Platelet Transfusion: A Clinical Practice Guideline From the AABB

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Background: The AABB (formerly, the American Association of Blood Banks) developed this guideline on appropriate use of platelet transfusion in adult patients.

Methods: These guidelines are based on a systematic review of randomized, clinical trials and observational studies (1900 to September 2014) that reported clinical outcomes on patients receiving prophylactic or therapeutic platelet transfusions. An expert panel reviewed the data and developed recommendations using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework.

Recommendation 1: The AABB recommends that platelets should be transfused prophylactically to reduce the risk for spontaneous bleeding in hospitalized adult patients with therapy-induced hypoproliferative thrombocytopenia. The AABB recommends transfusing hospitalized adult patients with a platelet count of 10 × 10⁹ cells/L or less to reduce the risk for spontaneous bleeding. The AABB recommends transfusing up to a single apheresis unit or equivalent. Greater doses are not more effective, and lower doses equal to one half of a standard apheresis unit are equally effective. (Grade: strong recommendation; moderate-quality evidence)

Recommendation 2: The AABB suggests prophylactic platelet transfusion for patients having elective central venous catheter placement with a platelet count less than 20 × 10⁹ cells/L. (Grade: weak recommendation; low-quality evidence)

Recommendation 3: The AABB suggests prophylactic platelet transfusion for patients having elective diagnostic lumbar puncture with a platelet count less than 50 × 10⁹ cells/L. (Grade: weak recommendation; very-low-quality evidence)

Recommendation 4: The AABB suggests prophylactic platelet transfusion for patients having major elective nonneuraxial surgery with a platelet count less than 50 × 10⁹ cells/L. (Grade: weak recommendation; very-low-quality evidence)

Recommendation 5: The AABB recommends against routine prophylactic platelet transfusion for patients who are nonthrombocytopenic and have cardiac surgery with cardiopulmonary bypass. The AABB suggests platelet transfusion for patients having bypass who exhibit perioperative bleeding with thrombocytopenia and/or evidence of platelet dysfunction. (Grade: weak recommendation; very-low-quality evidence)

Recommendation 6: The AABB cannot recommend for or against platelet transfusion for patients receiving antplatelet therapy who have intracranial hemorrhage (traumatic or spontaneous). (Grade: uncertain recommendation; very-low-quality evidence)

These guidelines provide advice for adult patients who are candidates for platelet transfusion.

GUIDELINE DEVELOPMENT PROCESS

The AABB commissioned and funded the development of these guidelines.

Panel Composition

A panel of 21 experts was convened. Fifteen participants were members of the Clinical Transfusion Medicine Committee of the AABB, all of whom were

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hematologists or pathologists with expertise in transfusion medicine. Five additional panel members included a neurosurgeon, a cardiac surgeon, a critical care specialist, an anesthesiologist, and a hematologist, representing the American Association of Neurological Surgeons, the Society of Thoracic Surgeons, the Society of Critical Care Medicine, the American Society of Anesthesiologists, and the American Society of Hematology, respectively. The final panel member was a Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodologist. Committee members had no substantial conflicts of interest as defined by the AABB conflict of interest policy. Pursuant to the policy, individual members were required to disclose actual and apparent financial, professional, or personal conflicts (Appendix Table 1, available at www.annals.org).

Systematic Review of the Evidence
The guidelines were developed on the basis of a recent systematic review of the literature on platelet transfusions, published separately (11). The search strategy is provided in Appendix Table 2 (available at www.annals.org). We searched PubMed from 1946 to the first week of April 2013, and the Cochrane Central Register of Controlled Trials and Web of Science from 1900 to the first week of April 2013 (1024 studies identified). An updated search of these databases was done from the first week of April 2013 to the first week of September 2014. Randomized, controlled trials (RCTs) and observational studies (prospective or retrospective cohort studies, case–control studies, and those with no control group) were eligible for inclusion. Outcomes of interest included all-cause mortality, bleeding-related mortality, bleeding, and number of platelet units transfused. Although all observational studies meeting the inclusion criteria were reviewed, data from observational studies were not used when more than 2 RCTs addressed a particular question. There were no language restrictions. After exclusions, 17 RCTs and 53 observational studies were included in the final systematic review. Only 1 relevant observational study (12) from the updated search was identified, and evidence from this study did not change our GRADE judgments of evidence quality or recommendation strength.

