

Platelet Transfusion

2025 AABB and ICTMG International Clinical Practice Guidelines

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IMPORTANCE Platelet transfusion is a frequent procedure with benefits and risks.

OBJECTIVE To provide recommendations in adult and pediatric populations in whom platelet transfusions are commonly performed.

EVIDENCE REVIEW Grading of Recommendations Assessment Development and Evaluation (GRADE) methodology was applied to findings from 21 randomized trials and 13 observational studies in contexts of limited randomized clinical trial data. Transfusion strategies using fewer (restrictive) vs greater (liberal) amounts of platelets were compared.

FINDINGS Evidence demonstrated that restrictive transfusion strategies probably did not cause increases in mortality or bleeding relative to liberal strategies across predefined clinical populations. Exceedingly low incidence of spinal hematoma was identified in patients with thrombocytopenia undergoing lumbar puncture. Because definitions of restrictive strategies varied across trials, recommendations reflect practical guidance. The following recommendations are strong recommendations with high/moderate-certainty evidence. For hypoproliferative thrombocytopenia in nonbleeding patients receiving chemotherapy or undergoing allogeneic stem cell transplant, platelet transfusion is recommended when platelet count is less than $10 \times 10^3/\mu\text{L}$. For consumptive thrombocytopenia in neonates without major bleeding, platelet transfusion is recommended when platelet count is less than $25 \times 10^3/\mu\text{L}$. In patients undergoing lumbar puncture, platelet transfusion is recommended when platelet count is less than $20 \times 10^3/\mu\text{L}$. In patients with consumptive thrombocytopenia due to Dengue without major bleeding, platelet transfusion is not recommended. The following recommendations are conditional recommendations with low/very low-certainty evidence. For hypoproliferative thrombocytopenia in nonbleeding adults undergoing autologous stem cell transplant or with aplastic anemia, prophylactic platelet transfusion is not recommended. In adults with consumptive thrombocytopenia without major bleeding, platelet transfusion is recommended when platelet count is less than $10 \times 10^3/\mu\text{L}$. In adults undergoing central venous catheter placement in compressible anatomic sites, platelet transfusion is recommended when platelet count is less than $10 \times 10^3/\mu\text{L}$. In adults undergoing interventional radiology, platelet transfusion is recommended when platelet count is less than $20 \times 10^3/\mu\text{L}$ for low-risk procedures and less than $50 \times 10^3/\mu\text{L}$ for high-risk procedures. For adults undergoing major nonneuraxial surgery, platelet transfusion is recommended when platelet count is less than $50 \times 10^3/\mu\text{L}$. For patients without thrombocytopenia undergoing cardiovascular surgery in the absence of major hemorrhage, including those receiving cardiopulmonary bypass, platelet transfusion is not recommended. For nonoperative intracranial hemorrhage in adults with platelet count greater than $100 \times 10^3/\mu\text{L}$, including those receiving antiplatelet agents, platelet transfusion is not recommended.

CONCLUSIONS AND RELEVANCE A consistent pattern of evidence supports the implementation of restrictive platelet transfusion strategies. Restrictive strategies reduce risk of adverse reactions, mitigate platelet shortages, and reduce costs. It is good practice to consider overall clinical context and alternative therapies in the decision to perform platelet transfusion.

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Platelet transfusions are a common intervention in different populations with thrombocytopenia or platelet dysfunction.¹ Thrombocytopenia is linked to bleeding and, because transfusions raise platelet counts, transfusions should reduce bleeding without causing harm.² Platelet units have a short shelf-life (5-7 days) and maintaining adequate supply to meet demand is challenging.³ While red blood cell transfusion usage has decreased in many countries, platelet usage has not.^{4,5} Risk of adverse events accompanies any transfusion, but occur more commonly after platelet transfusion⁶ (Table 1⁷⁻¹¹). Particularly in the US, clinicians' concerns about litigation after a bleeding event in a patient who did not undergo transfusion may also influence clinicians' behavior.

Randomized clinical trials (RCTs) have evaluated the effects of platelet transfusion.¹²⁻³¹ A typical trial design compares patients receiving fewer (restrictive) vs greater (liberal) amounts of platelets,³² although definitions for restrictive and liberal transfusion strategies vary between trials (Figure). The 2025 Association for the Advancement of Blood and Biotherapies (AABB) and the International Collaboration for Transfusion Medicine Guidelines (ICTMG) international clinical practice guidelines aimed to meet the need for updated recommendations for health care professionals and their patients, with practical advice on appropriate use of platelets.^{33,34}

Guideline Development Process

Panel Composition and Conflicts

We (the international platelet transfusion guidelines panel) followed Grading of Recommendations Assessment Development and Evaluation (GRADE) methodology to summarize evidence and formulate recommendations.^{35,36} The AABB and ICTMG commissioned and funded the guideline, recruiting patient partners and experts from relevant organizations across different resource settings (eTable 1 in the Supplement). Experts were selected for inclusion in the panel from the AABB clinical transfusion medicine committee, AABB members with prior guideline leadership experience, ICTMG's platelet guideline panel and leadership, and clinician experts from various specialties that commonly perform platelet transfusions. One investigator (G.G.) was our GRADE methodologist, supported by AABB. E.M.W.,²³ L.J.E.,²³ M.M.,²³ and S.J.S.^{23,28} were excluded from discussion and voting on topics of trials as primary investigators of those studies.

