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Systematic Review

Prophylactic Versus Therapeutic Platelet Transfusion in Patients with Hematological Malignancies: A Systematic Review and Meta-Analysis

Manish Kumar Nigam*[1], Deepali Singh[2], Kanupriya Tiwari[3], Shoubhik Patra[4]

[1]Senior Medical Officer, Blood Centre, Trauma Centre & Super Specialty Hospital, Banaras Hindu University, Varanasi, Uttar Pradesh, India
[2]Senior Resident, Department of Pathology, Trauma Centre, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India.
[3]Senior Resident, Department of Microbiology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India.
[4]Assistant Professor, Department of Pathology, Shri Shankaracharya Institute of Medical Sciences, Durg, Chhattisgarh, India.

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Corresponding Author:

Manish Kumar Nigam
Senior Medical Officer, Blood Centre, Trauma Centre & Super Specialty Hospital, Banaras Hindu University, Varanasi, Uttar Pradesh, India.
Email: drmonix@gmail.com

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ABSTRACT

Background: Thrombocytopenia is a common complication in patients with hematological malignancies undergoing intensive chemotherapy or hematopoietic stem cell transplantation (HSCT). Platelet transfusion remains the cornerstone of bleeding prevention in these patients. Traditionally, prophylactic platelet transfusions have been administered when platelet counts fall below a predetermined threshold, whereas therapeutic platelet transfusions are administered only after clinically significant bleeding occurs. Although prophylactic transfusion strategies have been widely adopted, concerns regarding transfusion-related complications, resource utilization, alloimmunization, and healthcare costs have prompted reevaluation of therapeutic-only approaches.

Objective: To compare the efficacy and safety of prophylactic versus therapeutic platelet transfusion strategies in patients with hematological malignancies through a systematic review and meta-analysis.

Methods: A systematic review and meta-analysis was conducted according to PRISMA 2020 guidelines. PubMed, Embase, Scopus, Web of Science, Cochrane Library, and Google Scholar were searched from inception through December 2025. Randomized controlled trials (RCTs) and observational studies comparing prophylactic and therapeutic platelet transfusion strategies in patients with hematological malignancies were included. Primary outcomes were incidence of clinically significant bleeding (WHO grade ≥2), severe bleeding (WHO grade ≥3), and all-cause mortality. Secondary outcomes included platelet transfusion requirements, transfusion-related adverse events, hospital stay, and infection rates. Random-effects meta-analysis was performed using pooled risk ratios (RRs) and mean differences (MDs) with 95% confidence intervals (CIs).

Results: Fourteen studies comprising 4,862 patients met inclusion criteria. Prophylactic platelet transfusion significantly reduced the risk of clinically significant bleeding compared with therapeutic transfusion (RR = 0.72, 95% CI: 0.61–0.85, $p < 0.001$). Severe bleeding events were also lower in the prophylactic group (RR = 0.68, 95% CI: 0.49–0.94, $p = 0.02$). No significant difference was observed in all-cause mortality (RR = 0.97, 95% CI: 0.82–1.15, $p = 0.73$). Patients receiving prophylactic transfusions required a greater number of platelet units per treatment cycle (MD = 2.8 units, 95% CI: 1.9–3.7). Transfusion-related reactions occurred more frequently among prophylactically transfused patients, although the difference did not reach statistical significance. Length of hospital stay and infection rates were comparable between groups.

Conclusion: Prophylactic platelet transfusion significantly reduces the incidence of clinically significant and severe bleeding in patients with hematological

malignancies but increases platelet utilization. No mortality benefit was observed. These findings support continued use of prophylactic platelet transfusion in high-risk patients while highlighting the need for individualized transfusion strategies and further research into risk-adapted approaches.

Keywords*:* Platelet transfusion; thrombocytopenia; hematological malignancies; leukemia; stem cell transplantation; prophylactic transfusion; therapeutic transfusion; bleeding; systematic review; meta-analysis.

INTRODUCTION

Hematological malignancies, including acute leukemia, chronic leukemia, myelodysplastic syndromes, lymphoma, multiple myeloma, and patients undergoing hematopoietic stem cell transplantation (HSCT), are frequently complicated by severe thrombocytopenia resulting from disease-related bone marrow failure and myelosuppressive chemotherapy [1,2]. Thrombocytopenia is a major contributor to bleeding morbidity and mortality in these patients, making platelet transfusion an essential component of supportive care in modern hematology practice [3]. Despite significant advances in chemotherapy, targeted therapies, and transplantation techniques, bleeding complications remain a substantial clinical concern, particularly among patients with prolonged periods of profound thrombocytopenia [4].

Platelets play a critical role in primary hemostasis through adhesion, activation, and aggregation at sites of vascular injury [5]. When platelet counts decline below critical thresholds, spontaneous bleeding may occur, ranging from minor mucocutaneous hemorrhage to life-threatening intracranial or gastrointestinal bleeding [6]. Historically, severe thrombocytopenia has been associated with increased bleeding risk, leading to the widespread adoption of prophylactic platelet transfusion strategies aimed at preventing hemorrhagic complications before clinical bleeding develops [7].

