Supplementary Materials

Corticosteroids and Thrombotic Risk in Immune Thrombocytopenia: A Systematic Review and Meta-Analysis

PROSPERO CRD420261504746

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Table S1. Full search strategies.

All searches were run by D.-C.P. on 28 September 2026. Structure of the bibliographic searches: ITP concept AND (thrombosis concept OR corticosteroid-safety arm), from 1 January 2000 onwards. Registry searches combined the ITP condition with corticosteroid and TPO-RA intervention terms. No search filters other than date and animal exclusion were applied. Records were exported and de-duplicated before screening (6587 records; 1920 duplicates removed; 4667 records screened).

Source	Platform / interface	Records	Export file
MEDLINE	PubMed (History #27)	1851	PubMed_2026-09-28.txt
Scopus	Elsevier (Search History #5)	3680	Scopus_2026-09-28.ris
CENTRAL	Cochrane Library, Issue 8 of 12, August 2026	552 (582 before year limit)	CENTRAL_2026-09-28.ris
LILACS	Virtual Health Library portal, LILACS filter	46	LILACS_2026-09-28.csv
ClinicalTrials.gov	clinicaltrials.gov	248 studies	CTgov_2026-09-28.csv
WHO ICTRP	trialsearch.who.int, Advanced Search	333 records (210 trials)	ICTRP_2026-09-28.xml
Total		6587	

S1.1. MEDLINE via PubMed (28 September 2026; 1851 records)

```
(("Purpura, Thrombocytopenic, Idiopathic"[Mesh] OR "immune thrombocytopenia"[tiab] OR "immune thrombocytopenic purpura"[tiab] OR "idiopathic thrombocytopenic purpura"[tiab] OR "idiopathic thrombocytopenia"[tiab] OR "autoimmune thrombocytopenia"[tiab] OR "autoimmune thrombocytopenic purpura"[tiab] OR "primary immune thrombocytopenia"[tiab] OR "ITP"[tiab]) AND (("Thrombosis"[Mesh] OR "Thromboembolism"[Mesh] OR "Venous Thromboembolism"[Mesh] OR "Pulmonary Embolism"[Mesh] OR "Stroke"[Mesh] OR "Ischemic Stroke"[Mesh] OR "Ischemic Attack, Transient"[Mesh] OR "Myocardial Infarction"[Mesh] OR "Mesenteric Ischemia"[Mesh] OR "Budd-Chiari Syndrome"[Mesh] OR thrombos*[tiab] OR thrombotic[tiab] OR thromboembol*[tiab] OR embolism*[tiab] OR VTE[tiab] OR DVT[tiab] OR stroke*[tiab] OR "myocardial infarction*"[tiab] OR "transient ischemic attack*"[tiab] OR "transient ischaemic attack*"[tiab] OR "Budd-Chiari"[tiab] OR "mesenteric ischemia"[tiab] OR "mesenteric ischaemia"[tiab]) OR "Adrenal Cortex Hormones/adverse effects"[Mesh] OR "Glucocorticoids/adverse effects"[Mesh] OR ((corticosteroid*[ti] OR glucocorticoid*[ti] OR steroid*[ti] OR dexamethasone[ti] OR prednisone[ti] OR prednisolone[ti] OR methylprednisolone[ti]) AND (adverse*[tiab] OR safety[tiab] OR complication*[tiab] OR "side effect*"[tiab] OR toxicit*[tiab] OR risks[tiab])))) AND ("2000/01/01"[dp] : "3000/12/31"[dp]) NOT ("Animals"[Mesh] NOT "Humans"[Mesh])
```

Run as a single query in PubMed Advanced Search (History #27). The corticosteroid-safety arm was added because a known relevant study (Kashiwagi 2025) contains no thrombosis term in its title, abstract, or indexing. Corticosteroid terms were restricted to the title to limit records that mention corticosteroids only incidentally.

S1.2. Scopus (28 September 2026; 3680 records)

```
TITLE-ABS-KEY ( "immune thrombocytopenia" OR "immune thrombocytopenic purpura" OR "idiopathic thrombocytopenic purpura" OR "idiopathic thrombocytopenia" OR "autoimmune thrombocytopenia" OR "autoimmune thrombocytopenic purpura" OR "primary immune thrombocytopenia" OR ITP ) AND ( TITLE-ABS-KEY ( thrombos* OR thrombotic OR thromboembol* OR embolism* OR VTE OR DVT OR stroke* OR "myocardial infarction*" OR "transient ischemic attack*" OR "transient ischaemic attack*" OR "Budd-Chiari" OR "mesenteric ischemia" OR "mesenteric ischaemia" ) OR ( TITLE ( corticosteroid* OR glucocorticoid* OR steroid* OR dexamethasone OR prednisone OR prednisolone OR methylprednisolone ) AND TITLE-ABS ( adverse* OR safety OR complication* OR "side effect*" OR toxicit* OR risks ) ) ) AND PUBYEAR > 1999 AND NOT ( TITLE-ABS-KEY ( mice OR mouse OR murine OR rat OR rats ) AND NOT TITLE-ABS-KEY ( patient* OR human* ) )
```

Advanced document search, Search History #5. Same logic as the PubMed strategy; Scopus was searched in place of Embase, to which the review team had no access.

S1.3. Cochrane CENTRAL (28 September 2026; 552 trials)

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("immune thrombocytopenia" OR "immune thrombocytopenic purpura" OR "idiopathic thrombocytopenic purpura" OR "idiopathic thrombocytopenia" OR "autoimmune thrombocytopenia" OR "autoimmune thrombocytopenic purpura" OR "primary immune thrombocytopenia" OR ITP) AND (thrombos* OR thrombotic OR thromboembol* OR embolism* OR VTE OR DVT OR stroke* OR "myocardial infarction" OR "myocardial infarctions" OR "transient ischemic attack" OR "transient ischaemic attack" OR "Budd Chiari" OR "mesenteric ischemia" OR "mesenteric ischaemia" OR ((corticosteroid* OR glucocorticoid* OR steroid* OR dexamethasone OR prednisone OR prednisolone OR methylprednisolone) AND (adverse* OR safety OR complication* OR "side effect" OR "side effects" OR toxicit* OR risks)))
```

Cochrane Library Search tab, single line, field set to Title Abstract Keyword; Year first published 2000–2026 applied on the results page (582 trials before the limit). Interface-imposed differences: no MeSH headings; phrase truncation replaced by explicit singular and plural forms; the corticosteroid-safety arm is searched in title, abstract, and keywords rather than title only.

S1.4. LILACS (28 September 2026; 46 records)

```
(mh:"Purpura, Thrombocytopenic, Idiopathic" OR tw:("immune thrombocytopenia" OR "idiopathic thrombocytopenic purpura" OR "trombocitopenia inmune" OR "trombocitopenia imune" OR "purpura trombocitopenica idiopatica" OR "purpura trombocitopenica" OR PTI OR ITP)) AND (mh:Thrombosis OR mh:Thromboembolism OR mh:"Pulmonary Embolism" OR mh:Stroke OR mh:"Myocardial Infarction" OR tw:(thrombos$ OR trombos$ OR thromboembol$ OR tromboembol$ OR embolism OR embolia
```

```
OR stroke OR "acidente vascular cerebral" OR "accidente cerebrovascular" OR "myocardial infarction" OR "infarto do miocardio" OR "infarto del miocardio") OR ti:(corticoster$ OR glucocortic$ OR steroid$ OR esteroid$ OR dexamet$ OR prednis$ OR corticoide$))
```

Virtual Health Library portal (lilacs.bvsalud.org), Database filter = LILACS. Spanish and Portuguese terms written without diacritics (the portal is accent-insensitive); $ is the VHL truncation symbol. The corticosteroid arm is simplified to a corticosteroid term in the title, without adverse-event terms, given the small size of LILACS. All 46 records were published from 2000 onwards.

S1.5. ClinicalTrials.gov (28 September 2026; 248 studies)

Condition/disease: immune thrombocytopenia OR idiopathic thrombocytopenic purpura OR ITP

Intervention/treatment: dexamethasone OR prednisone OR prednisolone OR methylprednisolone OR corticosteroid OR glucocorticoid OR eltrombopag OR romiplostim OR avatrombopag OR hetrombopag

Study starts from 01/01/2000; all recruitment statuses, ages, and study types. Thrombosis terms were not used because registries report thrombosis only within adverse-event results. The count before the date filter was not recorded. TARGET 020 (NCT04747080) was retrieved.

S1.6. WHO ICTRP (28 September 2026; 333 records for 210 trials)

Condition: immune thrombocytopenia OR idiopathic thrombocytopenic purpura OR ITP

Intervention: dexamethasone OR prednisone OR prednisolone OR methylprednisolone OR corticosteroid OR glucocorticoid OR eltrombopag OR romiplostim OR avatrombopag OR hetrombopag

Advanced Search; Condition AND Intervention; recruitment status ALL; date of registration 01/01/2000 to 28/09/2026.

S1.7. Other methods and search validation

Reference lists of the included studies and of relevant reviews were screened. One report identified in this way (Wang L 2019, Platelets) [71] was assessed and excluded because thrombosis was not reported. The strategies were validated against seven studies identified before the search (Lafaurie 2021, Ruggeri 2014, Kashiwagi 2025, Therme 2026, Lee 2026, Hamed 2023 and Demirci 2025); all seven were retrieved in PubMed and Scopus, and Hamed 2023, the only randomized trial among them, was retrieved in CENTRAL. The search strategies were not peer-reviewed by an information specialist. Databases that were freely accessible or available through the authors' institution were searched; databases requiring an additional subscription, including Chinese bibliographic databases, were not searched.

Table S2. Full-text reports excluded, with reasons.

