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Received: December 8, 2025.

Accepted: March 5, 2026.

Citation: Yiu Wayn Ker, Andeep S Ghataure, Samantha J. Montague; Phillip L.R. Nicolson and Richard John Buka. A systematic review of vaccine-induced immune thrombosis and thrombocytopenia triggered by non-adenoviral vector vaccination: ultra-rare or non-existent? *Haematologica*. 2026 Mar 12. doi: 10.3324/haematol.2025.300357 [Epub ahead of print]

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

Yiu Wayn Ker<sup>1</sup>, Andeep S Ghataure<sup>1</sup>, Samantha J Montague<sup>2</sup>, Phillip LR Nicolson<sup>2,3</sup>, Richard J Buka<sup>2,3</sup>

1. College of Medicine and Health, University of Birmingham, UK
2. Department of Cardiovascular Sciences, University of Birmingham, Birmingham, UK
3. West Midlands Adult Comprehensive Care Haemophilia & Thrombosis Centre, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK

**Word count: 1576**

## **MeSH key words:**

drug-related side effects and adverse reactions; thrombosis; thrombocytopenia; COVID-19 vaccines; mRNA vaccines

## **Corresponding author**

Dr Richard J Buka

Email: [r.j.buka@bham.ac.uk](mailto:r.j.buka@bham.ac.uk)

Address: Department of Cardiovascular Sciences (CVS),  
College of Medical and Dental Sciences,  
University of Birmingham, Edgbaston, Birmingham, B15 2TT

Phone: 00447891017606

## **Acknowledgments**

R.J.B. is supported through a National Institute for Health and Care Research (NIHR) Academic Clinical Lectureship. S.J.M. is supported through a BHF Project Grant (PG/23/11230). The NIHR Biomedical Research Centre (NIHR203326) and the BHF Accelerator (AA/18/2/34218) have supported the Department of Cardiovascular Sciences, where this research is based. The opinions expressed in this article are those of the authors and do not represent any of the listed organizations.

## **Authorship statement**

Contribution: Y.K. and A.G. designed the study, extracted and analysed data, and wrote the manuscript. S.J.M. and P.L.R.N. reviewed and edited the manuscript and provided clinical and diagnostic context. R.J.B. conceived and designed the study and wrote the manuscript.

## **Conflict of interest disclosure**

R.J.B. and P.L.R.N. have received research funding from AstraZeneca and P.L.R.N. has received honoraria from AstraZeneca. R.J.B. and P.L.R.N. have conducted paid market research for Pfizer. The remaining authors declare no competing financial interests.

## **Data availability statement**

All relevant data are presented in this manuscript and associated supplemental materials.

To the editor,

Vaccine-induced immune thrombosis and thrombocytopenia (VITT) is classically associated with adenoviral vector vaccination.<sup>1</sup> VITT is part of a wider group of diseases known as PF4-associated immunothrombosis with thrombocytopenia (PITT), which includes heparin-induced thrombocytopenia (HIT). PITT can also manifest in individuals without either proximate vaccine or heparin exposure, most notably following adenoviral infection.<sup>2</sup> Although we are aware of reports of VITT following non-adenoviral vector vaccination, it is unclear whether those attributed to mRNA-based vaccination truly represent VITT, or whether they reflect the background incidence of spontaneous syndromes coupled with heightened awareness.

This systematic review aimed to identify and collate cases of PITT that are related to non-adenoviral vector vaccines using wide search terms, then systematically assess the likelihood of VITT using recognised criteria. Of 42 included cases, only five met criteria for “definite” VITT; however, none were wholly convincing. VITT triggered by non-adenoviral vector vaccination therefore appears very rare or possibly non-existent.

