Version history

V0.1	25/3/21	Out for comments
V0.2	1/4/21	Spencer Keene comments
V0.3	5/4/21	Cathie Sudlow comments, updated relevant phenotypes, added tables
V0.4	7/4/21	Munir Pirmohamed comments, Cathie Sudlow comments, updated phenotypes, added post COVID analysis added pre COVID analysis, added skeleton tables post Angela Wood comments, added thrombophilia to phenotypes, altering of DVT codes after Spencer Keene suggestions
V0.5	8/4/21	Altered follow up time periods to 1,2,3,4,8,12,20,39 weeks, updated to shorter ICD-10 when possible, new COVID phenotypes matched to prior long covid application (but to be replaced by Spiros Denaxos' codes when available)
V0.6	9/4/21	Updated to include pregnancy related venous thrombosis codes and separate into a category, outcomes now in better table in appendix, updated tables and analyses
V0.7	11/4/21	Updated to include SAH, retinal infarction in list of codes, removed time since registration from population definition and changing practice

Lay summary

There have been a number of reports of vascular complications after coronavirus vaccination. The complication that is of most concern is a very rare condition of clotting of the veins in unusual places like the brain and the gut been associated with low levels of platelets.

We will study all adults alive in England at the beginning of the pandemic in 2020 with data included in the NHS Digital trusted research environment. We will find out which people had a disease involving blood clots in the arteries (like stroke or heart attack) or in the veins (like deep vein thrombosis, pulmonary embolism or clots in the veins of the brain or gut). We will also find out which of these people were diagnosed with low levels of platelets at the time of their blood clotting event.

We will compare the risk of developing one of these conditions among people who have had a Covid-19 vaccine versus those who have not had a vaccine. We will use statistical methods to account for differences between vaccinated and unvaccinated people (such as age, sex, ethnic group and previous medical history) that might affect the risk of these conditions. We will assess the risks for clotting events of different types, for different vaccines, for people who have had one or two vaccine doses, and for people with different characteristics. Our results will allow us to estimate whether Covid-19 vaccine is associated with an increased risk of one or more of these different types of clotting events, and if so by how much.

This research is needed to provide reliable information to medicines regulators, the Department of Health and Social Care, health professionals and the public about any risks associated with Covid-19 vaccines. Because the clotting events that might be affected are very rare, any increase in risk is likely to be very small. It will, therefore, be important to understand not only whether or not there is an increased risk but also the size of any increased risk and whether it only applies to particular groups of people. It will also be important to understand how any risk compares with the protective benefits of the vaccine, which are known to be substantial.

AUTHORS

BHF Data Science Centre

TITLE

SARS-CoV-2 vaccination and risk of major venous and arterial vascular events

BACKGROUND

After Astra Zeneca SARS-CoV-2 vaccination, there have been reports of intracranial venous sinus thrombosis, mesenteric thrombosis, thrombocytopenia and disseminated intravascular coagulation. Whether or not there is a causal association with the vaccine is uncertain. It has been proposed that this increased risk is due to antiplatelet antibodies leading to the particular haematological syndrome. Severe COVID-19 is also associated with increased antibody-mediated procoagulant platelets.[1]

Vaccination in adulthood against other infections leads to a transient increase in inflammatory markers as the immune system begins an acute inflammatory response. Although higher levels of markers associated with inflammation are associated with a higher risk of myocardial infarction and stroke, there is little evidence that vaccination in adults (other than against COVID) increases the risk of myocardial infarction or stroke, and in fact may reduce it. In the United Kingdom, a study in electronic health records demonstrated no increase in incident myocardial infarction or stroke after influenza vaccination, tetanus vaccination, or pneumococcal vaccination;[2] this finding was replicated in a cohort of older men who received pneumococcal vaccination (analysed as a time varying covariate) in the United States.[3]

There are epidemiological biases associated with vaccination. People who have vaccinated tend to be in better health, at least in the time when they received the vaccine. This is perhaps the reason why some studies have demonstrated that pneumococcal vaccination is associated with a reduced risk of myocardial infarction relative to the rest of the population that use a case control study design.[4]

Any increased risk in serious complications with the SARS-CoV-2 vaccination needs to be balanced against the risk of these complications with SARS-CoV-2 infection, and against the baseline rate of these events.