Values and Preferences

Recommendations were based on several values and preferences. While placing a high value on mortality reduction, the panel accepted the remaining possibility of a small increase in mortality or bleeding with a restrictive strategy. The panel placed high value on avoiding unnecessary exposure to platelets and conserving platelet transfusions for circumstances in which benefit is considered likely. The panel placed value on quality of life in chronic conditions, such as time away from activities and personal cost burdens for prophylactic platelet transfusion support. Values and preferences may vary depending on the acuity and severity of the patient's condition, and patients or family members in acute situations, following an informed consent process, may choose platelet transfusion in the face of substantial uncertainty of benefit.

Perspective

The primary perspective is the individual patient/family, including medical, psychological, and financial impacts. A secondary perspective is public health, including security of the blood supply.

Population, Intervention, Comparator, Outcome Questions

The panel recognized common rationales for platelet transfusions, and there was no strong clinical/biological basis for expecting relative effects of transfusion to vary significantly by population. The overarching PICO (population, intervention, comparator, outcome) question was "For patients in whom platelet transfusion might reduce bleeding, what is the impact of a restrictive vs a liberal strategy on mortality and bleeding?"

Specific populations of interest identified reflected the main clinical settings in which platelets may be administered.¹ (1) For non-bleeding patients with hypoproliferative thrombocytopenia (HPT), what is the impact of restrictive vs liberal platelet transfusion strategies on mortality and bleeding? A predefined subgroup was autologous stem cell transplant (SCT) recipients. (2) For patients with consumptive thrombocytopenia associated with critical illness, what is the impact of restrictive vs liberal platelet transfusion strategies on mortality and bleeding? Predefined subgroups were neonates and adults. (3) For patients with thrombocytopenia requiring invasive procedures, what is the impact of restrictive vs liberal platelet transfusion strategies on mortality and serious procedure-related bleeding? Predefined subgroups were patients undergoing central venous catheter (CVC) placement, lumbar puncture (LP), and interventional radiology procedures. (4) For patients undergoing cardiovascular surgery including those on cardiopulmonary bypass, what is the impact of restrictive vs liberal platelet transfusion strategies on mortality and bleeding? (5) For patients with intracranial hemorrhage (ICH), what is the impact of restrictive vs liberal platelet transfusion strategies on mortality and hemostasis? Predefined subgroups were patients with spontaneous and traumatic ICH.

Scope

Topics out of scope included platelet component types, platelet transfusion refractoriness, massive hemorrhage protocols, viscoelastic testing, and alternatives/adjuncts.

Evidence Review and Grading

Systematic Review

A systematic review³⁷ informed recommendations, with searches of RCTs and observational studies evaluating platelet transfusions published from 1950 to April 2024. Primary analyses focused on RCTs, but if they provided very low-certainty evidence, observational studies were considered. Eligible observational studies generated propensity-matched cohorts, except for LP, for which published spinal hematoma incidence data were synthesized.

Outcomes

A survey of ICTMG members on outcome importance rated mortality and clinically significant bleeding highly (eTable 2 in the Supplement). Definitions of significant bleeding were context-specific. Variation exists in definitions used between and within populations across trials.³⁸ Statistical criteria for interaction tests were

Table 1. Approximate Risks of Transfusion-Related Adverse Events

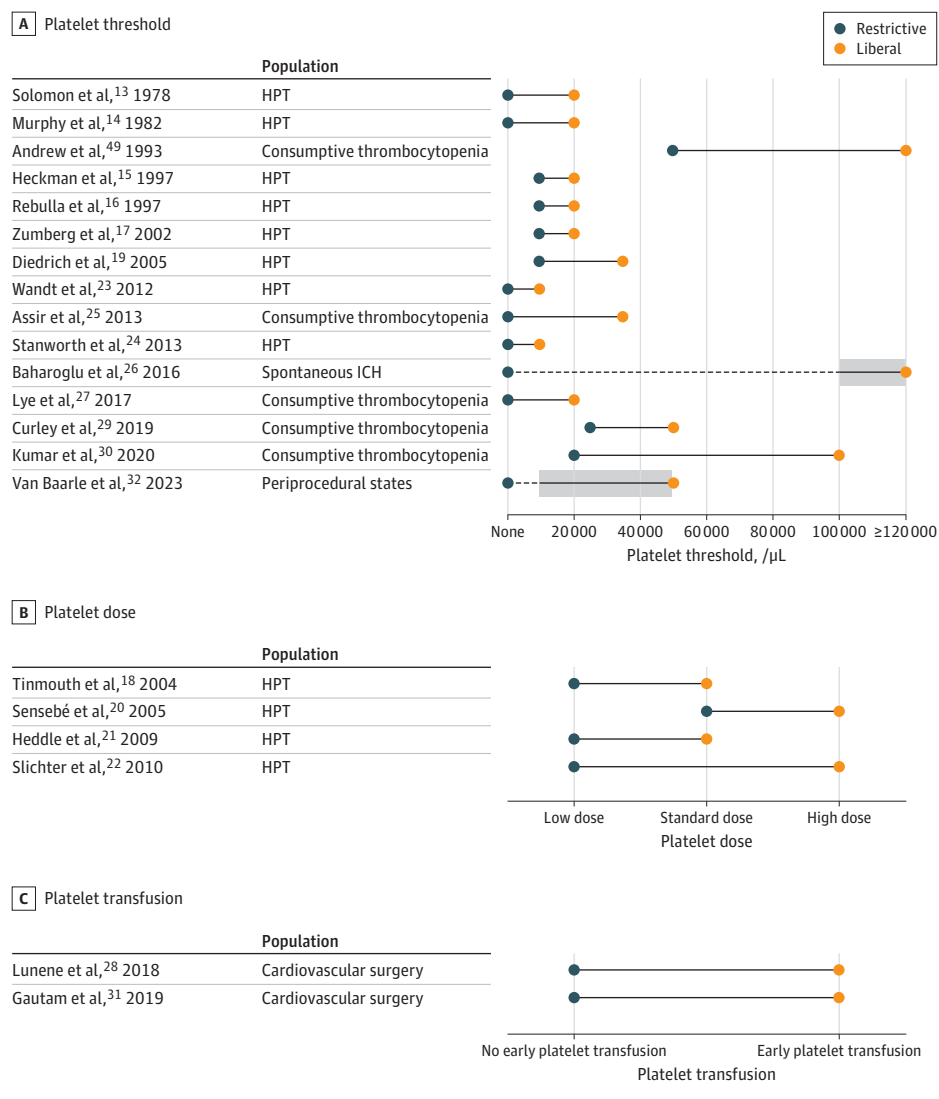
Reaction type	Source	Rate per transfusion episode	Rate per platelet transfused	No. needed to harm
Allergic	AABB Technical Manual	NA	10-30/1000	33-100 units
Anaphylactic	AABB Technical Manual	NA	0.02-0.05/1000	20 000-50 000 units
Febrile nonhemolytic	AABB Technical Manual	NA	1-10/1000	100-1000 units
Septic ^a	Hong et al, ⁷ 2016	NA	≤0.1/1000	10 000 units
TACO ^b	White et al, ⁸ 2025	6.6/1000 (95% CI, 2.9-11.8)	2.6/1000 (95% CI, 0.6-5.9)	385 units or 152 episodes
	Hendrickson et al, ⁹ 2016	8.0/1000	NA	125 episodes
TRALI	White et al, ¹⁰ 2024	NA	0.03/1000 (95% CI, 0.022-0.042)	33 333 units
	Hendrickson et al, ⁹ 2016	0.8/1000	NA	1250 episodes