No.	Study	Design	Reason for exclusion	Details
1	Kashiwagi 2025 [20]	Claims-database nested case–control (Japan)	Non-comparable outcome or exposure contrast	Composite outcome includes cerebral hemorrhage and angina; adjusted OR (2.16) not comparable with the pooled outcomes
2	Yang 2022 [54]	Retrospective case–control (China)	Non-comparable outcome or exposure contrast	Only a duration contrast (>8 vs ≤8 weeks) reported, not exposed vs unexposed; internal inconsistencies
3	Sarpatwari 2010 [8]	Population-based cohort (UK GPRD)	Exposure window not defined	Reviewer-calculated incidence-rate ratios only; exposure window unclear (time-fixed exposure)
4	Lee 2026 [55]	Retrospective cohort (Korea)	Corticosteroid exposure not separable	GC not separable from IVIg (GC ± IVIg group); only a group event rate reported
5	Demirci 2025 [56]	Nationwide retrospective study (Türkiye)	No denominator by exposure	Arterial cases only, no denominator by corticosteroid exposure
6	Wang JD 2024 [19]	Population-based cohort (Taiwan)	Thrombosis not reported or not separable	Thrombosis not separated from broader adverse-event composites
7	Ekstrand 2019 [57]	Two nationwide cohorts (Sweden, France)	Thrombosis not stratified by corticosteroid exposure	Not stratified by CS exposure; Swedish estimate not received; French arm overlaps FAITH
8	Goncalves 2024 [58]	Retrospective cohort	Thrombosis not stratified by corticosteroid exposure	Thrombosis not stratified by CS exposure
9	Palandri 2018 [59]	Single-center cohort (Italy)	Thrombosis not stratified by corticosteroid exposure	Thrombosis not stratified by CS exposure
10	Wei 2016 [60]	Randomized trial (China)	Thrombosis not reported or not separable	Thrombosis not reported in either arm; data not received
11	An 2021 (TARGET 020) [61]	Randomized trial, conference abstract	Thrombosis not reported or not separable	Conference abstract with no extractable thrombosis data
12	Zordan 2026 [62]	Target trial emulation (FAITH)	Corticosteroid exposure not separable	CS entered only as an adjustment covariate; population overlaps Lafaurie 2021
13	Garabet 2019 [63]	Randomized trials, conference abstract	Corticosteroid exposure not separable	CS-exposed arm not separable from rituximab arms
14	Nørgaard 2016 [64]	Population-based cohort, letter	Thrombosis not stratified by corticosteroid exposure	No CS-specific thrombosis data as published
15	Moulis 2018 (ASH abstract) [65]	Nationwide cohort (FAITH), conference abstract	Overlapping population (superseded report)	Earlier report of the FAITH cohort (2009–2015; corticosteroid aHR for VT 3.29, 2.39–4.53), superseded by Lafaurie 2021 (2009–2017)
16	Moulis 2017 (CARMEN) [66]	Prospective multicenter cohort (France)	Thrombosis not reported or not separable	Clinical epidemiology and treatment exposure of newly diagnosed ITP; thrombotic events not reported by corticosteroid exposure
17	Palandri 2016 [67]	Retrospective multicenter cohort (Italy)	Thrombosis not reported or not separable	Splenectomy rates and outcomes before and after new drugs; thrombosis not reported by corticosteroid exposure
18	Beyene 2024 [68]	Cross-sectional study (Ethiopia)	Thrombosis not reported or not separable	Health-related quality of life and corticosteroid complications; thrombotic events not reported
19	Valsecchi 2025 (ASH abstract) [69]	Administrative-database cohort (Italy), conference abstract	Thrombosis not reported or not separable	Corticosteroid-related events reported as composites by dose and intensity; no corticosteroid-free comparator; thrombosis not reported separately
20	Zhang L 2018 (ASH abstract) [70]	Single-arm pilot trial, conference abstract	Corticosteroid exposure not separable	Eltrombopag plus pulsed dexamethasone in all patients; corticosteroid exposure not separable from eltrombopag

Exclusion decisions were agreed by both reviewers (D.-C.P. and M.-A.G.) on 29 September 2026 (reports 1–14). Reports 15–20 had first been appraised during protocol development and were added on 24 October 2026 so that every assessed full text is accounted for. One further report identified through other methods (Wang L 2019) was excluded because thrombosis was not reported. CS, corticosteroid; GC, glucocorticoid; IVIg, intravenous immunoglobulin.

Table S3. Author data requests and replies.

Systematic review and meta-analysis of corticosteroids and thrombotic risk in immune thrombocytopenia (PROSPERO CRD420261504746). Updated 24 October 2026.

#	Study	Contacted author	Data requested	Reply (date) and content	Use in the review
1	Lafaurie 2021 (FAITH) [42]	M. Lafaurie	VT/AT events and person-time outside CS exposure; aHR for any thrombosis; aHR by duration, cumulative dose or recency	No reply by 29 Sep 2026 (treated as no data)	Published data used (adjusted set)
2	Therme 2026 (CARMEN-France) [44]	G. Moulis	VT events and person-time during and outside CS exposure; proportion on CS at VT (18/53 vs 40.0%); counts restricted to primary ITP	Reply 3 Oct 2026: published crude counts confirmed; person-time of CS exposure not calculated (multiple exposures, non-linear risk function) and not feasible in the coming months; 12 of 39 patients with primary ITP and VT were on CS at the time of thrombosis (39 = 53 patients with VT minus 14 with secondary ITP)	Published counts used (crude European set); additional information reported narratively
3	Ruggeri 2014 (GIMEMA ITP0311) [43]	F. Rodeghiero	Adult-only aHRs; VT/AT counts by steroid exposure with person-time; estimates excluding SVT and TIA	Reply by 1 Oct 2026: retired as department director; data not accessible	Published data used (adjusted and crude European sets)
4	Kashiwagi 2025 [20]	H. Kashiwagi	Adjusted ORs for VTE alone and arterial ischemic events alone, with exposure counts	No reply by 29 Sep 2026 (treated as no data)	Not included (non-comparable composite outcome)
5	Lee 2026 [55]	S.-M. Bang	Events and person-time with glucocorticoids without IVIg; events during GC therapy	No reply by 29 Sep 2026 (treated as no data)	Not included (GC not separable from IVIg)
6	Wang JD 2024 [19]	Y.-M. Chen; L.-N. Chien	VTE, ischemic stroke and MI separately by steroid exposure; aHRs by dose/intensity	No reply by 29 Sep 2026 (treated as no data)	Not included (thrombosis not reported separately)
7	Ekstrand 2019 (Swedish cohort) [57]	C. Ekstrand	AT/VTE events and person-time during and outside dispensed oral CS; time-varying aHR	E-mail of 27 Sep 2026 not delivered (server block).	Not included (not stratified by CS exposure)
8	Goncalves 2024 [58]	I. Goncalves	VTE/ATE events and person-time by CS exposure; patients on CS at index thrombosis; CS in Cox models	No reply by 29 Sep 2026 (treated as no data)	Not included (not stratified by CS exposure)
9	Palandri 2018 [59]	F. Palandri	Events during CS therapy; ever-treated patients with and without thrombosis; overlap with GIMEMA ITP0311	No reply by 29 Sep 2026 (treated as no data)	Not included (not stratified by CS exposure)
10	Wei 2016 [60]; Wang L 2019 [71]	M. Hou	Confirmation and number of thrombotic events per arm (HD-DXM, prednisone); overlap between studies	No reply by 29 Sep 2026 (treated as no data)	Not included (thrombosis not reported)
11	Mazzucconi 2024 (GIMEMA ITP0207) [51]	M.G. Mazzucconi	Confirmation and number of thrombotic events per arm (prednisone n = 59; HD-DXM n = 54)	Reply by 29 Sep 2026: no thromboembolic events in the study	Included, narrative synthesis (0/59 vs 0/54)
12	Huang 2018 [27]; Wang Y 2026 [48]	R. Yang	VT/AT counts by GC exposure; timing of exposure relative to the event; person-time	No reply by 29 Sep 2026 (treated as no data)	Published data used (crude prior-use set)

#	Study	Contacted author	Data requested	Reply (date) and content	Use in the review
13	Yang 2022 [54]	M. Zhao	Ever/never GC exposure by thrombosis status; composition of the ≤ 8-week group; reported proportion	E-mail of 27 Sep 2026 not delivered (inbox full); no reply	Not included (duration contrast only)
14	Mao 2026 [28]	Y. Hou	VT/AT counts by GC exposure; timing of exposure; adjusted OR	No reply by 29 Sep 2026 (treated as no data)	Published data used (crude prior-use set)
15	Demirci 2025 [56]	U. Demirci	Number of CS-treated patients and person-time; arterial events during CS therapy	No reply by 29 Sep 2026 (treated as no data)	Not included (no denominator by exposure)
16	Valsecchi 2025 (ASH abstract) [69]	D. Valsecchi	VTE, ischemic stroke and MI with person-time by CS dose/intensity group	E-mail address not listed in the abstract; sending not recorded	Not assessed as a full-text report
17	An 2021 (TARGET 020, ASH abstract) [61]	X. Zhang	Confirmation and number of thrombotic events per arm; status of full publication	No reply by 29 Sep 2026 (treated as no data)	Not included (abstract without extractable data)
18	Zhou F 2025 [47]	Corresponding author	Request content as sent (not held in the review file)	No reply by 29 Sep 2026 (treated as no data)	Published data used (crude prior-use set)
19	Liang H 2025 [46]	Corresponding author	Request content as sent (not held in the review file)	No reply by 29 Sep 2026 (treated as no data)	Published data used (crude prior-use set)
20	Zhang L 2026 [49]	Corresponding author	Request content as sent (not held in the review file)	No reply by 29 Sep 2026 (treated as no data)	Published data used (crude prior-use set)
21	Garabet 2019 (ASH abstract) [63]	W. Ghanima	Request content as sent (not held in the review file)	No reply by 29 Sep 2026 (treated as no data)	Not included (CS arm not separable from rituximab)

Requests 1–17 were drafted on 27 September 2026 and sent on 27–28 September 2026; requests 18–21 were sent on 28 September 2026. Request 12 also covered Wang Y 2026 (same center). Requests unanswered by 29 September 2026 were treated as yielding no data; replies received up to 3 October 2026 were used only to confirm published data or to inform the narrative synthesis. The contact period was subsequently extended to 24 October 2026; no further replies or data were received. Request 16 could not be sent (no e-mail address), and requests 7 and 13 were not delivered.

AT, arterial thrombosis; ATE, arterial thromboembolism; CS, corticosteroid; GC, glucocorticoid; HD-DXM, high-dose dexamethasone; IVIg, intravenous immunoglobulin; MI, myocardial infarction; SVT, superficial vein thrombosis; TIA, transient ischemic attack; VT, venous thrombosis; VTE, venous thromboembolism.

