Received: 6 February 2025 | Revised: 25 April 2025 | Accepted: 28 April 2025

DOI: 10.1111/trf.18277

REVIEW ARTICLE

Transfusion Medicine

TRANSFUSION

The clinical use of platelet transfusions: A systematic literature review and meta-analysis on behalf of the International Collaboration for Transfusion Medicine Guidelines

Rachel Jug[1] | **Ursula La Rocca**[2] | **Arwa Z. Al-Riyami**[3,4] | **Aarti Bathla**[5] | **Ryan A. Metcalf**[6] | **Sandra K. White**[6] | **Simon J. Stanworth**[7,8,9] | **Susan Nahirniak**[10,11]

[1]Department of Pathology, University of Cincinnati, Cincinnati, Ohio, USA

[2]Italian National Blood Center, National Institute of Health, Sapienza University of Rome, Rome, Italy

[3]Department of Hematology, Sultan Qaboos University Hospital, University Medical City, Muscat, Oman

[4]College of Medicine and Health Sciences, Sultan Qaboos University, Muscat, Oman

[5]Canadian Blood Services, Toronto, Canada

[6]Department of Pathology, University of Utah, Salt Lake City, Utah, USA

[7]NHS Blood and Transplant, University of Oxford, Oxford, UK

[8]Oxford University Hospitals NHS Trust, University of Oxford, Oxford, UK

[9]Radcliffe Department of Medicine, University of Oxford, Oxford, UK

[10]Department of Laboratory Medicine and Pathology, University of Alberta, Edmonton, Alberta, Canada

[11]Alberta Precision Laboratories, Edmonton, Alberta, Canada

Correspondence
Rachel Jug, Department of Pathology, University of Cincinnati, Cincinnati, OH, USA.
Email: jugrl@ucmail.uc.edu

Abstract

Background: Platelets are frequently transfused, but supply and potential harms highlight the importance of appropriate use.

Abbreviations: AABB, Association for the Advancement of Blood & Biotherapies; AMSTAR, A MeaSurement Tool to Assess quality of Systematic Reviews; CCRT, Cochrane Central Register of Controlled Trials; CIs, confidence intervals; CPB, cardiopulmonary bypass; CVC, central venous catheter; CVS, cardiovascular surgery; ECMO, extracorporeal membrane oxygenation; ECSTATIC, ECmo hemoSTAtic Transfusions In Children; HSCT, hematopoietic stem cell transplant; HT, hypoproliferative thrombocytopenia; ICH, intracranial hemorrhage; ICTMG, International Collaboration for Transfusion Medicine Guidelines; ICU, intensive care unit; LP, lumbar punctures; MA, meta-analysis; MCOS, matched cohort observational studies; NIHR, National Institute of Health Research; OR, odds ratios; PICO, Population, Intervention, Comparator, Outcome; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RBC, red blood cell; RCTs, randomized controlled trials; ROB, risk of bias; ROBINs, Risk Of Bias In Non-randomized Studies of Interventions; S-ICH, spontaneous ICH; SR, systematic review; TRALI, transfusion-related acute lung injury; WHO, World Health Organization.

This systematic review was conducted on behalf of the ICTMG (www.ICTMG.org). ICTMG receives funding from Canadian Blood Services (funded by the federal government (Health Canada) and the provincial and territorial ministries of health).

Canadian Blood Services does not have any role in the design and interpretation of the data and approval of the manuscript. The views herein do not necessarily reflect the views of Canadian Blood Services or the federal, provincial, or territorial governments of Canada.

Funding information
Canadian Blood Services

Study Design and Methods: Our systematic review (SR) followed a predefined protocol. Eligible studies included SRs, randomized controlled trials (RCTs), and matched cohort observational studies between 1946 and March 2025. Populations included were hypoproliferative thrombocytopenia, periprocedural prophylaxis, cardiovascular surgery, consumptive thrombocytopenia, and intracranial hemorrhage. The intervention was restrictive versus liberal platelet transfusion strategies on outcomes of mortality and bleeding. Duplicate screening and data extraction occurred. Meta-analysis used Mantel–Haenszel method of random effects model.

Results: Twenty-one RCTs, 24 observational studies, and 20 SRs were included. The evidence quality varied. For hypoproliferative thrombocytopenia, 11 RCTs were analyzed, with 9 RCTs at moderate risk of bias (ROB). Two RCTs were identified for dengue, with high ROB for bleeding. One RCT was identified each in cardiovascular surgery, intracranial hemorrhage, and periprocedural prophylaxis. Meta-analyses indicated no significant effect for outcomes of mortality or bleeding by strategy, but confidence intervals (CIs) were wide. Effect estimates were 1.32 [0.93, 1.86] for all-cause mortality in hypoproliferative thrombocytopenia, 0.80 [0.38, 1.70] in cardiovascular surgery, and 0.69 [0.47, 1.03] in critically ill neonates or dengue patients.

Discussion: A consistent lack of benefit with liberal platelet transfusion was observed across analyzed populations, although wide confidence intervals do not exclude clinically meaningful impacts. Important research gaps are highlighted in areas where the RCT data is limited.

KEYWORDS
platelet transfusion, platelets, systematic literature review, thrombocytopenia

1 | INTRODUCTION

Platelets are the second most transfused blood component.[1] Concerns about meeting demand for platelets have made conservation strategies key for blood suppliers' planning,[2] alongside the implementation of appropriate use informed by evidence-based standards. Despite a long history of conducting randomized controlled trials (RCTs) evaluating platelet transfusion safety and efficacy, most have been focused on populations with hematological malignancy. More recently, RCTs have been reported in non-hematology settings, with some revealing unexpected harms.[3,4] Prior systematic reviews (SR) are either outdated or address specific clinical settings (Table S1).

This SR and meta-analysis (MA) was commissioned by the International Collaboration for Transfusion Medicine Guidelines (ICTMG) to inform a collaborative clinical practice guideline with the AABB (Association for the Advancement of Blood & Biotherapies).[5] The scope was designed to cover broad clinical settings administering platelets, identifying those comparing restrictive versus liberal strategies, and included observational studies when RCTs were lacking. This review provides a baseline for iterative updates, which in turn will ensure that future guidelines can be informed and updated by new relevant literature.

2 | MATERIALS AND METHODS

This SR was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 checklist.[6] The protocol was registered on the National Institute of Health Research (NIHR) PROSPERO database (CRD42019147033). The working group identified Population, Intervention, Comparator, Outcome (PICO) questions in consultation with ICTMG and AABB. The populations of interest were: hypoproliferative thrombocytopenia (HT), periprocedural prophylaxis, cardiovascular surgery (CVS), consumptive thrombocytopenia, and intracranial hemorrhage (ICH). Studies in congenital thrombocytopenias, immune

thrombocytopenias, thrombotic thrombocytopenic purpura, heparin-induced thrombotic thrombocytopenia, vaccine-induced thrombotic thrombocytopenia, obstetric hemorrhages, and massive hemorrhage were deemed beyond scope and excluded. Interventions where platelets were used in combination with other agents (e.g., desmopressin) were also excluded. The focus was to inform clinical use of platelets and not to evaluate different types of manufactured platelet components (e.g., frozen, cold, or lyophilized). Interventional strategies were defined as liberal versus restrictive, broadly considered as using greater versus fewer amounts of platelets transfused respectively, to enable inclusion of studies with varied definitions, including different thresholds, different doses, and different timing of transfusions (Table S2). Restrictive also included "no prophylaxis." Critical outcomes included mortality (30-day and overall) and clinically significant hemorrhage defined in context-specific ways: World Health Organization (WHO) bleeding grades,[7] achieving hemostasis, hemorrhage volume, or frequency of bleeding cessation procedures.

2.1 | Study identification

Content experts identified key words further used to inform the development of a comprehensive search strategy. This strategy was used to search MEDLINE, Embase, Cochrane Central Register of Controlled Trials (CCRT), Cochrane database of Systematic Reviews, NHS Economic Evaluation database, Health Technology Assessment database, Ovid MED®E(R) Epub Ahead of Print, in-process and other non-indexed citations from inception (1946) to March 2025. Studies were also identified through retrieved systematic reviews (details in Appendix S1).

2.2 | Eligibility criteria

Study inclusion criteria were SRs, RCTs, and matched cohort observational studies (MCOS) reporting on our outcomes. MCOS were only included in the analysis if RCTs were single small trials or absent, and only if matched cohorts were adjusted.

2.3 | Screening and data extraction

Duplicate screening of references using DistillerSR software occurred in two stages, first for titles and abstracts, and then for full text. Four individuals reviewed for eligibility. Data extraction was performed in duplicate. Inconsistencies were resolved by consensus with a third reviewer.

2.4 | Assessment of risk of bias

Risk of bias (ROB) assessments were performed using established criteria for RCTs, MCOSs, and SRs. RCTs were assessed using the Cochrane ROB method. ROB assessments differed based on the outcome considered. Knowledge of treatment allocation was felt to be unlikely to influence the assessment of mortality; therefore, the risk of bias for this outcome was considered low. However, for bleeding, assessor blinding was helpful to reduce the risk of bias, even if patients and carers could not be.

For MCOS, we used the Risk Of Bias In Non-randomized Studies of Interventions (ROBINs) tool[8] (Table S3). Since our analysis only considered MCOS that adjusted for possible confounders before reporting on matched cohorts, the ROBINS assessment for the risk of confounding domain was anticipated to be low.

SRs were assessed using A MeaSurement Tool to Assess quality of Systematic Reviews (AMSTAR).[9] All assessments were performed in duplicate; conflicts were resolved with mutual consensus.

2.5 | Analysis

Both qualitative and quantitative data analyses were performed. Where RCT data were absent, meta-analysis incorporated MCOS data. Analysis included comparable effect measures across multiple studies when appropriate. Effect estimates for meta-analysis were presented as odds ratios (OR) with 95% confidence intervals (CIs) using RevMan web software (Version 8.14.0). Since the sampling frame across studies was randomly chosen and studies were from different geographies, a random effects model using Mantel–Haenszel methods was used. Statistical heterogeneity was assessed using a χ^2 test and quantified using the Higgins I^2 statistic, with I^2 values >50% defined a priori to reflect high heterogeneity. Findings were significant at 2-tailed $p < .05$. For scenarios with insufficient quantitative data for meta-analysis, data was summarized narratively.