Abbreviations: NA, not available; TACO, transfusion-associated circulatory overload; TRALI, transfusion-related acute lung injury.

^a Septic transfusion reaction rates may vary depending on the bacterial risk control strategy used.

^b The rate of TACO per patient (point estimate) is 22/1000 (number needed to harm = 45).

Figure. Restrictive and Liberal Transfusion Strategies Used Across Randomized Trials



Most trials used platelet count thresholds, with less using different platelet doses or varying timing of platelet transfusion. Gray shading indicates platelet count ranges of included patients in 2 trials; the dashed lines denote platelet count ranges that were not included in these trials. Although restrictive and liberal definitions varied across studies, in general, they refer to fewer vs greater amounts of platelets transfused. Sensebé et al, 2005: low-dose, $0.5 \times 10^{11}/10$ kg; high-dose, $1 \times 10^{11}/10$ kg; Tinmouth et al, 2004: low-dose, 3 prophylactic platelet transfusions (PLTs); standard-dose, 5 PLTs; Heddle et al, 2009: low-dose, $1.5-3.0 \times 10^{11}$ PLTs/product; standard dose, $3.0-6.0 \times 10^{11}$ platelets/transfusion; Slichter et al, 2010: low-dose, 1.1×10^{11} platelets/m²; high dose, 4.4×10^{11} platelets/m². HPT indicates hypoproliferative thrombocytopenia; ICH, intracranial hemorrhage.

applied to assess significant variation in effects, with application of the Instrument for Assessing the Credibility of Effect Modification Analyses criteria for credible effects.³⁹ The eAppendix (eTable 3) in the Supplement provides a summary of World Health Organization (WHO) bleeding grades.⁴⁰

Analysis

We applied Cochrane's Risk of Bias tool for RCTs⁴¹ and separate tools for observational studies.^{42,43} We followed GRADE to evaluate between-study variability and inferences regarding subgroup effects.^{39,44} Analyses were performed using Cochrane

Collaboration Review Manager.⁴⁵ Odds ratios (ORs) with 95% CIs were calculated using random effects models. Absolute risk differences (ARDs) were calculated by applying ORs to estimated baseline risks.⁴⁶ A sensitivity analysis in HPT evaluated the impact of a restrictive strategy on 30-day mortality.

Grading Evidence Certainty and Making Recommendations

We rated certainty in relation to thresholds of minimal important differences (MIDs)³⁵: mortality: 2%; grade 2-4 bleeding (or equivalent): 20%; and grade 3-4 bleeding (or equivalent): 5%. Using GRADE summary of findings,⁴⁷ the panel formulated recommendations using the GRADE evidence to decision framework.⁴⁸ Unless specified, recommendations apply to adult and pediatric patients. In the absence of unanimous agreement, a panel vote would be performed and an agreement threshold of greater than 50% was required to make a decision.

Results

Overview

Analyses of RCTs across clinical populations provided high- or moderate-certainty evidence that restrictive platelet transfusion strategies probably did not result in important increases in mortality (ARD, -0.4% [95% CI, -2.2% to 1.7%]), WHO grade 2-4 bleeding (ARD, 6.8% [95% CI, 0.9% to 12.8%]), or WHO grade 3-4 bleeding (ARD, 0.3% [95% CI, -1.4% to 2.4%]), as shown in **Table 2** and eFigures 1-3 in the **Supplement**. Given that specific definitions of restrictive and liberal in studies depended on clinical population, further analyses were undertaken by population.

Strong Recommendations (1.1-1.4)

The panel strongly recommends restrictive over liberal platelet transfusion strategies based on high- or moderate-certainty evidence in the 4 populations defined below. **Table 2** provides the summary of findings and **Table 3** summarizes all recommendations.