Therefore, a comprehensive assessment of vascular events after vaccination against SARS-CoV-2 and SARS-CoV-2 infection is needed.

RESEARCH HYPOTHESES

1. There is a higher risk for venous and arterial thrombosis or embolism after SARS-CoV-2 vaccination that varies with vaccine type, and is associated with thrombocytopenia.
2. There is a higher risk for venous and arterial thrombosis or embolism after SARS-CoV-2 infection.

DATA SOURCES

NHS Digital TRE for England

- Primary care data (GP Data for Pandemic Planning and Research via General Practice Extraction Service, GPES)
- Secondary Use Service (SUS) hospital data
- Pillar 1 and Pillar 2 SARS-CoV-2 infection laboratory testing data
- HES Admitted Patient Care
- Office of National Statistics death registration records
- Sentinel Stroke National Audit (SSNAP)
- Community dispensing data
- SARS-CoV-2 vaccination data

RESEARCH QUESTION

1. What is the age- and sex- specific incidence of each event in 2018 and 2019 (before pandemic) and 2020 onwards (during pandemic)?
2. In people who have had SARS-CoV-2 **vaccine** compared with people who have not, what is the excess risk (expressed as hazard ratios with time since vaccination) of first fatal or non-fatal stroke or MI ('arterial); cerebral sinus thrombosis, mesenteric or portal vein thrombosis, PE or DVT ('venous thromboembolism'); before and after adjustment for confounders (age, diabetes, poverty, ethnicity, sex etc.)?
3. In people who have had SARS-CoV-2 **infection** compared with people who have not, what is the excess risk (expressed as hazard ratios with time since infection) of first fatal or non-fatal stroke or MI ('arterial); cerebral sinus thrombosis, mesenteric or portal vein thrombosis, PE or DVT ('venous thromboembolism'); before and after adjustment for confounders (age, diabetes, poverty, ethnicity, sex etc.)?

DISCUSSION OF METHODS

We will use a time-dependent exposure (SARS-CoV-2 vaccine or infection) in a Cox regression model, separating follow-up time for all people into time before and time after vaccination, and estimating relative hazards of events of different types by week after vaccination. We will account for confounding by risk factors with time-independent covariates for cardiovascular risk factors and other covariates. We will look for heterogeneity in the estimate of the association between SARS-CoV-2 vaccination or infection and cardiovascular disease by vaccine type, time and prior risk factors.

STUDY POPULATION

Population for COVID and vaccine analyses

Patients will be included if they meet ALL of the following criteria:

- An age of ≥ 18 can be calculated on 1st January 2020 and have known sex;
- Registered with a GP practice in the linked data extract on 1st January 2020;
- Alive on 1st January 2020.

Exclude

- A SARS-CoV-2 infection recorded prior to 1st January 2020.

Population for pre-COVID risk

Whole population of England, estimated by mid-2019 population from ONS

EXPOSURE

PRIMARY -VACCINE

- Astra Zeneca
  - Batch number, dose number (first or second)
- Pfizer
  - Batch number, dose number (first or second)
- Moderna (when available)
  - Batch number, dose number (first or second)

PRIMARY – COVID INFECTION

- A positive PCR test and date of test available in laboratory data
-

SECONDARY – COVID INFECTION [needs to be updated when Spiros confirms they are ready]

		Test	
		+	-
Any clinical code (COVID)	+	1. Confirmed diagnosis	2. Clinical diagnosis only
	-	4. Asymptomatic [or asymptomatic code]	6. No known positive test or diagnosis

All detected: positive test or any clinical code (i.e. 1 or 2)

OUTCOMES

Note HES APC only has 4-character ICD-10 codes, and the following are ICD10 2019. See appendix for outcome code definitions

Composite events:

- **Arterial events:** first of ischaemic stroke or stroke or unknown type or myocardial infarction or other arterial thrombosis
- *Arterial events + thrombocytopenia* (i.e. any arterial code + any thrombocytopenia code present during in same spell or superspell), and no prior history of thrombocytopenia
- **Venous events:** first of pulmonary embolism or deep venous thrombosis in arm or leg or intracranial venous thrombosis or mesenteric thrombus or portal vein thrombus
- *Venous events + thrombocytopenia* (i.e. both codes present during same super-spell/spell) and no prior history of thrombocytopenia
- *ICVST + thrombocytopaenia ((*i.e. both codes present during same super-spell/spell) and no prior history of thrombocytopenia

Individual events of different types

Arterial

- Incident myocardial infarction in primary care or APC HES
- Incident ischaemic stroke or stroke of unknown type in primary care or APC HES
- Incident non-stroke non-MI arterial embolism in primary care or APC HES

Venous

- Pulmonary embolism in primary or APC HES;
- Deep vein thrombosis in APC HES
- Portal vein thrombosis in APC HES
- Other deep vein thrombosis in APC HES
- Thrombosis during pregnancy (excluding cerebral venous thrombosis) in APC HES
- Intracranial venous thrombosis during pregnancy in APC HES
- Intracranial venous thrombosis[5] in APC HES

Haematological

- Disseminated intravascular coagulation in APC HES
- Thrombotic thrombocytopenic purpura in APC HES
- Thrombocytopenia in APC HES

Other

- Intracerebral haemorrhage in primary care or APC HES
- Mesenteric thrombus (the definition could be venous or arterial) in APC HES
- Spinal stroke in APC HES

Date of onset defined as: of date of start of SUS or APC spell with event; OR date of GP consultation with event; OR death with event

CONFOUNDERS

Defined on 1st January 2020, with a look back in primary and secondary care for each patient:

- Sex — categorical, GP, where >1 sex recorded, excluded;
- Age in years — continuous, at 1st January 2020, GP, where age conflicts, exclude;
- Ethnicity — 5 categorical, most recent recorded prior to 1st January 2020, GP and if missing from HES;
- Deprivation — continuous, most recent recorded prior to 1st January 2020, in spine or GP data;
- Region: — East of England, London, Midlands, NE and Yorkshire, North West, South East, South West, Scotland, Wales, most recent residence prior to 1st January 2020, GP;

- Consultation rate: number of primary care contacts from 1/1/19 to 1/1/20, GP;
- Medications: total number of medications by BHF chapters prescribed 1/10/19–1/1/20, GP;
- Diabetes: yes/not recorded from start of record to 1st January 2020, GP or HES APC;
- Depression: yes/not recorded from start of record to 1st January 2020, GP or HES APC;
- Obesity: yes/not recorded from start of record to 1st January 2020 GP; or BMI>30 in GP record
- Cancer yes/not recorded from start of record to 1st January 2020, GP or HES APC;
- COPD yes/not recorded from start of record to 1st January 2020, GP or HES APC:
- CKD yes/not recorded from start of record to 1st January 2020, GP or HES APC;
- Liver disease: yes/not recorded from start of record to 1st January 2020, GP or HES APC;
- Major Surgery yes/not recorded from start of record to 1st January 2020, GP or HES APC;
- Hypertension yes/not recorded from start of record to 1st January 2020, GP or HES APC;
- Dementia yes/not recorded from start of record to date of linkage, GP or HES APC;
- Smoking current/ex-/never/unknown most recent prior to 1st January 2020, GP;
- Antiplatelet yes/no/unknown (unknown if patient's GP practice not in prescription extract) BNF chapter 2.9 at least one prescription 1/10/19–1/1/20, dispensing;
- BP lowering yes/no/unknown BNF chapter 2.5 at least one prescription 1/10/19–1/1/20, dispensing;
- Lipid lowering yes/no/unknown BNF chapter 2.12 at least one prescription 1/10/19–1/1/20, dispensing;
- Anticoagulant yes/no/unknown BNF chapter 2.8.2 at least one prescription 1/10/19–1/1/20, dispensing;
- COCP yes/no/unknown BNF chapter 7.3.1 at least one prescription 1/10/19–1/1/20, dispensing;
- HRT yes/no/unknown BNF chapter 6.4.1.1 at least one prescription 1/10/19–1/1/20, dispensing;
- History of stroke yes/not recorded from start of record to 1st January 2020, GP or HES APC;
- History of MI yes/not recorded from start of record to 1st January 2020, GP or HES APC;
- History of VTE yes/not recorded from start of record to 1st January 2020, GP or HES APC;
- History of thrombophilia yes/not recorded from start of record to 1st January 2020, GP or HES APC; defined as ICD-10 D68.5 D68.6; acquired or inherited
- History of coronavirus infection before vaccination, defined as a positive PCR test or a clinical episode of COVID (for vaccine analysis)
- Pregnancy For discussion
-