Table S4. Item-level JBI critical appraisal.

Risk-of-bias assessment – JBI critical appraisal checklists

Corticosteroids and Thrombotic Risk in Immune Thrombocytopenia: A Systematic Review and Meta-Analysis (PROSPERO CRD420261504746)

Final judgements – confirmed by the authors on 3 October 2026. These judgements correspond to Table 2 of the manuscript and to Supplementary Table S4.

Tools used

JBI Critical Appraisal Checklist for Cohort Studies (11 items) and for Case–Control Studies (10 items) (Moola et al., 2020), and the revised JBI Critical Appraisal Tool for the Assessment of Risk of Bias for Randomized Controlled Trials (13 items) (Barker et al., 2023). The item wording follows the published JBI checklists.

How the judgements were made

Judgements refer to the corticosteroid–thrombosis comparison used in this review, not to each study's primary aim. For the crude comparisons, the odds ratio was calculated by the reviewers from published counts, so confounding items are rated against that unadjusted comparison. Particular attention was given to exposure definition and timing, confounding by indication, outcome ascertainment and, for the trials, the reporting of thrombosis as a safety outcome. Following current JBI guidance, no summary score is calculated; each study receives an overall level of concern.

Legend

Y = Yes	**N** = No	**U** = Unclear	**NA** = Not applicable

Overall concern for the corticosteroid–thrombosis comparison

Low	**Low–moderate**	**Moderate**	**Moderate–high**	**High**	**Very high**

Contents: Part A – summary tables (landscape); Part B – individual checklists for each of the 12 included studies.

Part A. Summary of JBI judgements

Table A1. Cohort studies (n = 8)

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Overall concern	Main reasons
Lafaurie 2021 [42]	Y	Y	Y	Y	Y	Y	Y	Y	Y	NA	Y	**Low–moderate**	Residual confounding by disease activity cannot be excluded; outcome limited to hospitalized events.
Ruggeri 2014 [43]	U	Y	U	Y	Y	U	Y	Y	U	U	U	**Moderate–high**	Age range reported as 18–95 years in the text and 10–95 years in Table 1; VT includes superficial vein thrombosis and AT includes TIA.
Therme 2026 [44]	N	Y	U	N	N	U	Y	U	U	U	N	**High**	Secondary ITP (14.9%) included; population probably overlaps FAITH for 2013–2017.
Huang 2018 [27]	N	U	U	N	N	U	U	U	U	U	N	**High**	Corticosteroid exposure in 88.6% of patients without thrombosis.
Mao 2026 [28]	N	U	U	N	N	U	U	U	U	U	N	**High**	Possible outcome misclassification.
Liang H 2025 [46]	N	U	U	N	N	N	U	U	U	U	N	**Very high**	Mostly secondary (autoimmune) ITP; internally inconsistent counts in Table 1. Orientation of exposure counts confirmed from reported overall corticosteroid use (90.29%).
Wang Y 2026 [48]	N	U	U	N	N	U	U	U	U	U	N	**High**	Mixed age; arterial-dominant events (22 arterial, 7 venous, 4 both).
Kim KJ 2013 [45]	N	U	U	N	N	U	Y	U	U	U	N	**High**	Exposure counts derived by the reviewers from the per-patient listing; 36% later diagnosed with SLE; patients aged > 15 years included.

Q1. Were the two groups similar and recruited from the same population?
Q2. Were the exposures measured similarly to assign people to both exposed and unexposed groups?
Q3. Was the exposure measured in a valid and reliable way?
Q4. Were confounding factors identified?
Q5. Were strategies to deal with confounding factors stated?
Q6. Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?
Q7. Were the outcomes measured in a valid and reliable way?
Q8. Was the follow up time reported and sufficient to be long enough for outcomes to occur?
Q9. Was follow up complete, and if not, were the reasons to loss to follow up described and explored?
Q10. Were strategies to address incomplete follow up utilized?
Q11. Was appropriate statistical analysis used?

Table A2. Case–control studies (n = 2)

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Overall concern	Main reasons
Zhou F 2025 [47]	N	NA	Y	U	U	N	N	Y	U	N	High	Corticosteroid exposure in 95.4% of patients without thrombosis; minors possibly included.
Zhang L 2026 [49]	Y	Y	Y	U	U	Y	N	Y	U	N	Moderate–high	25 cases only; outcome restricted to pulmonary embolism.

Q1. Were the groups comparable other than the presence of disease in cases or the absence of disease in controls?
Q2. Were cases and controls matched appropriately?
Q3. Were the same criteria used for identification of cases and controls?
Q4. Was exposure measured in a standard, valid, and reliable way?
Q5. Was exposure measured in the same way for cases and controls?
Q6. Were confounding factors identified?
Q7. Were strategies to deal with confounding factors stated?
Q8. Were outcomes assessed in a standard, valid and reliable way for cases and controls?
Q9. Was the exposure period of interest long enough to be meaningful?
Q10. Was appropriate statistical analysis used?

Table A3. Randomised controlled trials (n = 2)

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Overall concern	Main reasons
Hamed 2023 [50]	U	U	Y	N	N	U	U	Y	U	N	N	U	Y	High	No corticosteroid-free arm; comparison of interest here is HD-DXM vs prednisolone + azathioprine.
Mazzucconi 2024 [51]	U	U	U	N	N	Y	U	Y	U	Y	Y	Y	Y	Moderate	No corticosteroid-free arm; thromboembolic events (0/59 vs 0/54) provided by the author.

Q1. Was true randomization used for assignment of participants to treatment groups?
Q2. Was allocation to treatment groups concealed?
Q3. Were treatment groups similar at baseline?
Q4. Were participants blind to treatment assignment?
Q5. Were those delivering the treatment blind to treatment assignment?
Q6. Were treatment groups treated identically other than the intervention of interest?
Q7. Were outcome assessors blind to treatment assignment?
Q8. Were outcomes measured in the same way for treatment groups?
Q9. Were outcomes measured in a reliable way?
Q10. Was follow up complete, and if not, were differences between groups in terms of their follow up adequately described and analyzed?
Q11. Were participants analyzed in the groups to which they were randomized?
Q12. Was appropriate statistical analysis used?
Q13. Was the trial design appropriate and any deviations from the standard RCT design (individual randomization, parallel groups) accounted for in the conduct and analysis of the trial?

Abbreviations: AT, arterial thrombosis; CTCAE, Common Terminology Criteria for Adverse Events; HD-DXM, high-dose dexamethasone; ITP, immune thrombocytopenia; MI, myocardial infarction; OR, odds ratio; PE, pulmonary embolism; SLE, systemic lupus erythematosus; SVT, superficial vein thrombosis; TIA, transient ischemic attack; VT, venous thrombosis; VTE, venous thromboembolism.

Part B. Individual JBI checklists

JBI Critical Appraisal Checklist for Cohort Studies

Reviewer: Review team	**Date:** 3 October 2026	**Author / year:** Lafaurie 2021	**Record number:** __01__

	Question	**Yes**	**No**	**Unclear**	**Not applicable**	**Support for judgement**
1.	Were the two groups similar and recruited from the same population?	☒	☐	☐	☐	All adults with incident primary ITP in the national health database; exposed and unexposed person-time from the same cohort.
2.	Were the exposures measured similarly to assign people to both exposed and unexposed groups?	☒	☐	☐	☐	Exposure from outpatient dispensing data for all patients.
3.	Was the exposure measured in a valid and reliable way?	☒	☐	☐	☐	Dispensing records with a duration algorithm (7-day grace period); exposure modelled as time-varying.
4.	Were confounding factors identified?	☒	☐	☐	☐	Age, sex, Evans syndrome, history of thrombosis, cancer, diabetes, renal and liver disease, other ITP treatments.
5.	Were strategies to deal with confounding factors stated?	☒	☐	☐	☐	Multivariable time-varying Cox models; Fine–Gray sensitivity analysis.
6.	Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?	☒	☐	☐	☐	First hospitalization for thrombosis after ITP diagnosis; history of thrombosis entered as a covariate.
7.	Were the outcomes measured in a valid and reliable way?	☒	☐	☐	☐	Hospital discharge ICD-10 codes; only hospitalized events captured.
8.	Was the follow up time reported and sufficient to be long enough for outcomes to occur?	☒	☐	☐	☐	Follow-up from ITP diagnosis to end of the study period (2009–2017).
9.	Was follow up complete, and if not, were the reasons to loss to follow up described and explored?	☒	☐	☐	☐	Administrative database with near-complete follow-up.
10.	Were strategies to address incomplete follow up utilized?	☐	☐	☐	☒	Not applicable (database follow-up).
11.	Was appropriate statistical analysis used?	☒	☐	☐	☐	Time-varying exposure; competing-risk sensitivity analysis; negative-control exposure (rituximab).

Overall appraisal: ☒ Include ☐ Exclude ☐ Seek further info	**Overall concern: Low–moderate**
Comments: Residual confounding by disease activity cannot be excluded; outcome limited to hospitalized events.	

JBI Critical Appraisal Checklist for Cohort Studies

Reviewer: Review team	**Date:** 3 October 2026	**Author / year:** Ruggeri 2014	**Record number:** _02__

	Question	Yes	No	Unclear	Not applicable	Support for judgement
1.	Were the two groups similar and recruited from the same population?	☐	☐	☒	☐	Ever- and never-exposed patients from the same centers, but likely to differ in disease severity.
2.	Were the exposures measured similarly to assign people to both exposed and unexposed groups?	☒	☐	☐	☐	Treatments recorded on a standardized electronic form for all patients.
3.	Was the exposure measured in a valid and reliable way?	☐	☐	☒	☐	Retrospective chart review; dose, timing and duration not recorded.
4.	Were confounding factors identified?	☒	☐	☐	☐	Age, sex, cardiovascular risk factors and splenectomy.
5.	Were strategies to deal with confounding factors stated?	☒	☐	☐	☐	Multivariable Cox model stratified by center.
6.	Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?	☐	☐	☒	☐	Previous thrombosis recorded but not an exclusion criterion.