Recommendation 1.1: in nonbleeding patients with hypoproliferative thrombocytopenia actively receiving chemotherapy or undergoing allogeneic stem cell transplant, platelet transfusion should be administered when the platelet count is less than $10 \times 10^3/\mu\text{L}$ (strong recommendation, moderate-certainty evidence).

Recommendation 1.2: in preterm neonates without major bleeding, platelet transfusion should be administered when the platelet count is less than $25 \times 10^3/\mu\text{L}$ (strong recommendation, high-certainty evidence).

Recommendation 1.3: in patients undergoing lumbar puncture, platelet transfusion should be administered when the platelet count is less than $20 \times 10^3/\mu\text{L}$ (strong recommendation, moderate-certainty evidence).

Recommendation 1.4: in patients with Dengue-related consumptive thrombocytopenia in the absence of major bleeding, the panel recommends no platelet transfusion (strong recommendation, moderate-certainty evidence).

Synopsis of Identified Evidence

See the **Supplement** for details of identified evidence. Twelve RCTs in patients with HPT compared restrictive vs liberal platelet transfusion strategies on all-cause mortality or bleeding.¹²⁻²³ For mortal-

ity, the ARD was 1.8% (95% CI, -0.4% to 4.8%). Three RCTs in critically ill preterm neonates compared restrictive vs liberal platelet transfusion strategies. With baseline mortality risk of 16.9%, the ARD was -4.5% (95% CI, -8.2% to 0.4%).^{28,29,49} Two RCTs in patients with Dengue and platelet counts less than $20 \times 10^3/\mu\text{L}$ to $30 \times 10^3/\mu\text{L}$ compared platelet transfusion with no platelet transfusion,^{24,26} but baseline risks of mortality were very low. Six (nonrandomized) pediatric and adult studies reported spinal hematoma rates after LP of 0.8 (95% CI, 0-10.4) per 1000 procedures when platelet counts prior to LP were less than $50 \times 10^3/\mu\text{L}$.⁵⁰⁻⁵⁵

Rationale for Strong Recommendations

Although some point estimates indicated a possible increase in mortality with a restrictive strategy approaching the minimally important difference (ARD of 1.8% favoring liberal strategy in HPT), the overall results across all conditions showed no suggestion of benefit for liberal strategies (ARD, -0.4% [95% CI, -2.2% to 1.7%]). Furthermore, a sensitivity analysis evaluating 30-day mortality in HPT showed an ARD point estimate of 0.4%. The panel judged a lack of evidence of important harm with restrictive strategies applying predefined minimally important differences of 2% for mortality.

Event rates of important outcomes were so low in LP that liberal platelet transfusion could not be expected to importantly reduce spinal hematoma incidence.

Presumed benefits of restrictive platelet transfusion strategies extend to minimizing transfusion-related patient harms, maintaining adequate supply for clinical situations (eg, bleeding) in which platelet transfusion may yield important benefits, and reducing health care expenditures, given that platelets have high acquisition costs and associated costs of blood banking and safe administration.^{4,56} Active surveillance has helped quantify risk of transfusion-related adverse events, but other potential negative effects of platelet transfusions (eg, immunomodulatory effects) are poorly understood.⁵⁷

Conditional Recommendations (2.1-2.7)

In the predefined clinical populations mentioned below, certainty of evidence was low or very low, with the exception of CVC placement at compressible anatomic sites (moderate certainty for grade 2-4 bleeding; very low certainty for grade 3-4 bleeding). The panel made conditional recommendations in favor of restrictive over liberal platelet transfusion.

Recommendation 2.1: in nonbleeding adult patients with hypoproliferative thrombocytopenia undergoing autologous SCT or with aplastic anemia, the panel recommends a no-prophylaxis strategy (conditional recommendation; low- to very low-certainty evidence).

Recommendation 2.2: in adult patients with consumptive thrombocytopenia due to critical illness (non-Dengue) and without major bleeding, platelet transfusion should be administered when the platelet count is less than $10 \times 10^3/\mu\text{L}$ (conditional recommendation; very low-certainty evidence).

Recommendation 2.3: in adult patients undergoing CVC placement at anatomic sites amenable to manual compression, platelet transfusion should be administered when the platelet count is less than $10 \times 10^3/\mu\text{L}$ (conditional recommendation; moderate- to very low-certainty evidence).

Recommendation 2.4: in adult patients undergoing interventional radiology procedures, platelet transfusion should be administered

