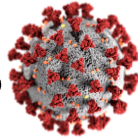


EVENT DEFINITION FORM

Event: thrombocytopenia
Outcome/covariate: outcome
Version: 1.0
Status: final

Contributing authors

authors	Role	Date
Miriam Sturkenboom	Codemapping	
Corinne Willame	Algorithm proposal	02 Sep 2020
Miriam Sturkenboom	Final code list	23-3-2021
Carlos Durán	Review narrow/possible assignment	26-03-2021
Miriam Sturkenboom	Updating final codes	8-8-2021



1. Event definition & validity classifications

Brighton Collaboration Criteria; Thrombocytopenia (Wise et al.)

TP is an abnormally low platelet count. Pathogenic mechanisms include insufficient production, abnormal distribution, or excessive destruction of platelets. Excessive destruction can be caused by microangiopathy, hereditary platelet abnormalities, or immunologic mechanisms. Immunologic TP can be caused by autoimmune mechanisms, neonatal isoimmunization, or a nonspecific immune response. Idiopathic TP (ITP) refers to TP without an identified etiology, although an autoimmune etiology is frequently suspected but not always verified through exhaustive exclusion of differential diagnoses

Level 1 of diagnostic certainty (confirmed TP)

Platelet count^a less than $150 \times 10^9 \text{ L}^{-1}$

AND

confirmed by blood smear examination OR the presence of clinical signs and symptoms of spontaneous bleeding^b

Level 2 of diagnostic certainty (unconfirmed TP)

Platelet count^a less than $150 \times 10^9 \text{ L}^{-1}$

Level 3 of diagnostic certainty

Not applicable

^a Measured by an automated hematology analyzer or assessed by hand count of platelets on a cell count slide.

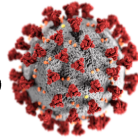
^b Presentations of spontaneous (i.e., non-traumatic) bleeding include purpura (i.e., petechiae, purpura sensu stricto, ecchymosis), hemorrhagic oozing of skin lesions including rashes, hematoma, bruising, hematemesis, hematochezia, occult bleeding per rectum, epistaxis, hemoptysis, hematuria, vaginal bleeding other than menstruation, conjunctival bleeding, intracranial bleeding.

2. Synonyms / lay terms used

Low platelet count

3. Laboratory tests done specific for event

Complete blood count (CBC). Peripheral blood smear



Full Blood Count (FBC) and smear show isolated thrombocytopenia. Bone marrow biopsy is required in patients over 60 years old to exclude myelodysplastic syndrome or lymphoproliferative disorders. (Ref BMJ) However, this practice is no longer recommended, since long-term monitoring of older adults with ITP has not revealed an increased incidence of MDS.^[5, 6]

Anemia from blood loss may be present, but it should be proportional to the amount, and the duration, of bleeding and may result in iron deficiency (evidence level IV). If anemia is found, the reticulocyte count may help define whether it the result of poor production or increased destruction of red blood cells (RBCs).

4. Diagnostic tests done specific for event

No specific test

5. Drugs used specific for event treatment

Combination therapy of corticosteroids, IV immunoglobulin, and platelet transfusion.

Romiplostim and eltrombopag, are FDA-approved for the treatment of ITP. Romiplostim is administered as a 1 to 10 µg/kg subcutaneous weekly injection

6. Procedures used specific for event treatment

Splenectomy

Platelet transfusion

7. Setting (outpatient specialist, in-hospital, GP, emergency room) where condition will be most frequently /reliably diagnosed

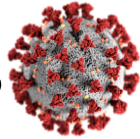
Outpatient and hospital

8. Diagnosis codes or algorithms used in different papers to extract the events in Europe/USA: seek literature for papers that have studied this event, and see how they extracted/measured the event.

