Supplementary materials

Supplementary table 1 Diagnosis codes for thrombocytopenia for the Truven MarketScan® (now Merative™ MarketScan®) analysis

ICD-10 code	Concept name
D69.3	Immune thrombocytopenic purpura
D75.82	HIT
D69.6	Thrombocytopenia

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HIT, heparin-induced thrombocytopenia; ICD-10, International Classification of Diseases, Tenth Revision.

Supplementary table 2 Diagnosis codes for thrombotic/thromboembolic events for the MarketScan analysis

ICD-10 code	Concept name
	Cerebral venous sinus thrombosis
G08	Intracranial and intraspinal phlebitis and thrombophlebitis
I63.6	Cerebral infarction due to cerebral venous thrombosis, nonpyogenic
I67.6	Nonpyogenic thrombosis of intracranial venous system
	Deep vein thrombosis
I80.21	Phlebitis and thrombophlebitis of iliac vein
I80.219	Phlebitis and thrombophlebitis of unspecified iliac vein
I82.2	Embolism and thrombosis of vena cava and other thoracic veins
I82.21	Embolism and thrombosis of superior vena cava
I82.210	Acute embolism and thrombosis of superior vena cava
I82.211	Chronic embolism and thrombosis of superior vena cava
I82.22	Embolism and thrombosis of inferior vena cava
I82.220	Acute embolism and thrombosis of inferior vena cava
I82.221	Chronic embolism and thrombosis of inferior vena cava
I82.29	Embolism and thrombosis of other thoracic veins

I82.290	Acute embolism and thrombosis of other thoracic veins
I82.291	Chronic embolism and thrombosis of other thoracic veins
I82.3	Embolism and thrombosis of renal vein
I82.4	Acute embolism and thrombosis of deep veins of lower extremity
I82.40x	Acute embolism and thrombosis of unspecified deep veins of lower extremity
I82.41x	Acute embolism and thrombosis of femoral vein
I82.42x	Acute embolism and thrombosis of iliac vein
I82.43x	Acute embolism and thrombosis of popliteal vein
I82.44x	Acute embolism and thrombosis of tibial vein
I82.49x	Acute embolism and thrombosis of other specified deep vein of lower extremity
I82.4Yx	Acute embolism and thrombosis of unspecified deep veins of proximal lower extremity
I82.4Zx	Acute embolism and thrombosis of unspecified deep veins of distal lower extremity
I82.62x	Acute embolism and thrombosis of deep veins of upper extremity
I82.8	Embolism and thrombosis of other specified veins
I82.81x	Embolism and thrombosis of superficial veins of lower extremities
I82.89	Embolism and thrombosis of other specified veins
I82.890	Acute embolism and thrombosis of other specified veins

I82.891	Chronic embolism and thrombosis of other specified veins
I82.9	Embolism and thrombosis of unspecified vein
I82.90	Acute embolism and thrombosis of unspecified vein
I82.91	Chronic embolism and thrombosis of unspecified vein
I82.A	Embolism and thrombosis of axillary vein
I82.A1x	Acute embolism and thrombosis of axillary vein
I82.B	Embolism and thrombosis of subclavian vein
I82.B1x	Acute embolism and thrombosis of subclavian vein
I82.C	Embolism and thrombosis of internal jugular vein
I82.C1x	Acute embolism and thrombosis of internal jugular vein
N48.81	Thrombosis of superficial vein of penis
	Intra-abdominal thrombosis
I74.0	Embolism and thrombosis of abdominal aorta
I74.09	Other arterial embolism and thrombosis of abdominal aorta
I74.5	Embolism and thrombosis of iliac artery
I81	Portal vein thrombosis
I82.0	Budd-Chiari syndrome

	Pulmonary embolism
I26.0	Pulmonary embolism with mention of acute cor pulmonale
I26.02	Saddle embolus of pulmonary artery with acute cor pulmonale
I26.09	Other pulmonary embolism with acute cor pulmonale
I26.9	Pulmonary embolism without mention of acute cor pulmonale
I26.92	Saddle embolus of pulmonary artery without acute cor pulmonale
I26.93	Single subsegmental pulmonary embolism without acute cor pulmonale
I26.94	Multiple subsegmental pulmonary emboli without acute cor pulmonale
I26.99	Other pulmonary embolism without acute cor pulmonale
	Other thromboses not otherwise classified
I63.01	Cerebral infarction due to thrombosis of vertebral artery
I63.011	Cerebral infarction due to thrombosis of right vertebral artery
I63.012	Cerebral infarction due to thrombosis of left vertebral artery
I63.013	Cerebral infarction due to thrombosis of bilateral vertebral arteries
I63.019	Cerebral infarction due to thrombosis of unspecified vertebral artery

ICD-10, International Classification of Diseases, Tenth Revision.

