA COVID-19 vaccine (second dose)	5	PE, DVT	NA, 123	ELISA negative PS exposure of washed platelets positive	Brighton TTS: Definite Brighton VITT: Possible UK Expert VITT: Possible
Esefeld (2025)⁹	TTS	62, M	Germany	Pfizer-BioNTech mRNA COVID-19 vaccine (second dose)	<7	PE, DVT	NA, 119	ELISA negative PS exposure of washed platelets positive	Brighton TTS: Definite Brighton VITT: Possible UK Expert VITT: Possible
Esefeld (2025)⁹	TTS	56, F	Germany	Pfizer-BioNTech mRNA COVID-19 vaccine (first dose)	10-20	Acral necrosis, Petechiae	NA, 63	ELISA negative PS exposure of washed platelets positive	Brighton TTS: Definite Brighton VITT: Possible UK Expert VITT: Possible

Esefeld (2025)⁹	TTS	13, M	Germany	Pfizer-BioNTech mRNA COVID-19 vaccine (second dose)	2	DIC, Petechiae, epistaxis, abdominal bleeding	NA, 54	ELISA negative PS exposure of washed platelets positive	Brighton TTS: Definite Brighton VITT: does not meet criteria UK Expert VITT: does not meet criteria
Esefeld (2025)⁹	TTS	66, M	Germany	Pfizer-BioNTech mRNA COVID-19 vaccine (first dose)	19	Splenic infarction, petechiae	NA, 29	ELISA negative PS exposure of washed platelets positive	Brighton TTS: Definite Brighton VITT: Possible UK Expert VITT: Possible
Esefeld (2025)⁹	TTS	62, M	Germany	Pfizer-BioNTech mRNA COVID-19 vaccine (second dose)	43	DVT, Stroke, Left ventricular thrombosis	NA, 23	ELISA negative PS exposure of washed platelets positive	Brighton TTS: Definite Brighton VITT: does not meet criteria UK Expert VITT: does not meet criteria
Esefeld (2025)⁹	TTS	50, F	Germany	Pfizer-BioNTech mRNA COVID-19 vaccine (second dose)	5	Stroke	NA, 127	ELISA negative PS exposure of washed platelets positive	Brighton TTS: Definite Brighton VITT: Possible UK Expert VITT: Possible
Esefeld (2025)⁹	TTS	29, M	Germany	Pfizer-BioNTech mRNA COVID-19 vaccine (first dose)	30	CVST	NA, 111	ELISA negative PS exposure of washed platelets negative	Brighton TTS: Definite Brighton VITT: Possible UK Expert VITT: Possible
Esefeld (2025)⁹	TTS	83, M	Germany	Pfizer-BioNTech mRNA COVID-19	20	Stroke	NA, 110	ELISA negative	Brighton TTS: Definite

				vaccine (second dose)				PS exposure of washed platelets negative			Brighton VITT: Possible
											UK Expert VITT: Possible
Esefeld (2025)⁹	TTS	20, F	Germany	Pfizer- BioNTech mRNA COVID-19 vaccine (third dose)	1	CVST, Petechiae	NA, 12	ELISA negative PS exposure of washed platelets negative			Brighton TTS: Definite Brighton VITT: does not meet criteria UK Expert VITT: does not meet criteria
Esefeld (2025)⁹	TTS	76, M	Germany	Pfizer- BioNTech mRNA COVID-19 vaccine (first dose)	NA	Stroke	NA, 11	ELISA negative PS exposure of washed platelets negative			Brighton TTS: Definite Brighton VITT: does not meet criteria UK Expert VITT: does not meet criteria
Esefeld (2025)⁹	TTS	80, M	Germany	Pfizer- BioNTech mRNA COVID-19 vaccine (second dose)	NA	CVST	NA, 76	ELISA negative PS exposure of washed platelets negative			Brighton TTS: Definite Brighton VITT: does not meet criteria UK Expert VITT: does not meet criteria
Esefeld (2025)⁹	TTS	61, F	Germany	Pfizer- BioNTech mRNA COVID-19 vaccine (second dose)	<7	DVT	NA, 65	ELISA negative PS exposure of washed platelets negative			Brighton TTS: Definite Brighton VITT: Possible UK Expert VITT: Possible
Goh (2022)¹⁰	VITT	76, M	Malaysia	Pfizer- BioNTech mRNA COVID-19	2	Axillary vein thrombosis , upper limb	116, 63	Hb 78 g/L WCC 8.7 x 10 ⁹ /L D-dimer 17400 ng/mL FEU ELISA OD 0.3 (NR <0.3)	Fondaparinux IVIG	Fatal	Brighton TTS: Definite Brighton VITT: Probable