Thrombocytopenia Codes (VAESCO)

-please note this is a broader category than Idiopathic thrombocytopenic purpura

READ-GPRD: 42P2.00, 42P2.11, C391211, D312.00, D313.00, D313.12, D313.15, D313000, D313012, D313111, D313200, D313300, D313y00, D313z00, D313z11, D314.00, D314100, D314y00, D314z00, D315.00, Dyu3200, G756100,



READ1309-THIN

42P2.00	Thrombocytopenia
42P2.11	Auto-immune thrombocytopenia
C391211	Thrombocytopenic eczema with immunodeficiency
D312.00	Other nonthrombocytopenic purpura
D313.00	Primary thrombocytopenia
D313.12	Idiopathic thrombocytopenic purpura
D313.15	Thrombocytopenic purpura
D313000	Idiopathic thrombocytopenic purpura
D313012	ITP - idiopathic thrombocytopenic purpura
D313111	Hereditary thrombocytopenia NEC
D313200	Thrombocytopenic purpura with absent radius
D313300	[X]Essential thrombocytopenia NOS
D313y00	Other specified primary thrombocytopenia
D313z00	Primary thrombocytopenia NOS
D313z11	Essential thrombocytopenia NOS
D314.00	Secondary thrombocytopenia
D314100	Thrombocytopenia due to drugs
D314y00	Other specified secondary thrombocytopenia
D314z00	Secondary thrombocytopenia NOS
D315.00	Thrombocytopenia NOS
Dyu3200	[X]Other primary thrombocytopenia
G756100	Thrombotic thrombocytopenic purpura

D313.11 Evan's syndrome

ICD-9: 279.12*, 283.11*, 284.1*, 287.3, 287.5, 287.4, 446.6, 776.1*

* Please note:

279.12 wiskott-aldrich syndrome (X-linked recessive disease)

283.11 Haemolytic-uraemic syndrome (Not an isolated thrombocytopenia)

284.1: are drug-induced bone marrow suppression, a non-immune phenomenon

284.11 antineoplastic chemotherapy induced pancytopenia

284.12 other drug induced pancytopenia

284.19 other pancytopenia

287.3

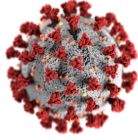
287.30 primary thrombocytopenia,unspecified

287.31 immune thrombocytopenic purpura

287.32 Evans' syndrome (autoimmune disorder)

287.33 congenital and hereditary thrombocytopenic purpura

287.39 other primary thrombocytopenia

**287.4**

287.41 posttransfusion purpura (ADR following blood/platelet transfusion)

287.49 other secondary thrombocytopenia

287.5 thrombocytopenia unspecified

446.6 thrombotic microangiopathy

776.1 transient neonatal thrombocytopenia

ICD-10: D59.3**, D61**, D69.3, D69.4, D69.5, D69.6, D82.0** M31.1**ICPI:** B82***, B83*****Evaluation of thrombocytopenia algorithms Sentinel ([Mini-Sentinel Methods - 11 - 16 HOIs for Surveillance Preparedness](#))¹**

For defining the outcome of thrombocytopenia, the workgroup principally proposes the following composite algorithm based on published literature and expert advice: at least one inpatient, any position, diagnosis of the following ICD-9 codes: 287.1 [*qualitative platelet defects*], 287.30, 287.31, 287.32, 287.33 [*congenital and hereditary thrombocytopenic purpura*], 287.39, 287.4, 287.5, 289.84. The workgroup decided to add a code specific for HIT (289.84) to Galdarossa's algorithm. This code has not yet been validated but holds great potential to identify HIT specifically in the absence of laboratory values. The workgroup does not prefer to recommend studies using non-US data based on concerns with generalizability; however, the paper by Galdarossa et al. is the only published validation study evaluating the new codes for thrombocytopenia. Therefore, as a secondary algorithm, the workgroup proposes the algorithm from Galdarossa et al.: at least one inpatient diagnosis of the following ICD-9 codes, in any position: 287.1, 287.30, 287.31, 287.32, 287.33, 287.39, 287.4, 287.5. This secondary algorithm may be preferred if HIT is not of interest.