TIME VARYING COVARIATES

- Calendar month of exposure.

EFFECT MODIFIERS (see definitions in confounders)

- Age continuous variable

- Sex: categorical;
- Ethnicity: categorical, as defined in 'confounders';
- Medication: yes/no for each of antiplatelet, BP lowering, lipid lowering, anticoagulant, as defined in 'confounders';
- Diabetes yes/not known, as defined in 'confounders';
- Deprivation continuous variable (figured by fifths of deprivation distribution) , as defined in 'confounders';
- Calendar month

CENSORING FOR SURVIVAL METHODS

The cohort study will be censored at the first of:

- Death;
- Event of interest;
- Transfer to another nation or to a GP practice out of the linked data;

ANALYSES

Events in previous years

- Number of patients with at least one fatal or non-fatal venous or arterial events in different age and sex groups in 2018, 2019 and 2020, and incidence estimated with mid-2019 population
- Consider incidence of first ever events (i.e. no prior event in APC record)

Table of characteristics

- Distribution of baseline characteristics at 1/1/20 by SARS-CoV-2 vaccine type (AZ, Pfizer, none) versus rest of population
- Distribution of baseline characteristics at 1/1/20 by SARS-CoV-2 infection versus rest of population

Incidence of events per 100,000

- Incidence of each composite and individual outcome event by SARS-CoV-2 vaccine type (AZ, Pfizer, none) by week post vaccination and by sex and age groups (0-50; 50-70; over 70) from 1/12/20 to latest extract, and by date of 1st and second dose
- Incidence of each composite and individual outcome event by SARS-CoV-2 infection (yes/no) by week post infection and by sex and age groups (0-50; 50-70; over 70) from 1/1/20 to 1/12/20
- Number of events in each age and sex group in year 1/1/19 to 1/1/20, using ONS mid-year figures to estimate incidence

Proportional increase in incidence of events

- Kaplan Meier plots for time to event in SARS-CoV-2 vaccine and rest of population
- Cox regression estimating relative incidence comparing follow up time from vaccination in people with SARS-CoV-2 vaccine (for each vaccine) with rest of population, with and without confounders, for each of the fatal or non-fatal outcomes.
- Cox regression estimating relative incidence comparing follow up time from SARS-CoV-2 infection in people with SARS-CoV-2 vaccine with rest of population, with and without confounders, for each of the fatal or non-fatal outcomes.

Sensitivity analyses

- For the composite outcomes 'all venous' and all arterial'
    - With and without thrombocytopenia
    - With and without: a history of MI, stroke, thrombophilia, oral contraceptive, history of thrombophilia
    - For post-vaccine analyses, before and after mid-March 2021
- Consider predictive model if enough cases

FIGURES AND TABLES (IN DISCUSSION)

Table 1 Number of patients with at least one fatal or non-fatal venous event of different types in the year 1/1/19 to 31/12/19 in HES APC and ONS death

Later to calculate rate per 100,000 of population per year with number of events in APC HES year 1/1/19 to 31/12/19 as numerator, and mid-year 2019 population as numerator