Table 2. Summary of Findings of Overall Combined Studies and Populations^a

		No. of events/No. of patients (%)					
Outcomes	No. of participants (No. of trials)	Restrictive platelet strategy	Liberal platelet strategy	Risk differences (95% CI)	Odds ratio (95% CI)	Certainty of the evidence (GRADE)	Summary
Overall population							
All-cause mortality	4867 (20 RCTs)	255/2424 (10.5)	268/2443 (11.0)	-0.4% (-2.2% to 1.7%) 22 fewer to 17 more deaths per 1000	0.96 (0.78 to 1.18)	High	Restrictive probably results in little to no difference in all-cause mortality
WHO grades 2-4 bleeding or equivalent	2860 (11 RCTs)	589/1414 (41.7)	544/1446 (37.6)	6.8% (0.9% to 12.8%) 9 to 128 more patients per 1000 experiencing grade 2-4 bleeding with restrictive	1.32 (1.04 to 1.68)	Moderate ^b	Restrictive probably results in little or no difference in grade 2-4 bleeding or equivalent
WHO grades 3-4 bleeding or equivalent	3433 (11 RCTs)	148/1705 (8.7)	146/1728 (8.4)	0.3% (-1.9% to 3.0%) 19 fewer to 30 more patients per 1000 experiencing grade 3-4 bleeding with restrictive	1.04 (0.76 to 1.41)	Moderate ^b	Restrictive probably results in little or no difference in grade 3-4 bleeding
Hypoproliferative thrombocytopenia							
All-cause mortality	2851 (11 RCTs)	104/1417 (7.3)	91/1434 (6.3)	1.8% (-0.4% to 4.8%) 4 fewer to 48 more deaths per 1000 with restrictive	1.32 (0.93 to 1.86)	Moderate ^c	Restrictive probably results in little or no difference in mortality
WHO grades 2-4 bleeding or equivalent	2487 (10 RCTs)	567/1229 (46.1)	535/1258 (42.5)	5.2% (0.0% to 10.5%) 0 to 105 more patients per 1000 experiencing grade 2-4 bleeding	1.23 (1.00 to 1.53)	Moderate ^b	Restrictive probably results in little or no difference in grade 2-4 bleeding
WHO grades 3-4 bleeding or equivalent	2016 (6 RCTs)	82/1001 (8.2)	68/1015 (6.7)	1.5% (-0.8% to 4.4%) 8 fewer to 44 more patients per 1000 experiencing grade 3-4 bleeding	1.24 (0.88 to 1.75)	Moderate ^b	Restrictive probably results in little or no difference in grade 3-4 bleeding
Consumptive thrombocytopenia: neonates							
All-cause mortality	852 (3 RCTs)	53/426 (12.4)	72/426 (16.9)	-4.5% (-8.2% to 0.4%) 82 fewer to 4 more deaths per 1000 with restrictive	0.69 (0.47 to 1.03)	High	Restrictive results in little or no increase in harm
WHO grades 3-4 bleeding or equivalent	854 (3 RCTs)	44/426 (10.3)	59/428 (13.8)	-2.7% (-6.0% to 2.8%) 60 fewer to 28 more patients per 1000 experiencing grade 3-4 bleeding with restrictive	0.72 (0.39 to 1.31)	Moderate ^b	Restrictive probably results in little or no difference in grade 3-4 bleeding
Lumbar puncture ^d							
Hematoma incidence, PLT<50 000	4418 (6 studies)	42/4418 (1.0)		0.78 (0.00 to 10.02) Events per 1000 procedures	NA	Moderate ^b	Restrictive probably results in little or no difference in hematoma rates given very low baseline risk
Hematoma incidence, PLT<20 000	324 (4 studies)	0/324		0.00 (0.00 to 2.96) Events per 1000 procedures	NA	Moderate ^b	Restrictive probably results in little or no difference in hematoma rates given very low baseline risk
Consumptive thrombocytopenia due to Dengue: adults							
All-cause mortality	453 (2 RCTs)	0/226	1/227 (0.4)	-0.3% (-0.4% to 2.5%) 4 fewer to 25 more deaths per 1000 with restrictive	0.30 (0.01 to 7.47)	Moderate ^c	Restrictive probably results in little or no difference in mortality

(continued)

Table 2. Summary of Findings of Overall Combined Studies and Populations^a (continued)

		No. of events/No. of patients (%)					
Outcomes	No. of participants (No. of trials)	Restrictive platelet strategy	Liberal platelet strategy	Risk differences (95% CI)	Odds ratio (95% CI)	Certainty of the evidence (GRADE)	Summary
Hypoproliferative thrombocytopenia							
WHO grades 2-4 bleeding or equivalent: Autologous transplant subgroup	698 (3 RCTs)	130/353 (36.8)	103/346 (29.8)	19.5% (−7.7% to 47.2%) 77 fewer to 472 more patients per 1000 experiencing grade 2-4 bleeding	2.30 (0.67 to 7.88)	Very low ^c	Effect is very uncertain
WHO grades 3-4 bleeding or equivalent: Autologous transplant subgroup	622 (2 RCTs)	4/314 (1.3)	0/308	0.6% (−0.1% to 6.1%) 1 fewer to 61 more patients per 1000 experiencing grade 3-4 bleeding	4.68 (0.53 to 41.38)	Low ^c	Restrictive possibly results in little or no difference in grade 3-4 bleeding
Consumptive thrombocytopenia: adults							
All-cause mortality	3324 (2 adjusted observational studies)	368/1662 (22.1)	434/1662 (26.1)	−4.1% (−6.8% to −1.2%) 68 to 12 fewer deaths per 1000 individuals with restrictive	0.80 (0.68 to 0.94)	Very low ^c	Effect is very uncertain
CVC placement ^e							
WHO grades 2-4 bleeding or equivalent: Compressible sites	232 (1 RCT)	8/115 (7.0)	7/117 (6.0)	1.0% (−3.4% to 11.6%) 34 fewer to 116 more patients per 1000 experiencing grade 2-4 bleeding	1.18 (0.41 to 3.35)	Moderate ^b	Restrictive probably results in little or no difference in bleeding for compressible sites
WHO grades 3-4 bleeding or equivalent: Compressible sites	232 (1 RCT)	6/115 (5.2)	4/117 (3.4)	1.8% (−1.9% to 13.2%) 19 fewer to 132 more patients per 1000 experiencing grade 3-4 bleeding	1.56 (0.43 to 5.66)	Very low ^{b,c}	Effect is very uncertain
Periprocedural settings (interventional radiology)							
Periprocedural RBC transfusion	521 (1 adjusted observational study)	69/342 (20.2)	48/179 (26.8)	−6.6% (−12.6% to 1.0%) 126 fewer to 10 more periprocedural RBC transfusions per 1000 individuals with restrictive	0.69 (0.45 to 1.05)	Very low ^c	Effect is very uncertain
ICU admission	521 (1 adjusted observational study)	91/342 (26.6)	65/179 (36.3)	−9.7% (−16.5% to −1.5%) 165 to 15 fewer ICU admissions per 1000 individuals with restrictive	0.64 (0.43 to 0.94)	Very low ^c	Effect is very uncertain
Cardiovascular surgery: adults							
All-cause mortality (RCT)	122 (1 RCT)	19/61 (31.1)	22/61 (36.1)	−4.9% (−18.5% to 12.9%) 185 fewer to 129 more deaths per 1000 individuals with restrictive	0.80 (0.38 to 1.70)	Very low ^c	Effect is very uncertain
All-cause mortality (observational)	10 036 (4 adjusted observational studies)	142/5187 (2.7)	143/4849 (2.9)	−0.6% (−1.8% to 2.0%) 18 fewer to 20 more deaths per 1000 individuals with restrictive	0.79 (0.37 to 1.72)	Very low ^c	Effect is very uncertain
Cardiovascular surgery: neonates							
All-cause mortality	42 (1 RCT)	0/21	0/21	0.0% (−2.3% to 27.2%) 23 fewer to 272 more deaths per 1000 individuals with restrictive	Not estimable	Very low ^c	Effect is very uncertain