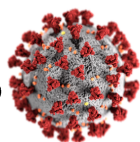
9. Experience of participating data sources in extracting the events prior to ACCESS

AEMPS (BIFAP) has experience in extracting this event within the ADVANCE project.

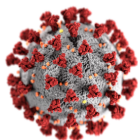
10. Codes used

Coding system	Code	Code name	Concept	Algorithm
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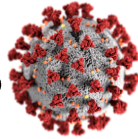
¹ https://www.sentinelinitiative.org/sites/default/files/surveillance-tools/validations-literature/Mini-Sentinel_16_HOIs_Surveillance-Preparedness.pdf



ICD10/CM	D59.3	Haemolytic-uraemic syndrome	C0019061	Possible
ICD10/CM	D69.3	Hemorrhagic (thrombocytopenic) purpura	C2873806	Narrow
ICD10/CM	D69.3	Idiopathic thrombocytopenic purpura	C0398650	Narrow
ICD10/CM	D69.3	Tidal platelet dysgenesis	C0272282	Narrow
ICD10/CM	D69.4	Other primary thrombocytopenia	C0477317	Narrow
ICD10/CM	D69.41	Evans syndrome	C0272126	Possible
ICD10/CM	D69.49	Other primary thrombocytopenia	C0477317	Narrow
ICD10/CM	D69.5	Secondary thrombocytopenia	C0154301	Narrow
ICD10/CM	D69.6	Thrombocytopenia, unspecified	C0040034	Narrow
ICD10/CM	M31.1	Thrombotic thrombocytopenic purpura	C0034155	Narrow
ICD10/CM	D75.82	Heparin induced thrombocytopenia		possible
ICD9CM	283.11	Hemolytic-uremic syndrome	C0019061	Possible
ICD9CM	287.31	Immune thrombocytopenic purpura	C0398650	Narrow
ICD9CM	287.32	Evans' syndrome	C0272126	Possible
ICD9CM	287.39	Other primary thrombocytopenia	C0477317	Narrow
ICD9CM	287.4	Secondary thrombocytopenia	C0154301	Narrow
ICD9CM	287.5	Thrombocytopenia, unspecified	C0040034	Narrow
ICD9CM	446.6	Thrombotic microangiopathy	C2717961	Narrow
ICD9CM	289.94	Heparin induced thrombocytopenia		possible
ICPC2P	B83006	Idiopath Thrombocytopenic Purp	C0398650	Narrow
ICPC2P	B83012	Thrombocytopenia	C0040034	Narrow
ICPC	B83.02	ITP		narrow
RCD2	42P2.	Thrombocytopenia	C0040034	Narrow
RCD2	D1113	Haemolytic-uraemic syndrome	C0019061	Possible
RCD2	D313.	Primary thrombocytopenia	C0857305	Narrow
RCD2	D3130	Thrombocytopen purp-idiopathic	C0398650	Narrow
RCD2	D3133	[X]Essent thrombocytopenia NOS	C0677060	Narrow
RCD2	D313z	Primary thrombocytopenia NOS	C0677060	Narrow
RCD2	D314.	Secondary thrombocytopenia	C0154301	Narrow
RCD2	D314z	Secondary thrombocytopenia NOS	C0154301	Narrow
RCD2	D315.	Thrombocytopenia NOS	C0040034	Narrow
RCD2	Dyu32	[X]Oth primry thrombocytopenia	C0477317	Narrow
RCD2	Dyu32	[X]Oth primry thrombocytopenia	C0477317	Narrow
RCD2	G756.	Thrombotic microangiopathy	C0034155	Narrow
RCD2	G756.	Thrombotic microangiopathy	C2717961	Narrow
RCD2	G756z	Thrombotic microangiopathy NOS	C2717961	Narrow
RCD2	D3143	Heparin induced thrombocytopenia		Possible
SCTSPA	13172003	enfermedad de Werlhof	C0398650	Narrow
SCTSPA	28505005	púrpura trombocitopénica idiopática aguda	C0272292	Narrow
SCTSPA	32273002	púrpura trombocitopénica idiopática	C0398650	Narrow
SCTSPA	48788004	trombocitopenia cíclica	C0272282	Narrow
SCTSPA	70786006	trombocitopenia	C0040034	Narrow