	First intracranial venous thrombosis and intracranial venous thrombosis during pregnancy		**First portal vein thrombosis**		**First Other vein thrombosis**		**First lower limb thrombosis**		**First Pulmonary embolism**		**First Mesenteric thrombosis**		**Thrombosis during pregnancy**	**All venous events**	
ICD10 codes	G08x, I67.6, I63.6	G08x, I67.6, I63.6, O22.5, O87.3	I81		I82.2, I82.3, I82.8, I82.9		I80.1, I80.2, I80.3		I26.0, 126.9		K55		O87.1, O87.9, O88.2	Any venous event	
Age group (defined 1/1/19)	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Female	Male	Female
0-18															
19-29															
30-39															
40-49															
50-59															
60-69															
70-79															
80-89															
90+															

Table 2 – repeat table 1 for 1/1/20 to 31/12/20, 1/1/18 to 31/12/218

Table 3 Number of patients with at least one fatal and non-fatal arterial events of different types in the year 1/1/19 to 31/12/19 in ONS and HES APC

Later to calculate rate per 100,000 of population per year with number of events in APC HES year 1/1/19 to 31/12/19 as numerator, and mid-year 2019 population as numerator

	First myocardial infarction		**First ischaemic stroke**		**First stroke uncertain**		**First retinal infarction**		**First spinal stroke**		**First haemorrhagic stroke**		**First other arterial thrombus**		**All venous events**	
ICD10 codes	I21x, I22x, I23x, I24.2		I63x		I64x		H34x		G95.1		I61x		I74x		Any venous event	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
0-18																
19-29																
30-39																
40-49																
50-59																
60-69																
70-79																
80-89																
90+																

Table 4 – repeat table 3 for 1/1/20 to 31/12/20, 1/1/18 to 31/12/218

Table 5 – baseline characteristics of patients with and without SARS CoV-2 **vaccination** on date of linkage (?worthwhile) rows as per https://app.box.com/file/784295677240

	Exposed	Un-exposed
	N, %	N, %
Sex Female Male		
Age in decades 0-9 10-19 20-29 30-39 40-49 50-59 60-69 70-79 80-89 >90		
Ethnicity Asian or Asian British Black or Black British Mixed Other Ethnic groups Unknow White Missing		
Deprivation tenths 1 2 3 4 5 6 7 8 9 10 Missing		
Region East Midland East of England London North East North West South East South West West Midlands Yorkshire and The Humber Missing		
Medical history		
Smoking Current Ex-smoker Never-smoker Missing		
Any Stroke Yes No		
MI Yes		

No		
VTE Yes No		
Thrombophilia Yes No		
Coronavirus infection prior to vaccination Yes No		
Diabetes Yes No		
Depression Yes No		
Obesity Yes No		
Cancer Yes No		
COPD Yes No		
Liver disease Yes No		
CKD Yes No		
Major Surgery last yr Yes No		
Dementia Yes No		
Medication		
Antiplatelet Yes No		
BP lowering Yes No		
Lipid lower Yes No		
Anticoagulant Yes No		
COCP Yes No		
HRT Yes No		
Age at start Mean (sd)		
Number of GP previous year Mean (sd)		

missing		
BMI Mean (sd) missing		

Table 6 - baseline characteristics of patients with and without SARS CoV-2 **infection** on date of linkage (rows as per table 5

Table 7 baseline characteristics of patients (as per table 5) by ICVT diagnosis within 2 months of vaccination

Table 8 baseline characteristics of patients (as per table 5) by ever any venous diagnosis within 2 months of vaccination

Table 9 baseline characteristics of patients (as per table 5) by ever any arterial diagnosis within 2 months of vaccination

Table 10 baseline characteristics of patients (as per table 5) by ICVT diagnosis within 2 months of infection

Table 11 baseline characteristics of patients (as per table 5) by ever any venous diagnosis within 2 months of infection

Table 12 baseline characteristics of patients (as per table 5) by ever any arterial diagnosis within 2 months of infection

Figure 1 a-z – HR of each event (starting with ICVT) by days (0-7; 8-14; 15-21; 22-28; 29-56; 57-84; 85-140;; 141-273) since **COVID vaccine** (as per Jenny's figures), adjusting for age and other confounders etc..by AZ and Pfizer vaccine

Figure 2 a-z – HR of each event by days (0-13; 14-27; 28-41; 42-56; 56-70) since **COVID infection** (as per Jenny's figures), adjusting for age and other confounders etc..