Supplementary table 3 Incident and overall* event rates per 1M person/21 days for TTS and by type of thrombosis/thromboembolism in adults aged ≥18 years in the MarketScan database (2019: pre-pandemic)

	Algorithm 1		Algorithm 2	
Thrombosis type†	**Events**	**Event rate per 1M person-21-days (95% CI)**	**Events**	**Event rate per 1M person-21-days (95% CI)**
Incident event rates				
All thrombotic/thromboembolic events	902	5.6 (5.3 to 6.0)	1028	6.4 (6.0 to 6.8)
CVST	22	0.1 (0.1 to 0.2)	24	0.15 (0.1 to 0.2)
DVT	613	3.8 (3.5 to 4.1)	715	4.5 (4.1 to 4.8)
Intra-abdominal	124	0.8 (0.6 to 0.9)	129	0.8 (0.7 to 1.0)
PE	363	2.3 (2.0 to 2.5)	408	2.5 (2.3 to 2.8)
Overall event rates				
All thrombotic/thromboembolic events	1783	11.1 (10.6 to 11.6)	1971	12.2 (11.7 to 12.8)
CVST	32	0.2 (0.1 to 0.3)	35	0.2 (0.15 to 0.3)
DVT	1188	7.4 (7.0 to 7.8)	1327	8.2 (7.8 to 8.7)
Intra-abdominal	267	1.7 (1.5 to 1.9)	282	1.75 (1.6 to 2.0)
PE	596	3.7 (3.4 to 4.0)	657	4.1 (3.8 to 4.4)

*Incident event counts exclude patients with thrombosis that occurred in 365 days prior to first thrombosis in 2019. Overall event counts include these patients. The first encounter in 2019 with thrombosis was categorised by subtype. Patients who had more than one subtype during this encounter were counted in each contributing type, but only once in the overall count; hence the counts of events by subtype exceed the overall count.

†All occurring with thrombocytopenia following the criteria for the algorithm used.

1M, 1 million; CI, confidence interval; CVST, cerebral venous sinus thrombosis; DVT, deep vein thrombosis; PE, pulmonary embolism; PY, person-years; TTS, thrombosis with thrombocytopenia syndrome.

Supplementary table 4 Incident and overall background TTS event rates per 1M person/21 days by age and sex from the MarketScan database (2019: pre-pandemic)

	Algorithm 1		Algorithm 2	
Event type and age group	**Event rate per 1M person-21-days (95% CI)**	**Event rate per 1M person-21-days (95% CI)**	**Event rate per 1M person-21-days (95% CI)**	**Event rate per 1M person-21-days (95% CI)**
	Female	**Male**	**Female**	**Male**
Incident event rates				
0–17 years	0.2 (0.1 to 0.6)	0.3 (0.1 to 0.6)	0.2 (0.08 to 0.6)	0.2 (0.07 to 0.5)
18–49 years	2.6 (2.2 to 3.1)	2.6 (2.2 to 3.1)	2.7 (2.2 to 3.2)	3.1 (2.6 to 3.7)
50–64 years	5.6 (4.8 to 6.5)	9.1 (8.0 to 10.3)	6.6 (5.7 to 7.6)	10.8 (9.6 to 12.1)
≥65 years	17.9 (14.6 to 21.8)	30.3 (25.4 to 35.7)	20.8 (17.2 to 24.9)	32.2 (27.2 to 37.9)
Overall event rates				
0–17 years	0.6 (0.3 to 1.0)	1.0 (0.6 to 1.5)	0.5 (0.3 to 0.9)	0.9 (0.6 to 1.4)
18–49 years	4.6 (4.0 to 5.3)	4.5 (3.9 to 5.1)	4.9 (4.3 to 5.6)	5.0 (4.4 to 5.7)
50–64 years	11.3 (10.1 to 12.5)	19.4 (17.8 to 21.1)	12.7 (11.5 to 14.0)	21.7 (20.0 to 23.5)
≥65 years	35.1 (30.4 to 40.4)	60.6 (53.7 to 68.1)	39.8 (34.7 to 45.3)	64.9 (57.7 to 72.6)

1M, 1 million; CI, confidence interval; PY, person-years; TTS, thrombosis with thrombocytopenia syndrome.