7.	Were the outcomes measured in a valid and reliable way?	☒	☐	☐	☐	Objective criteria (imaging for VTE/SVT; clinical/imaging criteria for stroke, TIA and MI).
8.	Was the follow up time reported and sufficient to be long enough for outcomes to occur?	☒	☐	☐	☐	Median follow-up 38.2 months (3,888 patient-years).
9.	Was follow up complete, and if not, were the reasons to loss to follow up described and explored?	☐	☐	☒	☐	Losses to follow-up not reported.
10.	Were strategies to address incomplete follow up utilized?	☐	☐	☒	☐	Not described.
11.	Was appropriate statistical analysis used?	☐	☐	☒	☐	Ever-use entered as a fixed covariate (immortal-time bias); timing of corticosteroids relative to events not modelled.

Overall appraisal: ☒ Include ☐ Exclude ☐ Seek further info	**Overall concern: Moderate–high**
Comments: Age range reported as 18–95 years in the text and 10–95 years in Table 1; VT includes superficial vein thrombosis and AT includes TIA.	

JBI Critical Appraisal Checklist for Cohort Studies

Reviewer: Review team	**Date:** 3 October 2026	**Author / year:** Therme 2026	**Record number:** __03__

	Question	Yes	No	Unclear	Not applicable	Support for judgement
1.	Were the two groups similar and recruited from the same population?	☐	☒	☐	☐	Never-exposed group small (n = 239) and likely to differ in disease severity.
2.	Were the exposures measured similarly to assign people to both exposed and unexposed groups?	☒	☐	☐	☐	Registry case report form for all patients.
3.	Was the exposure measured in a valid and reliable way?	☐	☐	☒	☐	Ever exposure without dose or timing.
4.	Were confounding factors identified?	☐	☒	☐	☐	No confounders considered for the corticosteroid comparison (crude comparison by the reviewers).
5.	Were strategies to deal with confounding factors stated?	☐	☒	☐	☐	No adjustment.
6.	Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?	☐	☐	☒	☐	Previous VT recorded but not an exclusion criterion.
7.	Were the outcomes measured in a valid and reliable way?	☒	☐	☐	☐	Registry-reported VT with imaging confirmation.
8.	Was the follow up time reported and sufficient to be long enough for outcomes to occur?	☐	☐	☒	☐	Follow-up not reported by exposure group.
9.	Was follow up complete, and if not, were the reasons to loss to follow up described and explored?	☐	☐	☒	☐	Not reported.
10.	Were strategies to address incomplete follow up utilized?	☐	☐	☒	☐	Not reported.
11.	Was appropriate statistical analysis used?	☐	☒	☐	☐	Crude odds ratio; ever-use exposure.

Overall appraisal: ☒ Include ☐ Exclude ☐ Seek further info	**Overall concern: High**
Comments: Secondary ITP (14.9%) included; population probably overlaps FAITH for 2013–2017.	

JBI Critical Appraisal Checklist for Cohort Studies

Reviewer: Review team	**Date:** 3 October 2026	**Author / year:** Huang 2018	**Record number:** __04__

	Question	Yes	No	Unclear	Not applicable	Support for judgement
1.	Were the two groups similar and recruited from the same population?	☐	☒	☐	☐	Only 9 of 46 patients with thrombosis and 247 of 2171 without thrombosis were unexposed; the small unexposed group probably differed in disease severity and time since diagnosis.
2.	Were the exposures measured similarly to assign people to both exposed and unexposed groups?	☐	☐	☒	☐	Glucocorticoid use abstracted retrospectively from the inpatient records of a single referral center (2005–2017); abstraction procedure not described.
3.	Was the exposure measured in a valid and reliable way?	☐	☐	☒	☐	History of glucocorticoid treatment recorded without dose, duration or timing relative to the event; only 15 of 46 patients were receiving glucocorticoids at the event.
4.	Were confounding factors identified?	☐	☒	☐	☐	Age, smoking, hypertension and diabetes compared between groups, but not considered for the corticosteroid comparison.
5.	Were strategies to deal with confounding factors stated?	☐	☒	☐	☐	No multivariable analysis; corticosteroid use compared by χ^2 test only (P = 0.075).
6.	Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?	☐	☐	☒	☐	Previous thrombosis recorded in 26 patients (1.2%) but not an exclusion criterion.
7.	Were the outcomes measured in a valid and reliable way?	☐	☐	☒	☐	Events (34 of 36 arterial events were ischemic strokes) identified from medical records; imaging confirmation not reported for all events.
8.	Was the follow up time reported and sufficient to be long enough for outcomes to occur?	☐	☐	☒	☐	Follow-up duration not reported (inpatients 2005–2017).
9.	Was follow up complete, and if not, were the reasons to loss to follow up described and explored?	☐	☐	☒	☐	Losses to follow-up not reported.
10.	Were strategies to address incomplete follow up utilized?	☐	☐	☒	☐	Not described.
11.	Was appropriate statistical analysis used?	☐	☒	☐	☐	Crude comparison; exposure not treated as time-varying; odds ratio calculated by the reviewers.

Overall appraisal: ☒ Include ☐ Exclude ☐ Seek further info	**Overall concern: High**
Comments: Corticosteroid exposure in 88.6% of patients without thrombosis.	

JBI Critical Appraisal Checklist for Cohort Studies

Reviewer: Review team	**Date:** 3 October 2026	**Author / year:** Mao 2026	**Record number:** __05__

	Question	Yes	No	Unclear	Not applicable	Support for judgement
1.	Were the two groups similar and recruited from the same population?	☐	☒	☐	☐	Unexposed patients (15 with and 108 without thrombosis) not described separately; selection based on inpatient records.
2.	Were the exposures measured similarly to assign people to both exposed and unexposed groups?	☐	☐	☒	☐	First-line treatment abstracted from the records of inpatients at one center (2018–2022); abstraction method not described.
3.	Was the exposure measured in a valid and reliable way?	☐	☐	☒	☐	Glucocorticoid use recorded as part of first-line treatment, without dose, duration or timing relative to the event.
4.	Were confounding factors identified?	☐	☒	☐	☐	Age, disease duration, coronary heart disease and platelet count considered for the prediction model, not for the corticosteroid comparison.
5.	Were strategies to deal with confounding factors stated?	☐	☒	☐	☐	Corticosteroids not entered into the multivariable logistic model (univariable P = 0.925).
6.	Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?	☐	☐	☒	☐	Not stated whether thrombosis before ITP diagnosis or before treatment was excluded.
7.	Were the outcomes measured in a valid and reliable way?	☐	☐	☒	☐	Imaging-based ascertainment, but pulmonary embolism appears to have been counted with arterial events (32 arterial, 6 venous, 2 mixed).
8.	Was the follow up time reported and sufficient to be long enough for outcomes to occur?	☐	☐	☒	☐	Follow-up not reported.
9.	Was follow up complete, and if not, were the reasons to loss to follow up described and explored?	☐	☐	☒	☐	Losses to follow-up not reported.
10.	Were strategies to address incomplete follow up utilized?	☐	☐	☒	☐	Not described.
11.	Was appropriate statistical analysis used?	☐	☒	☐	☐	Crude comparison; exposure not treated as time-varying; odds ratio calculated by the reviewers.

Overall appraisal: ☒ Include ☐ Exclude ☐ Seek further info	**Overall concern: High**
Comments: Possible outcome misclassification.	

JBI Critical Appraisal Checklist for Cohort Studies

Reviewer: Review team	**Date:** 3 October 2026	**Author / year:** Liang H 2025	**Record number:** _06__

	Question	Yes	No	Unclear	Not applicable	Support for judgement
1.	Were the two groups similar and recruited from the same population?	☐	☒	☐	☐	Mostly secondary (autoimmune) ITP (254 of 350 patients); exposed and unexposed patients likely to differ in underlying disease.
2.	Were the exposures measured similarly to assign people to both exposed and unexposed groups?	☐	☐	☒	☐	Hospitalized patients (January–June 2024) at one center; exposure abstracted from records, method not described.
3.	Was the exposure measured in a valid and reliable way?	☐	☐	☒	☐	Corticosteroid use recorded without dose, duration or time window; order of the published counts inferred from the reported overall use (90.29%).
4.	Were confounding factors identified?	☐	☒	☐	☐	D-dimer, platelet count and Padua score considered for the prediction model, not for the corticosteroid comparison.
5.	Were strategies to deal with confounding factors stated?	☐	☒	☐	☐	Corticosteroids not entered into the multivariable model (univariable P = 0.295).
6.	Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?	☐	☒	☐	☐	82% of events occurred within ±6 months of ITP diagnosis; temporality relative to exposure not established.
7.	Were the outcomes measured in a valid and reliable way?	☐	☐	☒	☐	Arterial and venous events identified from the records of a six-month admission window; imaging confirmation not reported for all events.
8.	Was the follow up time reported and sufficient to be long enough for outcomes to occur?	☐	☐	☒	☐	Six-month window of hospitalized patients; follow-up not reported.
9.	Was follow up complete, and if not, were the reasons to loss to follow up described and explored?	☐	☐	☒	☐	Losses to follow-up not reported.
10.	Were strategies to address incomplete follow up utilized?	☐	☐	☒	☐	Not described.
11.	Was appropriate statistical analysis used?	☐	☒	☐	☐	Crude comparison; internally inconsistent comorbidity counts in the baseline table.

Overall appraisal: ☒ Include ☐ Exclude ☐ Seek further info	**Overall concern: Very high**
Comments: Mostly secondary (autoimmune) ITP; internally inconsistent counts in Table 1. Orientation of exposure counts confirmed from reported overall corticosteroid use (90.29%).	

JBI Critical Appraisal Checklist for Cohort Studies

Reviewer: Review team	**Date:** 3 October 2026	**Author / year:** Wang Y 2026	**Record number:** __07__

	Question	Yes	No	Unclear	Not applicable	Support for judgement
1.	Were the two groups similar and recruited from the same population?	☐	☒	☐	☐	Glucocorticoid use 48.5% among patients with and 46.5% among patients without thrombosis; unexposed patients probably differed in disease phase and prior treatment.
2.	Were the exposures measured similarly to assign people to both exposed and unexposed groups?	☐	☐	☒	☐	Hospitalization history at one referral center (2018–2025); abstraction method not described.