Figure 3-x: Forest plot for each event type for **COVID vaccine** exposure, beginning all ICVT, then all venous then all arterial, and consider whether to do all events later. For each HR, adjusted for all confounders bar that in the rows (e.g. when presenting by time, adjusted for age etc..) Average HR over the first 70 days for non-time exposure. These could be produced outside TRE (if no small n…)

	Exposed		**Unexposed**		**HR (unadj)**	**95%CI**	**HR (adj)**	**95%CI**
	Event	**N**	**Event**	**N**				
Vaccine								
Astra Zeneca								
Pfizer								
Dose								
1st								
2nd								
Week since vaccine								
0-1								
1-2								
3-4								
5-8								
9-12								
13-20								
21-39								
Age groups								
0-19								
20-39								
40-59								
60-79								

80+								
Sex								
Male								
Female								
Ethnicity								
Black or Black British Mixed Other Ethnic groups Unknown White Missing								
Thrombocytopenia								
Yes								
No								
Thrombophilia								
Yes								
No								
Prior venous event								
Yes								
No								
Prior COVID infection								
Yes								
No								
OCP or HRT								
Yes								
No								
Anticoagulant								
Yes No								
Antiplatelet								
Yes No								

Columns – n/N (%) exposed // n/N (%) unexposed // forest plot figure, point estimate, size, 95%CI // unadjusted HR (95%CI) adjusted HR (95%CI)
Rows - by days since vaccine 0-13; 14-27; 28-41; 42-56; 56-70 // by age decades // female, male // presence of thrombocytopenia // by thrombophilia // by COCP or HRT //by ethnicity // by anticoagulant // by antiplatelet

Figure 4-x: Forest plot for each event type for **COVID infection** exposure, beginning all venous then all arterial, then ICVT – consider further later. For each HR, adjusted for all confounders bar that in the rows (e.g. when presenting by time, adjusted for age etc..). These could be produced outside TRE (if no small n…)

	Exposed		**Unexposed**		**HR (unadj)**	**95%CI**	**HR (adj)**	**95%CI**
	Event	N	Event	N				
Days since COVID								
0-1								
1-2								
3-4								
5-8								
9-12								
13-20								
21-39								
Age								

0-19								
20-39								
40-59								
60-79								
80+								
Sex								
Male								
Female								
Ethnicity								
Black or Black British Mixed Other Ethnic groups Unknown White Missing								
History of stroke or MI								
Yes								
No								
COVID severity								
As per Spiros' definitions								
Diabetes								
Yes								
No								
Anticoagulant								
Yes No								
Antiplatelet								
Yes No								

Columns – n/N (%) exposed // n/N (%) unexposed // forest plot figure, point estimate, size, 95%CI // unadjusted HR (95%CI) adjusted HR (95%CI)
Rows - by days since infection 0-13; 14-27; 28-41; 42-56; ; 56-70 // by age decades // female, male // presence of COVID severity // by prior history of stroke; prior history of MI; prior history of diabetes //by ethnicity // by anticoagulant // by antiplatelet //by COVID severity //

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Appendix: outcome definitions

Composite events, composed of more than one phenotype	
Arterial event	First of first of *ischaemic stroke* or *stroke of unknown type* or *myocardial infarction* or *other arterial embolism*
Arterial events + thrombocytopenia	Any *arterial event* + any *thrombocytopenia* code present during in same spell or superspell), and no prior history of *thrombocytopenia*
Venous event	first of *pulmonary embolism* or *deep venous thrombosis* or *other deep vein thrombosis* or *portal vein thrombosis* or *intracranial venous thrombosis*
Venous events + thrombocytopenia	Any *venous event* + any *thrombocytopenia* code present during in same spell or superspell), and no prior history of *thrombocytopenia*