SCTSPA	74576004	trombocitopenia adquirida	C0154301	Narrow
SCTSPA	75331009	síndrome de Evans	C0272126	Possible
SCTSPA	78129009	púrpura trombocitopénica trombótica	C0034155	Narrow
SCTSPA	111407006	síndrome urémico hemolítico	C0019061	Possible
SCTSPA	123308008	síndrome urémico hemolítico - RETIRADO -	C0019061	Possible
SCTSPA	126729006	microangiopatía trombótica	C2717961	Narrow
SCTSPA	128091003	trombocitopenia autoinmunitaria	C0242584	Narrow
SCTSPA	154826009	trombocitopenia secundaria	C0154301	Narrow
SCTSPA	154827000	Thrombocytopenia NOS	C0040034	Narrow
SCTSPA	191318001	trombocitemia esencial, SAI	C0677060	Narrow
SCTSPA	191326009	plaquetopenia, SAI	C0040034	Narrow
SCTSPA	191435001	[X]otra trombocitopenia primaria	C0477317	Narrow
SCTSPA	195360005	microangiopatía trombótica, SAI	C2717961	Narrow
SCTSPA	234481002	trombocitopenia esencial, SAI	C0677060	Narrow
SCTSPA	234490009	púrpura trombocitopénica autoinmune	C0398650	Narrow
SCTSPA	267537007	trombocitopenia secundaria, SAI	C0154301	Narrow
SCTSPA	302215000	trastorno trombocitopénico	C0040034	Narrow
SCTSPA	302873008	púrpura trombocitopénica	C0857305	Narrow
SCTSPA	415116008	recuento plaquetario por debajo del rango de referencia	C0392386	Possible
SCTSPA	415116008	trombocitopenia	C0040034	Narrow
SNOMEDCT_US	2897005	Auto-immune thrombocytopenia	C0242584	Narrow
SNOMEDCT_US	13172003	Autoimmune thrombocytopenic purpura	C0398650	Narrow
SNOMEDCT_US	28505005	Acute idiopathic thrombocytopenic purpura	C0272292	Narrow
SNOMEDCT_US	28505005	Acute idiopathic thrombocytopenic purpura	C0272292	Narrow
SNOMEDCT_US	32273002	Idiopathic thrombocytopenic purpura	C0398650	Narrow
SNOMEDCT_US	48788004	Cyclic thrombocytopenia	C0272282	Narrow
SNOMEDCT_US	70786006	Decreased platelet count	C0392386	Possible
SNOMEDCT_US	70786006	Thrombocytopenia	C0040034	Narrow
SNOMEDCT_US	74576004	Acquired thrombocytopenia	C0154301	Narrow
SNOMEDCT_US	75331009	Evans syndrome	C0272126	Possible
SNOMEDCT_US	78129009	Thrombotic thrombocytopenic purpura	C0034155	Narrow
SNOMEDCT_US	78129009	Thrombotic microangiopathy	C2717961	Narrow
SNOMEDCT_US	111407006	Hemolytic uremic syndrome	C0019061	Possible
SNOMEDCT_US	123308008	Haemolytic uraemic syndrome	C0019061	Possible
SNOMEDCT_US	126729006	Thrombotic microangiopathy	C2717961	Narrow
SNOMEDCT_US	128091003	Autoimmune thrombocytopenia	C0242584	Narrow
SNOMEDCT_US	142969008	Thrombocytopenia	C0040034	Narrow
SNOMEDCT_US	154822006	Thrombocytopenic purpura	C0857305	Narrow
SNOMEDCT_US	154825008	Ideopath thrombocytopenic pur	C0398650	Narrow
SNOMEDCT_US	154826009	Secondary thrombocytopenia	C0154301	Narrow
SNOMEDCT_US	154827000	Thrombocytopenia NOS	C0040034	Narrow
SNOMEDCT_US	155443009	Thrombotic thrombocytopenic purpura	C0034155	Narrow