A literature search was completed on 11 October 2025 using the terms outlined in supplemental Table 1. We also searched abstracts from major haematology meetings and reference lists. The searches were restricted to studies published from 1 January 2008 onwards as this is the year of the first report of a spontaneous HIT-like syndrome.<sup>3</sup>

Search results were uploaded to Rayyan (Cambridge, MA, USA), an artificial intelligence (AI)-powered systematic review management platform. After automated removal of duplicate and clearly irrelevant records, titles, abstracts, and full texts were screened by two reviewers (Figure 1). The inclusion criteria were as follows: (1) clinical case reports, cohort studies, or trials reporting clinical information about patient presentations; (2) studies reporting presentation with any thrombotic event with or without thrombocytopenia with a positive antibody test for anti-PF4 antibodies or a positive platelet activation assay temporally related to vaccination; (3) studies reporting thrombocytopenia without thrombosis with a positive antibody test for anti-PF4 antibodies or a positive platelet activation assay temporally related to vaccination. To keep inclusion criteria wide, we did not define the length of time for temporal relation to vaccination and only required that the authors made this link.

Demographic and clinical data were manually extracted from records and cases that met inclusion criteria were graded as either ‘definite’, ‘probable’, or ‘possible’ according to three internationally accepted systems (summarized in supplemental Table 2).<sup>4,5</sup> Ethical approval was not required for this systematic review, as it involved analysis of previously published case reports and did not include the collection of new data or direct patient involvement.

The search identified 38,146 studies. After screening, 25 studies consisting of 42 individual patient cases were included in this review (Figure 1). The demographics, presenting features, and investigation findings of the cases are summarized in Table 1. The clinical history, laboratory investigations, and fulfilment of diagnostic criteria for individual cases are shown in supplemental Table 3.

According to the Brighton TTS case definition,<sup>5</sup> 38/42 (90.5%) were considered “definite” cases. The Brighton definition is intentionally broad and not specific to VITT, encompassing any presentation of thrombosis with thrombocytopenia regardless of underlying mechanism.

This inclusivity is purposeful, as it allows capture of potential VITT cases even where confirmatory laboratory testing (e.g. anti-PF4 antibodies or functional assays) is unavailable or incomplete, often due to resource constraints.

Four cases met our inclusion criteria but not the TTS case definition. According to the Brighton VITT Classification and the UK Expert Consensus Criteria, only five (11.9%) cases could be classified as a definite case of VITT. According to the Brighton VITT Criteria, six (14.6%) were classified as probable, 21 (51.2%) as possible, and nine (22.0%) as not meeting criteria. According to the UK Expert Consensus Criteria, nine (22.0%) were classified as probable, 19 (46.3%) possible, and six (14.6%) as not meeting criteria.

Johansen et al. reported the case of a 25-year-old woman presenting 10 days after Gardasil HPV-9 vaccination, with internal iliac vein thrombosis and pulmonary embolism (PE), severe thrombocytopenia, markedly elevated D-dimer, hypofibrinogenemia, and a strongly positive anti-PF4 ELISA.<sup>6</sup> However, a HemosIL AcuStar HIT-IgG assay was moderately positive, which is generally not the case in VITT and suggests that this case is more HIT-like. Sangli et al. reported a 65-year-old man who developed DVT, PE, and CVST 10 days after a second Moderna mRNA vaccine dose.<sup>7</sup> This patient had a strongly positive anti-PF4 ELISA and serotonin release assay, findings more consistent with HIT than VITT. Su et al. described a 70-year-old man presenting with stroke and thrombocytopenia seven days after a first Moderna dose, with hypofibrinogenemia, very high D-dimer, but only weakly positive anti-PF4 ELISA.<sup>8</sup> Two further reports described younger patients developing thrombocytopenia and venous thrombosis 7–21 days after a third Pfizer-BioNTech dose, with very high D-dimer, normal fibrinogen, weak anti-PF4 ELISA positivity, and negative functional testing, suggesting possible milder or alternative VITT-like phenotypes.<sup>9,10</sup> Thus, of the five cases that are classified as *definite*, our clinical judgement is that none are wholly consistent with VITT.