				vaccine (first dose)		haematoma, stroke		PT 16.5 s APTT 26.5 s Fibrinogen 0.7 g/L				UK Expert: Probable
Gurjar (2022) ¹¹	TTS	56, F	USA	Moderna mRNA COVID-19 vaccine (second dose)	96	CVST	139, NA	WCC 10.1×10 ⁹ /L Hb 128 g/L D-dimer 16666 ng/mL PT 12 s APTT 30.8 s	Platelet factor-4 (PF-4) antibody negative	UFH Thrombectomy	Recovery	Brighton TTS: Definite Brighton VITT: Possible UK Expert: Possible
Hosseinzadeh (2022) ¹²	VITT	85, M	Iran	Sinopharm BBIBP-CoV vaccine (first dose)	5	Splenic vein thrombosis	51, 15	Hb 120 g/L WCC 2.8×10 ⁹ /L D-dimer >3200 ng/mL APTT 28 s	ELISA OD 2.178	Rivaroxaban IVIG	Recovery	Brighton TTS: Definite Brighton VITT: Probable UK Expert VITT: Probable
Johansen (2022) ¹³	VITT	25, F	Norway	Gardasil 9 HPV vaccine	8	Internal iliac vein thrombosis, PE	47, 17	Hb 146 g/L WCC 11.4×10 ⁹ /L D-dimer 35000 ng/mL FEU APTT 29 s INR 1.2 Fibrinogen 1.0 g/L	ELISA OD 3.827 CLIA 2.52	LMWH Fondaparinux IVIG	Recovery	Brighton TTS: Definite Brighton VITT: Definite UK Expert VITT: Definite
Kim CS (2022) ¹⁴	TTS	85, F	Korea	Pfizer-BioNTech mRNA COVID-19 vaccine (first dose)	15, PE diagnosed day 49 days post-vaccination	Immune-mediated neuropathy, PE	4, NA	Hb 124 g/L WCC 2.8×10 ⁹ /L D-dimer 52690 ng/mL FEU Fibrinogen 3.97 g/L	ELISA OD 0.71 CLIA 0.6	Apixaban IVIG	Recovery	TTS: Definite Brighton VITT: Probable UK Expert VITT: Probable
Kim EJ (2023) ¹⁵	VITT	58, M	Korea	Pfizer-BioNTech mRNA COVID-19 vaccine (first dose)	7	PE, DVT	119, NA	D-dimer 23600 ng/mL INR 1.39 APTT 37.8 s	NA	Actilyse LMWH Rivaroxaban	Recovery	Brighton TTS: Definite Brighton VITT: Possible UK Expert VITT: Probable
Ling (2022) ¹⁶	VITT	27, F	Singapore	Pfizer-BioNTech mRNA COVID-19	7	DVT	10, 10	Hb 112 g/L WCC 12.5×10 ⁹ /L D-dimer 9050 ng/mL FEU	ELISA OD 0.922 (addition of heparin)	Rivaroxaban IVIG	Recovery	Brighton TTS: Definite

				vaccine (third dose)				Fibrinogen 3.97 g/L PT normal APTT normal	leads to 78% inhibition) HIPA lack of aggregation at low and high concentration heparin (negative)		Brighton VITT: Definite UK Expert VITT: Definite (if 5-30 days post viral exposure)
Lin (2023)¹⁷	VITT	28, M	Taiwan	Pfizer-BioNTech mRNA COVID-19 vaccine (third dose)	21	PE, DVT, CVST	32, NA	WCC 10.1×10 ⁹ /L Hb 154 g/L D-dimer >7650 ng/ml FEU APTT 34.2 s PT 10.5 s Fibrinogen 4.31 g/L	ELISA OD 0.793 Dabigatran IVIG	Recovery	Brighton TTS: Definite Brighton VITT: Definite UK Expert VITT: Definite
Mouta Nunes de Oliveira (2022)¹⁸	Probable VITT	37, F	Brazil	Pfizer-BioNTech mRNA COVID-19 vaccine (first dose)	20	DVT	NA, 30	D-dimer 4625 ng/mL FEU	ELISA negative Functional platelet activating assay negative		Brighton TTS: Definite Brighton VITT: Probable UK Expert VITT: Possible
Rodriguez (2021)¹⁹	VITT	78, M	Spain	Pfizer-BioNTech mRNA COVID-19 vaccine (second dose)	2	PE, DVT	117, NA	Hb 140 g/L WCC 9.44×10 ⁹ /L D-dimer >35000 ng/mL FEU Fibrinogen 5.54 g/L PT 11.7 s APTT 29 s	Enzyme immunoassay test (Aeskulisa) OD 1.846 Asserachrom 2.07 times higher than the cut-off OD (0.28) "HIPA" - describing LTA with PRP - 39% platelet aggregation with 1 IU/ml UFH	Apixaban Recovery	Brighton TTS: Definite Brighton VITT: Probable UK Expert VITT: Probable