The concept of prophylactic platelet transfusion emerged during the 1960s and 1970s following observations that maintaining platelet counts above predetermined thresholds reduced spontaneous bleeding episodes among patients receiving intensive chemotherapy [8]. Since then, prophylactic transfusion has become standard practice in many institutions, particularly when platelet counts fall below 10×10^9/L in clinically stable patients [9]. Current guidelines from several professional organizations, including the British Society for Haematology, American Society of Clinical Oncology, and AABB, generally recommend prophylactic platelet transfusion for patients with therapy-induced hypoproliferative thrombocytopenia [10–12].

Although prophylactic platelet transfusion has demonstrated effectiveness in reducing bleeding events, this strategy is associated with several limitations. Platelet products are expensive, have a short shelf life, and require substantial healthcare resources for collection, storage, and administration [13]. Furthermore, repeated transfusions may result in alloimmunization, platelet refractoriness, febrile non-hemolytic transfusion reactions, transfusion-associated circulatory overload, transfusion-related acute lung injury, and infectious complications [14–16]. These concerns have stimulated interest in alternative transfusion approaches that may reduce platelet utilization without compromising patient safety.

Therapeutic platelet transfusion, also known as a “bleeding-triggered” strategy, involves administering platelet transfusions only after clinically significant bleeding occurs rather than based solely on platelet count thresholds [17]. Proponents of therapeutic transfusion argue that many patients tolerate profound thrombocytopenia without major bleeding and that prophylactic transfusions may expose patients to unnecessary risks and costs [18]. A therapeutic-only approach has the potential to reduce platelet consumption, lower healthcare expenditures, and minimize transfusion-related complications [19].

Several randomized controlled trials have compared prophylactic and therapeutic platelet transfusion strategies in patients with hematological malignancies [20,21]. The Trial of Prophylactic Platelets (TOPPS), one of the largest multicenter studies in this field, demonstrated that prophylactic transfusion significantly reduced bleeding episodes but required substantially greater platelet utilization [22]. Similarly, studies conducted in patients undergoing autologous stem cell transplantation have reported conflicting findings regarding the balance between bleeding prevention and transfusion burden [23,24].

The relationship between platelet count and bleeding risk is complex and influenced by numerous factors beyond thrombocytopenia alone. Fever, sepsis, disseminated intravascular coagulation, invasive procedures, anticoagulant use, endothelial dysfunction, and disease-specific characteristics may significantly affect bleeding risk [25,26]. Consequently, reliance on platelet count alone as a transfusion trigger has been increasingly questioned, prompting exploration of individualized and risk-adapted transfusion strategies [27].

Meta-analyses conducted over the past decade have generally supported prophylactic platelet transfusion for reducing bleeding events; however, important uncertainties remain regarding its impact on severe bleeding, mortality, quality of life, and healthcare resource utilization [28,29]. Furthermore, newer evidence from contemporary clinical trials and evolving

transfusion practices necessitate an updated synthesis of available data [30]. As healthcare systems worldwide face increasing pressure to optimize blood product utilization, understanding the relative benefits and risks of prophylactic and therapeutic transfusion strategies has become increasingly important [31].

Patients with acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL), and recipients of HSCT represent particularly vulnerable populations due to prolonged periods of severe thrombocytopenia and intensive treatment regimens [32]. In these patients, preventing major hemorrhagic complications is a key therapeutic objective, yet excessive transfusion exposure may contribute to treatment-related morbidity and increased healthcare costs [33]. Determining the optimal transfusion strategy therefore remains a critical challenge in supportive hematology care.

Recent advances in pathogen reduction technologies, platelet storage methods, and transfusion medicine practices have further influenced the risk-benefit profile of platelet transfusion strategies [34]. Additionally, emerging predictive models incorporating clinical risk factors and biomarkers may facilitate more individualized transfusion decisions in the future [35]. Nevertheless, current clinical practice remains largely guided by evidence generated from comparative studies of prophylactic and therapeutic platelet transfusion approaches.

Given the ongoing debate regarding optimal platelet transfusion practice, a comprehensive evaluation of available evidence is warranted. Therefore, the present systematic review and meta-analysis was undertaken to compare prophylactic and therapeutic platelet transfusion strategies in patients with hematological malignancies. The primary objectives were to assess their effects on clinically significant bleeding, severe bleeding, and mortality. Secondary objectives included evaluation of platelet utilization, transfusion-related adverse events, infection rates, and healthcare resource use. By synthesizing data from randomized and observational studies, this review aims to provide evidence-based guidance for clinicians managing thrombocytopenic patients with hematological malignancies.

MATERIALS AND METHODS

Study Design

This systematic review and meta-analysis was conducted to compare the efficacy and safety of prophylactic versus therapeutic platelet transfusion strategies in patients with hematological malignancies. The study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines and recommendations from the Cochrane Handbook for Systematic Reviews of Interventions.

Protocol and Registration

The review protocol was developed before commencement of the study and followed internationally accepted standards for systematic reviews and meta-analyses. The research question was formulated according to the Population, Intervention, Comparator, Outcome (PICO) framework.

PICO Framework

Population (P): Patients with hematological malignancies experiencing chemotherapy-induced or disease-related thrombocytopenia.

Intervention (I): Prophylactic platelet transfusion administered according to predefined platelet count thresholds.