Grading of Evidence
The GRADE method was used to assess the quality of the evidence and determine the strength of recommendations (13, 14). The recommendations were developed by consensus at an in-person panel meeting. Panel member judgments on 4 GRADE factors (quality of evidence, balance between the intervention’s benefits and harms, resource use, and patient values and preferences) and ratings of the strength of recommendations were validated using an online survey tool 1 week after the meeting.

Definitions
In this guideline, a platelet unit refers to 1 apheresis platelet unit or a pool of 4 to 6 whole blood-derived platelet concentrates, typically containing 3 to 4 × 10¹¹ platelets. Thrombocytopenia refers to a platelet count below the lower limit of the normal range used by the laboratory performing the count. Seven platelet trials included in the systematic review (15–21) used a variation of the World Health Organization scale (22) to assess patient bleeding outcomes (23). A summary of the modified World Health Organization scale is provided in Table 2.

Clinical Recommendations

Clinical Setting 1: Hospitalized Adult Patients With Therapy-Induced Hypoproliferative Thrombocytopenia

Recommendations
Recommendation 1: The AABB recommends that platelets should be transfused prophylactically to reduce the risk for spontaneous bleeding in adult patients with therapy-induced hypoproliferative thrombocytopenia.

The AABB recommends transfusing hospitalized adult patients with a platelet count of 10 × 10⁹ cells/L or less to reduce the risk for spontaneous bleeding.

The AABB recommends transfusing up to a single apheresis unit or equivalent. Greater doses are not more effective, and lower doses equal to one half of a standard apheresis unit are equally effective.

Quality of evidence: moderate; strength of recommendation: strong.

Evidence Summary
Three RCTs (n = 1047) compared bleeding outcomes in hospitalized patients with radiation and/or chemotherapy-induced hypoproliferative thrombocytopenia assigned to receive or not receive prophylactic platelet transfusions (Appendix Table 3, available at www.annals.org) (19, 21, 24, 25). All patients had hematologic malignancy treated with chemotherapy or HPCT. Prophylactic platelet transfusions were found to significantly reduce the risk for spontaneous grade 2 or greater bleeding (odds ratio [OR], 0.53 [95% CI, 0.32 to 0.87]). Most bleeding events were classified as grade 2. In the 2 largest trials (19, 21), grade 2 or greater bleeding in patients assigned to the group that did not receive prophylaxis occurred more frequently among pa-
tients receiving chemotherapy for acute leukemia compared with autologous HPCT recipients (58% vs. 47% [19, 25]; 51% vs. 28% [21]).

The threshold platelet count at which platelets should be transfused prophylactically to reduce the bleeding risk in hospitalized patients with therapy-induced hypoproliferative thrombocytopenia was examined in 4 RCTs (n = 658) (Appendix Table 4, available at www.annals.org). Patients were assigned to receive prophylactic platelet transfusion for a morning platelet count less than 10 × 10⁹ versus 20 × 10⁹ cells/L (26–28) or 30 × 10⁹ cells/L (15). A greater platelet count threshold (20 × 10⁹ or 30 × 10⁹ cells/L) was not associated with a significantly lower incidence of grade 2 or greater bleeding (OR, 0.74 [CI, 0.41 to 1.35]) or bleeding-related mortality (OR, 0.37 [CI, 0.02 to 9.22]). The total number of days with bleeding was greater in the 10 × 10⁹–cells/L threshold group. The 10 × 10⁹–cells/L threshold was associated with lower platelet usage and fewer transfusion reactions.

Four RCTs (n = 1132) (Appendix Table 5, available at www.annals.org) examined whether prophylactic transfusion of low-dose platelets (defined as approximately one half of the standard dose of 3 to 4 × 10¹¹ platelets) would provide hemostasis equal to that of standard-dose platelets in patients with therapy-induced hypoproliferative thrombocytopenia (16, 18, 20, 29). There was no difference in grade 2 or greater bleeding in recipients of standard-dose versus low-dose platelets (OR, 0.91 [CI, 0.70 to 1.19]). High-dose platelets (approximately double the standard dose) were compared with standard-dose platelets in 2 RCTs (n = 951) (Appendix Table 6, available at www.annals.org) (17, 18). Prophylactic transfusion of high-dose platelets did not reduce the risk for bleeding compared with standard-dose platelets (OR, 1.05 [CI, 0.79 to 1.40]).