Individual events	Phenotype	Code	description
Arterial	Incident myocardial infarction	I21	Acute myocardial infarction
Arterial	Incident myocardial infarction	I22	Subsequent myocardial infarction
Arterial	Incident myocardial infarction	I23	Certain current complications following acute myocardial infarction
Arterial	Incident myocardial infarction	primary care codes, type=1	SNOMED codes
Arterial	Retinal infarction	H34x	Retinal vascular occlusion
Arterial	Ischaemic stroke	I63x	Cerebral infarction
Arterial	Ischaemic stroke	primary care codes type=1	SNOMED codes
Arterial	Stroke of unknown type	I64x	Stroke, not specified as haemorrhage or infarction
Arterial	Stroke of unknown type	Primary care codes =1	SNOMED codes
Arterial	Stroke, subarachnoid haemorrhage	I60x	Nontraumatic subarachnoid haemorrhage
Arterial	Other arterial embolism	I74x	Arterial embolism and thrombosis
Venous	Pulmonary embolism	I26.0	Pulmonary embolism without mention of acute cor pulmonale
Venous	Pulmonary embolism	I26.9	Pulmonary embolism with mention of acute cor pulmonale
Venous	Deep vein thrombosis	I80.1	Phlebitis and thrombophlebitis of femoral vein
Venous	Deep vein thrombosis	I80.2	Phlebitis and thrombophlebitis of other deep vessels of lower extremities
Venous	Deep vein thrombosis	I80.3	Phlebitis and thrombophlebitis of lower extremities, unspecified
Venous	Portal vein thrombosis	I81	Portal vein thrombosis
Venous	Other deep vein thrombosis	I82.2	Embolism and thrombosis of vena cava
Venous	Other deep vein thrombosis	I82.3	Embolism and thrombosis of renal vein
Venous	Other deep vein thrombosis	I82.8	Embolism and thrombosis of other specified veins
Venous	Other deep vein thrombosis	I82.9	Embolism and thrombosis of unspecified vein
Venous	Thrombosis during pregnancy and puerperium	O22.3	Deep phlebothrombosis in pregnancy

Venous	Thrombosis during pregnancy and puerperium	O87.1	Deep phlebothrombosis in the puerperium
Venous	Thrombosis during pregnancy and puerperium	O87.9	Venous complication in the puerperium, unspecified
Venous	Thrombosis during pregnancy and puerperium	O88.2	Obstetric blood-clot embolism
Venous	Cerebral venous thrombosis during pregnancy and puerperium	O22.5	Cerebral venous thrombosis in pregnancy
Venous	Cerebral venous thrombosis during pregnancy and puerperium	O87.3	Cerebral venous thrombosis in the puerperium
Venous	Cerebral venous thrombosis	G08	Intracranial and intraspinal phlebitis and thrombophlebitis
Venous	Cerebral venous thrombosis	I67.6	Nonpyogenic thrombosis of intracranial venous system
Venous	Cerebral venous thrombosis	I63.6	Cerebral infarction due to cerebral venous thrombosis, nonpyogenic
Haematological	Thrombocytopenia	D69.3	Idiopathic thrombocytopenic purpura
Haematological	Thrombocytopenia	D69.4	Other primary thrombocytopenia
Haematological	Thrombocytopenia	D69.5	Secondary thrombocytopenia
Haematological	Thrombocytopenia	D69.6	Thrombocytopenia, unspecified
Haematological	Disseminated intravascular coagulation	D65	Disseminated intravascular coagulation
Haematological	Thrombotic thrombocytopenic purpura	M31.1	Thrombotic microangiopathy
Uncertain classification	Mesenteric thrombus	K55.0	Acute vascular disorders of intestine (arterial or venous)
Uncertain classification	Intracerebral haemorrhage	I61	Intracerebral haemorrhage
Arterial	Spinal stroke	G95.1	Vascular myelopathies (arterial or venous)