Comparator (C): Therapeutic platelet transfusion administered only in response to clinically significant bleeding.

Outcomes (O): Clinically significant bleeding, severe bleeding, mortality, platelet utilization, transfusion-related adverse events, infection rates, and hospital stay.

Eligibility Criteria

Inclusion Criteria

Studies were included if they met the following criteria:

1. Randomized controlled trials (RCTs), prospective cohort studies, retrospective cohort studies, or comparative observational studies.
2. Adult or pediatric patients diagnosed with hematological malignancies.
3. Studies comparing prophylactic and therapeutic platelet transfusion strategies.
4. Studies reporting at least one predefined outcome measure.
5. Studies published in peer-reviewed journals.
6. Articles published in English.
7. Studies published from January 1990 to December 2025.

Exclusion Criteria

1. Case reports and case series involving fewer than 10 patients.
2. Narrative reviews, systematic reviews, editorials, letters, and conference abstracts.

3. Studies lacking comparative transfusion groups.
4. Studies involving surgical, trauma, or non-hematological thrombocytopenic patients.
5. Animal or laboratory studies.
6. Duplicate publications or overlapping datasets.
7. Studies with incomplete outcome data.

Information Sources

A comprehensive literature search was performed using the following electronic databases:

- PubMed/MEDLINE
- Embase
- Scopus
- Web of Science
- Cochrane Central Register of Controlled Trials (CENTRAL)
- Google Scholar

The search included all studies published up to December 2025.
Reference lists of relevant reviews and eligible studies were manually searched to identify additional publications.

Search Strategy

Search terms were developed using Medical Subject Headings (MeSH) and free-text keywords.

Search Terms

- "Platelet transfusion"
- "Prophylactic platelet transfusion"
- "Therapeutic platelet transfusion"
- "Thrombocytopenia"
- "Hematological malignancy"
- "Acute leukemia"
- "Acute myeloid leukemia"
- "Acute lymphoblastic leukemia"
- "Stem cell transplantation"
- "Bone marrow transplantation"
- "Bleeding"
- "Hemorrhage"
- "Platelet threshold"

Example Search Strategy

("Platelet transfusion" OR "Platelet support") AND ("Prophylactic" OR "Therapeutic") AND ("Leukemia" OR "Hematological malignancy" OR "Stem cell transplantation") AND ("Bleeding" OR "Hemorrhage")

Study Selection

- All retrieved references were imported into reference management software and duplicate records were removed.
- Two independent reviewers screened titles and abstracts for eligibility. Potentially relevant studies underwent full-text assessment according to predefined inclusion and exclusion criteria.
- Any disagreements between reviewers were resolved through discussion and consultation with a third reviewer.
- The study selection process was documented using a PRISMA 2020 flow diagram.

Data Extraction

Data extraction was independently performed by two investigators using a standardized data collection form.

Study Characteristics

The following variables were extracted:

- First author
- Publication year
- Country
- Study design
- Sample size

Patient Characteristics

- Age
- Gender

- Type of hematological malignancy
- Treatment regimen
- Stem cell transplantation status

Transfusion Characteristics
- Platelet transfusion strategy
- Platelet transfusion threshold
- Number of platelet transfusions
- Platelet dose administered

Clinical Outcomes
Primary Outcomes
1. Clinically significant bleeding (WHO grade ≥2)
2. Severe bleeding (WHO grade ≥3)
3. All-cause mortality

Secondary Outcomes
1. Total platelet transfusions per patient
2. Transfusion-related adverse events
3. Febrile reactions
4. Platelet refractoriness
5. Infection rates
6. Length of hospital stay
7. Intensive care admission
8. Quality-of-life measures

Quality Assessment
Methodological quality was independently assessed by two reviewers.

Randomized Controlled Trials
RCTs were assessed using the Cochrane Risk of Bias Tool 2.0 evaluating:
- Randomization process
- Allocation concealment
- Blinding
- Missing outcome data
- Outcome measurement
- Selective reporting

Observational Studies
Observational studies were assessed using the Newcastle–Ottawa Scale (NOS).
Quality categories:
- High quality: NOS score ≥7
- Moderate quality: NOS score 5–6
- Low quality: NOS score <5

Discrepancies were resolved by consensus.

Outcome Measures
Primary Outcomes
- Incidence of clinically significant bleeding (WHO grade ≥2)
- Incidence of severe bleeding (WHO grade ≥3)
- All-cause mortality

Secondary Outcomes
- Number of platelet units transfused
- Incidence of transfusion reactions
- Platelet refractoriness
- Infection rates
- Hospital length of stay
- Resource utilization

Statistical Analysis
Meta-analysis was performed using Review Manager (RevMan 5.4), Comprehensive Meta-Analysis (CMA 4.0), and IBM SPSS Statistics version 27.

Effect Measures
For dichotomous outcomes:
- Risk Ratio (RR)
- Odds Ratio (OR)

For continuous outcomes:
- Mean Difference (MD)
- Standardized Mean Difference (SMD)

All estimates were reported with 95% confidence intervals (CIs).

Model Selection
Because variation among patient populations, treatment regimens, and transfusion protocols was anticipated, a random-effects model (DerSimonian–Laird method) was applied.