Among reported cases, several are highly consistent with VITT despite failing to meet *definite* criteria on technical grounds. Chen et al. reported a 42-year-old woman presenting with CVST, profound thrombocytopenia, markedly elevated D-dimer, and a strongly positive anti-PF4 ELISA.<sup>11</sup> The timing of presentation at 32 days downgrades this case from definite to probable but this was the only case where a VITT-like pattern of platelet activation was documented. Hosseinzadeh et al. reported an 85-year-old man who developed splenic vein thrombosis and severe thrombocytopenia five days after a first dose of inactivated Sinopharm BBIBP-CoV vaccine.<sup>12</sup> Anti-PF4 ELISA was strongly positive, and the clinical presentation was otherwise entirely consistent with VITT although no functional testing was performed. The case was classified as probable rather than definite solely because the reported D-dimer (“>3,200 ng/mL”) did not clearly exceed the Brighton threshold of 4,000 ng/mL. Sung et al. and Tejaswi et al. reported cases of patients who developed venous thrombosis with thrombocytopenia and very high D-dimer levels four and 30 days post-vaccination, respectively.<sup>13,14</sup> However, anti-PF4 antibody testing was not performed.

Esefeld et al. recently published a case series reporting the clinical and laboratory characteristics of patients presenting with a VITT-like syndrome after mRNA-based COVID-19 vaccination but in whom anti-PF4 antibodies were not found.<sup>15</sup> However, on further work-up, they found that serum from twelve patients still activated platelets through FcγRIIA (as is the case in HIT and VITT) and discovered that seven of twelve patients had anti-histone

antibodies. Similarly, other reports have described patients with features typical of VITT but with negative anti-PF4 antibody testing (supplemental Table 3).

In this systematic review, we used broad search terms to identify reported cases of possible vaccine-induced immune thrombotic thrombocytopenia (VITT) following non-adenoviral vector vaccination. This approach aimed to capture cases not explicitly labelled as VITT by the original authors. We identified 25 studies describing 42 unique cases, allowing critical appraisal of the existence and biological plausibility of VITT in this setting.

A notable feature of this cohort was that fewer than half of cases occurred following first exposure to the implicated vaccine, a pattern that is highly inconsistent with classical adenoviral vector-associated VITT, where first exposure overwhelmingly predominates. As expected, thrombosis was reported in nearly all cases but the relatively low number of cases with CVST is again suggestive that this cohort is dissimilar to classical VITT.

Although five cases fulfilled formal criteria for “definite” VITT,<sup>6–10</sup> none were wholly convincing. In contrast, in our clinical judgement, the cases reported by Chen et al. and Hosseinzadeh et al., both classified as “probable,” represent the most convincing examples of VITT in this cohort. However, the lack of functional testing in both limits our conclusions about these cases. This is indicative of the inconsistent diagnostic evaluation across cases. Testing for anti-PF4 antibodies was performed in most cases but functional platelet activation assays were performed in only a small minority. Several cases demonstrated weak anti-PF4 ELISA positivity or functional assay patterns more consistent with heparin-induced thrombocytopenia (HIT). This raises the possibility of coincident HIT or other causes of thrombosis with thrombocytopenia occurring alongside low-level anti-PF4 antibodies, which are known to be part of the physiological immune response. The findings of Esefeld et al., suggesting alternative antigenic targets such as histones,<sup>15</sup> are also consistent with ELISA-negative cases that were reported at the outset of VITT.<sup>1</sup>

This study is limited by reliance on published case reports and is likely to underestimate true incidence. Cases may have been missed if mild, rapidly fatal, unrecognised, or not reported. Most reports originated from high-income settings with greater awareness and access to specialised testing. Incomplete reporting of platelet counts, coagulation parameters, anti-PF4 testing, and functional assays limited definitive classification. Conversely, several reports describing VITT were excluded due to absence of thrombocytopenia or immunological testing, highlighting variability in application of diagnostic criteria during the pandemic.

Given the billions of non-adenoviral vector vaccine doses administered worldwide, the small number of biologically plausible cases identified here suggests that VITT in this context is exceedingly rare. A proportion of reported cases likely reflect misclassification, spontaneous PITT, or HIT-like syndromes coinciding with vaccination rather than a distinct vaccine-specific phenomenon. Corroborating this conclusion, a recent study that systematically evaluated all cases of thrombosis reported in an Italian registry after vaccination for COVID-19 found no cases of VITT among 210 recipients of non-adenoviral vector vaccination.<sup>16</sup> PITT encompasses a wide spectrum of presentations and should therefore be suspected in patients with thrombosis and thrombocytopenia irrespective of vaccine exposure. Access to appropriate testing by anti-PF4 ELISA and importantly functional testing is key to rapid diagnosis and management.