3 | RESULTS

In total, 21 RCTs, 24 MCOS, and 20 SRs were included in the analysis (Figure 1). Twenty SRs were identified: six on HT states,[10–15] four on peri-procedural,[14,16–18] three on critical illness,[13,15,19] one on CVS[20] and 10 on ICH[14,21–29] (Table S1).

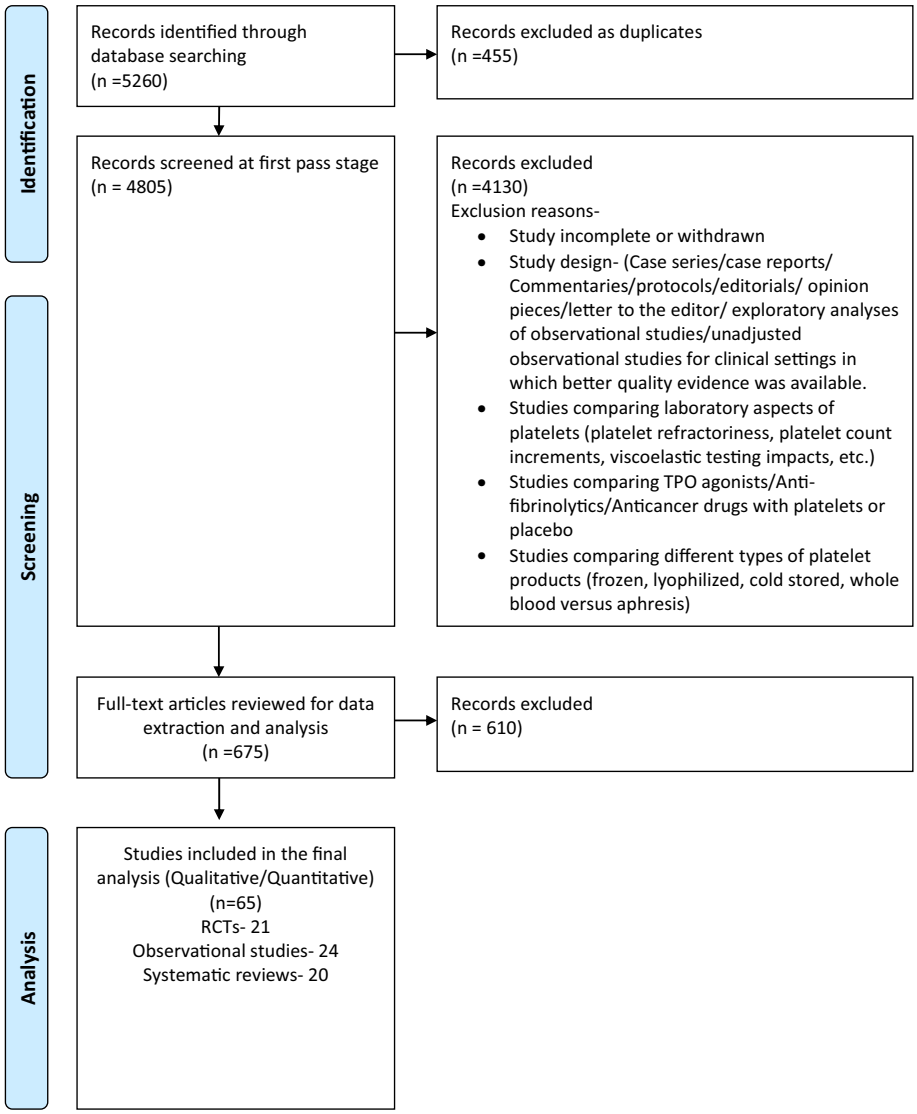

FIGURE 1 PRISMA diagram (searches from April 2022–April 2024).

3.1 | Clinical setting 1—Hypoproliferative thrombocytopenia

3.1.1 | Background

Patients with HT due to acquired bone marrow disorders represent a large proportion of platelet recipients. A subgroup of interest for this analysis included autologous hematopoietic stem cell transplant (HSCT) recipients.

3.1.2 | Evidence summary and quality assessments

RCTs

Eleven RCTs[30–40] (2860 participants) were analyzed: three compared prophylactic versus therapeutic strategies,[34–36] four focused on platelet dose,[31,33,39,40] and four compared different platelet count thresholds[30,32,37,38] for prophylactic transfusion. The settings of the trials were mixed populations of patients with hematological malignancies and/or undergoing stem cell transplantation; three trials included some with solid tumors.[41–43] One did not complete recruitment.[44] No single RCT evaluating platelet thresholds in pediatric patients was identified; the PLADO RCT was the only threshold trial that included children.[33] The secondary age-adjusted analysis of PLADO reported an increased risk of bleeding in children receiving HSCT.[45] High ROB was found for Heckman 1997, Diedrich 2005, and Rebulla 1997, with a moderate ROB for the remaining studies[37,39] (Figure S1).

One RCT with low ROB[35] included a restrictive arm more stringent than other trials' and accounted for a substantial majority of the difference in the absolute number of events between restrictive and liberal arms in the pooled meta-analysis for Grade 2–4 bleeding, shifting the OR toward favoring liberal. Despite this, no overall statistical benefit was observed. Three RCTs with

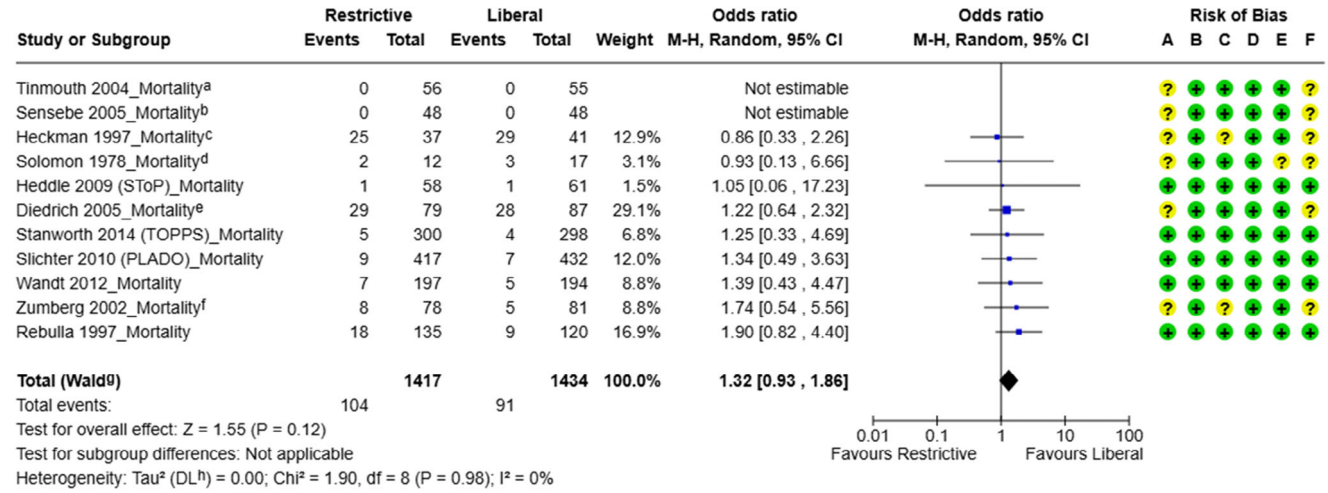

FIGURE 2 Forest plot for overall mortality in patients with hematological malignancies. [a]Domain A has some concerns—the study states it was randomized but provides minimal detail about how randomization was performed (e.g., no info on sequence generation method) or whether allocation was concealed. [b]Domain A has some concerns—the method of sequence generation is not detailed (e.g., no mention of computer randomization, block size, etc.) Besides, Allocation concealment is not reported, which leaves open the possibility of selection bias. [c]Domain A has some concerns—no detail on random sequence generation—we do not know whether it was truly random (e.g., computer-generated) or quasi-random (e.g., alternate assignment). Besides, No description of allocation concealment and no reporting of baseline characteristics in a table or formal statistical comparison, so it is difficult to judge whether randomization achieved balance. Domain C has some concerns—two patients with severe clinical events were excluded after randomization, and their missing outcomes could plausibly be related to the true outcome, introducing potential bias. [d]Domain A has some concerns—study mentions randomization but does not provide details on sequence generation or allocation concealment. Domain E has some concerns—mortality data are likely reported post hoc; the lack of protocol or trial registration raises concerns about selective reporting. [e]Domain A has some concerns—study used alternate assignment; it is a quasi-random method and is predictable, meaning clinicians could predict the next group allocation, so there is a risk of selection bias. [f]Domain A has some concerns—randomization method and allocation concealment were not described. Domain C has some concerns—five patients were excluded after randomization. For mortality, these exclusions could bias results—especially if failure to engraft or protocol violations, as mentioned by the author, may be associated with a higher risk of mortality.

moderate ROB suggest prophylactic transfusion did not reduce Grade 2–4 bleeding in autologous HSCT patients compared to patients receiving intensive myeloablative chemotherapy or allograft HSCT[35,36,40] (Figure S2).

Meta-analysis

All-cause mortality—Based on 11 RCTs, the estimated OR for all-cause mortality between restrictive and liberal platelet strategies in patients with HT was 1.32 [0.93–1.86] (Figure 2).

Thirty-day mortality—A sensitivity analysis for 30-day mortality was conducted for five RCTs reporting this parameter.[31,33–35,40] The OR was 1.23 (0.60–2.51) (Figure S3).

WHO Grade 2–4 bleeding and 3, 4 bleeding or equivalent: Ten RCTs reported on WHO Grade 2–4 bleeding (or equivalent)[30–33,35,37–40,46] with an OR of 1.23 [1.00, 1.53] (Figure S1). For WHO Grade 3 and 4 bleeding (or equivalent), data from six RCTs[31–35,38] showed an OR of 1.24 [0.88–1.75] (Figure S4).