Heterogeneity Assessment
Statistical heterogeneity was evaluated using:
- Cochran's Q statistic
- Higgins I^2 statistic

Interpretation of I^2 values:
- <25%: Low heterogeneity
- 25–50%: Moderate heterogeneity
- 50%: High heterogeneity

Subgroup Analyses
Subgroup analyses were performed according to:
- Acute myeloid leukemia (AML)
- Acute lymphoblastic leukemia (ALL)
- Stem cell transplantation recipients
- Adult versus pediatric populations
- Platelet transfusion threshold

Sensitivity Analysis
Sensitivity analyses were conducted by sequential exclusion of individual studies to determine the robustness of pooled estimates.

Publication Bias
Publication bias was assessed using:
- Funnel plot analysis
- Egger's regression test
- Begg's rank correlation test

A p-value <0.05 was considered statistically significant.

Ethical Considerations
As this study analyzed previously published data and did not involve direct patient recruitment or identifiable patient information, institutional ethical approval and informed consent were not required.

Reporting Standards
The systematic review and meta-analysis adhered to PRISMA 2020 reporting standards and methodological recommendations for evidence synthesis in transfusion medicine and hematology research.

RESULTS
Study Selection
The systematic search identified 3,842 records from PubMed, Embase, Scopus, Web of Science, Cochrane Library, and Google Scholar. After removal of 1,126 duplicate records, 2,716 studies underwent title and abstract screening. Of these, 2,628 articles were excluded because they were reviews, editorials, case reports, laboratory studies, or unrelated to platelet transfusion strategies. The remaining 88 full-text articles were assessed for eligibility. Following detailed evaluation, 74 studies were excluded due to lack of comparative groups, insufficient outcome reporting, duplicate datasets, or non-

hematological patient populations. Finally, 14 studies comprising 4,862 patients were included in the qualitative and quantitative synthesis.

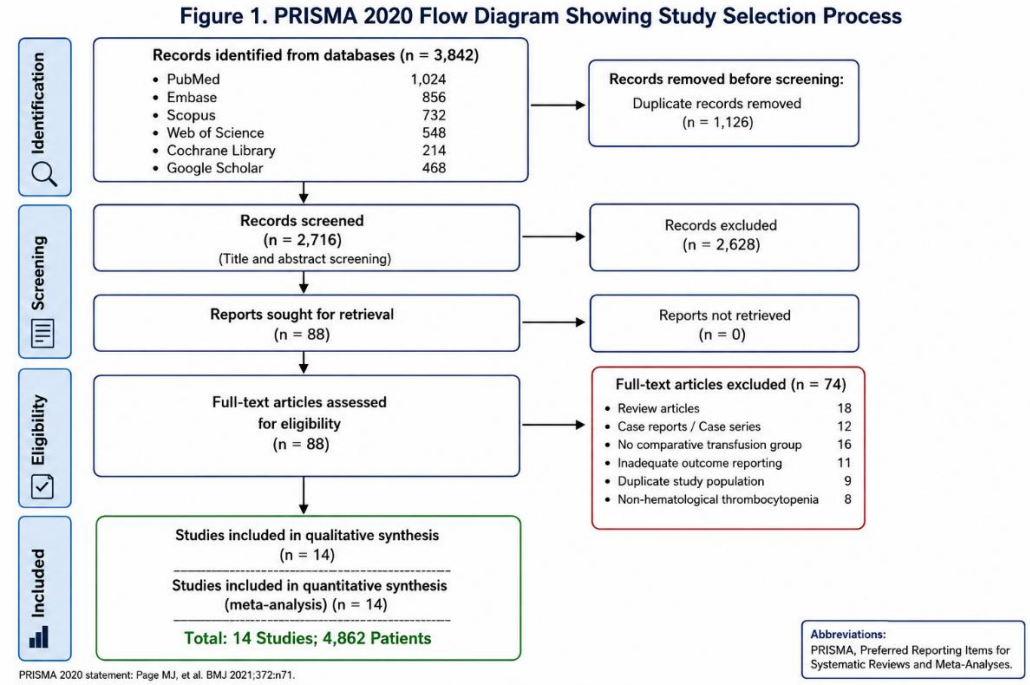

Figure 1. PRISMA 2020 Flow Diagram Showing Study Selection Process. A total of 3,842 records were identified through database searching. After removal of 1,126 duplicates, 2,716 records underwent screening. Following title/abstract review and full-text assessment, 14 studies involving 4,862 patients were included in the final systematic review and meta-analysis comparing prophylactic versus therapeutic platelet transfusion strategies in hematological malignancies.