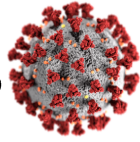
SNOMEDCT_US	155443009	Thrombotic thrombocytopenic purpura	C0034155	Narrow
SNOMEDCT_US	165556002	Auto-immune thrombocytopenia	C0242584	Narrow
SNOMEDCT_US	165556002	Thrombocytopenia	C0040034	Narrow
SNOMEDCT_US	191315003	Evan's syndrome	C0272126	Possible
SNOMEDCT_US	191315003	Idiopathic purpura	C0398650	Narrow
SNOMEDCT_US	191315003	Thrombocytopenic purpura	C0857305	Narrow
SNOMEDCT_US	191315003	Thrombocytopenic purpura	C0857305	Narrow
SNOMEDCT_US	191316002	Idiopathic purpura	C0398650	Narrow
SNOMEDCT_US	191318001	[X]Essential thrombocytopenia NOS	C0677060	Narrow
SNOMEDCT_US	191320003	Essential thrombocytopenia NOS	C0677060	Narrow
SNOMEDCT_US	191325008	Secondary thrombocytopenia NOS	C0154301	Narrow
SNOMEDCT_US	191326009	Thrombocytopenia NOS	C0040034	Narrow
SNOMEDCT_US	191435001	[X]Other primary thrombocytopenia	C0477317	Narrow
SNOMEDCT_US	195359000	Thrombotic thrombocytopenic purpura	C0034155	Narrow
SNOMEDCT_US	195360005	Thrombotic microangiopathy NOS	C2717961	Narrow
SNOMEDCT_US	234481002	Essential thrombocytopenia NOS	C0677060	Narrow
SNOMEDCT_US	234490009	Immune thrombocytopenic purpura	C0398650	Narrow
SNOMEDCT_US	267537007	Secondary thrombocytopenia NOS	C0154301	Narrow
SNOMEDCT_US	267564008	Thrombocytopenic purpura	C0857305	Narrow
SNOMEDCT_US	267567001	Ideopath thrombocytopenic pur	C0398650	Narrow
SNOMEDCT_US	275758003	Autoimmune thrombocytopenia	C0242584	Narrow
SNOMEDCT_US	302215000	Thrombocytopenic disorder	C0040034	Narrow
SNOMEDCT_US	302873008	Thrombocytopenic purpura	C0857305	Narrow
SNOMEDCT_US	360402008	Moschcowitz syndrome	C0034155	Narrow
SNOMEDCT_US	415116008	Platelet count below reference range	C0392386	Possible
SNOMEDCT_US	415116008	Thrombocytopenia	C0040034	Narrow
SNOMEDCT_US	32273002	Idiopathic thrombocytopenic purpura		narrow
SNOMEDCT_US	73162004	Post-transfusion purpura		possible
SNOMEDCT_US	73397007	Heparin induced thrombocytopenia		possible
SNOMEDCT_US	85589009	Thrombocytopenic purpura with absent radius		narrow
SNOMEDCT_US	191322006	Thrombocytopenia due to drugs		possible
SNOMEDCT_US	267534000	Primary thrombocytopenia		narrow

11. References

Wise RP, Bonhoeffer J, Beeler J, Donato H, Downie P, Matthews D, Pool V, Riise-Bergsaker M, Tapiainen T, Varricchio F; Brighton Collaboration Thrombocytopenia Working Group. Thrombocytopenia: case definition and guidelines for collection, analysis, and presentation

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10.1016/j.vaccine.2007.02.067. Epub 2007 Mar 12. PMID: 17493712.

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