WHO Grade 2–4 bleeding and 3, 4 bleeding or equivalent in autologous transplant subgroup: The data for WHO Grade 2–4 bleeding (or equivalent) was reported from three RCTs[35,36,40] with an OR of 2.30 [0.67, 7.88] (Figure S2).

For WHO Grade 3 and 4 bleeding (or equivalent), data was obtained from two RCTs[35,36] with an OR of 4.68 [0.53, 41.38] (Figure S5).

3.2 | Clinical setting 2—Peri-procedural states

3.2.1 | Background

Platelets are often administered prior to procedures in patients with thrombocytopenia with the goal of reducing bleeding risk.

3.2.2 | Evidence summary and quality assessments

RCTs

We identified one RCT in thrombocytopenic patients undergoing central venous catheter (CVC) placement.[47] This trial randomized patients with platelet counts

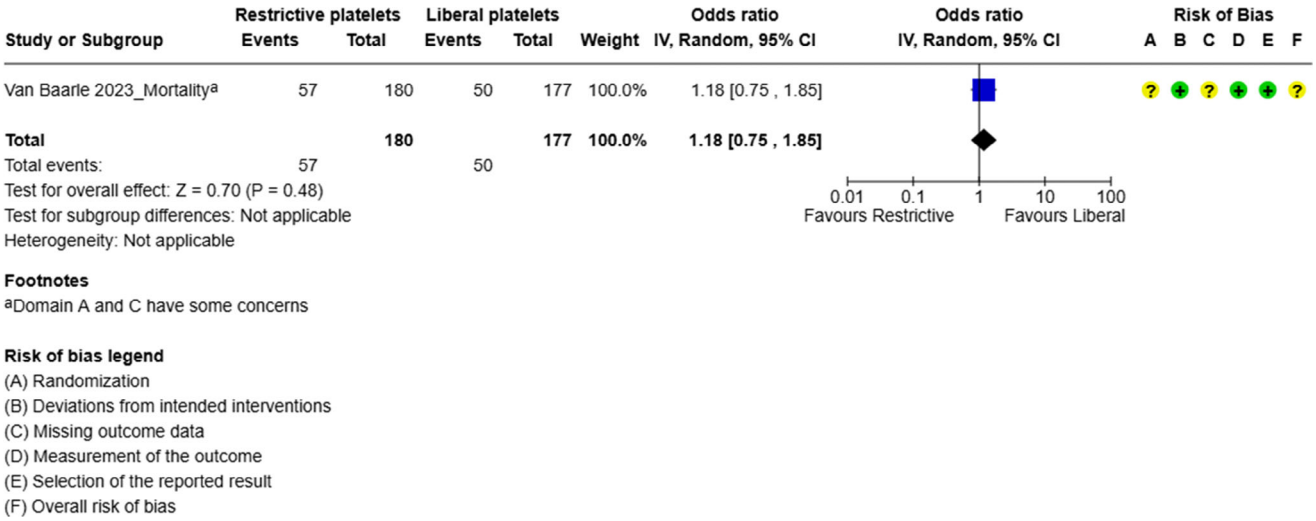

FIGURE 3 All-cause mortality in patients undergoing CVC placement. [a]Domain A has some concerns—the lack of blinding for patients and treating physicians could introduce performance bias. Domain C has some concerns—the trial reported missing data for the primary outcome (CVC-related bleeding) as 7.2% but did not clearly report missingness for the mortality outcome. There was no clear indication whether the patients with missing bleeding outcome data also had missing mortality data.

between 10,000-50,000/μL undergoing ultrasound-guided CVC placement in the hematology ward or intensive care unit (ICU) to platelets or no transfusion. The primary outcome was Grade 2–4 bleeding, with higher rates reported in the restrictive arm. Subgroup analyses suggested the observed difference varied by anatomic site, with no difference at compressible (internal jugular/femoral) sites. Average hematoma size was notably larger in the liberal group. This RCT had moderate ROB.

Observational studies

For CVC placement, one small prospective study found no differences in mortality or major bleeding between patients receiving platelets or not during catheter implantation.[48] One MCOS[49] of platelets prior to interventional radiology procedures in 2060 patients with platelet counts <100,000/μL had 203 patients (9.9%) receiving a platelet transfusion. There was no difference in mortality or need for red blood cell (RBC) transfusion between propensity-matched cohorts. Also, at thresholds ≤50,000/μL, there was no difference in need for RBC transfusion. A total of six MCOS were identified that assessed spinal hematoma incidence in patients with platelet counts <50,000/μL just prior to the lumbar punctures (LP).[50–55] Four of these studies also reported data for a subset of patients with platelet counts <20,000/μL.[51,52,54,55] Overall reported incidence rates of this complication were exceedingly low.

Meta-analysis

All-cause mortality—The estimated effect between restrictive and liberal platelet strategies in patients undergoing CVC placement extracted from one RCT[47] was 1.18 [0.75, 1.85] (Figure 3).

WHO Grade 2–4 bleeding—The estimated OR for Grade 2–4 CVC related bleeding reported from one RCT[47] was 3.56 [1.35, 9.36] for hematology ward patients and 1.33 [0.29, 6.16] for ICU patients (Figure S6).

Peri-procedural RBC transfusion and ICU admission; interventional radiology—One MCOS[49] on patients undergoing interventional radiology procedures reported an OR of 0.64 [0.43, 0.94] for ICU admission (Figure S7) and an OR of 0.69 [0.45, 1.05] for peri-procedural RBC transfusion (Figure S8). The ROB for this study was low (Table S4).

Spinal hematoma—Meta-analysis of spinal hematoma incidence showed a rate of 0/1000 lumbar puncture procedures [0–2.96] for patients with platelet counts <20,000/μL (four studies, 324 patients) and 0.78/1000 lumbar puncture procedures [0–10.02] for patients with platelet counts <50,000/μL (six studies, 4418 patients) (Figure S9).

3.3 | Clinical setting 3—Cardiovascular surgery, including extracorporeal membrane oxygenation

3.3.1 | Background

Patients undergoing CVS with or without CPB may develop thrombocytopenia but may also have added complications of platelet dysfunction secondary to bypass or anti-platelet agents.

3.3.2 | Evidence summary and quality assessments

RCTs

Our review identified three RCTs: two in adults[56,57] and one in neonates.[58] In the CVS setting, all studies involved patients on CPB except for one RCT.[57] Lunen 2018[56] randomized patients with ruptured abdominal aortic aneurysm to receive two preoperative platelets versus none upon transport to vascular surgery. No significant effect on postoperative complications, length of ICU and hospital stay, or mortality was observed with a low ROB. Gautam 2020[58] randomized neonatal patients undergoing elective open heart surgery to receive 10 mL/kg of platelets during the rewarming phase after cross-clamp release and before termination of CPB versus platelets only at the end of bypass but had a moderate ROB for bleeding and low ROB for mortality.

No RCTs were identified addressing platelet transfusion in patients undergoing extracorporeal membrane oxygenation (ECMO).

Observational studies

Our literature review identified four adjusted observational studies in patients undergoing CVS[59–62] that assessed mortality in platelet recipients versus those not receiving platelets.

Meta-analysis

The OR for all-cause mortality between restrictive and liberal platelet transfusion strategies in adult CVS patients not on CPB based on one RCT[56] was 0.80 [0.38, 1.70]. In neonatal CVS patients, the OR for all-cause mortality between restrictive and liberal platelet strategies could not be estimated (0 events in both arms)[54] (Figure 4).

Due to the paucity of RCTs in this subgroup, four MCOS were included in the meta-analysis. The OR for all-cause mortality between restrictive and liberal strategies in CVS was 0.79 [0.37, 1.72] (Figure 5). The ROB for all four studies was low (Table S4).

3.4 | Clinical setting 4—Consumptive thrombocytopenia

3.4.1 | Background

Thrombocytopenia is a common observation in critical illness, and platelets are frequently administered to ICU patients.

3.4.2 | Evidence summary and quality assessments

RCTs

Two RCTs in adults with dengue fever reported on all-cause mortality.[63,64] Lye 2017[63] compared platelets plus supportive care versus supportive care alone in adults with dengue fever and thrombocytopenia with a moderate ROB. Assir 2013[64] randomized patients to platelets compared to no platelets but had a moderate ROB.

In critically ill neonates, three RCTs reporting all-cause mortality were identified.[4,65,66] The[4] *Planet-2/MATISSE* trial recruited 660 neonates to demonstrate that the primary outcomes of death or major bleeding up to day 28 were greater in the liberal compared to the restrictive arm (defined by platelet thresholds of 50 and 25 $\times$ 10^9/L, respectively). Subgroup analysis suggested this effect was independent of predicted baseline risk with a low ROB. Kumar 2019[65] identified a higher risk of harm in critically ill neonates with patent ductus arteriosus treated with liberal transfusion strategies and an insignificant mortality benefit associated with restrictive strategies, with a low ROB. Andrew 1993[66] evaluated the impact of platelets on 152 premature infants with thrombocytopenia, demonstrating with a low ROB that liberal transfusion had no reduction in mortality or incidence of ICH.

Observational studies

The literature informing practice in non-dengue adult ICU patients is not supported by RCTs but by three MCOS.[67–69] Warner 2019[67] analyzed a retrospective cohort study of adults admitted to surgical, medical, or combined ICUs comparing outcomes between those who did versus did not receive prophylactic platelets. A propensity score-matched analysis of an ICU database[68] assessed mortality outcomes in septic patients with platelets ≤150,000/μL who did or did not receive platelet transfusions. Another propensity score-matched analysis assessed 30-day all-cause mortality in burn patients with thrombocytopenia who did or did not receive platelet transfusions.[69] The ROB for all three was low (Table S4).