Supplementary table 5 Incident and overall* TTS event rates and by type of thrombosis/thromboembolism in adults aged ≥18 years in the MarketScan database (2017 to 2019: pre-pandemic)

	Algorithm 1			Algorithm 2		
	Events	Event rate per 100K py (95% CI)	Event rate per 1M-person-21-days (95% CI)	Events	Event rate per 100K py (95% CI)	Event rate per 1M-person-21-days (95% CI)
Incident event rates						
All thrombotic/thromboembolic events						
2017	1477	14.1 (13.4 to 14.8)	8.1 (7.7 to 8.5)	1608	15.4 (14.6 to 16.1)	8.8 (8.4 to 9.3)
2018	982	10.7 (10.0 to 11.4)	6.1 (5.8 to 6.5)	1078	11.7 (11.0 to 12.5)	6.7 (6.3 to 7.2)
2019	902	9.8 (9.1 to 10.4)	5.6 (5.3 to 6.0)	1028	11.1 (10.5 to 11.8)	6.4 (6.0 to 6.8)
CVST						
2017	8	0.1 (0.0 to 0.2)	0.04 (0.0 to 0.1)	9	0.1 (0.0 to 0.2)	0.05 (0.0 to 0.1)
2018	12	0.1 (0.1 to 0.2)	0.08 (0.0 to 0.1)	12	0.1 (0.1 to 0.2)	0.08 (0.0 to 0.1)
2019	22	0.2 (0.1 to 0.4)	0.14 (0.1 to 0.2)	24	0.3 (0.2 to 0.4)	0.15 (0.1 to 0.2)
DVT						
2017	966	9.2 (8.7 to 9.8)	5.3 (5.0 to 5.6)	1068	10.2 (9.6 to 10.8)	5.9 (5.5 to 6.2)
2018	680	7.4 (6.9 to 8.0)	4.3 (3.9 to 4.6)	750	8.2 (7.6 to 8.8)	4.7 (4.4 to 5.0)

2019	613	6.6 (6.1 to 7.2)	3.8 (3.5 to 4.1)	715	7.7 (7.2 to 8.3)	4.5 (4.1 to 4.8)
Intra-abdominal						
2017	163	1.6 (1.3 to 1.8)	0.9 (0.8 to 1.0)	166	1.6 (1.4 to 1.8)	0.9 (0.8 to 1.1)
2018	110	1.2 (1.0 to 1.4)	0.7 (0.6 to 0.8)	125	1.4 (1.1 to 1.6)	0.8 (0.7 to 0.9)
2019	124	1.3 (1.1 to 1.6)	0.8 (0.6 to 0.9)	129	1.4 (1.2 to 1.7)	0.8 (0.7 to 1.0)
PE						
2017	618	5.9 (5.4 to 6.4)	3.4 (3.1 to 3.7)	675	6.4 (6.0 to 7.0)	3.7 (3.4 to 4.0)
2018	393	4.3 (3.9 to 4.7)	2.5 (2.2 to 2.7)	424	4.6 (4.2 to 5.1)	2.7 (2.4 to 2.9)
2019	363	3.9 (3.5 to 4.4)	2.3 (2.0 to 2.5)	408	4.4 (4.0 to 4.9)	2.5 (2.3 to 2.8)
Overall event rates						
All thrombotic/thromboembolic events						
2017	2746	26.1 (25.2 to 27.1)	15.0 (14.5 to 15.6)	2890	27.5 (26.5 to 28.5)	15.8 (15.2 to 16.4)
2018	1936	21.0 (20.1 to 22.0)	12.1 (11.6 to 12.6)	2063	22.4 (21.4 to 23.4)	12.9 (12.3 to 13.4)
2019	1783	19.3 (18.4 to 20.2)	11.1 (10.6 to 11.6)	1971	21.3 (20.4 to 22.3)	12.2 (11.7 to 12.8)
CVST						
2017	23	0.2 (0.1 to 0.3)	0.1 (0.1 to 0.2)	23	0.2 (0.1 to 0.3)	0.1 (0.1 to 0.2)
2018	17	0.2 (0.1 to 0.3)	0.1 (0.1 to 0.2)	17	0.2 (0.1 to 0.3)	0.1 (0.1 to 0.2)
2019	32	0.3 (0.2 to 0.5)	0.2 (0.1 to 0.3)	35	0.4 (0.3 to 0.5)	0.2 (0.2 to 0.3)