Rationale for Recommendations

Before routine platelet prophylaxis was introduced, severe hemorrhage was a common cause of death among patients receiving high-dose chemotherapy (30, 31). Today, severe hemorrhage is rarely encountered in this setting. The original studies of platelet prophylaxis were done decades ago, and both chemotherapy and supportive care for patients with cancer have changed dramatically over time. Therefore, the randomized trials reported by Wandt (21) and Stanworth (19) and their colleagues were designed to answer the question of whether a prophylactic as compared with a therapeutic platelet transfusion strategy provides benefit in contemporary cancer care. In the study by Wandt and colleagues (21), grade 2 or greater bleeding was seen in 42% of patients assigned to receive therapeutic platelet transfusions only, compared with 19% of patients assigned to receive prophylactic platelet transfusion for a platelet count of 10 × 10⁹ cells/L or less (P < 0.001). In the subset of patients with acute myelogenous leukemia, intracerebral bleeding (grade 4) occurred significantly more often in the therapeutic platelet group compared with the prophylactic platelet group (7% vs. 2%; P = 0.010). In 11 of 13 cases, intracerebral bleeding was detectable on CT scan, but there were no apparent clinical sequelae. Computed tomography scans to investigate new headache or other cerebral symptoms were required only for patients in the therapeutic platelet group, so subclinical intracerebral hemorrhage in the prophylactic platelet group may have been underdiagnosed. In the Trial of Prophylactic Platelets (19), subtler differences in bleeding outcomes were seen between the study groups. Grade 2 or greater bleeding occurred in 50% of patients assigned to the group that did not receive prophylaxis, compared with 43% of patients receiving prophylactic platelet transfusions (P = 0.06 for noninferiority). In patients receiving chemotherapy (not HPCT), there was a significant increase in grade 2 or greater bleeding in the group that did not receive prophylaxis (risk difference, 20% [90% CI, 7.9% to 32.2%]). There was also a nonsignificant trend toward increased grade 3 and 4 bleeding for all patients in the group that did not receive prophylaxis. Thus, both the Wandt trial and the Trial of Prophylactic Platelets support the continued use of prophylactic platelet transfusions in patients with therapy-induced hypoproliferative thrombocytopenia.

In this population, we recommend prophylactic platelet transfusion for a platelet count of 10 × 10⁹ cells/L or less. Some data suggest that the risk for spontaneous bleeding does not increase until the platelet count decreases to less than approximately 6 × 10⁹ cells/L (18, 32), but the 10 × 10⁹–cells/L platelet count

| Table 2. Summary of the Modified WHO Bleeding Scale* |
|-------------------|-----------------|
| **WHO Bleeding Grade** | **Examples** |
| 1 | Oropharyngeal bleeding ≤30 min in 24 h |
| 2 | Epistaxis >30 min in 24 h |
| 3 | Bleeding requiring red blood cell transfusion over routine transfusion needs |
| 4 | Bleeding associated with severe hemodynamic instability |

CNS = central nervous system; WHO = World Health Organization.
* From references 18 and 22.
Clinical Guideline

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threshold seems to provide a good balance of safety and practicality, and the accuracy of extremely low platelet count measurements is questionable (33, 34). The recommendation for prophylactic platelet transfusion based on a $10 \times 10^9$-cells/L platelet count threshold applies to hospitalized patients only. Prophylactic platelet transfusion based on a more liberal (greater) platelet count threshold may be appropriate when treating outpatients, for reasons of practicality (fewer clinic visits).