Meta-analysis

The effect on all-cause mortality between restrictive and liberal platelet strategies in critically ill adult patients with dengue extracted from two RCTs[63,64] was an OR of 0.30 [0.01, 7.47]. The OR for all-cause mortality between restrictive and liberal platelet strategies in critically ill neonates based on three RCTs was 0.69 [0.47, 1.03]. A combined OR for all ages was 0.69 [0.47, 1.01] (Figure 6). The OR reported for critically ill adults from the three MCOS that reported overall mortality[67,68] was 0.80 (0.68, 0.94) (Figure S10).

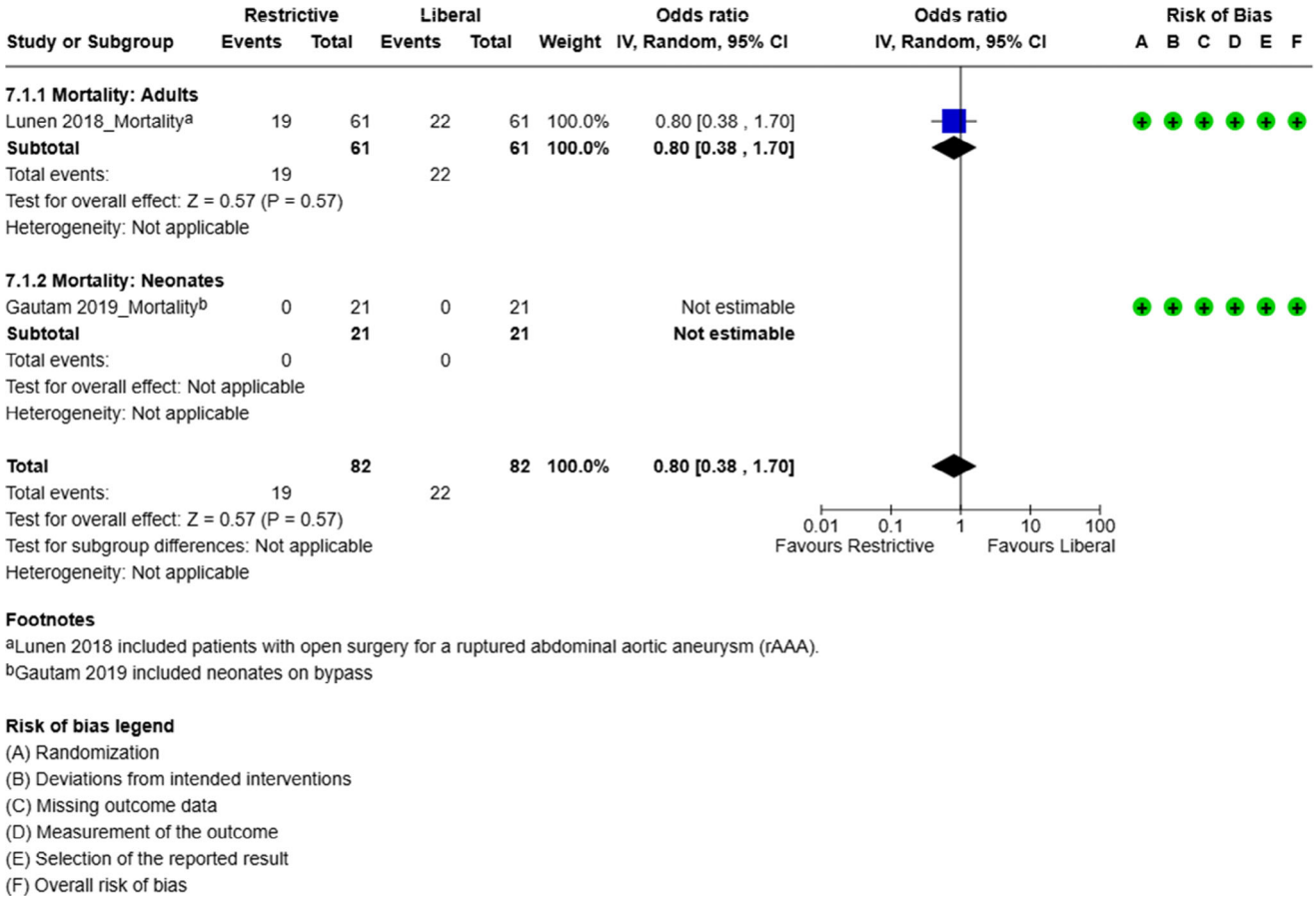

FIGURE 4 All-cause mortality in patients undergoing cardiovascular surgery.

3.5 | Clinical setting 5—Intracranial hemorrhage

3.5.1 | Background

Platelets are often used as empiric or threshold-driven transfusion support in ICH given concerns about the risk of ongoing bleeding in a critical site.

3.5.2 | Evidence summary and quality assessments

RCTs

The PATCH RCT[3] randomized adults with spontaneous ICH (S-ICH), anti-platelet medication use for at least 7 days preceding the hemorrhage, and a Glasgow coma scale of 8–15 who were able to have platelets initiated within 6 h of symptom onset and within 90 min of imaging but were not planned for a surgical evacuation. A total of 190 patients were enrolled; 97 were randomized to platelets and 93 to standard care. The mortality outcome at 3 months was higher in those randomized to platelets, 32% (31/97) compared to 22.6% (21/93) of those in the control arm with an OR 0.62 [0.33, 1.19] but there was a high ROB (Figure 7).

Observational studies

Only one appropriately adjusted MCOS assessing platelet transfusions in S-ICH patients on antiplatelet therapy was identified.[70] It found the use of platelets was not a significant predictor for a negative outcome (mortality OR 1.00 [0.13, 7.59]) (Figure S11) with a low risk of bias (Table S4).

Fifteen unadjusted observational studies[71–85] (Figure 8), two of which[84,85] were not included in previous SRs, evaluated platelet transfusion in the clinical setting of anti-platelet associated traumatic ICH in adults. There were 1745 participants across the studies. Most of these studies had serious issues with confounding; quality was low, resulting in a high ROB.

4 | DISCUSSION

Two broad themes emerged from our SR. First, no consistent evidence supported the superiority of liberal platelet

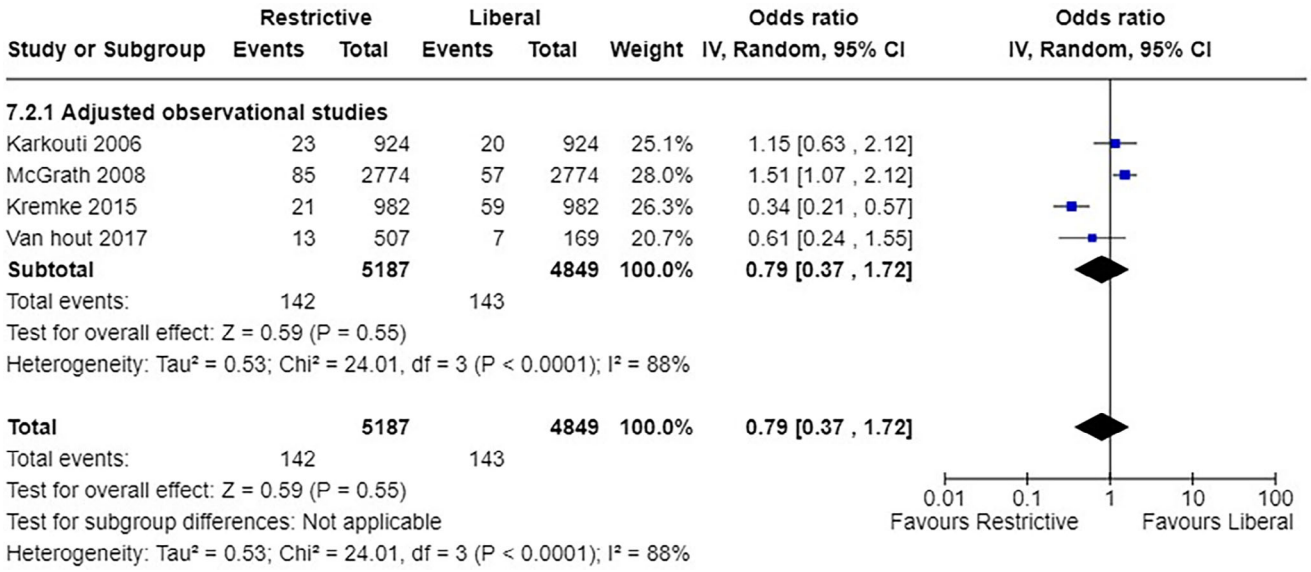

FIGURE 5 All-cause mortality in adults undergoing cardiovascular surgery.