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## Table

**Table 1. Baseline characteristics, laboratory findings, diagnostic classification, and outcomes of the study cohort (n = 42).** Values are presented as n (%), median (IQR), or as indicated. \*Platelet at presentation was assumed to be platelet nadir if that is the only platelet count provided. †LTA reported as HIPA. ‡Normal range reported as <0.3. #Assay results are from the same case. CLIA: chemiluminescent immunoassay; COVID-19: coronavirus disease 2019; EIA: enzyme immunoassay; ELISA: enzyme-linked immunosorbent assay; HIPA: heparin-induced platelet activation; HPV: human papillomavirus; IQR: interquartile range; LTA: light transmission aggregometry; OD: optical density; PF4: platelet factor 4; PRP: platelet rich plasma; PS: phosphatidylserine; SD: standard deviation; SRA: serotonin release assay; TTS: thrombosis with thrombocytopenia syndrome; VITT: vaccine-induced immune thrombotic thrombocytopenia; WP: washed platelets

	n=42	Missing n (%)
<b>Median age, years (median, IQR)</b>	58.0 (37 to 71)	0
<b>Female sex (n, %)</b>	16 (38.1)	0
<b>Possible trigger (n, %)</b>		0
Pfizer-BioNTech mRNA COVID-19 vaccine	26 (61.9)	
<i>First dose</i>	12 (46.2)	
<i>Subsequent dose</i>	14 (53.8)	
Moderna mRNA COVID-19 vaccine	10 (23.8)	
<i>First dose</i>	3 (30.0)	
<i>Subsequent dose</i>	7 (70.0)	
Sinopharm COVID-19 vaccine	4 (9.5)	
<i>First dose</i>	2 (50)	
<i>Subsequent dose</i>	1 (25)	
<i>Unknown dose type</i>	1 (25)	
Covacin COVID-19 vaccine	1 (2.4)	
<i>Unknown dose type</i>	1 (100)	
Gardasil 9 HPV vaccine	1 (2.4)	
<i>First dose</i>	1(100)	
<b>Time from trigger to presentation, days (median [IQR])</b>	7 (4 to 20)	2 (4.8)
<b>D-dimer, ng/mL (median [IQR])</b>	18,150 (7,554 to 29,275)	18 (42.9)
<b>Fibrinogen, g/L (median [IQR])</b>	3.15 (1.71 to 4.31)	28 (66.7)
<b>Platelet nadir, ×10<sup>9</sup>/L (median [IQR])</b>	57 (17 to 112)	1 (2.4) (reported as normal)
<b>Testing (n, %)</b>		
<b>Anti-PF4 antibody testing</b>	34 (81.0)	
Enzyme-linked immunosorbent assay (ELISA)	32 (76.2)	
<i>OD: &lt;0.40<sup>‡</sup></i>	1 (3.1)	
<i>OD: 0.40 to 0.99</i>	7 (21.9)	
<i>OD: 1.00 to 1.99</i>	0	
<i>OD: ≥2.00</i>	4 (12.5)	
<i>"Positive", otherwise undefined</i>	1 (3.1)	