(continued)

Table 2. Summary of Findings of Overall Combined Studies and Populations^a (continued) (continued)

Outcomes	No. of participants (No. of trials)	No. of events/No. of patients (%)		Risk differences (95% CI)	Odds ratio (95% CI)	Certainty of the evidence (GRADE)	Summary
		Restrictive platelet strategy	Liberal platelet strategy				
Spontaneous intracranial hemorrhage							
All-cause mortality	190 (1 RCT)	21/93 (22.6)	31/97 (32.0)	−9.4% (−18.7% to 3.8%) 187 fewer to 38 more deaths per 1000 individuals with restrictive	0.62 (0.33 to 1.19)	Low ^{b,c}	Restrictive results in little or no difference in mortality

Abbreviations: GRADE, Grading of Recommendations Assessment Development and Evaluation; NA, not applicable; RCT, randomized clinical trial; WHO, World Health Organization.

^a Included randomized trial data were based on the primary analysis reported for a given trial (intention to treat or per protocol). The WHO bleeding scale is on a semiquantitative scale ranging from 0 (no bleeding) to 4 (life-threatening bleeding). The degree of bleeding in trials is typically determined by study staff who evaluate patients at intervals specified by the trial. Ideally, bleeding outcome assessors are blinded, but this was not always the case. For additional detail on typical definitions of important bleeding (ie, grades 2, 3, and 4), see Supplement 1. The certainty of evidence was determined using GRADE methodology and synthesizing effect estimates across multiple studies, when applicable. GRADE considers imprecision, inconsistency, indirectness, and risk of bias. Imprecision depended on predefined minimal

important differences (MIDs). The MIDs chosen by the panel were: 2% for mortality, 5% for grade 3-4 bleeding or equivalent, and 20% for grade 2-4 bleeding or equivalent.

^b Downgraded for risk of bias.

^c Downgraded for imprecision.

^d Lumbar puncture evidence was synthesized from observational studies reporting incidence of spinal hematoma where platelet counts were measured before the procedure. Although most did not receive any platelet transfusion, those who did were only included if the platelet count was remeasured prior to the procedure and found to be less than $50 \times 10^3/\mu\text{L}$ or $20 \times 10^3/\mu\text{L}$.

^e Compressible sites refer to internal jugular and femoral vein central venous catheter placements, as opposed to the subclavian vein which may be less amenable to manual compression.

when the platelet count is less than $20 \times 10^3/\mu\text{L}$ for low-risk procedures and less than $50 \times 10^3/\mu\text{L}$ for high-risk procedures (conditional recommendation; very low-certainty evidence).

Recommendation 2.5: in adult patients undergoing major non-neuraxial surgery, platelet transfusion should be administered when the platelet count is less than $50 \times 10^3/\mu\text{L}$ (conditional recommendation; very low-certainty evidence).

Recommendation 2.6: in nonthrombocytopenic patients undergoing cardiovascular surgery in the absence of major hemorrhage, including those undergoing cardiopulmonary bypass, the panel recommends no platelet transfusion (conditional recommendation; very low-certainty evidence).

Recommendation 2.7: in adult patients with spontaneous or traumatic, nonoperative intracranial hemorrhage when the platelet count is greater than $100 \times 10^3/\mu\text{L}$, including for those receiving antiplatelet agents, the panel recommends no platelet transfusion (conditional recommendation; low- to very low-certainty evidence).

Synopsis of Identified Evidence

Full details of the identified evidence are shown in the Supplement. Three RCTs evaluated patients with HPT undergoing autologous SCT.^{17,22,23} For WHO grade 2-4 bleeding, the ARD was 19.5% (95% CI, −7.7% to 47.2%). Direct evidence comparing platelet transfusion strategies in adults patients with consumptive thrombocytopenia with critical illness was limited to 2 (nonrandomized) observational studies with propensity-matched cohorts.^{58,59} The ARD for mortality was −4.1% (95% CI, −6.8% to 1.2%). One RCT compared no platelet transfusion vs platelet transfusion among adults undergoing CVC placement with pretransfusion platelet counts of $10 \times 10^3/\mu\text{L}$ to $50 \times 10^3/\mu\text{L}$.³¹ Direct evidence comparing restrictive vs liberal strategies in patients undergoing a variety of low- and high-risk interventional radiology procedures was limited to a single observational study with propensity-matched cohorts.⁶⁰ Evidence in cardiovascular surgery included 3 small RCTs and 4 obser-

vational studies with propensity-matched cohorts.^{27,30,61,62} One RCT evaluated the impact of platelet transfusion following non-operative spontaneous ICH.²⁵ The ARD for mortality was −9.4% (95% CI, −18.7% to 3.8%).