3.	Was the exposure measured in a valid and reliable way?	☐	☐	☒	☐	Glucocorticoid use during the hospitalization history, without dose, duration or timing relative to the event.
4.	Were confounding factors identified?	☐	☒	☐	☐	Sex, age, hypertension, diabetes and smoking compared between groups, but not considered for the corticosteroid comparison.
5.	Were strategies to deal with confounding factors stated?	☐	☒	☐	☐	Univariable analysis only (OR 1.08, 0.54–2.15); no multivariable model.
6.	Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?	☐	☐	☒	☐	Thrombosis after the diagnosis of thrombocytopenia; earlier thrombosis not clearly excluded.
7.	Were the outcomes measured in a valid and reliable way?	☐	☐	☒	☐	Events (22 arterial, 7 venous, 4 both) identified from inpatient records; outpatient events not captured.
8.	Was the follow up time reported and sufficient to be long enough for outcomes to occur?	☐	☐	☒	☐	Follow-up not reported (inpatient records only).
9.	Was follow up complete, and if not, were the reasons to loss to follow up described and explored?	☐	☐	☒	☐	Losses to follow-up not reported.
10.	Were strategies to address incomplete follow up utilized?	☐	☐	☒	☐	Not described.
11.	Was appropriate statistical analysis used?	☐	☒	☐	☐	Crude comparison; exposure not treated as time-varying; mixed-age population.

Overall appraisal: ☒ Include ☐ Exclude ☐ Seek further info	**Overall concern: High**
Comments: Mixed age; arterial-dominant events (22 arterial, 7 venous, 4 both).	

JBI Critical Appraisal Checklist for Cohort Studies

Reviewer: Review team	**Date:** 3 October 2026	**Author / year:** Kim KJ 2013	**Record number:** __08__

	Question	Yes	No	Unclear	Not applicable	Support for judgement
1.	Were the two groups similar and recruited from the same population?	☐	☒	☐	☐	137 of 165 patients received steroids; the 28 unexposed patients probably had milder disease; 36% later met criteria for SLE.
2.	Were the exposures measured similarly to assign people to both exposed and unexposed groups?	☐	☐	☒	☐	Treatment modality abstracted from the records of one center (2002–2012).
3.	Was the exposure measured in a valid and reliable way?	☐	☐	☒	☐	Steroid treatment recorded as ever/never; exposure at the event available only from the per-patient listing of cases.
4.	Were confounding factors identified?	☐	☒	☐	☐	Traditional risk factors and antiphospholipid antibodies identified, but not for the corticosteroid comparison.
5.	Were strategies to deal with confounding factors stated?	☐	☒	☐	☐	Steroids not included in the Cox model (study aim: antiphospholipid antibodies); counts derived by the reviewers.
6.	Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?	☐	☐	☒	☐	Thromboembolic events after ITP diagnosis; earlier events not clearly excluded.
7.	Were the outcomes measured in a valid and reliable way?	☒	☐	☐	☐	Objective clinical and imaging criteria for thrombotic events.
8.	Was the follow up time reported and sufficient to be long enough for outcomes to occur?	☐	☐	☒	☐	Mean follow-up 63.4 months for the cohort, not reported by exposure group.
9.	Was follow up complete, and if not, were the reasons to loss to follow up described and explored?	☐	☐	☒	☐	Losses to follow-up not reported.
10.	Were strategies to address incomplete follow up utilized?	☐	☐	☒	☐	Not described.
11.	Was appropriate statistical analysis used?	☐	☒	☐	☐	Crude comparison by the reviewers; exposure not treated as time-varying.

Overall appraisal: ☒ Include ☐ Exclude ☐ Seek further info	**Overall concern: High**
Comments: Exposure counts derived by the reviewers from the per-patient listing; 36% later diagnosed with SLE; patients aged > 15 years included.	

JBI Critical Appraisal Checklist for Case Control Studies

Reviewer: Review team	**Date:** 3 October 2026	**Author / year:** Zhou F 2025	**Record number:** __09__

	Question	Yes	No	Unclear	Not applicable	Support for judgement
1.	Were the groups comparable other than the presence of disease in cases or the absence of disease in controls?	☐	☒	☐	☐	Patients with and without thrombosis differ in age and comorbidity; no matching.
2.	Were cases and controls matched appropriately?	☐	☐	☐	☒	Not applicable (unmatched comparison).
3.	Were the same criteria used for identification of cases and controls?	☒	☐	☐	☐	Same hospital cohort and diagnostic criteria.
4.	Was exposure measured in a standard, valid and reliable way?	☐	☐	☒	☐	Exposure from medical records; timing for patients without thrombosis not defined.
5.	Was exposure measured in the same way for cases and controls?	☐	☐	☒	☐	Not described whether the same exposure window applied to both groups.
6.	Were confounding factors identified?	☐	☒	☐	☐	Not considered for the corticosteroid comparison.
7.	Were strategies to deal with confounding factors stated?	☐	☒	☐	☐	No adjustment.
8.	Were outcomes assessed in a standard, valid and reliable way for cases and controls?	☒	☐	☐	☐	Imaging-confirmed thrombosis.
9.	Was the exposure period of interest long enough to be meaningful?	☐	☐	☒	☐	Exposure window not defined.
10.	Was appropriate statistical analysis used?	☐	☒	☐	☐	Crude odds ratio with a zero cell (Haldane–Anscombe correction applied by the reviewers).

Overall appraisal: ☒ Include ☐ Exclude ☐ Seek further info	**Overall concern: High**
Comments: Corticosteroid exposure in 95.4% of patients without thrombosis; minors possibly included.	

JBI Critical Appraisal Checklist for Case Control Studies

Reviewer: Review team	**Date:** 3 October 2026	**Author / year:** Zhang L 2026	**Record number:** __10__

	Question	Yes	No	Unclear	Not applicable	Support for judgement
1.	Were the groups comparable other than the presence of disease in cases or the absence of disease in controls?	☒	☐	☐	☐	Controls drawn from the same adult primary ITP cohort.
2.	Were cases and controls matched appropriately?	☒	☐	☐	☐	Matched 1:3 on sex, age and time.
3.	Were the same criteria used for identification of cases and controls?	☒	☐	☐	☐	Same cohort and diagnostic criteria for cases and controls.
4.	Was exposure measured in a standard, valid and reliable way?	☐	☐	☒	☐	Steroid exposure from records; dose not reported.
5.	Was exposure measured in the same way for cases and controls?	☐	☐	☒	☐	Window for controls (matched follow-up) approximates that of cases but is not fully described.
6.	Were confounding factors identified?	☒	☐	☐	☐	Antiphospholipid antibodies and comorbidities compared between groups.
7.	Were strategies to deal with confounding factors stated?	☐	☒	☐	☐	Not applied to steroid exposure in the estimate used here (crude, unmatched OR).
8.	Were outcomes assessed in a standard, valid and reliable way for cases and controls?	☒	☐	☐	☐	PE confirmed by CT pulmonary angiography or other imaging.
9.	Was the exposure period of interest long enough to be meaningful?	☐	☐	☒	☐	Duration of exposure not reported.
10.	Was appropriate statistical analysis used?	☐	☒	☐	☐	Unmatched OR used because a conditional analysis is not possible from published data.

Overall appraisal: ☒ Include ☐ Exclude ☐ Seek further info	**Overall concern: Moderate–high**
Comments: 25 cases only; outcome restricted to pulmonary embolism.	

JBI Critical Appraisal Tool for the Assessment of Risk of Bias for Randomized Controlled Trials (revised 2023)

Reviewer: Review team	**Date:** 3 October 2026	**Author / year:** Hamed 2023	**Record number:** __11__

	Question	Yes	No	Unclear	Not applicable	Support for judgement
1.	Was true randomization used for assignment of participants to treatment groups?	☐	☐	☒	☐	Patients "randomly assigned"; sequence generation not described.
2.	Was allocation to treatment groups concealed?	☐	☐	☒	☐	Allocation concealment not described.
3.	Were treatment groups similar at the baseline?	☒	☐	☐	☐	Baseline characteristics reported as comparable ($p > 0.05$).
4.	Were participants blind to treatment assignment?	☐	☒	☐	☐	No blinding described (oral and intravenous regimens).
5.	Were those delivering the treatment blind to treatment assignment?	☐	☒	☐	☐	No blinding described.
6.	Were treatment groups treated identically other than the intervention of interest?	☐	☐	☒	☐	All arms received one month of HD-DXM and weekly visits; other co-interventions not described.
7.	Were outcome assessors blind to treatment assignment?	☐	☐	☒	☐	Assessor blinding not described.
8.	Were outcomes measured in the same way for treatment groups?	☒	☐	☐	☐	Adverse events graded by CTCAE in all arms.
9.	Were outcomes measured in a reliable way?	☐	☐	☒	☐	Method of thrombosis ascertainment not described.
10.	Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed?	☐	☒	☐	☐	37 withdrawals and 4 losses to follow-up; distribution by arm not reported.
11.	Were participants analyzed in the groups to which they were randomized?	☐	☒	☐	☐	Completers only (per-protocol analysis).
12.	Was appropriate statistical analysis used?	☐	☐	☒	☐	Analysis of completers; thrombosis not formally compared between the two corticosteroid arms.
13.	Was the trial design appropriate and any deviations from the standard RCT design (individual randomization, parallel groups) accounted for in the conduct and analysis of the trial?	☒	☐	☐	☐	Parallel-group, individually randomized design.

Overall appraisal: ☒ Include ☐ Exclude ☐ Seek further info	**Overall concern: High**
Comments: No corticosteroid-free arm; comparison of interest here is HD-DXM vs prednisolone + azathioprine.	

JBI Critical Appraisal Tool for the Assessment of Risk of Bias for Randomized Controlled Trials (revised 2023)

Reviewer: Review team	**Date:** 3 October 2026	**Author / year:** Mazzucconi 2024	**Record number:** __12__

	Question	**Yes**	**No**	**Unclear**	**Not applicable**	**Support for judgement**
1.	Was true randomization used for assignment of participants to treatment groups?	☐	☐	☒	☐	Randomized (GIMEMA ITP0207); method of sequence generation not reported in sufficient detail.