Sangli (2021) ²⁰	VITT	65, M	USA	Moderna mRNA COVID-19 vaccine (second dose)	10	PE, DVT, CVST	14, NA	Fibrinogen 2.91 g/L D-dimer 18900 ng/mL APTT 156 s INR 3.9	ELISA OD 2.855 SRA 51% release with low dose UFH, 6% release with high dose UFH	UFH Bivalirudin IVIG Plasma exchange	Fatal	Brighton TTS: Definite Brighton VITT: Definite UK Expert: Definite
Shrestha (2022) ²¹	Unsure	51, M	USA	Moderna mRNA COVID-19 vaccine (first dose)	1	Portal vein thrombosis, superior mesenteric vein thrombosis	144, 121	D-dimer <150 ng/mL	NA	UFH Apixaban	Recovery	Brighton TTS: Definite Brighton VITT: does not meet criteria UK Expert VITT: Possible
Sistanizad (2023) ²²	VITT	18, M	Iran	Sinopharm HB02 COVID-19 vaccine (first dose)	3	PE	104, 57	WCC 4×10 ⁹ /L Hb 130 g/L D-dimer 2622 ng/mL PT 17.7 s Fibrinogen 3.39 g/L	NA	Apixaban IVIG	Recovery	Brighton TTS: Definite Brighton VITT: does not meet criteria UK Expert VITT: Possible
Sung (2022) ²³	Probable VITT	34, F	Korea	Pfizer-BioNTech mRNA COVID-19 vaccine (first dose)	21	Budd-Chiari syndrome, PE	57, NA	D-dimer 11530 ng/mL FEU	NA	Direct oral anticoagulant IVIG	Recovery	Brighton TTS: Definite Brighton VITT: Possible UK Expert VITT: Possible
Su (2021) ²⁴	VITT	70, M	Taiwan	Moderna mRNA COVID-19 vaccine (first dose)	7	Stroke	77, 17	D-dimer 28550 ng/mL FEU PT 14.5 s APTT 34.7 s Fibrinogen 0.63 g/L	ELISA OD 0.679	IVIG Plasma exchange	Fatal	Brighton TTS: Definite Brighton VITT: Definite UK Expert VITT: Definite
Suto (2024) ²⁵	Vaccine-induced	80, M	Japan	Moderna mRNA COVID-19	6	Superior mesenteric vein	113, NA	Hb 169 g/L WCC 10.4×10 ⁹ /L	Anti-PF4 testing	UFH Apixaban	Recovery	Brighton TTS: Definite

				vaccine (first dose, after 4 doses of Pfizer)		thrombosis , portal vein thrombosis		D-dimer 19800 ng/mL APTT 29.5 s INR 0.93 Fibrinogen 5.39 g/L	(5U/ml) negative			Brighton VITT: Possible UK Expert VITT: Probable
Tejaswi (2023) ²⁶	VITT	19, F	India	Covacin COVID-19 vaccine	7	CVST	43, NA	D-dimer 7457 ng/mL PT 18.8 s	NA	Fondaparinux Platelet transfusion Plasma exchange	Recovery	Brighton TTS: Definite Brighton VITT: Possible UK Expert VITT: Probable
Zaheri (2022) ²⁷	VITT	46, F	Iran	Sinopharm BBIBP-CorV COVID-19 vaccine (second dose)	3	DVT, PE	67.5, NA	Hb 129 g/L WCC 17.1×10 ⁹ /L D-dimer 67000 ng/mL APTT 30 s PT 16 s Fibrinogen 2.06 g/L	ELISA “positive”	Dabigatran IVIG	Recovery	TTS: Definite Brighton TTS: Probable UK Expert: Probable

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