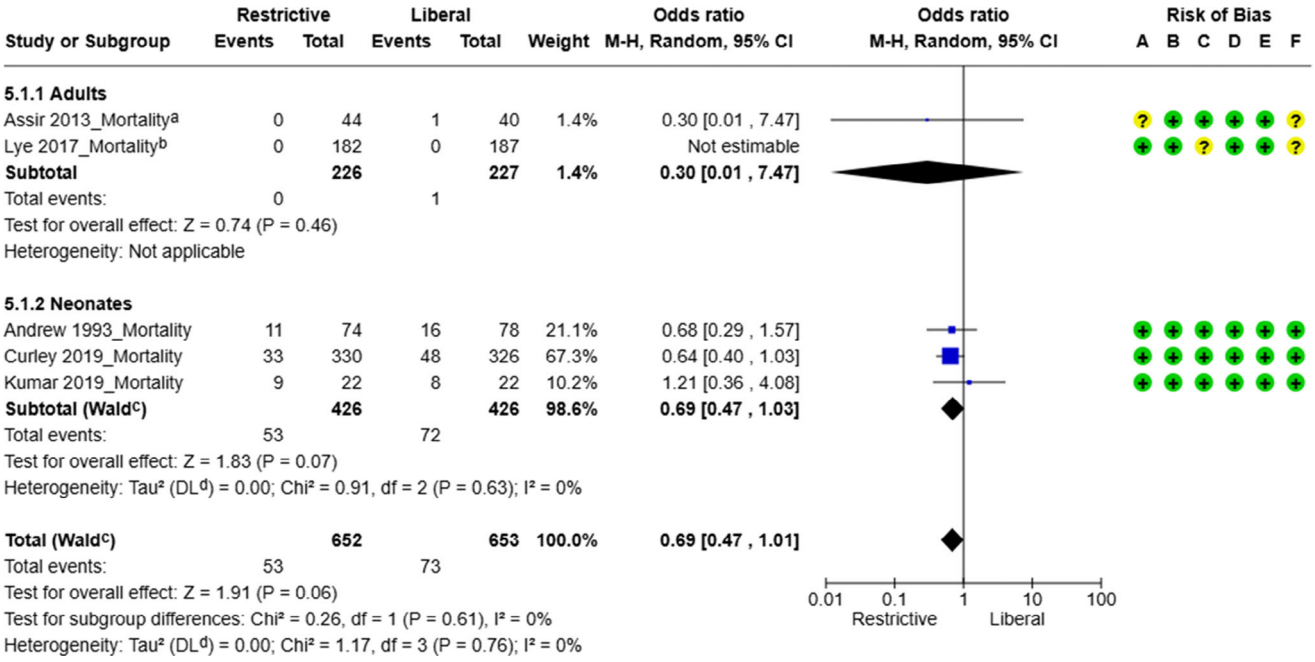

FIGURE 6 All-cause mortality in critically ill patients with Dengue and critically ill neonates, respectively. [a]Domain A has some concerns—the study mentions random allocation but lacks information on the randomization method and allocation concealment. Besides, Baseline characteristics between groups were not comprehensively reported. [b]Domain C has some concerns—the study reported zero deaths, lack of clarity about how completely and systematically mortality was assessed and captured across both groups.

transfusion strategies to reduce mortality or bleeding across the evaluated clinical settings. Second, the amount of data, levels of evidence, and evidence certainty varied considerably between different populations, often displaying wide confidence intervals for meta-analyses, precluding definitive exclusion of clinically significant effects that might be identified in future larger trials if undertaken. Overall, the findings support the general implementation of restrictive policies for platelet transfusion, minimizing exposure to platelets, which have risks, for recipients. Risks of platelets are well recognized, including transfusion-transmitted infections, transfusion-related acute lung injury (TRALI), immunomodulation and sensitization, in addition to acute transfusion

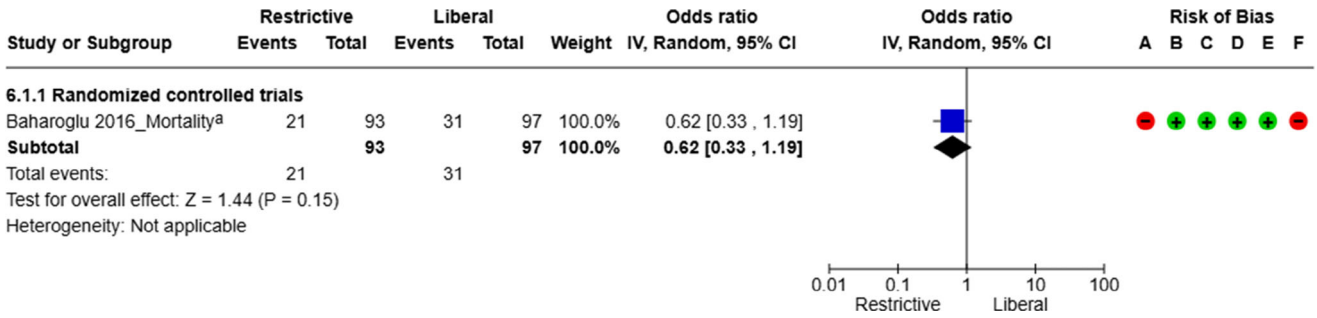

FIGURE 7 All-cause mortality in adults presenting with spontaneous intra-cranial hemorrhage. [a]Domain A has a high risk of bias—lack of allocation concealment and open-label design introduce a high risk of selection bias. Besides, baseline imbalances in a key prognostic factor (ICH volume) provide evidence that the randomization was not effectively achieved.

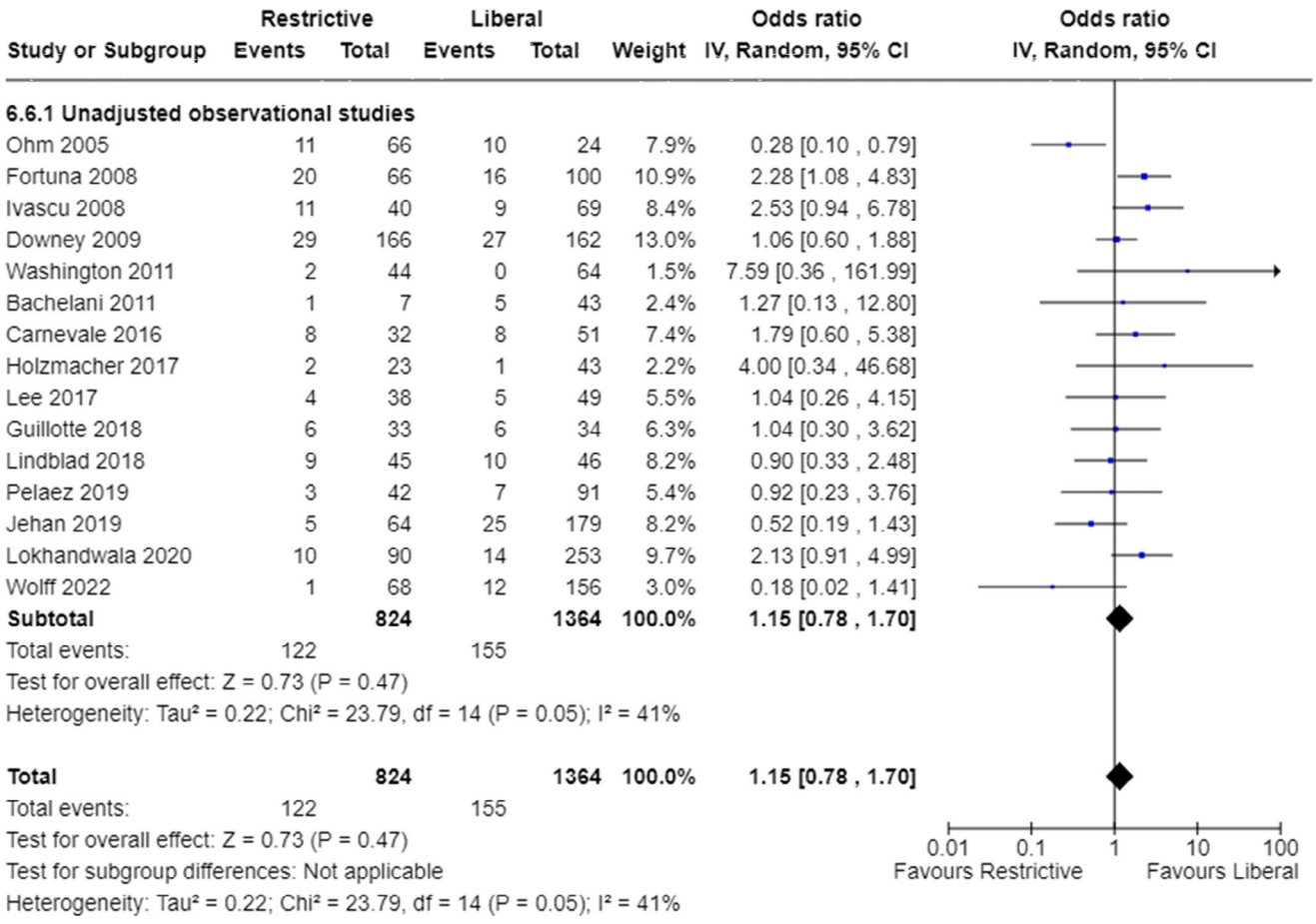

FIGURE 8 All-cause mortality in adults presenting with traumatic Intra-cranial hemorrhage; unadjusted observational studies.

reactions.[86] The overall support for restrictive platelet practices is reinforced by the signals of harm reported in selected RCTs in the liberal compared to restrictive arms.[3,4]

Our review evaluated the evidence for platelets in populations beyond HT where platelets are commonly administered. A large multi-institutional platelet transfusion audit showed the top medical specialties ordering platelets included hematology/oncology (38.9%), intensive care (17%), surgery (12.5%), and internal medicine/pediatrics (11.8%).[87] When mapping the identified literature to specific populations, HT was the most widely researched clinical setting in this review by number of RCTs, and for our primary outcome (mortality), 11 RCTs were identified including a total of 2851 patients. However, only two RCTs[63,64] ($n = 453$) for critically ill patients with consumptive thrombocytopenia, one RCT[3] ($n = 190$) with spontaneous-ICH, one RCT[56] ($n = 122$)

for CVS, and one RCT[47] ($n = 357$) in the peri-procedural patient population. No RCTs were identified related to traumatic-ICH.

A number of specific findings in our review warrant additional discussion. Within the HT population, an analysis of outcomes for autologous HSCT patients suggested prophylactic transfusion did not reduce Grade 2–4 bleeding[35,36,40] in comparison to patients receiving intensive myeloablative chemotherapy or allograft HSCT, who did see a benefit. This might reflect differences in the intensity of myeloablative treatments between groups. For the outcome of Grade 2–4 bleeding or equivalent in HT, liberal platelet transfusion was favored (1.23 [1.00, 1.53]), but the clinical significance of many Grade 2 bleeding events is controversial and the effect size with respect to patient values and preferences may not justify the strategy. While the overall trend across clinical populations supported restrictive practices being safe and/or at least as good as liberal, the PACER trial[47] in the peri-procedural population reported that for patients on the hematology ward a liberal strategy was favored with respect to Grade 2–4 bleeding. With recognition of this trial's limitations, including sample size across two sub-populations for ICU and hematology wards, anatomic site for line insertion, and risk of bias with respect to outcome assessors knowing treatment arm assignment, further evaluation by the ongoing larger international trial is anticipated.[88]

Our review's findings are consistent with results in other SRs identified by our search strategy, although most of these reviews focused on specific populations (Table S1). Lin et al.[29] reviewed platelet transfusion in the setting of ICH and Yanagawa et al.[20] reviewed platelet transfusion in the setting of CVS, both report non-superiority of platelet transfusions, consistent with our meta-analysis. A broad SR published in 2015 covered HT, peri-procedural, and ICH settings is missing more recent RCTs and adjusted observational studies.