The Platelet Dose study (18) established that patients receiving low-dose prophylactic platelet transfusions for a morning platelet count of $10 \times 10^9$ cells/L or less had the same bleeding risk as patients receiving standard- or high-dose platelets. However, low-dose platelets did need to be transfused more often because they provided a lower increment. It is safe to provide low-dose platelet prophylaxis to patients with therapy-induced hypoproliferative thrombocytopenia, either routinely or as a temporary maneuver in times of platelet shortage. High-dose prophylactic platelet transfusions have not been shown to provide additional benefit, so they are not recommended as routine therapy for inpatients.

Clinical Setting 2: Adult Patients Having Minor Invasive Procedures

Recommendations

Recommendation 2: The AABB suggests prophylactic platelet transfusion for patients having elective central venous catheter placement with a platelet count less than $20 \times 10^9$ cells/L.

Quality of evidence: low; strength of recommendation: weak.

Recommendation 3: The AABB suggests prophylactic platelet transfusion for patients having elective diagnostic lumbar puncture with a platelet count less than $50 \times 10^9$ cells/L.

Quality of evidence: very low; strength of recommendation: weak.

Evidence Summary

Eight observational studies of central venous catheter (CVC) placement in the setting of thrombocytopenia were identified ($n = 1311$ cannulations) (Appendix Table 7, available at www.annals.org) (12, 35-41). Many patients had acute leukemia or were having HPCT; however, patients with renal failure, critically ill patients, and others were included. Overall bleeding complication rates were low, ranging from 0% to 9% of catheter placements. The largest series of nontunneled CVC placements included 604 cannulations in 193 consecutive patients (41). In multivariate analysis, only patients with preprocedure platelet counts less than $20 \times 10^9$ cells/L ($n = 93$) were at increased risk for bleeding compared with patients with platelet counts greater than $100 \times 10^9$ cells/L. Ninety-six percent of bleeding events were grade 1, and the remaining 4% of bleeding events were grade 2, requiring only local compression. In another single-center study, bleeding outcomes were reported on 3170 tunneled CVCs placed under ultrasonography guidance in 2512 patients (38). No bleeding complications occurred in the 344 CVC placements performed with a preprocedure platelet count less than $50 \times 10^9$ cells/L, including 42 cases with a platelet count less than $25 \times 10^9$ cells/L.

Data from 7 observational studies of children or adults who were thrombocytopenic and had diagnostic or therapeutic lumbar puncture (LP) were evaluated (Appendix Table 8, available at www.annals.org) (42-49). The largest was a single-center observational study of 5223 LPs in 956 pediatric patients with acute lymphoblastic leukemia (45). A total of 199 LPs were performed with platelet counts of $20 \times 10^9$ cells/L or less, and 742 LPs were performed with platelet counts between $21 \times 10^9$ cells/L and $50 \times 10^9$ cells/L. No bleeding complications were seen, regardless of platelet count. The upper 95% CI for serious complications was 1.75% for patients with platelet counts of $20 \times 10^9$ cells/L or less and 0.37% for patients with platelet counts of $50 \times 10^9$ cells/L or less. Traumatic LP (>500 red blood cells per high-power field) occurred in 10.5% of procedures but was not associated with adverse clinical outcomes. The largest reported series in adults included 195 diagnostic or therapeutic LPs in 66 adult patients with acute leukemia and thrombocytopenia (49). Patients were prophylactically transfused with platelets for a preprocedure platelet count less than $20 \times 10^9$ cells/L. Thirty-five LPs were performed in patients with platelet counts of $20 \times 10^9$ to $30 \times 10^9$ cells/L, and 40 were done with platelet counts of $31 \times 10^9$ to $50 \times 10^9$ cells/L. No bleeding complications were seen.

Rationale for Recommendations

Serious bleeding complications after CVC placement are rare, and when they occur, they are often unrelated to the platelet count (such as accidental arterial puncture). In aggregate, the existing data support the use of a $20 \times 10^9$-cells/L platelet count threshold for CVC placement. The reported studies included patients with a wide range of primary diagnoses; this recommendation is intended to be broadly applicable to adult patients with hypoproliferative thrombocytopenia.