2.	Was allocation to treatment groups concealed?	☐	☐	☒	☐	Allocation concealment not reported in sufficient detail.
3.	Were treatment groups similar at the baseline?	☐	☐	☒	☐	Baseline comparability not reported in sufficient detail.
4.	Were participants blind to treatment assignment?	☐	☒	☐	☐	Open-label trial.
5.	Were those delivering the treatment blind to treatment assignment?	☐	☒	☐	☐	Open-label trial.
6.	Were treatment groups treated identically other than the intervention of interest?	☒	☐	☐	☐	Protocol-defined management in both arms.
7.	Were outcome assessors blind to treatment assignment?	☐	☐	☒	☐	Not described.
8.	Were outcomes measured in the same way for treatment groups?	☒	☐	☐	☐	Adverse events recorded by Common Toxicity Criteria (v3.0) in both arms.
9.	Were outcomes measured in a reliable way?	☐	☐	☒	☐	Thrombosis not a pre-specified outcome; event counts from the corresponding author.
10.	Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed?	☒	☐	☐	☐	Losses to follow-up few and reported by arm in the flow diagram.
11.	Were participants analyzed in the groups to which they were randomized?	☒	☐	☐	☐	Intention-to-treat analysis.
12.	Was appropriate statistical analysis used?	☒	☐	☐	☐	Appropriate for the trial outcomes.
13.	Was the trial design appropriate and any deviations from the standard RCT design (individual randomization, parallel groups) accounted for in the conduct and analysis of the trial?	☒	☐	☐	☐	Parallel-group, individually randomized design.

Overall appraisal: ☒ Include ☐ Exclude ☐ Seek further info	**Overall concern: Moderate**
Comments: No corticosteroid-free arm; thromboembolic events (0/59 vs 0/54) provided by the author.	

Table S5. Protocol amendment log (version 1.0 to version 1.1).

PROSPERO CRD420261504746. Version 1.0: 12 September 2026; version 1.1 (Amendment 1): 3 October 2026. Amendment 1 was made after the searches had been run (28 September 2026) and the eligible studies identified. Part A (items 1–19): Amendment 1. Part B (items B1–B10): subsequent changes (24 October 2026); a corresponding update of the PROSPERO record is planned.

No.	Protocol section	Version 1.0	Version 1.1	Rationale
1	4 Information sources	MEDLINE, Embase, CENTRAL	MEDLINE, Scopus, CENTRAL, LILACS	No institutional access to Embase; LILACS widens geographic coverage
2	5 Search strategy	ITP AND thrombosis concepts only; no exposure terms	Corticosteroid-safety arm added; registry searches use intervention terms	A known relevant study was not retrieved by thrombosis terms; registries record thrombosis only in adverse-event results
3	5 Search strategy	Peer review of strategies by an information specialist	Not performed	Not available within the review timeline
4	3.1 Population	Adults ≥ 18 years	Mixed-age rule, with sensitivity analysis	Several cohorts include a minority of younger patients without age-specific data
5	3.2, 3.4 Exposure and outcomes	—	Non-separable exposure and composites with hemorrhagic or non-thrombotic events excluded	A corticosteroid-specific thrombosis estimate cannot be extracted from such studies
6	3.3 Comparator	TPO-RA as secondary comparator; no comparator required	No corticosteroid exposure; regimen comparisons and TPO-RA narrative	Primary analysis is now comparative
7	3.5 Study designs	SCCS, adjusted cohorts, RCTs, uncontrolled case series	Unadjusted cohorts and case–control designs added; case series removed	Few adjusted studies; single-arm proportions not interpretable
8	2, 3.4, 9 Primary analysis	Proportional meta-analysis of event rates (Freeman–Tukey/logit)	Pooled adjusted relative estimates, venous and arterial separately	Follow-up and exposure definitions too heterogeneous for pooled proportions
9	9 Secondary analysis	—	Crude odds ratios pooled by exposure-definition subgroup, with subgroup test	Exposure definition expected to modify the estimates
10	9 Model	Random effects (estimator unspecified)	REML with Wald-type CI; HKSJ as sensitivity analysis	HKSJ unstable with two studies
11	9 Sensitivity analyses	High risk of bias; primary vs secondary ITP	Additional exclusions, leave-one-out, Fine–Gray substitution	Address specific features of the included studies
12	7, 9 Meta-regression	Dose, duration and follow-up as mandatory covariates	Not performed; narrative	Fewer than ten studies; dose not reported in poolable form
13	9 TPO-RA comparison	Pooled rates by exposure	Narrative	Insufficient within-study data
14	9 Reporting bias	Funnel plot and Egger's test where ≥ 10 studies	Unchanged rule; not applicable	No pooled estimate included ten or more studies
15	8 Risk of bias	JBI checklists (cohort, case series, RCT); four-level hierarchy	JBI cohort, case–control and revised RCT tool (2023); revised hierarchy	Change in eligible designs
16	9 Triangulation	Negative-control outcomes	Negative-control exposures where reported	Negative-control exposure available in an included cohort; no negative-control outcome reported
17	9 Certainty	GRADE implied (RevMan optional)	GRADE stated explicitly; evidence profile and SoF table	Clarification

No.	Protocol section	Version 1.0	Version 1.1	Rationale
18	7 Author contact	—	Unanswered requests by 29 September 2026 treated as no data	Review timeline
19	11 Timeline	Planned dates	Actual and revised dates	Searches later than planned; journal deadline extended
B1	9 Primary analysis	Adjusted HRs pooled separately for VT and AT (REML)	Adjusted HRs presented by study; VT estimates combined only as a sensitivity analysis; AT estimates not combined	One cohort carries 97% of the weight; exposure definitions differ
B2	9 Secondary analysis	Subgroups "European ever-use" and "Asian prior-use"; overall crude OR reported for completeness	Subgroups relabelled "European cohorts" and "Asian hospital-based series"; no overall crude OR	Neither subgroup defines an exposure window; subgroups differ in several respects
B3	8 Risk of bias	JBI checklists	JBI primary; ROBINS-E added for the two adjusted cohorts (Table S7)	Time-varying confounding and immortal time not addressed by JBI
B4	7 Data extraction	—	Multivariable corticosteroid estimates (Asian series), incidence per person-time and exposure at the event extracted (Tables S8 and S9)	Completeness of data extraction; absolute risks
B5	7 Author contact	Requests unanswered by 29 September 2026 treated as no data	Contact period extended to 24 October 2026; no further replies	Completeness of author data
B6	9 Narrative synthesis	—	Corticosteroid estimates from excluded studies with composite outcomes summarized (Table S10)	Use of all available corticosteroid estimates
B7	9 Triangulation	E-values for the pooled VT estimate	E-values for the nationwide-cohort aHR; limitations of the E-value and of the negative-control exposure stated	Transparency about residual confounding
B8	9 Zero-event trials	Narrative only	Exact (Clopper–Pearson) 95% CIs reported	Precision of zero-event results
B9	9 Certainty	VT inconsistency not serious; AT risk of bias not serious; absolute effects not calculated	VT inconsistency not assessable; AT risk of bias serious; absolute effect for VT derived	Certainty assessment aligned with the study-level presentation
B10	6 Study selection	26 full-text reports in the flow diagram	32 full-text reports (6 appraised during protocol development added)	Every assessed full text accounted for

Source: protocol version 1.1, Section 12. Section numbers refer to the protocol.

CI, confidence interval; HKSJ, Hartung–Knapp–Sidik–Jonkman; ITP, immune thrombocytopenia; JBI, Joanna Briggs Institute; RCT, randomized controlled trial; REML, restricted maximum likelihood; SCCS, self-controlled case series; SoF, Summary of Findings; TPO-RA, thrombopoietin receptor agonist.

Table S6. GRADE evidence profile.

Certainty of evidence – GRADE evidence profile and summary of findings

Corticosteroids and Thrombotic Risk in Immune Thrombocytopenia: A Systematic Review and Meta-Analysis (PROSPERO CRD420261504746)

Final ratings – confirmed by the authors on 3 October 2026 and revised on 24 October 2026. Layout follows the GRADEpro GDT evidence profile and summary-of-findings formats. The ratings correspond to Table 4 of the manuscript.

Question: Corticosteroid exposure compared with no corticosteroid exposure for thrombosis in patients with immune thrombocytopenia (ITP)
Setting: Inpatient and outpatient care; France, Italy, China, Korea and Egypt
Bibliography: studies included in this systematic review (12 studies; 10 in the meta-analysis)

Color key

Not serious	Serious	Very serious	HIGH ⊕⊕⊕⊕	MODERATE ⊕⊕⊕◯	LOW ⊕⊕◯◯	VERY LOW ⊕◯◯◯

Table G1. GRADE evidence profile

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Corticosteroid exposure	No corticosteroid exposure	Relative (95% CI)	Absolute (95% CI)		
Venous thrombosis – adjusted hazard ratios (corticosteroid exposure vs no exposure) – Follow-up: median 38 months (Ruggeri 2014); up to 8 years of database follow-up (Lafaurie 2021)												
2	Observational (cohort)	not serious[a]	not assessable[b]	not serious[c]	not serious[d]	Publication bias not assessable; strong association not used to upgrade[e]	11,025 participants; 307 VT events (time-varying exposure – exposed and unexposed groups not separable)		**aHR 3.55 (2.74 to 4.58); not combined**	11 more per 1000 person-years (8 more to 16 more)[f]	⊕⊕◯◯ **LOW**	**CRITICAL**
Arterial thrombosis – adjusted hazard ratios (corticosteroid exposure vs no exposure) – Follow-up: median 38 months (Ruggeri 2014); up to 8 years of database follow-up (Lafaurie 2021)												
2	Observational (cohort)	serious[s]	serious[g]	not serious[c]	serious[h]	Publication bias not assessable	11,025 participants; 689 AT events (time-varying exposure)		**aHR 1.15 (0.94 to 1.41); not combined**	2 more per 1000 person-years (1 fewer to 6 more)[f]	⊕◯◯◯ **VERY LOW**	**CRITICAL**
Any thrombosis – crude odds ratios, European cohorts (ever-use exposure) – Follow-up: median 38 months (Ruggeri); registry follow-up (Therme)												
2	Observational (cohort)	serious[i]	not serious	serious[j]	not serious	Publication bias not assessable	87/1717 (5.1%)	9/572 (1.6%)	**OR 3.48 (1.73 to 7.01)**	37 more per 1000 (from 11 more to 85 more)[k]	⊕◯◯◯ **VERY LOW**	**CRITICAL**
Any thrombosis – crude odds ratios, Asian hospital-based series (prior use, window not defined) – Follow-up: not reported												
7	Observational (5 cohorts, 2 case–control)	serious[l]	not serious	serious[m]	serious[n]	Publication bias not assessable	234/3911 (6.0%)[o]	62/1492 (4.2%)[o]	**OR 0.82 (0.59 to 1.14)**	Not calculated[o]	⊕◯◯◯ **VERY LOW**	**CRITICAL**
Any thrombosis – randomised comparisons of corticosteroid regimens (HD-DXM vs prednisone-based) – Follow-up: 12 to 44 months												
2	Randomized trials	serious[p]	not applicable	serious[q]	very serious[r]	none	HD-DXM: 0/159 (0%)	Prednisone-based: 0/169 (0%)	**Not estimable**	Not estimable	⊕◯◯◯ **VERY LOW**	**CRITICAL**

CI: confidence interval; HR: hazard ratio; OR: odds ratio; HD-DXM: high-dose dexamethasone; RCT: randomized controlled trial; SLE: systemic lupus erythematosus; TIA: transient ischemic attack; AT: arterial thrombosis; VT: venous thrombosis.