A strength of our review was the rigorous systematic, standardized protocol use, and evaluation of evidence patterns using relative effects across various clinical populations administering platelet transfusions. Limitations of our review reflected the limited available evidence, especially for patient cohorts apart from HT. Due to inconsistent reporting, Red cell transfusion rate was not included as a surrogate marker for bleeding outside of IR procedures. Although our primary outcome was overall mortality, this may not be the most clinically relevant measure across all populations. Further work will explore this issue in more detail, using analyses at different mortality timepoints when sufficient data exist. Our pre-defined populations of interest may also overlap. Impaired bone marrow production could be a feature of critical illness thrombocytopenia despite predominating in HT.

We identified research implications in multiple clinical settings. There was a notable lack of RCTs related to platelet transfusion strategies in CPB and ECMO, although one ongoing (ECmo hemoSTAtic Transfusions In Children (ECSTATIC): NIH project number 1R34HL159119-01A1). No large RCTs informing platelet transfusion strategies in adult critically ill patients without dengue exist. The RCT by Van Baarle evaluated CVC placement in a mixed population of patients and raised possible divergent results between patients admitted to ICU versus hematology wards, and by compressibility of anatomic site. Ongoing larger trials can fully evaluate how the risk profile for pre-procedure platelets varies by type of procedure and baseline patient characteristics.[88] There were no RCTs comparing platelet strategies in other interventional radiology or major surgery settings. Some of these have trials underway.[89,90] Our findings provide a basis for ongoing updates of evidence and will be of value to inform guidelines; the results support restrictive use of platelets across different clinical settings, but also direct funders and policymakers to areas of research uncertainties. Transfusion services are facing challenges meeting platelet demands, and our review provides an evidence synthesis to inform quality improvement initiatives and development of mitigation strategies/hortage plans.

AUTHOR CONTRIBUTIONS

Susan Nahirniak, Rachel Jug, Ursula La Rocca, and Arwa Z. Al-Riyami performed the screening. Susan Nahirniak, Rachel Jug, Ursula La Rocca, and Arwa Z. Al-Riyami extracted the data. Aarti Bathla, Ryan A. Metcalf, Sandra K. White, and Simon J. Stanworth analyzed the data. Aarti Bathla, Ryan A. Metcalf, and Sandra K. White performed the meta-analysis and developed forest plots. Susan Nahirniak, Simon J. Stanworth, Rachel Jug, Aarti Bathla, Arwa Z. Al-Riyami, Ursula La Rocca, and Sandra K. White performed risk of bias assessments. Rachel Jug, Susan Nahirniak, Simon J. Stanworth, Arwa Z. Al-Riyami, Ursula La Rocca, Aarti Bathla, and Ryan A. Metcalf drafted the initial manuscript. All authors participated in the review and development of the manuscript.

ACKNOWLEDGMENTS

Non-author contributors: Aaron Tobian, Johns Hopkins Hospital, United States; Andreas Greinacher, University of Greifswald, Germany; Brittney Williams (Society of Cardiovascular Anesthesiologists representative), United States; Catherine Moltzan, Cancer Care Manitoba, Canada; Chee-Loong Saw, McGill University Health Centre, Canada; Cian O'Kelly, Alberta Health services, Canada; Daniela Filipescu, World Federation of Societies of Anaesthesiologists (WFSA representative),

Romania; Dean Fergusson, Ottawa Hospital Research Institute, Canada; Erica Wood, Monash University, Australia; Gopal Patidar, All India Institute of Medical Sciences, India; Heather Hume, University of Montreal, Canada; Ibe Onyekachi Ewa, Ebonyi State University, Nigeria; Jeannie Callum, Kingston Health Sciences Center, Canada; Jennifer Muszynski (Society of Critical Care Medicine representative), United States; Katerina Pavenski, Unity Health Toronto, Canada; Lise Estcourt, National Health Services Blood & Transplant, United Kingdom; Manjusha Pawagi (Patient representative) Canada; Marc Leone (European Society of Anesthesiology and Intensive Care (ESAIC) representative), France; Mark Fung, University of Vermont Medical Center, United States; Michael Murphy, National Health Service Blood & Transplant, United Kingdom; Michelle Zeller (Representative from American Society of Hematologists), Canada; Morten Moeller (ESAIC representative), Denmark; Oluwafemi Ajayi, Afe Babalola University, Nigeria; Peter Kranke (ESA representative), Wuerzburg, Germany; Ralph Vassalo, Blood System Inc, United States; Raman Uberoi, John Radcliffe Hospital, United Kingdom; Ravi Patel, Emory University School of Medicine, United States; Vernon Louw, University of Cape Town and Groote Schuur Hospital, South Africa; Zbigniew M. Szczepiorkowski, Dartmouth-Hitchcock Medical Center, United States. The authors also thank Thomasin Addams Webber for assistance with the literature search and Kimberly Figures and Sophie Chargé for administrative assistance. The authors would also like to acknowledge the three infants born to two of our authors during this systematic review process.

CONFLICT OF INTEREST STATEMENT

Aarti Bathla is currently employed with the Canadian Blood Services. Ryan A. Metcalf reports having served as a scientific advisor for Werfen. Rachel Jug, Susan Nahirniak, Simon J. Stanworth, Sandra K. White, Ursula La Rocca, and Arwa Z. Al-Riyami have no relevant conflicts of interest.

ORCID

Arwa Z. Al-Riyami https://orcid.org/0000-0001-8649-0650
Ryan A. Metcalf https://orcid.org/0000-0001-6074-7147
Simon J. Stanworth https://orcid.org/0000-0002-7414-4950

REFERENCES

1. Kaufman RM, Djulbegovic B, Gernsheimer T, Kleinman S, Tinmouth AT, Capocelli KE, et al. Platelet transfusion: a clinical practice guideline from the AABB. Ann Intern med. 2015;162(3):205–13.
2. Chowdhury F, Estcourt L, Murphy MF. Mitigating the impact of blood shortages in England. Br J Haematol. 2024;204(5):1660–71.
3. Baharoglu MI, Cordonnier C, Al-Shahi Salman R, de Gans K, Koopman MM, Brand A, et al. Platelet transfusion versus standard care after acute stroke due to spontaneous cerebral haemorrhage associated with antiplatelet therapy (PATCH): a randomised, open-label, phase 3 trial. Lancet. 2016;387(10038):2605–13. https://doi.org/10.1016/S0140-6736(16)30392-0
4. Curley A, Stanworth SJ, Willoughby K, Fustolo-Gunnink SF, Venkatesh V, Hudson C, et al. Randomized trial of platelet-transfusion thresholds in neonates. N Engl J med. 2019;380(3):242–51.
5. Metcalf RA, Nahirniak S, Guyatt G, et al. Platelet transfusion: 2025 AABB and ICTMG International Clinical Practice Guidelines. JAMA. Published online May 29, 2025. doi:10.1001/jama.2025.7529
6. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. https://doi.org/10.1136/bmj.n71
7. Estcourt LJ, Heddle N, Kaufman R, McCullough J, Murphy MF, Slichter S, et al. The challenges of measuring bleeding outcomes in clinical trials of platelet transfusions. Transfusion. 2013;53(7):1531–43.
8. Sterne JA, Hernan MA, Reeves BC, Savovic J, Berkman ND, Viswanathan M, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ. 2016;355:i4919.
9. Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ. 2017;358:j4008.
10. Anthon CT, Granholm A, Sivapalan P, Zellweger N, Pène F, Puxty K, et al. Prophylactic platelet transfusions versus no prophylaxis in hospitalized patients with thrombocytopenia: a systematic review with meta-analysis. Transfusion. 2022;62(10):2117–36.
11. Christou G, Iyengar A, Shorr R, Tinmouth A, Saidenberg E, Maze D, et al. Optimal transfusion practices after allogeneic hematopoietic cell transplantation: a systematic scoping review of evidence from randomized controlled trials. Transfusion. 2016;56(10):2607–14.
12. Crighton GL, Estcourt LJ, Wood EM, Trivella M, Doree C, Stanworth S. A therapeutic-only versus prophylactic platelet transfusion strategy for preventing bleeding in patients with haematological disorders after myelosuppressive chemotherapy or stem cell transplantation. Cochrane Database Syst Rev. 2015;(9):Cd010981.
13. Fustolo-Gunnink SF, Huisman EJ, van der Bom JG, van Hout FMA, Makineli S, Lopriore E, et al. Are thrombocytopenia and platelet transfusions associated with major bleeding in preterm neonates? A systematic review. Blood Rev. 2019;36:1–9. https://doi.org/10.1016/j.blre.2018.10.001
14. Kumar A, Mhaskar R, Grossman BJ, Kaufman RM, Tobian AA, Kleinman S, et al. Platelet transfusion: a systematic review of the clinical evidence. Transfusion. 2015;55(5):1116–27; quiz 5.
15. Newland A, Bentley R, Jakubowska A, Liebman H, Lorens J, Peck-Radosavljevic M, et al. A systematic literature review on the use of platelet transfusions in patients with thrombocytopenia. Hematology. 2019;24(1):679–719.
16. Estcourt LJ, Malouf R, Hopewell S, Doree C, Van Veen J. Use of platelet transfusions prior to lumbar punctures or epidural