Rationale for Conditional Recommendations

For populations with conditional recommendations, restrictive strategies also showed lack of clear evidence of harm but less evidence certainty. Relative effects were consistent and point estimates for absolute effects of mortality and/or bleeding were consistent with what the panel judged to be unimportant effects based on the MIDs. Of note, the panel felt mortality was not a practically applicable outcome for minor procedures. For WHO grade 2-4 bleeding in patients undergoing autologous SCT, there was inconsistency due to greater difference in event rates between groups in a study.²² Inconsistency was not observed for the outcome of WHO grade 3-4 bleeding events. The panel chose the subpopulation of autologous SCT for a no-prophylaxis recommendation given that duration of thrombocytopenia is typically short. The benefit from prophylactic platelet transfusion is less likely in this HPT subpopulation compared with the HPT subpopulation for which the panel made a strong recommendation to transfuse platelets when the platelet count is less than $10 \times 10^3/\mu\text{L}$.⁶³ In contrast, although the duration of thrombocytopenia in aplastic anemia is often prolonged, the panel conditionally recommended a no-prophylaxis strategy given value placed on quality of life.

Although the upper bounds of the CIs for mortality and/or bleeding included important harm for a restrictive strategy in autologous SCT, CVC placement at compressible anatomic sites (grade 3-4 bleeding only), cardiovascular surgery, and spontaneous ICH, there remained no clear evidence of a benefit to a liberal transfusion strategy. Relative effects appeared consistent, and the panel saw no compelling reason for relative effects to vary by population.

Accordingly, the panel suggested implementation of restrictive strategies to avoid undesirable effects of transfusion while

Table 3. Recommendations for Platelet Transfusion

Population	Recommendation and guidance	Certainty of the evidence ^a	Summary justification
1. Strong recommendations			
1.1: Nonbleeding patients with hypoproliferative thrombocytopenia actively receiving chemotherapy or undergoing allogeneic stem cell transplant (SCT)	Platelet transfusion should be administered when the platelet count is $<10 \times 10^3/\mu\text{L}$	Moderate	The data support no benefit with liberal strategies and a platelet count threshold $<10 \times 10^3/\mu\text{L}$ is practical for implementation
1.2: Preterm neonates without major bleeding	Platelet transfusion should be administered when the platelet count is $<25 \times 10^3/\mu\text{L}$	High	The data support no benefits with liberal policies of $<50 \times 10^3/\mu\text{L}$ and the possibility of harm.
1.3: Patients undergoing lumbar puncture	Platelet transfusion should be administered when the platelet count is $<20 \times 10^3/\mu\text{L}$	Moderate	A platelet count threshold $<20 \times 10^3/\mu\text{L}$ is practical for implementation, and minimizes need for platelet transfusion, while recognizing the extremely low event rate estimate
1.4: Patients with Dengue-related consumptive thrombocytopenia in the absence of major bleeding	No platelet transfusion	Moderate	The data support no benefits with use of platelets as prophylaxis and possibility of harm
2. Conditional recommendations			
2.1: Nonbleeding adult patients with hypoproliferative thrombocytopenia undergoing autologous SCT or with aplastic anemia	No-prophylaxis strategy	Low to very low	The evidence includes subgroup analyses of bleeding outcomes in trials
2.2: Adult patients with consumptive thrombocytopenia due to critical illness (non-Dengue) and without major bleeding	Platelet transfusion should be administered when the platelet count is $<10 \times 10^3/\mu\text{L}$	Very low	Lack of direct randomized trial data; a platelet count threshold $<10 \times 10^3/\mu\text{L}$ is practical for implementation and minimizes requirements for platelet transfusions with attendant risks
2.3: Adult patients undergoing central venous catheter (CVC) placement at anatomic sites amenable to manual compression	Platelet transfusion should be administered when the platelet count is $<10 \times 10^3/\mu\text{L}$	Moderate to very low	A platelet count threshold $<10 \times 10^3/\mu\text{L}$ is practical for implementation and minimizes need for platelet transfusion
2.4: Adult patients undergoing interventional radiology procedures	Platelet transfusion should be administered when the platelet count is $<20 \times 10^3/\mu\text{L}$ for low-risk procedures and $<50 \times 10^3/\mu\text{L}$ for high-risk procedures ⁵	Very low	A platelet count threshold $<20 \times 10^3/\mu\text{L}$ or $<50 \times 10^3/\mu\text{L}$ is practical for implementation; recognizes the varying degrees of bleeding risk by procedure
2.5: Adult patients undergoing major nonneuraxial surgery	Platelet transfusion should be administered when the platelet count is $<50 \times 10^3/\mu\text{L}$	Very low	A platelet count threshold $<50 \times 10^3/\mu\text{L}$ is practical for implementation; recognizes the degree of potential risk of severe bleeding for these procedures
2.6: Nonthrombocytopenic patients undergoing cardiovascular surgery in the absence of major hemorrhage, including those receiving cardiopulmonary bypass	No platelet transfusion	Very low	The limited data available support no benefit with use of platelets
2.7: Adult patients with spontaneous or traumatic, nonoperative intracranial hemorrhage with platelet counts $>100 \times 10^3/\mu\text{L}$, including those receiving antiplatelet agents	No platelet transfusion	Low to very low	The limited data available support no benefit with use of platelets and the possibility of harm

^a The certainty of evidence was determined using GRADE methodology and synthesizing effect estimates across multiple studies, when applicable. GRADE considers imprecision, inconsistency, indirectness, and risk of bias. Imprecision depended on predefined minimal important differences (MIDs). The MIDs chosen by the panel were 2% for mortality, 5% for grade 3-4 bleeding or equivalent, and 20% for grade 2-4 bleeding or equivalent.

accepting the remaining possibility of harm based on the upper bounds of some CIs.