Explanations

a. The nationwide cohort (Lafaurie 2021), which provides almost all the information for VT, was judged at low–moderate concern with JBI (time-varying exposure, multivariable adjustment, null negative-control exposure) and at high risk of bias with ROBINS-E (confounding by disease activity, bleeding and hospitalization; Table S7); because observational evidence starts at low certainty, this was not used to downgrade further. The Italian cohort (Ruggeri 2014) was at moderate–high concern. Not downgraded.

b. Inconsistency not assessable: one cohort provides almost all the information, so the estimates are not combined; both point estimates exceed 1 (3.55 and 2.2).

c. Ruggeri 2014 may include patients aged 10–17 years, counts superficial vein thrombosis as venous and TIA as arterial; Lafaurie 2021 captures hospitalized events only. Not judged sufficient to downgrade.
d. Confidence interval excludes no effect; 307 VT events (292 in Lafaurie 2021, 15 in Ruggeri 2014).
e. Fewer than ten studies, so publication bias could not be assessed. The large magnitude (HR > 2) was not used to upgrade because the estimate rests mainly on one cohort and residual confounding by indication remains plausible.
f. Absolute effect derived from the nationwide cohort: rate without exposure approximately 4.4 per 1000 person-years for VT and 14.6 for AT (from the published overall rates and rates during exposure), multiplied by (aHR − 1); approximate (Table S9).
g. Conflicting point estimates (1.15 and 5.3); not combined.
h. The Italian estimate is very imprecise (95% CI 0.9 to 40.6), and the CI of the nationwide cohort (0.94 to 1.41) includes no effect and appreciable harm. AT events: 661 in Lafaurie 2021 and 28 in Ruggeri 2014.
i. Unadjusted odds ratios calculated by the reviewers; ever-use exposure is susceptible to immortal-time bias and confounding by indication.
j. Outcomes differ (any thrombosis in Ruggeri 2014, VT only in Therme 2026); Ruggeri 2014 is a mixed-age cohort.
k. Assumed risk without exposure = pooled risk in unexposed patients of the two cohorts (9/572 = 16 per 1000); risk with exposure calculated from the pooled OR.
l. Unadjusted odds ratios; exposure window not defined; one study at very high risk of bias (Liang H 2025).
m. Prior use without a time window is not equivalent to current exposure; several series are dominated by arterial events; secondary ITP, SLE and minors included.
n. 95% CI 0.59 to 1.14 includes no effect and an appreciable reduction in risk.
o. Counts are exposed/total among patients with and without thrombosis pooled across case-based and case–control designs; they are not risks, so absolute effects were not calculated.
p. Both trials open-label; thrombosis is not a pre-specified outcome; one trial analyzed completers only (Hamed 2023).
q. Both trials compare corticosteroid regimens; neither has a corticosteroid-free comparator, which is the comparison of interest.
r. No events among 328 participants (exact 95% CI 0 to 1.1%).
s. Arterial evidence: the Italian cohort (moderate–high concern with JBI; very high risk of bias with ROBINS-E; ever-use exposure; transient ischaemic attacks included) provides a substantial share of the information, and arterial events in the nationwide cohort were identified from hospital discharge codes.

Table G2. Summary of findings

Corticosteroid exposure compared with no corticosteroid exposure for thrombosis in patients with ITP

Patient or population: patients with ITP (predominantly adults) **Setting:** inpatient and outpatient care **Exposure:** systemic corticosteroids **Comparison:** no corticosteroid exposure (RCT row: alternative corticosteroid regimen)

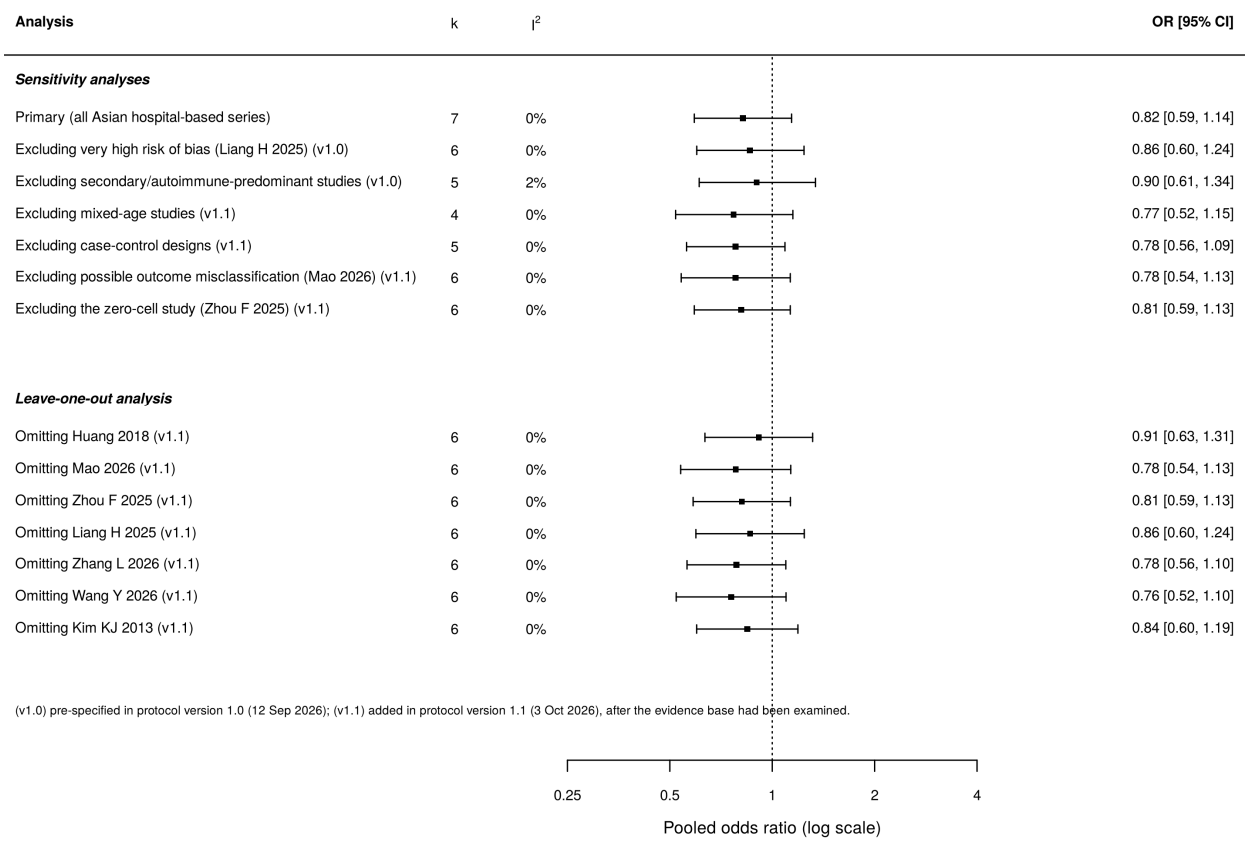
Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk without corticosteroid exposure	Risk with corticosteroid exposure				
Venous thrombosis (adjusted)	4 per 1000 person-years[f]	16 per 1000 person-years (12 to 20)[f]	**aHR 3.55 (2.74 to 4.58), nationwide cohort; not combined**	11,025 (2 cohort studies)	⊕⊕◯◯ **LOW**	Current corticosteroid exposure may increase the risk of venous thrombosis. The estimate comes almost entirely from one nationwide cohort; the estimates of the two cohorts are not combined.
Arterial thrombosis (adjusted)	15 per 1000 person-years[f]	17 per 1000 person-years (14 to 21)[f]	**aHR 1.15 (0.94 to 1.41), nationwide cohort; not combined**	11,025 (2 cohort studies)	⊕◯◯◯ **VERY LOW**	The evidence is very uncertain about the effect of corticosteroid exposure on arterial thrombosis.
Any thrombosis (crude; European cohorts)	16 per 1000	53 per 1000 (27 to 101)[k]	**OR 3.48 (1.73 to 7.01)**	2289 (2 cohort studies)	⊕◯◯◯ **VERY LOW**	Unadjusted estimate calculated by the reviewers; concordant with the adjusted venous estimate.
Any thrombosis (crude; Asian hospital-based series)	—[o]	—[o]	**OR 0.82 (0.59 to 1.14)**	5403 (7 observational studies)	⊕◯◯◯ **VERY LOW**	Prior use without a defined exposure window; the evidence is very uncertain.
Any thrombosis (RCTs; HD-DXM vs prednisone-based regimens)	0 per 1000	0 per 1000 (exact 95% CI 0 to 11)[r]	**Not estimable**	328 (2 RCTs)	⊕◯◯◯ **VERY LOW**	No events in either arm; no corticosteroid-free comparator.

*The risk with corticosteroid exposure (and its 95% CI) is based on the assumed risk without exposure and the relative effect of the exposure (and its 95% CI). Superscript letters refer to the explanations under Table G1.