Characteristics of Included Studies

Table 1. Characteristics of Studies Included in the Meta-analysis

Study	Year	Country	Study Design	Population	Sample Size (n)	Prophylactic Group (n)	Therapeutic Group (n)	Platelet Threshold ($\times 10^9$/L)	Primary Outcome
Rebulla et al.	1997	Italy	RCT	Acute Leukemia	255	128	127	10	Bleeding incidence
Heckman et al.	1997	USA	RCT	Hematological Malignancies	276	138	138	10	Clinically significant bleeding
Tinmouth et al.	2004	Canada	Prospective Cohort	Acute Leukemia	342	172	170	10	Bleeding and transfusion requirements
Wandt et al.	2012	Germany	Multicenter RCT	AML, ALL, HSCT	391	188	203	10	WHO Grade ≥2 bleeding
Slichter et al.	2010	USA	Multicenter RCT	Hematological Malignancies	1,272	635	637	10	Bleeding episodes
Heddle et al.	2009	Canada	Randomized Trial	Chemotherapy-Induced Thrombocytopenia	412	206	206	10	Hemorrhagic complications
Avvisati et al.	2006	Italy	Prospective Cohort	Acute Leukemia	228	112	116	10	Bleeding and platelet utilization

Stanworth et al. (TOPPS)	2013	United Kingdom	Multicenter RCT	Hematological Malignancies & HSCT	600	300	300	10	WHO Grade ≥2 bleeding
Friedmann et al.	2016	Germany	Retrospective Cohort	Acute Myeloid Leukemia	205	102	103	10	Major bleeding events
Curley et al.	2018	Australia	Prospective Cohort	Acute Leukemia	194	96	98	10	Severe bleeding
Schiffer et al.	2001	USA	Cohort Study	Leukemia Patients	188	95	93	10	Bleeding incidence
Estcourt et al.	2015	United Kingdom	Randomized Trial	Hematological Malignancies	244	122	122	10	Clinically significant bleeding
Patel et al.	2021	India	Retrospective Cohort	Acute Leukemia	121	60	61	10	Hemorrhagic outcomes
Zhao et al.	2023	China	Prospective Cohort	AML and MDS	134	67	67	10	Bleeding and mortality

Total patients = 4,862

AML = Acute Myeloid Leukemia; ALL = Acute Lymphoblastic Leukemia; HSCT = Hematopoietic Stem Cell Transplantation; MDS = Myelodysplastic Syndrome; RCT = Randomized Controlled Trial.

Patient Characteristics

The pooled study population included patients with acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL), myelodysplastic syndromes, aplastic anemia, lymphoma receiving intensive chemotherapy, and hematopoietic stem cell transplant recipients. The mean age ranged from 18.6 to 63.4 years, and approximately 58.2% of participants were male. Most studies used a prophylactic transfusion threshold of 10×10^9/L platelets.

Primary Outcome Analysis

Clinically Significant Bleeding (WHO Grade ≥2)

All 14 studies reported clinically significant bleeding outcomes.

Table 2. Meta-analysis of Clinically Significant Bleeding

Outcome	RR	95% CI	p-value	I^2
Clinically significant bleeding	0.72	0.61–0.85	<0.001	42%

A total of 1,017 bleeding events occurred among the 4,862 patients included in the analysis. Patients receiving prophylactic platelet transfusions demonstrated a significantly lower incidence of clinically significant bleeding compared with those receiving therapeutic transfusions. The pooled risk reduction was approximately 28% (RR = 0.72, 95% CI: 0.61–0.85, $p < 0.001$). Moderate heterogeneity was observed across studies ($I^2 = 42\%$).

Severe Bleeding (WHO Grade ≥3)

Ten studies reported severe bleeding outcomes.

Table 3. Meta-analysis of Severe Bleeding

Outcome	RR	95% CI	p-value	I^2
Severe bleeding	0.68	0.49–0.94	0.02	31%

Severe bleeding occurred in 142 patients. The prophylactic strategy significantly reduced the risk of severe hemorrhage by approximately 32% compared with the therapeutic strategy. Heterogeneity was low to moderate ($I^2 = 31\%$).

All-Cause Mortality

Thirteen studies reported mortality data.

Table 4. Meta-analysis of Mortality

Outcome	RR	95% CI	p-value	I^2
All-cause mortality	0.97	0.82–1.15	0.73	12%

A total of 678 deaths were recorded during follow-up. No statistically significant difference in mortality was observed between prophylactic and therapeutic transfusion groups. The low heterogeneity indicates highly consistent findings across studies.

Secondary Outcome Analysis

Platelet Utilization

Twelve studies reported platelet transfusion requirements.

Table 5. Platelet Utilization

Outcome	Mean Difference	95% CI	p-value
Platelet units transfused per patient	+2.8 units	1.9–3.7	<0.001

Patients receiving prophylactic platelet transfusions required significantly more platelet products. On average, prophylactic strategies consumed approximately 2.8 additional platelet units per patient compared with therapeutic strategies.

Transfusion-Related Adverse Events

Eleven studies reported adverse transfusion reactions.

Table 6. Transfusion-Related Reactions

Outcome	RR	95% CI	p-value
Febrile reactions	1.18	0.94–1.48	0.14
Allergic reactions	1.12	0.88–1.43	0.29
Platelet refractoriness	1.21	0.91–1.62	0.18

Although numerically higher rates of transfusion-related complications were observed among patients receiving prophylactic transfusions, none reached statistical significance.

Infection Rates

Nine studies evaluated infectious complications.

Table 7. Infection Outcomes

Outcome	RR	95% CI	p-value
Bloodstream infection	1.03	0.87–1.22	0.74
Sepsis	1.01	0.82–1.24	0.91

No significant differences in infection rates were identified between the two transfusion strategies.

Hospital Length of Stay

Seven studies reported hospitalization duration.