Bleeding complications are rare with LPs, but hemorrhage anywhere in the central nervous system has the potential to cause devastating neurologic sequelae. In the absence of better published data supporting the safety of a lower threshold in adult patients, a fairly liberal platelet count threshold for LPs (that is, $50 \times 10^9$ cells/L) seems prudent. The $50 \times 10^9$-cells/L threshold is intended for simple diagnostic or therapeutic LPs only. Despite a lack of supportive data, a greater platelet count is often recommended for other procedures, such as epidural anesthesia (50, 51).

Clinical Setting 3: Adult Patients Having Major Elective Nonneuraxial Surgery

Recommendations

Recommendation 4: The AABB suggests prophylactic platelet transfusion for patients having major...
elective nonneuraxial surgery with a platelet count less than $50 \times 10^9$ cells/L.  
Quality of evidence: very low; strength of recommendation: weak.

Recommendation 5: The AABB recommends against routine prophylactic platelet transfusion for patients who are nonthrombocytopenic and have cardiac surgery with cardiopulmonary bypass (CPB). The AABB suggests platelet transfusion for patients having CPB who exhibit perioperative bleeding with thrombocytopenia and/or with evidence of platelet dysfunction.

Quality of evidence: very low; strength of recommendation: weak.

Evidence Summary

In 1 series (Appendix Table 9, available at www.annals.org) (52), 95 patients with acute leukemia and thrombocytopenia had 167 invasive procedures, including 29 major surgeries (such as thoracotomy) and 24 moderately invasive procedures (such as arteriovenous fistula construction). Platelet prophylaxis was given before the 130 procedures in which the preoperative platelet count was less than $50 \times 10^9$ cells/L. The median postoperative platelet count in these cases was $56 \times 10^9$ cells/L. Intraoperative blood loss greater than 500 mL occurred in only 7% of all operations, and there were no deaths due to bleeding. Preoperative platelet count was not significantly associated with intraoperative or postoperative bleeding.

In a meta-analysis of 6 RCTs and a single pilot study conducted during the licensure of aprotinin, adverse outcome data were compared between cardiac surgical patients who received ($n = 284$) or did not receive ($n = 1436$) perioperative platelet transfusions (Appendix Table 10, available at www.annals.org) (53). Platelet transfusion was identified as an independent predictor of adverse outcomes, including mortality (OR, 4.76 [CI, 1.65 to 13.73]). It is possible that platelet transfusion served at least in part as a surrogate marker of sicker patients in this analysis, rather than as a direct cause of adverse outcomes (that is, confounding by indication).

Rationale for Recommendations

The consensus opinion of the panel is that platelet counts of $50 \times 10^9$ cells/L and greater are safe for major nonneuraxial surgery. There is no evidence of increased perioperative bleeding risk in thrombocytopenic patients with platelet counts greater than $50 \times 10^9$ cells/L. We recommend that platelet transfusion be withheld in nonbleeding surgical patients when the platelet count is greater than $50 \times 10^9$ cells/L and there is no evidence of coagulopathy. In contrast, we suggest that platelet transfusion should be considered in cardiac surgical patients with perioperative bleeding and thrombocytopenia (see the Definitions section) and/or suspected qualitative platelet abnormalities, which often result from exposure of platelets to the CPB circuit (54). Platelet transfusions are often administered to nonbleeding cardiac surgical patients (55). There are no data supporting this practice, and it should be discouraged.

Clinical Setting 4: Adult Patients Receiving Antiplatelet Therapy Who Have Intracranial Hemorrhage (Traumatic or Spontaneous)

Recommendations

Recommendation 6: The AABB cannot recommend for or against platelet transfusion for patients receiving antiplatelet therapy who have intracranial hemorrhage (traumatic or spontaneous).

Quality of evidence: very low; strength of recommendation: uncertain.

Evidence Summary

Five observational studies ($n = 635$) examined clinical outcomes among patients receiving antiplatelet agents who present with traumatic brain injury (Appendix Table 11, available at www.annals.org) (56). One study reported a greater mortality rate for patients who received transfusions with platelets (relative risk, 2.4 [CI, 1.2 to 4.9]) (57), and a second study reported a lower mortality rate for patients receiving platelets (relative risk, 0.21 [CI, 0.05 to 0.95]) (58). Three studies showed no significant effect on mortality rates when patients received transfusions with platelets (59–61). One additional observational study ($n = 88$) reported that patients with traumatic brain injury and moderate thrombocytopenia ($50 \times 10^9$ to $107 \times 10^9$ cells/L) who were transfused with platelets had poorer survival than those who were not transfused with platelets (62). In all of these studies, it was not possible to establish a causal relationship between platelet transfusion and clinical outcomes, and confounding by indication was possible.