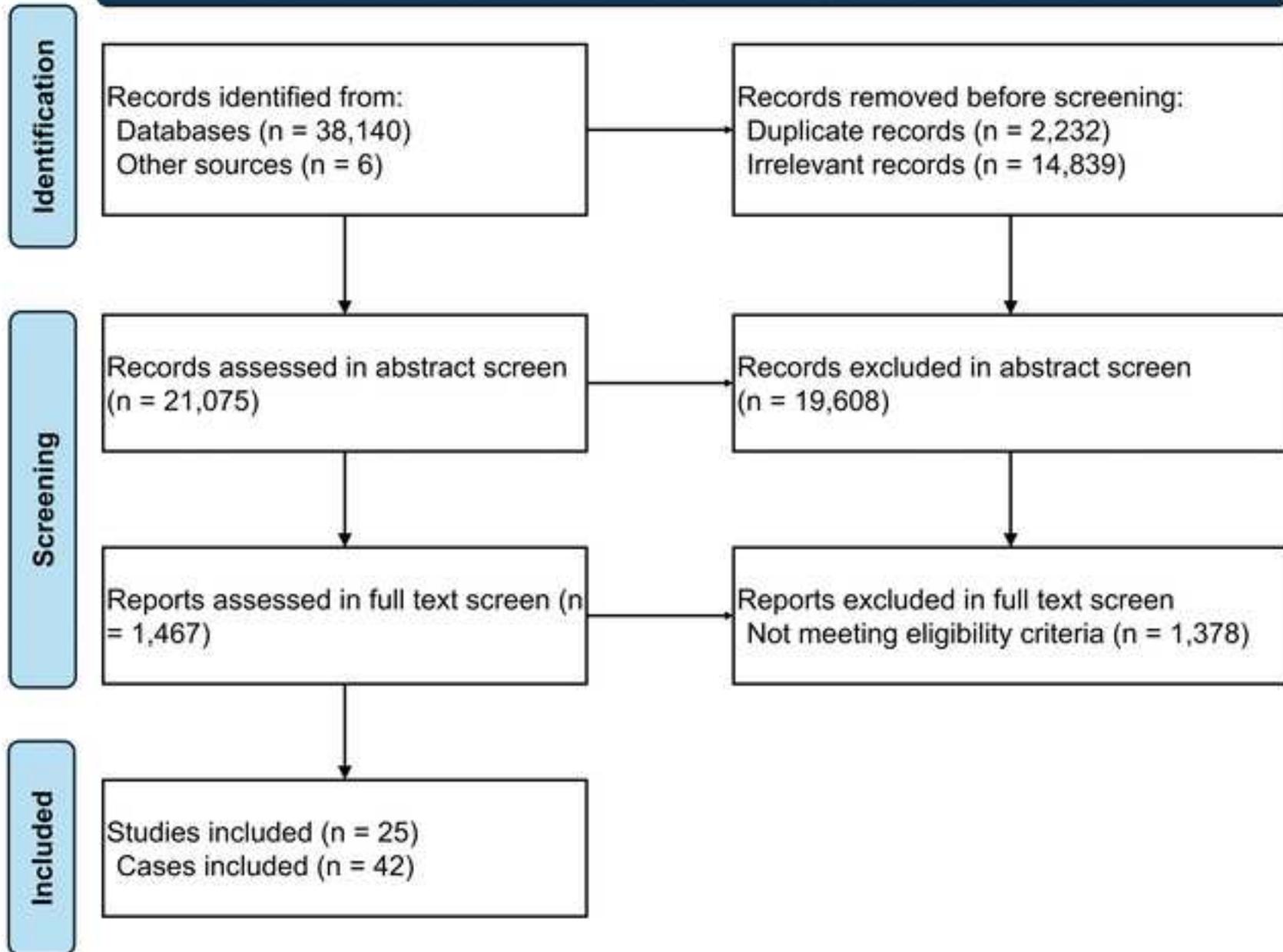
<i>"Negative", otherwise undefined</i>	19 (59.4)
Chemiluminescent immunoassay (CLIA)	2 (4.8)
<i>&lt;1 U/mL</i>	1 (50.0)
<i>1 to 5 U/mL</i>	1 (50.0)
Enzyme immunoassay (EIA)	1 (2.4)
<i>OD: 1.00 to 1.99</i>	1 (100.0)*
<i>OD: ≥2.0</i>	1 (100.0)*
Gel agglutination assay	1 (2.4)
<i>Negative</i>	1 (100.0)
PF4 antibody test, not defined	2 (4.8)
<i>Negative</i>	2 (100.0)
<b>Functional platelet activation testing (n, %)</b>	23 (54.7)
Heparin-induced platelet activation (HIPA) – WP	1 (2.4)
<i>Negative</i>	1 (100.0)
Serotonin release assay (SRA) – WP	1 (2.4)
<i>Positive - 51% release with low concentration heparin, inhibited by high concentration heparin</i>	1 (100.0)
Light transmission aggregometry (LTA) – PRP	1 (2.4)
<i>Positive - 39% aggregation in presence of low concentration heparin</i>	1 (100.0)
Flow cytometry – WP	19 (45.2)
<i>Negative</i>	6 (31.6)
<i>Positive - defined as mean + 3 SD of negative control for phosphatidylserine exposure</i>	12 (63.2)
<i>Positive – 66% P-selectin expression</i>	1 (5.2)
Functional platelet activation assay, not defined	1 (2.4)
<i>Negative</i>	1 (100.0)
<b>Thrombosis (n, %)</b>	40 (95.2)
Site of thrombosis	
<i>Deep vein thrombosis</i>	18 (42.9)
<i>Pulmonary embolism</i>	17 (40.5)
<i>Cerebral venous sinus thrombosis</i>	8 (19.0)
<i>Ischemic stroke</i>	6 (14.3)
<i>Portal vein thrombosis</i>	2 (4.8)
<i>Superior mesenteric vein thrombosis</i>	2 (4.8)
<i>Splanchnic vein thrombosis (otherwise undefined)</i>	2 (4.8)
<i>Splenic vein thrombosis</i>	1 (2.4)
<i>Axillary vein thrombosis</i>	1 (2.4)
<i>Internal iliac vein thrombosis</i>	1 (2.4)
<i>Budd-Chiari syndrome</i>	1 (2.4)
<i>Splenic infarction</i>	1 (2.4)
<i>Disseminated intravascular coagulation</i>	1 (2.4)
<i>Acral Necrosis</i>	1 (2.4)
<i>None</i>	1 (2.4)
<b>VITT Diagnostic Classification (n, %)</b>	
Brighton TTS	
<i>Definite</i>	38 (90.5)
<i>Probable</i>	0 (0.0)
<i>Possible</i>	0 (0.0)
<i>Did not meet criteria</i>	4 (9.5)
Brighton VITT	