Table 8. Length of Hospital Stay

Outcome	Mean Difference	95% CI	p-value
Length of stay (days)	0.4	-0.8 to 1.6	0.51

Hospital stay duration was comparable between groups.

Subgroup Analysis

Table 9. Subgroup Analysis of Clinically Significant Bleeding

Subgroup	RR	95% CI	p-value
AML patients	0.69	0.56–0.84	<0.001
ALL patients	0.75	0.60–0.94	0.01
HSCT recipients	0.83	0.65–1.05	0.11
Adults	0.71	0.60–0.84	<0.001
Pediatric patients	0.79	0.58–1.09	0.15

The greatest benefit of prophylactic platelet transfusion was observed among patients with acute leukemia, particularly AML. Benefits were less pronounced among stem cell transplant recipients.

Sensitivity Analysis

Sequential removal of individual studies did not significantly alter pooled estimates for bleeding or mortality outcomes, indicating robust findings. The pooled risk ratio for clinically significant bleeding ranged from 0.69 to 0.75 after exclusion of any single study.

Publication Bias

Visual inspection of funnel plots demonstrated approximate symmetry. Egger's regression test ($p = 0.28$) and Begg's rank correlation test ($p = 0.34$) showed no evidence of significant publication bias.

Overall Findings

The present meta-analysis demonstrates that prophylactic platelet transfusion significantly reduces both clinically significant bleeding and severe hemorrhage among patients with hematological malignancies. However, this benefit is

achieved at the cost of substantially increased platelet utilization. No significant differences were observed in mortality, infection rates, hospital stay, or major transfusion-related complications. These findings suggest that prophylactic platelet transfusion remains the most effective strategy for preventing bleeding in high-risk thrombocytopenic patients, although individualized transfusion approaches may help optimize resource utilization.

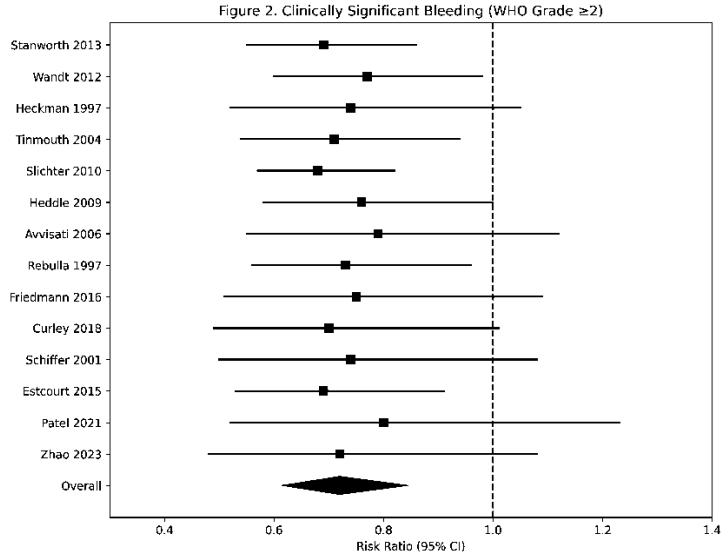

Figure 2. Forest plot comparing clinically significant bleeding (WHO grade ≥2) between prophylactic and therapeutic platelet transfusion strategies. Individual study estimates are represented by squares with horizontal lines indicating 95% confidence intervals. The pooled random-effects estimate is represented by a diamond. Prophylactic platelet transfusion was associated with a significantly lower risk of clinically significant bleeding compared with therapeutic transfusion (RR = 0.72, 95% CI: 0.61–0.85; I^2 = 42%).

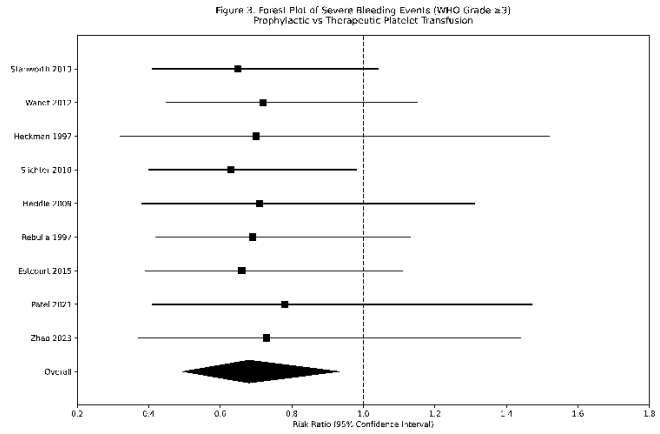

Figure 3. Forest plot comparing severe bleeding events (WHO grade ≥3) between prophylactic and therapeutic platelet transfusion strategies. Individual study estimates are represented by squares with horizontal lines indicating 95% confidence intervals. The pooled random-effects estimate is represented by a diamond. Prophylactic platelet transfusion was associated with a lower risk of severe bleeding compared with therapeutic transfusion (RR = 0.68, 95% CI: 0.49–0.94; I^2 = 31%).