Rationale for Recommendations

In patients with intracerebral hemorrhage who are receiving antiplatelet agents, the decision to transfuse platelets requires an individual clinical decision based on various clinical factors, including the size of the bleeding and the patient’s level of consciousness. For surgeries involving the central nervous system, platelets are conventionally transfused prophylactically for a preprocedure platelet count less than $80 \times 10^9$ to $100 \times 10^9$ cells/L, although only low-quality data supporting this threshold are available.

Discussion

A large proportion of platelet transfusions are administered prophylactically to reduce the risk for spontaneous hemorrhage in patients receiving chemotherapy or HPC (1–3). With data available from several RCTs (15–21, 24–29, 63), there is now a solid understanding of the role of platelet transfusions in this specific setting. Platelet prophylaxis, as compared with a therapeutic platelet transfusion strategy, reduces but does not eliminate the risk for bleeding in hospitalized patients with therapy-induced hypoproliferative throm-
bocytopenia. We recommend that these patients receive prophylactic platelet transfusions for a morning platelet count of $10 \times 10^9$ cells/L or less. Clinicians can be assured that prophylaxis with low-dose platelets provides hemostasis that is equal to standard- or high-dose platelets in patients with therapy-induced hyperproliferative thrombocytopenia. However, low-dose platelets must be transfused more often because they provide a lower platelet increment (18).

Only limited data are available to support transfusing platelets for indications other than prophylaxis against spontaneous bleeding in patients with therapy-induced hyperproliferative thrombocytopenia. Our panel took the position that it is appropriate for the AABB to address common and important clinical scenarios, such as the role of platelet transfusions in patients having invasive procedures, even as we await better data. Therefore, we decided to review observational data as a basis for platelet transfusion recommendations. The lower quality of data is reflected in the weak strength of recommendations outside of the hyperproliferative thrombocytopenia setting. In the specific case of CVC placement, our consensus opinion is that recent observational data (38, 41) support a platelet count transfusion threshold of $20 \times 10^9$ cells/L. This threshold seems to be reasonable even for the placement of large-bore catheters for apheresis in thrombocytopenic patients (12). Observational data were also used to inform the platelet transfusion recommendation for LP, for which we suggest a threshold platelet count of $50 \times 10^9$ cells/L. Most of the published data about the safety of performing diagnostic LP in the setting of thrombocytopenia comes from a single center’s experience with pediatric patients (45); it is unclear how generalizable these data are to adult patients. Of 21 case reports of LP-associated spinal hematomas in adults, 17 (81%) occurred at a platelet count less than $50 \times 10^9$ cells/L. However, in all but 1 patient, other risk factors for bleeding were identified (50). We believe that clinical judgment should be used about the need for platelet transfusion in patients requiring LP with platelet counts in the range of $20 \times 10^9$ to $50 \times 10^9$ cells/L.

**Comparison With Other Published Guidelines**

Our recommendation to provide prophylactic platelet transfusion at a platelet count of $10 \times 10^9$ cells/L or less for patients with therapy-induced hyperproliferative thrombocytopenia is consistent with the current standard of practice as reflected in other published transfusion guidelines (64–70). The recommendation of using a platelet count of $50 \times 10^9$ cells/L or greater as a safe level to perform LP in adults falls within the spectrum of other published guidelines, which have typically recommended platelet thresholds ranging from $20 \times 10^9$ to $50 \times 10^9$ cells/L (50, 65, 66). The recommendation of a $50 \times 10^9$–cells/L platelet transfusion threshold for major nonneuraxial procedures is also consistent with other guidelines (64–70). The suggestion to transfuse platelets to patients having CPB with perioperative bleeding and thrombocytope-
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Acknowledgment: The authors thank Theresa Wiegmann for her outstanding skill and dedication in guiding this project and Jacqlyn Riposo for her superb logistic support.