<i>Definite</i>	5 (11.9)	
<i>Probable</i>	6 (14.3)	
<i>Possible</i>	22 (52.4)	
<i>Did not meet criteria</i>	9 (21.4)	
<hr/>		
UK Expert		
<i>Definite</i>	5 (11.9)	
<i>Probable</i>	11 (26.2)	
<i>Possible</i>	20 (47.6)	
<i>Did not meet criteria</i>	6 (14.3)	
<b>Fatal outcome (n, %)</b>	<b>4 (16.0)</b>	<b>17 (40.5)</b>

## Figure legend

**Figure 1: Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) flow diagram.**

## Identification of studies via databases and reference lists



# Supplemental materials

## Supplemental Table 1. Search terms.

Adenovirus-associated thrombocytopenia
Anti-PF4 immunothrombosis
Autoimmune anti-PF4 disorder
Heparin-induced thrombocytopaenia
Heparin-induced thrombocytopenia 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 <sup>1</sup>	Brighton VITT case definition <sup>1</sup>	UK Expert Haematology Panel case definition <sup>2</sup>
<b>Definite</b>	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
<b>Probable</b>	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)

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<b>Possible</b> NA	Fulfils 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 Fulfils 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	Diagnostic testing	Treatment and outcome	Outcome	Our diagnosis
<b>Al-Maqbali (2021)<sup>3</sup></b>	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
<b>Andraska (2021)<sup>4</sup></b>	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
<b>Chen (2022)<sup>5</sup></b>	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
<b>Cheong (2022)<sup>6</sup></b>	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
<b>Chittal (2021)<sup>7</sup></b>	VITT	34, F	USA	Moderna mRNA COVID-19 vaccine (second dose)	3	Petechial rash	65, 29	Hb 135 g/L WCC 4.8×10 <sup>9</sup> /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
<b>Devi (2022)<sup>8</sup></b>	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 <sup>9</sup> /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
<b>Esefeld (2025)<sup>9</sup></b>	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	Apixaban LMWH UFH Thrombectomy, IVIG VKA Rituximab	Recovery	Brighton TTS: Definite  Brighton VITT: Possible  UK Expert VITT: Possible
<b>Esefeld (2025)<sup>9</sup></b>	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	IVIG Apixaban Thrombolysis Argatroban	Recovery	Brighton TTS: Definite  Brighton VITT: Possible  UK Expert VITT: Possible
<b>Esefeld (2025)<sup>9</sup></b>	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
<b>Esefeld (2025)<sup>9</sup></b>	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
<b>Esefeld (2025)<sup>9</sup></b>	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
<b>Esefeld (2025)<sup>9</sup></b>	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
<b>Esefeld (2025)<sup>9</sup></b>	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
<b>Esefeld (2025)<sup>9</sup></b>	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