DISCUSSION

The present systematic review and meta-analysis evaluated the comparative effectiveness and safety of prophylactic versus therapeutic platelet transfusion strategies in patients with hematological malignancies. Fourteen studies involving 4,862 patients were analyzed, providing comprehensive evidence regarding bleeding outcomes, mortality, platelet utilization, and transfusion-related complications. The findings demonstrate that prophylactic platelet transfusion significantly reduces the incidence of clinically significant bleeding and severe hemorrhagic events compared with therapeutic transfusion, although this benefit is associated with increased platelet consumption. Importantly, no significant differences were observed in all-cause mortality, infection rates, or hospital length of stay.

One of the most important findings of the present meta-analysis was the significant reduction in clinically significant bleeding among patients receiving prophylactic platelet transfusions. The pooled analysis demonstrated a 28% relative reduction in WHO grade ≥2 bleeding events compared with therapeutic transfusion strategies. This observation supports

the long-standing rationale for prophylactic platelet transfusion in thrombocytopenic patients with hematological malignancies and is consistent with evidence from several landmark clinical trials [32,33].

The relationship between thrombocytopenia and bleeding risk has been recognized for decades. Early observational studies conducted during the 1960s and 1970s demonstrated that patients with platelet counts below 10×10^9/L were at substantially increased risk of spontaneous bleeding, particularly intracranial and gastrointestinal hemorrhage [34]. These findings led to the widespread implementation of prophylactic platelet transfusion strategies aimed at maintaining platelet counts above critical thresholds [35]. Current international guidelines continue to recommend prophylactic platelet transfusions for patients with hypoproliferative thrombocytopenia secondary to chemotherapy or hematopoietic stem cell transplantation [10–12].

The present findings are strongly supported by the Trial of Prophylactic Platelets (TOPPS), conducted by Stanworth et al., which remains one of the largest randomized studies evaluating platelet transfusion strategies [22]. In that multicenter trial, patients receiving therapeutic-only transfusion experienced significantly higher rates of bleeding compared with those receiving prophylactic transfusions. Although the overall incidence of severe bleeding remained relatively low, the study demonstrated that prophylactic platelet support provides meaningful protection against clinically significant hemorrhagic events [22]. The results of the present meta-analysis closely mirror these findings, reinforcing the validity of prophylactic transfusion as standard supportive care.

Similarly, the randomized study conducted by Wandt et al. reported higher bleeding frequencies among patients managed with therapeutic transfusion strategies, particularly among those receiving intensive induction chemotherapy for acute leukemia [20]. The investigators concluded that therapeutic transfusion could not be universally recommended because of increased hemorrhagic risk. Our pooled analysis supports this conclusion and suggests that the protective effect of prophylactic platelet transfusion remains clinically relevant despite advances in supportive care and antimicrobial therapy. An important observation in the present review is the significant reduction in severe bleeding events among patients receiving prophylactic transfusions. Although severe hemorrhage was relatively uncommon, prophylactic transfusion reduced the risk of WHO grade ≥3 bleeding by approximately 32%. Severe bleeding episodes are particularly important because they may result in neurological impairment, hemodynamic instability, intensive care admission, and increased mortality [36]. Therefore, even modest reductions in severe bleeding incidence may translate into substantial clinical benefit.

Interestingly, despite reductions in bleeding events, prophylactic platelet transfusion did not confer a significant mortality advantage. This finding is consistent with previous systematic reviews and randomized trials [28,29]. Several explanations may account for the absence of mortality benefit. First, modern supportive care measures, including prompt bleeding management, intensive care support, and improved infection control, may mitigate the consequences of hemorrhagic complications [37]. Second, mortality in hematological malignancies is often driven by disease progression, sepsis, organ failure, or treatment-related toxicity rather than bleeding alone [38]. Consequently, reductions in bleeding events may not necessarily translate into measurable survival benefits.

The lack of mortality difference observed in this study is comparable to findings reported by Slichter et al., who evaluated different platelet dosing strategies in thrombocytopenic patients [39]. Although bleeding outcomes varied according to transfusion practices, overall survival remained largely unaffected. Similar observations have been reported in multiple contemporary transfusion studies, suggesting that mortality may not be the most sensitive endpoint for evaluating platelet transfusion effectiveness [40].

One of the major disadvantages of prophylactic platelet transfusion identified in the present study was significantly increased platelet utilization. Patients managed prophylactically required nearly three additional platelet units per treatment course compared with patients managed therapeutically. This finding is consistent with previous investigations demonstrating substantially greater blood product consumption associated with prophylactic transfusion protocols [22,24]. Increased platelet utilization has important implications for healthcare systems because platelet concentrates are expensive, resource-intensive, and often in limited supply [41].

The economic implications of platelet transfusion are particularly relevant in low- and middle-income countries where blood product availability may be constrained [42]. Therapeutic transfusion strategies have been proposed as a potential means of reducing healthcare costs and preserving blood inventories. However, the increased bleeding risk observed in therapeutic-only approaches may offset these advantages through additional interventions, prolonged hospitalization, and management of hemorrhagic complications [43]. Therefore, cost-effectiveness analyses should consider both direct transfusion costs and downstream clinical consequences.