DVT						
2017	1790	17.0 (16.3 to 17.8)	9.8 (9.3 to 10.3)	1870	17.8 (17.0 to 18.6)	10.2 (9.8 to 10.7)
2018	1293	14.0 (13.3 to 14.8)	8.1 (7.6 to 8.5)	1374	14.9 (14.1 to 15.7)	8.6 (8.1 to 9.0)
2019	1188	12.8 (12.1 to 13.6)	7.4 (7.0 to 7.8)	1327	14.3 (13.6 to 15.1)	8.2 (7.8 to 8.7)
Intra-abdominal						
2017	341	3.2 (2.9 to 3.6)	1.9 (1.7 to 2.1)	361	3.4 (3.1 to 3.8)	2.0 (1.8 to 2.2)
2018	251	2.7 (2.4 to 3.1)	1.6 (1.4 to 1.8)	274	3.0 (2.6 to 3.3)	1.7 (1.5 to 1.9)
2019	267	2.9 (2.5 to 3.3)	1.7 (1.5 to 1.9)	282	3.0 (2.7 to 3.4)	1.8 (1.6 to 2.0)
PE						
2017	967	9.2 (8.6 to 9.8)	5.3 (5.0 to 5.6)	1043	9.9 (9.3 to 10.6)	5.7 (5.4 to 6.1)
2018	685	7.4 (6.9 to 8.0)	4.3 (4.0 to 4.6)	729	7.9 (7.3 to 8.5)	4.5 (4.2 to 4.9)
2019	596	6.4 (5.9 to 7.0)	3.7 (3.4 to 4.0)	657	7.1 (6.6 to 7.7)	4.1 (3.8 to 4.4)

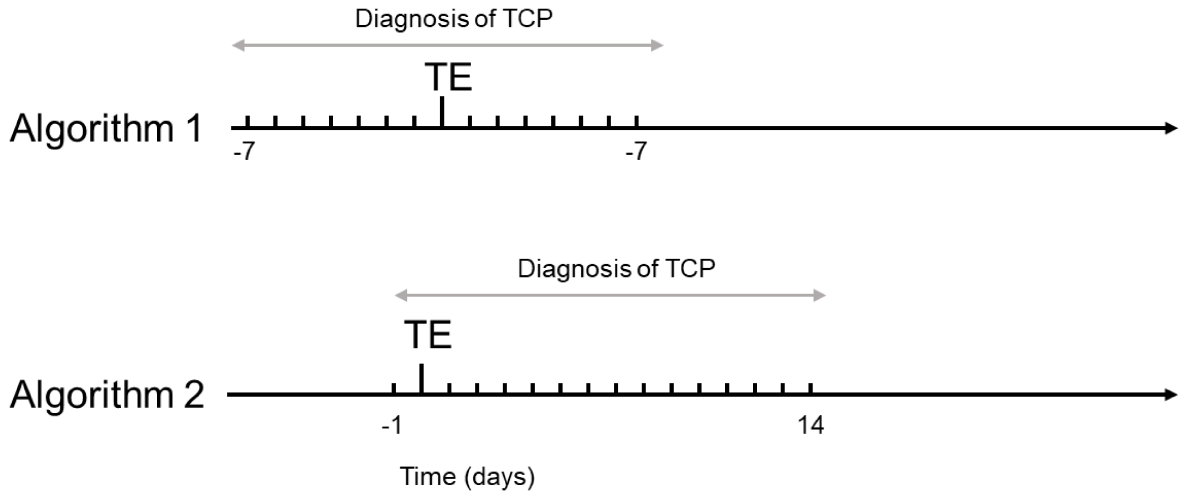
1M, 1 million; CI, confidence interval; CVST, cerebral venous sinus thrombosis; DVT, deep vein thrombosis; PE, pulmonary embolism; PY, person-years; TTS, thrombosis with thrombocytopenia syndrome.

Supplementary table 6 Definition of TTS across studies

Study	Definition of TE	Definition of TCP	Period used to identify an overlap of TE and TCP events	Period used to extract TTS events from the database
ACCESS[1]	VTE (DVT and PE), arterial (CAD narrow, and ischaemic stroke), VTE or arterial, CVST (broad)	Diagnosis codes for TCP (primary and secondary)	+/- 10 days	The latest of having 1 year of valid data in the data source, or 1 January 2017 (2010 for Denmark, 2014 for Germany)
Burn et al[2]	Diagnosis codes for individual events of: CVST, DVT, PE, SVT, myocardial infarction or ischemic stroke	Diagnosis code for TCP or a measurement of 10 000–150 000 platelets per µL of blood	+/- 10 days	1 January 2017 to 31 December 2019
Original MarketScan analysis [Algorithm 1] [3]	See supplementary table 2	See supplementary table 1	+/- 7 days	1 January 2019 to 31 December 2019

CAD, coronary artery disease; CVST, cerebral venous sinus thrombosis; DVT, deep vein thrombosis; PE, pulmonary embolism; SVT, splanchnic vein thrombosis; TCP, thrombocytopenia; TE, thrombotic event; TTS, thrombosis with thrombocytopenia syndrome; VTE, venous thromboembolism; –, not available.

Supplementary figure 1 Algorithm definitions for the Truven MarketScan® (now Merative™ MarketScan®) analysis



TE, thrombotic/thromboembolic event; TCP, thrombocytopenia.

Supplementary references

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