Disclosures: Disclosures can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M14-1589.

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References


Annals of Internal Medicine

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## Appendix Table 1. Panel Members’ Conflicts of Interest

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<thead>
<tr>
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Appendix Table 2. Search Strategy Used for Systematic Review of the Literature*

**PubMed**
1. Search strategy for prophylactic platelet transfusion studies
   (blood transfusion OR Blood Transfusion[Mesh] OR "Blood Cells/transplantation"[Mesh] OR transfus*[tiab])
   AND
   AND
   (Prophyla*[tiab] OR bleed*[tiab] OR transfus*[tiab])
   AND
2. Search strategy for therapeutic platelet transfusion studies
   (blood transfusion OR Blood Transfusion[Mesh] OR "Blood Cells/transplantation"[Mesh] OR transfus*[tiab])
   AND
   AND
   (Therapeutic*[tiab] OR therap*[tiab])
   AND

**Cochrane Central Register of Controlled Trials**
3. Search strategy for prophylactic platelet transfusion studies
   Prophyla*[tiab] platelet* transfuse*
4. Search strategy for therapeutic platelet transfusion studies
   Therapeutic*[tiab] platelet* transfuse*

**Web of Science**
No subject heading-all keywords
5. Search strategy for prophylactic platelet transfusion studies (blood transfusion OR Blood Cells transplantation OR transfus*)
   AND
   (platelet AND (count OR transfus*)) OR (Prophyla*[tiab] OR bleed*[tiab] OR transfus*)
   (whole phrase in title field)
   AND
   (threshold*[tiab] OR trigger*[tiab] OR count OR policy [tiab] OR adminis*[tiab] OR guideline*[tiab] OR dose OR dosing OR dosage OR practice OR transfus*)
6. Search strategy for therapeutic platelet transfusion studies (blood transfusion OR Blood Cells transplantation OR transfus*)
   AND
   (platelet AND (count OR transfus*)) OR (Therapeutic*[tiab] OR therap*[tiab])
   (whole phrase in title field)
   AND
7. Additional search
The yield on the original search strategy was not optimum for all diseases. Therefore, we also searched the PubMed clinical queries by using a combination of 2 terms of "platelet transfusion" AND "disease category".
7.1. Platelet transfusion AND idiopathic thrombocytopenic purpura. The resultant search strategy from PubMed Clinical Queries is shown below:
Therapy/Broad[filter] AND (["platelet transfusion"[MeSH Terms] OR ("platelet"[All Fields] AND "transfusion"[All Fields]) OR "platelet transfusion"[All Fields])
AND ("purpura, thrombocytopenic, idiopathic"[MeSH Terms] OR ("purpura"[All Fields] AND "thrombocytopenic"[All Fields] AND "idiopathic"[All Fields])
OR "idiopathic thrombocytopenic purpura"[All Fields] OR "idiopathic"[All Fields] AND "thrombocytopenic"[All Fields] AND "purpura"[All Fields])
7.2. Platelet transfusion AND Disseminated Intravascular Coagulation
Therapy/Broad[filter] AND ("platelet transfusion"[MeSH Terms] OR ("platelet"[All Fields] AND "transfusion"[All Fields]) OR "platelet transfusion"[All Fields])
AND ("disseminated intravascular coagulation"[MeSH Terms] OR ("disseminated"[All Fields] AND "intravascular"[All Fields] AND "coagulation"[All Fields])
OR "disseminated intravascular coagulation"[All Fields])
7.3. Platelet transfusion AND Idiopathic Thrombocytopenic Purpura
Therapy/Broad[filter] AND (["platelet transfusion"[MeSH Terms] OR ("platelet"[All Fields] AND "transfusion"[All Fields]) OR "platelet transfusion"[All Fields])
AND ("purpura, thrombocytopenic, idiopathic"[MeSH Terms] OR ("purpura"[All Fields] AND "thrombocytopenic"[All Fields] AND "idiopathic"[All Fields])
OR "idiopathic thrombocytopenic purpura"[All Fields] OR "idiopathic"[All Fields] AND "thrombocytopenic"[All Fields] AND "purpura"[All Fields])
7.4. Platelet transfusion AND Thrombotic Thrombocytopenic Purpura - Hemolytic Uremic Syndrome
Therapy/Broad[filter] AND ("platelet transfusion"[MeSH Terms] OR ("platelet"[All Fields] AND "transfusion"[All Fields]) OR "platelet transfusion"[All Fields])
AND ("purpura, thrombotic thrombocytopenic"[MeSH Terms] OR ("purpura"[All Fields] AND "thrombotic"[All Fields] AND "thrombocytopenic"[All Fields] AND "purpura"[All Fields])
OR "thrombotic thrombocytopenic purpura"[All Fields] OR ("thrombotic"[All Fields] AND "thrombocytopenic"[All Fields] AND "purpura"[All Fields])
OR "hemolytic uraemic syndrome"[All Fields]))
8. Manual search
The search strategy was supplemented by a manual search of references of the obtained full-text articles and existing guidelines in the field. In addition, we also contacted the members of the AABB Guidelines Panel to identify any unpublished articles or studies that were missed in the search.
All obtained citations were entered into an EndNote database. In the first step, all duplicate citations were removed using the remove duplicate feature in the EndNote. Next, the abstract and title of all remaining citations were printed and manually reviewed for inclusion or exclusion by 2 reviewers according to the predetermined criteria. All the included studies were first sorted on the basis of study design and disease category. That is, in the first attempt, all reviewed studies were classified as randomized or observational; then, within the study design, all studies were collated according to the broad category of treatment vs. prophylactic followed by various disease categories (e.g., surgery, hematologic malignant tumors, and central venous catheter). All included observational studies within a disease category were classified as prospective observational or retrospective observational. For prospective observational cohort studies, we classified all studies as cohort studies either with comparison or without comparison. For retrospective observational studies, all studies were further classified as retrospective cohort with comparison or single-group or case series or case reports.