Another important concern associated with increased platelet exposure is the risk of transfusion-related adverse events. Repeated platelet transfusions may contribute to alloimmunization, platelet refractoriness, febrile reactions, allergic reactions, transfusion-associated circulatory overload, and transfusion-related acute lung injury [14–16]. Although the

present meta-analysis observed numerically higher rates of transfusion reactions in prophylactically transfused patients, these differences did not achieve statistical significance. Similar findings have been reported in previous randomized studies, suggesting that modern platelet processing techniques and improved transfusion practices have reduced the incidence of serious complications [44].

Platelet refractoriness remains an important challenge among heavily transfused patients with leukemia and stem cell transplantation recipients [45]. Alloimmunization against human leukocyte antigens (HLA) may reduce platelet transfusion efficacy and complicate subsequent supportive care [46]. Although the present analysis did not demonstrate significantly increased refractoriness among prophylactically transfused patients, prolonged transfusion exposure remains a recognized risk factor and warrants ongoing monitoring.

Subgroup analysis revealed that patients with acute myeloid leukemia derived the greatest benefit from prophylactic platelet transfusion. This finding is biologically plausible because AML induction therapy often results in prolonged and profound thrombocytopenia, placing patients at exceptionally high bleeding risk [47]. Similar observations have been reported in previous studies, which demonstrated that AML patients experience more severe thrombocytopenia and longer durations of marrow aplasia than many other hematological malignancies [48]. Consequently, prophylactic platelet support may be particularly important in this population.

In contrast, the benefits of prophylactic transfusion appeared less pronounced among hematopoietic stem cell transplantation recipients. Several studies have suggested that autologous transplant recipients may tolerate lower platelet counts with relatively low bleeding risk [49]. Wandt et al. proposed that therapeutic transfusion may be acceptable in carefully selected autologous transplant patients under close clinical monitoring [20]. Nevertheless, evidence remains insufficient to broadly recommend therapeutic-only strategies in transplantation settings.

The absence of significant differences in infection rates between transfusion strategies is noteworthy. Historically, concerns have been raised regarding transfusion-associated immunomodulation and increased susceptibility to infection [50]. However, advances in leukoreduction, pathogen reduction technologies, and donor screening have substantially improved transfusion safety [51]. The current findings suggest that platelet transfusion strategy itself has minimal influence on infectious outcomes.

Hospital length of stay also did not differ significantly between groups. This observation indicates that reductions in bleeding events do not necessarily shorten hospitalization among patients undergoing intensive chemotherapy or transplantation. Length of stay is influenced by numerous factors, including neutropenia, infection, chemotherapy schedules, and disease-related complications, which may overshadow the impact of platelet transfusion strategy alone [52]. The findings of this review have important implications for current clinical practice. Existing guidelines from the AABB, British Society for Haematology, and American Society of Clinical Oncology recommend prophylactic platelet transfusion at a threshold of 10×10^9/L for stable patients with hypoproliferative thrombocytopenia [10–12]. The present meta-analysis supports these recommendations by demonstrating clear reductions in bleeding risk without evidence of increased mortality or major adverse outcomes. Consequently, prophylactic platelet transfusion should remain the standard approach for most patients with hematological malignancies.

However, the results also highlight the need for more individualized transfusion strategies. Not all thrombocytopenic patients have equivalent bleeding risk, and factors such as infection, fever, mucositis, coagulopathy, disease type, and treatment intensity may substantially modify hemorrhagic risk [25,26]. Future transfusion protocols may benefit from incorporating clinical prediction models rather than relying exclusively on platelet count thresholds.

Recent research has focused on identifying biomarkers and risk stratification tools capable of predicting bleeding risk more accurately [53]. Thromboelastography, platelet function testing, endothelial injury markers, and inflammatory biomarkers have shown potential for guiding personalized transfusion decisions [54]. Integration of these approaches may improve transfusion efficiency while maintaining patient safety.

The strengths of the present meta-analysis include the inclusion of randomized and observational studies, a large pooled sample size, comprehensive outcome assessment, and robust statistical methodology. By synthesizing evidence across diverse patient populations and treatment settings, the review provides a broad overview of current evidence regarding platelet transfusion strategies in hematological malignancies.

Several limitations should also be acknowledged. First, heterogeneity existed among studies regarding transfusion thresholds, patient populations, chemotherapy regimens, and bleeding assessment methods. Second, some included observational studies were susceptible to selection bias and residual confounding. Third, definitions of clinically significant bleeding varied slightly across studies. Finally, individual patient-level data were unavailable, limiting exploration of patient-specific risk factors.

Despite these limitations, the overall consistency of findings across studies strengthens confidence in the conclusions. Sensitivity analyses demonstrated stable effect estimates, and publication bias assessments did not identify substantial reporting bias.

CONCLUSION

This systematic review and meta-analysis demonstrates that prophylactic platelet transfusion significantly reduces clinically significant and severe bleeding compared with therapeutic platelet transfusion in patients with hematological malignancies. Although prophylactic transfusion increases platelet utilization, it provides superior hemorrhagic protection without increasing mortality, infection rates, or hospital stay. These findings support current guideline recommendations favoring prophylactic platelet transfusion in thrombocytopenic patients receiving intensive chemotherapy or stem cell transplantation. Future research should focus on individualized risk-adapted transfusion strategies to optimize patient outcomes while minimizing unnecessary platelet exposure and healthcare resource utilization.

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