Good Practice Statement

The panel considered it good clinical practice to also consider symptoms, signs, other laboratory parameters, bleeding history, medications, patients' values and preferences, alternative therapies, and overall clinical context when deciding to perform a platelet transfusion on a particular patient. It is possible that this recommendation, although not intended for legal proceedings but rather as a guide for patient care, may reassure clinicians contemplating not admin-

istering unnecessary platelet transfusions whose behavior may be influenced by worries about litigation.

Discussion

This guideline advocates for restrictive platelet transfusion strategies. There was no consistent evidence across RCTs to support benefit of platelets impacting clinical outcomes. The panel applied and analyzed the restrictive vs liberal paradigm to platelet transfusion and found no significant varying effect by population for mortality

and bleeding. Hematoma incidence was very low across the observational literature for thrombocytopenic patients undergoing LP, and it is highly unlikely that liberal platelet transfusion achieves important benefit.⁵⁰⁻⁵⁵

Definitions of restrictive strategies varied by population and even by trial among the same populations (Figure). Ideally a single restrictive strategy that is easy to implement for clinicians could be adopted widely, but heterogeneity of trial protocols limits options for standardized guidance. The most restrictive policy is no prophylaxis strategy—a therapeutic-only strategy—which has been tested in some but not all populations (Figure). A summary of policies tested in trials alongside practical recommendations for restrictive policies by population is provided in Table 3.

Although some recommendations were similar to previous guidelines^{33,34,64} (HPT, interventional radiology, major nonneuroaxial surgery, and cardiovascular surgery), the current guideline introduces new recommendations in certain groups, including neonates and those with Dengue. Some prior recommendations were less restrictive (LP, autologous SCT, CVC placement) or no recommendation was made (ICH).^{33,34} Although some clinicians may wish to consider less-restrictive platelet transfusion strategies for diagnostic LP with the intent of reducing likelihood of traumatic LP, the relevance of this outcome may be questioned given it is unlikely to impact treatment.⁶⁵

The panel made a strong recommendation for a restrictive strategy in preterm neonates, although the meta-analyses were dominated by results of a single trial.²⁸ There was heterogeneity in the enrolled neonatal population in this study (eg, by gestational and postnatal age), although secondary analysis of this trial failed to identify significant differences in effects by varying baseline risk.⁶⁶ A future trial is due to begin in 2026.⁶⁷

For CVC placement, a 2023 RCT showed variation in grade 2-4 bleeding by anatomic site, with no difference in event rates at compressible sites using restrictive or liberal strategies.³¹ The Instrument for Assessing the Credibility of Effect Modification Analyses judged the effect modification to be of moderate credibility (eTable 4 in the Supplement). However, the importance of reported bleeding events in this study is unclear, with small numbers of mixed populations enrolled. A larger international RCT evaluating multiple platelet thresholds is ongoing.^{68,69}

RCTs in clinical settings, including different age groups, for which data are absent or very low certainty, could provide additional certainty supporting recommendations. Research should develop personalized approaches to platelet transfusion incorporating a range of individual factors. It was noted that for many populations in whom

baseline risks represent an important incidence of bleeding, rates of bleeding remained important irrespective of transfusion strategy tested; alternative approaches to reduce risk should be developed. See further descriptions in the Supplement. We will consider updating guidelines as new and important published trial data become available.

Strengths of this guideline include adherence to standards for trustworthy guidelines, application of GRADE, identification of consistent patterns in the relative impacts of platelet transfusion strategies across populations, involvement of patient partners, the variety of physician expert participants, and its international applicability.

Limitations

This guideline also has limitations. Patients with thrombocytopenia are heterogeneous for factors relevant to bleeding risk, which may not be captured by inclusion criteria in trials or baseline features of enrolled patients. This reiterates the importance of clinical judgment and application of the good practice statement. Evidence in some settings was very low certainty. Baseline risk was not always clear when there was variation in event rates across studies. The panel made judgements about MIDIs for key outcomes, informed by values and preferences that considered the potential negative effects of liberal transfusion strategies. Some uncertainty persists about the impact of different platelet strategies on mortality. MIDIs vary by guideline panels and may impact evidence certainty ratings. More conservative MIDIs could have downgraded evidence certainty in some settings and the possibility of conditional rather than strong recommendations might have arisen. The panel incorporated the value of indirect evidence given the lack of significant variation in relative effects across populations and the common rationale for use of platelets, which may not be valid. The panel considered a framework to ensure guideline quality (Appraisal of Guidelines for Research and Evaluation II) and plans to address the domain of applicability with future implementation work (described in the Supplement).⁷⁰

Conclusions

Restrictive transfusion strategies should be implemented. Recommendations may not apply to all individual patient scenarios, as noted in the good practice statement, and for conditional recommendations, clinicians should carefully consider the individual patient's values and preferences in the decision.³⁵

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