GRADE Working Group grades of evidence

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

Figure S1. Sensitivity and leave-one-out analyses (Asian hospital-based series).



Upper panel: sensitivity analyses, labelled by protocol version – (v1.0) pre-specified in protocol version 1.0 (12 September 2026); (v1.1) added in protocol version 1.1 (3 October 2026), after the evidence base had been examined. Lower panel: leave-one-out analysis (added in version 1.1); each row shows the pooled estimate after omission of the named study. Pooled crude odds ratios from random-effects (REML) models; the dashed line marks the null (OR = 1). CI, confidence interval; OR, odds ratio.

Table S7. ROBINS-E assessment of the two adjusted cohorts.

Risk Of Bias In Non-randomized Studies – of Exposures (ROBINS-E; Higgins et al., Environ Int 2024). Result assessed: adjusted hazard ratio for VT and AT with corticosteroid exposure vs no exposure. Assessed independently by two reviewers; JBI remains the primary risk-of-bias tool for all 12 included studies (Table S4). Judgement levels: low; some concerns; high; very high.

Domain	Lafaurie 2021 (aHR, time-varying exposure)	Ruggeri 2014 (aHR, ever-use exposure)
D1 Confounding	High – adjusted for age, sex, Evans syndrome, previous thrombosis, cancer, diabetes, renal and liver disease, cardiovascular drugs and other ITP treatments (time-varying); disease activity, bleeding, hospitalization and immobilization not measured (IVIg adjustment and the null negative-control exposure only partly address this)	High – adjusted only for sex, age group, number of cardiovascular risk factors and splenectomy; disease severity, other ITP treatments and hospitalization not considered
D2 Measurement of the exposure	Some concerns – outpatient dispensing with a duration algorithm (7-day grace period); in-hospital corticosteroids (e.g. intravenous methylprednisolone) not captured; adherence unknown	High – ever-use entered as a fixed covariate; dose, timing and duration not recorded; exposure not related in time to the event (immortal time)
D3 Selection of participants into the study (or analysis)	Low – inception cohort of all adults with incident primary ITP; follow-up from diagnosis	Some concerns – retrospective inclusion of treated patients at tertiary centers; age range 10–95 years in the baseline table (possible inclusion of minors)
D4 Post-exposure interventions	Some concerns – later ITP treatments and antithrombotic drugs modelled as time-varying covariates; some may be consequences of corticosteroid response	Some concerns – subsequent treatments not modelled
D5 Missing data	Low – national administrative data with near-complete follow-up	Some concerns – losses to follow-up not reported
D6 Measurement of the outcome	Some concerns – primary hospital discharge diagnoses (hospitalized events only); possible detection bias during hospital stays	Some concerns – objective criteria, but VT includes superficial vein thrombosis and AT includes TIA; retrospective record review
D7 Selection of the reported result	Low – VT and AT analyzed separately as planned; Cox and Fine–Gray models and subgroups reported	Some concerns – corticosteroid estimate is one of several risk factors in multivariable models; model specification not pre-registered
Overall risk of bias	High (driven by confounding)	Very high (high risk of bias in two domains)
Predicted direction of bias	Confounding: probably away from the null (overestimation); exposure misclassification: probably towards the null	Confounding: away from the null; ever-use exposure (immortal time): towards the null; net direction unpredictable

Table S8. Multivariable analyses in the Asian hospital-based series and corticosteroid exposure at the time of the event.

Part A. Whether corticosteroids were entered into a multivariable model. None of the seven series reported a corticosteroid estimate adjusted for other factors.

Study	Multivariable model and entry rule	Corticosteroids entered	Corticosteroid estimate reported	Variables in the final model
Huang 2018 [27]	No (χ^2 comparisons only)	No	Univariable comparison only (P = 0.075)	–
Mao 2026 [28]	Logistic; univariable P < 0.05 entered	No (univariable P = 0.925)	Univariable OR 0.97 (0.49–1.92)	Age, ITP duration > 1 year, coronary heart disease, platelet count
Zhou F 2025 [47]	Logistic; univariable P < 0.1 entered	No (not estimable: all 15 cases exposed; P = 0.999)	Univariable OR not estimable	Coronary artery disease, dyslipidemia, TPO-RA treatment
Liang H 2025 [46]	Backward stepwise logistic; univariable P < 0.1 entered	No (univariable P = 0.295)	Univariable comparison only	Padua score, D-dimer, platelet count
Zhang L 2026 [49]	Cox (PE); univariable P < 0.1 entered	No (steroid use did not differ, P = 0.51; not a candidate variable)	None	History of thrombosis, active malignancy
Wang Y 2026 [48]	No (univariable logistic only)	No	Univariable OR 1.08 (0.54–2.15)	–
Kim KJ 2013 [45]	Cox with pre-selected covariates (aim: antiphospholipid antibodies)	No (not among the covariates)	None	Age, diabetes, hypertension, dyslipidemia, smoking, pregnancy/puerperium, SLE, LAC, aCL, anti-β2GPI

Part B. Corticosteroid exposure at the time of the thrombotic event (descriptive; the proportion receiving corticosteroids at a random time point is not reported, so these are not risk estimates).

Study	Outcome	On corticosteroids at the event	Source / note
Lafaurie 2021 [42]	VT (hospitalized)	136/292 (46.6%)	Events during periods of corticosteroid exposure (Table II)
Lafaurie 2021 [42]	AT (hospitalized)	142/661 (21.5%)	Events during periods of corticosteroid exposure (Table III)
Ruggeri 2014 [43]	Any	21/43 (49%)	Taking steroids at the time of the event (Results)
Therme 2026 [44]	VT	18/53 (34.0%)	Printed as 40.0% in the publication
Therme 2026 (author reply) [44]	VT, primary ITP	12/39 (30.8%)	Author reply, 3 October 2026
Huang 2018 [27]	Any	15/46 (32.6%)	Only 3 receiving glucocorticoids for > 1 month; 25/46 receiving no ITP treatment

Table S9. Incidence rates per person-time and absolute rates.

Rates per 1000 person-years (PY). Published values unless stated otherwise; derived values are approximate (rounded published rates; total person-time not censored at the first event).

Study	Outcome	Period	Rate per 1000 PY (95% CI)	Value type
Lafaurie 2021 [42]	VT	All follow-up (292 events; 40,954 PY)	7.3 (6.5–8.2)	Published
Lafaurie 2021 [42]	VT	Periods of corticosteroid exposure (136 events)	24.8 (21.0–29.4)	Published
Lafaurie 2021 [42]	VT	Periods without exposure (156 events; ≈35,470 PY)	4.4 (3.7–5.1)	Derived
Lafaurie 2021 [42]	AT	All follow-up (661 events)	16.8 (15.6–18.1)	Published
Lafaurie 2021 [42]	AT	Periods of corticosteroid exposure (142 events)	26.3 (22.3–31.0)	Published
Lafaurie 2021 [42]	AT	Periods without exposure (519 events; ≈35,555 PY)	14.6 (13.4–15.9)	Derived
Ruggeri 2014 [43]	VT / AT	All follow-up, not by exposure (15 / 28 events; 3888 PY)	3.9 (2.3–6.5) / 7.1 (4.9–10.4)	Published (per 100 PY × 10)
Therme 2026 [44]	VT	All follow-up, not by exposure (53 events; 2352.3 PY)	22.5 (16.9–29.5)	Derived; person-time by exposure not calculated (author reply)
Kim KJ 2013 [45]	Any	All follow-up, not by exposure (21 events)	15.2	Published
Huang 2018 [27]; Mao 2026 [28]; Zhou F 2025 [47]; Liang H 2025 [46]; Zhang L 2026 [49]; Wang Y 2026 [48]	Any/PE	–	Not reported	Follow-up or person-time not reported

Absolute excess during corticosteroid exposure (nationwide cohort) = rate without exposure × (aHR − 1): VT 4.4 × (3.55 − 1) ≈ 11.2 (7.7–15.7) additional hospitalizations per 1000 PY of exposure; AT 14.6 × (1.15 − 1) ≈ 2.2 (−0.9 to 6.0). Calculations in File S1 (sheet Person_time) and File S2.

Table S10. Corticosteroid estimates from excluded studies with composite outcomes.

Both studies are listed in Table S2 and were not combined with the outcomes of this review.

Study	Design; population	Outcome	Exposure contrast	Adjusted estimate (95% CI)	Reason not pooled
Kashiwagi 2025 [20]	Nested case–control, Japanese claims database (153 cases; 765 risk-set-sampled controls)	Thromboembolism composite: MI, angina, stroke, cerebral hemorrhage, peripheral arterial disease, VTE	Any CS prescription vs none (cohort entry to index date)	aOR 2.16 (1.48–3.14)	Composite includes hemorrhagic and non-thrombotic events
Kashiwagi 2025 [20]	As above	As above	Duration > 0–< 15 / 15–< 60 / ≥ 60 days vs none	aOR 2.25 (1.39–3.66) / 2.71 (1.50–4.87) / 1.72 (1.02–2.91)	As above
Kashiwagi 2025 [20]	As above	As above	Cumulative dose > 0–< 500 / 500–< 1500 / ≥ 1500 mg vs none	aOR 2.32 (1.41–3.82) / 1.73 (0.87–3.44) / 2.21 (1.38–3.55)	As above
Wang JD 2024 [19]	Population-based cohort, Taiwan (2,691 adults, all receiving steroids)	Cardiovascular disorders (dyslipidemia, hypertension, heart failure, ischemic heart disease); neuropsychiatric disorders (cerebrovascular disease, psychiatric disorders)	High vs low prednisolone-equivalent daily dose (> 10 vs ≤ 10 mg), time-dependent	aIRR 2.61 (2.28–2.99) cardiovascular; 2.91 (2.29–3.69) neuropsychiatric	No thrombosis-specific outcome; no corticosteroid-free comparator

aIRR, adjusted incidence rate ratio; aOR, adjusted odds ratio; CS, corticosteroid; MI, myocardial infarction; VTE, venous thromboembolism. Kashiwagi 2025: adjusted for sex, age, malignancy, pulmonary and liver disease. Wang JD 2024: adjusted for age, sex, Charlson comorbidity index and first-line regimen.

Supplementary references cited in Table S2 (and Table S3 where indicated)

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