anaesthesia for the prevention of complications in people with thrombocytopenia. Cochrane Database Syst Rev. 2018;4(4): Cd011980. https://doi.org/10.1002/14651858.CD011980.pub3
17. Estcourt LJ, Stanworth SJ, Doree C, Hopewell S, Trivella M, Murphy MF. Comparison of different platelet count thresholds to guide administration of prophylactic platelet transfusion for preventing bleeding in people with haematological disorders after myelosuppressive chemotherapy or stem cell transplantation. Cochrane Database Syst Rev. 2015;(11):Cd010983.
18. Karasneh J, Christoforou J, Walker JS, Manfredi M, Dave B, Diz Dios P, et al. World workshop on Oral Medicine VII: platelet count and platelet transfusion for invasive dental procedures in thrombocytopenic patients: a systematic review. Oral Dis. 2019;25(Suppl 1):174–81.
19. Rajapakse S, de Silva NL, Weeratunga P, Rodrigo C, Fernando SD. Prophylactic and therapeutic interventions for bleeding in dengue: a systematic review. Trans R Soc Trop med Hyg. 2017;111(10):433–9.
20. Yanagawa B, Ribeiro R, Lee J, Mazer CD, Cheng D, Martin J, et al. Platelet transfusion in cardiac surgery: a systematic review and meta-analysis. Ann Thorac Surg. 2021;111(2):607–14. https://doi.org/10.1016/j.athoracsur.2020.04.139
21. Al-Shahi Salman R, Law ZK, Bath PM, Steiner T, Sprigg N. Haemostatic therapies for acute spontaneous intracerebral haemorrhage. Cochrane Database Syst Rev. 2018;(4):Cd005951.
22. Alvikas J, Myers SP, Wessel CB, Okonkwo DO, Joseph B, Pelaez C, et al. A systematic review and meta-analysis of traumatic intracranial hemorrhage in patients taking prehospital antiplatelet therapy: is there a role for platelet transfusions? J Trauma Acute Care Surg. 2020;88(6):847–54.
23. Brogi E, Corbella D, Coccolini F, Gamberini E, Russo E, Agnoletti V, et al. The role of platelet transfusions after intracranial hemorrhage in patients on antiplatelet agents: a systematic review and meta-analysis. World Neurosurg. 2020;141:455–66. e13.
24. Leong LB, David TK. Is platelet transfusion effective in patients taking antiplatelet agents who suffer an intracranial hemorrhage? J Emerg med. 2015;49(4):561–72. https://doi.org/10.1016/j.jemermed.2015.02.023
25. Morris NA, Patel N, Galvagno SM Jr, Ludeman E, Schwartzbauer GT, Pourmand A, et al. The effect of platelet transfusion on functional independence and mortality after antiplatelet therapy associated spontaneous intracerebral hemorrhage: a systematic review and meta-analysis. J Neurol Sci. 2020;417:117075.
26. Nishijima DK, Zehtabchi S, Berrong J, Legome E. Utility of platelet transfusion in adult patients with traumatic intracranial hemorrhage and preinjury antiplatelet use: a systematic review. J Trauma Acute Care Surg. 2012;72(6):1658–63.
27. Thorn S, Guting H, Mathes T, Schafer N, Maegele M. The effect of platelet transfusion in patients with traumatic brain injury and concomitant antiplatelet use: a systematic review and meta-analysis. Transfusion. 2019;59(11):3536–44.
28. Batchelor J, Grayson A. A meta-analysis to determine the effect on survival of platelet transfusions in patients with either spontaneous or traumatic antiplatelet medication-associated intracramal haemorrhage. BMJ Open. 2012;2:e000588.
29. Lin Y, Liu Y, Liu L, Zhang L, Lin Y, Yu J, et al. Platelet transfusion for spontaneous intracerebral hemorrhage with prior antiplatelet: a systematic review and meta-analysis. Medicine (Baltimore). 2023;102(46):e36072.
30. Heckman KD, Weiner GJ, Davis CS, Strauss RG, Jones MP, Burns CP. Randomized study of prophylactic platelet transfusion threshold during induction therapy for adult acute leukemia: 10,000/microL versus 20,000/microL. J Clin Oncol. 1997; 15(3):1143–9.
31. Heddle NM, Cook RJ, Tinmouth A, Kouroukis CT, Hervig T, Klapper E, et al. A randomized controlled trial comparing standard- and low-dose strategies for transfusion of platelets (SToP) to patients with thrombocytopenia. Blood. 2009;113(7): 1564–73.
32. Rebulla P, Finazzi G, Marangoni F, Avvisati G, Gugliotta L, Tognoni G, et al. The threshold for prophylactic platelet transfusions in adults with acute myeloid leukemia Gruppo Italiano Malattie Ematologiche Maligne dell'Adulto. N Engl J med. 1997;337(26):1870–5. https://doi.org/10.1056/NEJM199712253372602
33. Slichter SJ, Kaufman RM, Assmann SF, McCullough J, Triulzi DJ, Strauss RG, et al. Dose of prophylactic platelet transfusions and prevention of hemorrhage. N Engl J med. 2010;362(7):600–13.
34. Solomon J, Bofenkamp T, Fahey JL, Chillar RK, Beutel E. Platelet prophylaxis in acute non-lymphoblastic leukaemia. Lancet. 1978;1(8058):267.
35. Stanworth SJ, Estcourt LJ, Powter G, Kahan BC, Dyer C, Choo L, et al. A no-prophylaxis platelet-transfusion strategy for hematologic cancers. N Engl J med. 2013;368(19):1771–80.
36. Wandt H, Schaefer-Eckart K, Wendelin K, Pilz B, Wilhelm M, Thalheimer M, et al. Therapeutic platelet transfusion versus routine prophylactic transfusion in patients with haematological malignancies: an open-label, multicentre, randomised study. Lancet. 2012;380(9850):1309–16.
37. Zumberg MS, del Rosario ML, Nejame CF, Pollock BH, Garzarella L, Kao KJ, et al. A prospective randomized trial of prophylactic platelet transfusion and bleeding incidence in hematopoietic stem cell transplant recipients: 10,000/L versus 20,000/microL trigger. Biol Blood Marrow Transplant. 2002; 8(10):569–76. https://doi.org/10.1053/bbmt.2002.v8.pm12434952
38. Diedrich B, Remberger M, Shanwell A, Svahn BM, Ringden O. A prospective randomized trial of a prophylactic platelet transfusion trigger of 10 × 10(9) per L versus 30 × 10(9) per L in allogeneic hematopoietic progenitor cell transplant recipients. Transfusion. 2005;45(7):1064–72.
39. Sensebe L, Giraudeau B, Bardiaux L, Deconinck E, Schmidt A, Bidet ML, et al. The efficiency of transfusing high doses of platelets in hematologic patients with thrombocytopenia: results of a prospective, randomized, open, blinded end point (PROBE) study. Blood. 2005;105(2):862–4.
40. Tinmouth A, Tannock IF, Crump M, Tomlinson G, Brandwein J, Minden M, et al. Low-dose prophylactic platelet transfusions in recipients of an autologous peripheral blood progenitor cell transplant and patients with acute leukemia: a randomized controlled trial with a sequential Bayesian design. Transfusion. 2004;44(12):1711–9.
41. Kellum A, Jagiello-Gruszfeld A, Bondarenko IN, Patwardhan R, Messam C, Mostafa Kamel Y. A randomized, double-blind, placebo-controlled, dose ranging study to assess