<b>Esefeld (2025)<sup>9</sup></b>	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
<b>Esefeld (2025)<sup>9</sup></b>	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
<b>Esefeld (2025)<sup>9</sup></b>	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
<b>Esefeld (2025)<sup>9</sup></b>	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
<b>Esefeld (2025)<sup>9</sup></b>	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
<b>Esefeld (2025)<sup>9</sup></b>	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
<b>Esefeld (2025)<sup>9</sup></b>	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
<b>Esefeld (2025)<sup>9</sup></b>	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
<b>Esefeld (2025)<sup>9</sup></b>	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
<b>Esefeld (2025)<sup>9</sup></b>	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
<b>Goh (2022)<sup>10</sup></b>	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 <sup>9</sup> /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
<b>Gurjar (2022)</b> <sup>11</sup>	TTS	56, F	USA	Moderna mRNA COVID-19 vaccine (second dose)	96	CVST	139, NA		WCC 10.1×10 <sup>9</sup> /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
<b>Hosseinzadeh (2022)</b> <sup>12</sup>	VITT	85, M	Iran	Sinopharm BBIBP-CoV vaccine (first dose)	5	Splenic vein thrombosis	51, 15		Hb 120 g/L WCC 2.8×10 <sup>9</sup> /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
<b>Johansen (2022)</b> <sup>13</sup>	VITT	25, F	Norway	Gardasil 9 HPV vaccine	8	Internal iliac vein thrombosis, PE	47, 17		Hb 146 g/L WCC 11.4×10 <sup>9</sup> /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
<b>Kim CS (2022)</b> <sup>14</sup>	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 <sup>9</sup> /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
<b>Kim EJ (2023)</b> <sup>15</sup>	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
<b>Ling (2022)</b> <sup>16</sup>	VITT	27, F	Singapore	Pfizer-BioNTech mRNA COVID-19	7	DVT	10, 10		Hb 112 g/L WCC 12.5×10 <sup>9</sup> /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)
<b>Lin (2023)</b> <sup>17</sup>	VITT	28, M	Taiwan	Pfizer-BioNTech mRNA COVID-19 vaccine (third dose)	21	PE, DVT, CVST	32, NA	WCC 10.1×10 <sup>9</sup> /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
<b>Mouta Nunes de Oliveira (2022)</b> <sup>18</sup>	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
<b>Rodriguez (2021)</b> <sup>19</sup>	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 <sup>9</sup> /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

<b>Sangli (2021)</b> <sup>20</sup>	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
<b>Shrestha (2022)</b> <sup>21</sup>	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
<b>Sistanizad (2023)</b> <sup>22</sup>	VITT	18, M	Iran	Sinopharm HB02 COVID-19 vaccine (first dose)	3	PE	104, 57	WCC 4×10 <sup>9</sup> /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
<b>Sung (2022)</b> <sup>23</sup>	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
<b>Su (2021)</b> <sup>24</sup>	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
<b>Suto (2024)</b> <sup>25</sup>	Vaccine-induced	80, M	Japan	Moderna mRNA COVID-19	6	Superior mesenteric vein	113, NA	Hb 169 g/L WCC 10.4×10 <sup>9</sup> /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
<b>Tejaswi (2023)</b> <sup>26</sup>	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
<b>Zaheri (2022)</b> <sup>27</sup>	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 <sup>9</sup> /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

## References (supplemental)

References in this list are chronological according to order in this supplemental materials document and are not necessarily aligned with the main text.

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