the efficacy and safety of eltrombopag in patients receiving carboplatin/paclitaxel for advanced solid tumors. Curr med Res Opin. 2010;26(10):2339–46. https://doi.org/10.1185/03007995.2010.510051
42. Natale R, Charu V, Schütte W, Albert I, Tehenes S, McCoy J, et al. 9248 safety of romiplostim for treatment of chemotherapy-induced thrombocytopenia (CIT) in patients with advanced non-small cell lung cancer (NSCLC). Eur J Cancer Suppl. 2009;7(2):574.
43. Winer ES, Safran H, Karaszewska B, Richards DA, Hartner L, Forget F, et al. Eltrombopag with gemcitabine-based chemotherapy in patients with advanced solid tumors: a randomized phase I study. Cancer med. 2015;4(1):16–26.
44. Malouf R, Ashraf A, Hadjinicolaou AV, Doree C, Hopewell S, Estcourt LJ. Comparison of a therapeutic-only versus prophylactic platelet transfusion policy for people with congenital or acquired bone marrow failure disorders. Cochrane Database Syst Rev. 2018;5:Cd012342.
45. Josephson CD, Glynn SA, Kleinman SH, Blajchman MA. A multidisciplinary "think tank": the top 10 clinical trial opportunities in transfusion medicine from the National Heart, Lung, and Blood Institute-sponsored 2009 state-of-the-science symposium. Transfusion. 2011;51(4):828–41. https://doi.org/10.1111/j.1537-2995.2010.02898.x
46. Murphy S, Litwin S, Herring LM, Koch P, Remischovsky J, Donaldson MH, et al. Indications for platelet transfusion in children with acute leukemia. Am J Hematol. 1982;12(4):347–56.
47. van Baarle FLF, van de Weerdt EK, van der Velden W, Ruiterkamp RA, Tuinman PR, Ypma PF, et al. Platelet transfusion before CVC placement in patients with thrombocytopenia. N Engl J med. 2023;388(21):1956–65.
48. Ray CE Jr, Shenoy SS. Patients with thrombocytopenia: outcome of radiologic placement of central venous access devices. Radiology. 1997;204(1):97–9.
49. Warner MA, Woodrum D, Hanson A, Schroeder DR, Wilson G, Kor DJ. Preprocedural platelet transfusion for patients with thrombocytopenia undergoing interventional radiology procedures is not associated with reduced bleeding complications. Transfusion. 2017;57(4):890–8.
50. Kozak M, Hallan DR, Stoltzfus M, Rizk E. Lumbar puncture in thrombocytopenia: the floor is not firm. Cureus. 2023;15(7):e42019.
51. Ning S, Kerbel B, Callum J, Lin Y. Safety of lumbar punctures in patients with thrombocytopenia. Vox Sang. 2016;110(4):393–400.
52. van Veen JJ, Nokes TJ, Makris M. The risk of spinal haematoma following neuraxial anaesthesia or lumbar puncture in thrombocytopenic individuals. Br J Haematol. 2010;148(1):15–25.
53. Chung HH, Morjaria S, Frame J, Riley M, Zhang AW, Martin SC, et al. Rethinking the need for a platelet transfusion threshold of 50 × 10(9)/L for lumbar puncture in cancer patients. Transfusion. 2020;60(10):2243–9.
54. Foerster MV, Pedrosa Fde P, da Fonseca TC, Couceiro TC, Lima LC. Lumbar punctures in thrombocytopenic children with cancer. Paediatr Anaesth. 2015;25(2):206–10.
55. Howard SC, Gajjar A, Ribeiro RC, Rivera GK, Rubnitz JE, Sandlund JT, et al. Safety of lumbar puncture for children with acute lymphoblastic leukemia and thrombocytopenia. Jama. 2000;284(17):2222–4.
56. Lunen TB, Johansson PI, Jensen LP, Homburg KM, Roeder OC, Lonn L, et al. Administration of platelets to ruptured abdominal aortic aneurysm patients before open surgery: a prospective, single-blinded, randomised study. Transfus med. 2018;28(5):386–91.
57. Simon TL, Akl BF, Murphy W. Controlled trial of routine administration of platelet concentrates in cardiopulmonary bypass surgery. Ann Thorac Surg. 1984;37(5):359–64.
58. Gautam NK, Pierre J, Edmonds K, Pawelek O, Griffin E, Xu Z, et al. Transfusing platelets during bypass rewarming in neonates improves postoperative outcomes: a randomized controlled trial. World J Pediatr Congenit Heart Surg. 2020;11(1):71–6.
59. Karkouti K, Wijeysundera DN, Yau TM, Callum JL, Meineri M, Wasowicz M, et al. Platelet transfusions are not associated with increased morbidity or mortality in cardiac surgery. Can J Anaesth. 2006;53(3):279–87.
60. Kremke M, Hansen MK, Christensen S, Tang M, Andreasen JJ, Jakobsen CJ. The association between platelet transfusion and adverse outcomes after coronary artery bypass surgery. Eur J Cardiothorac Surg. 2015;48(5):e102–9.
61. McGrath T, Koch CG, Xu M, Li L, Mihaljevic T, Figueroa P, et al. Platelet transfusion in cardiac surgery does not confer increased risk for adverse morbid outcomes. Ann Thorac Surg. 2008;86(2):543–53.
62. van Hout FM, Hogervorst EK, Rosseel PM, van der Bom JG, Bentala M, van Dorp EL, et al. Does a platelet transfusion independently affect bleeding and adverse outcomes in cardiac surgery? Anesthesiology. 2017;126(3):441–9. https://doi.org/10.1097/ALN.0000000000001518
63. Lye DC, Archuleta S, Syed-Omar SF, Low JG, Oh HM, Wei Y, et al. Prophylactic platelet transfusion plus supportive care versus supportive care alone in adults with dengue and thrombocytopenia: a multicentre, open-label, randomised, superiority trial. Lancet. 2017;389(10079):1611–8.
64. Khan Assir MZ, Kamran U, Ahmad HI, Bashir S, Mansoor H, Anees SB, et al. Effectiveness of platelet transfusion in dengue fever: a randomized controlled trial. Transfus med Hemother. 2013;40(5):362–8.
65. Kumar J, Dutta S, Sundaram V, Saini SS, Sharma RR, Varma N. Platelet transfusion for PDA closure in preterm infants: a randomized controlled trial. Pediatrics. 2019;143(5):2018–565.
66. Andrew M, Vegh P, Caco C, Kirpalani H, Jefferies A, Ohlsson A, et al. A randomized, controlled trial of platelet transfusions in thrombocytopenic premature infants. J Pediatr. 1993;123(2):285–91.
67. Warner MA, Chandran A, Frank RD, Kor DJ. Prophylactic platelet transfusions for critically ill patients with thrombocytopenia: a single-institution propensity-matched cohort study. Anesth Analg. 2019;128(2):288–95.
68. He S, Fan C, Ma J, Tang C, Chen Y. Platelet transfusion in patients with sepsis and thrombocytopenia: a propensity score-matched analysis using a large ICU database. Front med (Lausanne). 2022;9:830177.
69. Xiao K, Xiong W, Liu Q, Deng H, Zhang Z, Yu K, et al. The impact of platelet transfusion on prognosis in adult burn

patients with thrombocytopenia: a propensity score matching analysis. Burns. 2024;50(9):107237.
70. Arnone GD, Kumar P, Wonais MC, Esfahani DR, Campbell-Lee SA, Charbel FT, et al. Impact of platelet transfusion on intracerebral hemorrhage in patients on antiplatelet therapy-an analysis based on intracerebral hemorrhage score. World Neurosurg. 2018;111:e895–904.
71. Fortuna GR, Mueller EW, James LE, Shutter LA, Butler KL. The impact of preinjury antiplatelet and anticoagulant pharmacotherapy on outcomes in elderly patients with hemorrhagic brain injury. Surgery. 2008;144(4):598–603; discussion—5.
72. Guillotte AR, Herbert JP, Madsen R, Hammer RD, Litofsky NS. Effects of platelet dysfunction and platelet transfusion on outcomes in traumatic brain injury patients. Brain Inj. 2018; 32(13–14):1849–57.
73. Holzmacher JL, Reynolds C, Patel M, Maluso P, Holland S, Gamsky N, et al. Platelet transfusion does not improve outcomes in patients with brain injury on antiplatelet therapy. Brain Inj. 2018;32(3):325–30.
74. Ivascu FA, Howells GA, Junn FS, Bair HA, Bendick PJ, Janczyk RJ. Predictors of mortality in trauma patients with intracranial hemorrhage on preinjury aspirin or clopidogrel. J Trauma. 2008;65(4):785–8.
75. Jehan F, Zeeshan M, Kulvatunyou N, Khan M, O'Keeffe T, Tang A, et al. Is there a need for platelet transfusion after traumatic brain injury in patients on P2Y12 inhibitors? J Surg Res. 2019;236:224–9.
76. Lee AT, Gagnidze A, Pan SR, Sookplung P, Nair B, Newman SF, et al. Preoperative Low-dose aspirin exposure and outcomes after emergency neurosurgery for traumatic intracranial hemorrhage in elderly patients. Anesth Analg. 2017; 125(2):514–20.
77. Lindblad C, Thelin EP, Nekludov M, Frostell A, Nelson DW, Svensson M, et al. Assessment of platelet function in traumatic brain injury-a retrospective observational study in the neurocritical care setting. Front Neurol. 2018;9:15.
78. Ohm C, Mina A, Howells G, Bair H, Bendick P. Effects of antiplatelet agents on outcomes for elderly patients with traumatic intracranial hemorrhage. J Trauma. 2005;58(3):518–22.
79. Pelaez CA, Spilman SK, Bell CT, Eastman DK, Sidwell RA. Not all head injured patients on antiplatelet drugs need platelets: integrating platelet reactivity testing into platelet transfusion guidelines. Injury. 2019;50(1):73–8.
80. Washington CW, Schuerer DJ, Grubb RL Jr. Platelet transfusion: an unnecessary risk for mild traumatic brain injury patients on antiplatelet therapy. J Trauma. 2011;71(2):358–63. https://doi.org/10.1097/TA.0b013e318220ad7e
81. Downey DM, Monson B, Butler KL, Fortuna GR Jr, Saxe JM, Dolan JP, et al. Does platelet administration affect mortality in elderly head-injured patients taking antiplatelet medications? Am Surg. 2009;75(11):1100–3. https://doi.org/10.1177/000313480907501115
82. Bachelani AM, Bautz JT, Sperry JL, Corcos A, Zenati M, Billiar TR, et al. Assessment of platelet transfusion for reversal of aspirin after traumatic brain injury. Surgery. 2011;150(4):836–43.
83. Carnevale JA, Segar DJ, Powers AY, Shah M, Doberstein C, Drapcho B, et al. Blossoming contusions: identifying factors contributing to the expansion of traumatic intracerebral hemorrhage. J Neurosurg. 2018;129(5):1305–16.
84. Wolff C, Muakkassa F, Marley R, El-Khatib A, Docherty C, Muakkassa L, et al. Routine platelet transfusion in patients with traumatic intracranial hemorrhage taking antiplatelet medication: is it warranted? Can J Surg. 2022;65(2):E206–11.
85. Lokhandwala AM, Asmar S, Khurrum M, Chehab M, Bible L, Castanon L, et al. Platelet transfusion after traumatic intracranial hemorrhage in patients on antiplatelet agents. J Surg Res. 2021;257:239–45.
86. Bolton-Maggs PH, Cohen H. Serious hazards of transfusion (SHOT) haemovigilance and progress is improving transfusion safety. Br J Haematol. 2013;163(3):303–14. https://doi.org/10.1111/bjh.12547
87. Hill-Strathy M, Pinkerton PH, Thompson TA, Wendt A, Collins A, Cohen R, et al. Evaluating the appropriateness of platelet transfusions compared with evidence-based platelet guidelines: an audit of platelet transfusions at 57 hospitals. Transfusion. 2021;61(1):57–71.
88. Stanworth SJ, Shah A, Doidge J, Watkinson P. The ongoing dilemma of prophylactic platelet transfusions pre-procedure and the development of evidence-based recommendations. Transfus med. 2023;33(5):428–30.
89. ECMO hemostatic transfusions in children [Internet]. 2023 [March 31, 2025]. Available from: https://clinicaltrials.gov/study/NCT05796557
90. Watkinson P, Noble H. A study to define the platelet count below which critically ill patients should receive a platelet transfusion before an invasive procedure. In: IRcA, editor. ISRCTN79371664.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Jug R, La Rocca U, Al-Riyami AZ, Bathla A, Metcalf RA, White SK, et al. The clinical use of platelet transfusions: A systematic literature review and meta-analysis on behalf of the International Collaboration for Transfusion Medicine Guidelines. Transfusion. 2025. https://doi.org/10.1111/trf.18277