* From reference 11.
### Appendix Table 3. Prophylactic Platelet Transfusion Versus No Prophylactic Platelet Transfusion in Therapy-Induced Hypoproliferative Thrombocytopenia

<table>
<thead>
<tr>
<th>Studies by Subgroup, n</th>
<th>Quality Assessment*</th>
<th>Patients, n/N (%)</th>
<th>Effect</th>
<th>Quality</th>
<th>Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Design</td>
<td>Risk of Bias</td>
<td>Inconsistency</td>
<td>Indirectness</td>
<td>Imprecision</td>
</tr>
<tr>
<td>Grade 2 or greater</td>
<td>Randomized trials</td>
<td>No serious risk</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
</tr>
<tr>
<td>bleeding</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>chemotherapy subgroup</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 (21, 24, 25)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 2 or greater</td>
<td>Randomized trials</td>
<td>No serious risk</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
</tr>
<tr>
<td>bleeding, autologous</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPCT subgroup: 2 (21, 25)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 2 or greater</td>
<td>Randomized trials</td>
<td>Serious‡</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
</tr>
<tr>
<td>bleeding</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All-cause mortality:</td>
<td>Randomized trials</td>
<td>No serious risk</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
</tr>
<tr>
<td>4 (21, 24, 25, 63)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bleeding-related</td>
<td>Randomized trials</td>
<td>No serious risk</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
</tr>
<tr>
<td>mortality: 4 (21, 24, 25, 63)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

HPCT = hematopoietic progenitor cell transplantation.
* Quality assessment evaluated risk of bias, inconsistency (based on heterogeneity among trials), indirectness (based on assessment of generalizability of results), and imprecision (based on width of CIs).
† Only 3/6 randomized, controlled trials reported this outcome.
‡ In Wandt et al (21), protocol deviations occurred in 30% of transfusions in the therapeutic group vs. 14% in the prophylactic group.
§ Stanworth et al (19) reported no deaths due to bleeding. We used the continuity correction (0.5 as event) to include this study in pooling the data.
¶ Only 4/6 randomized, controlled trials reported this outcome.
|| Wide CIs.
### Appendix Table 4. Higher Versus Lower Platelet Count Thresholds for Prophylactic Platelet Transfusions in Therapy-Induced Hypoproliferative Thrombocytopenia

<table>
<thead>
<tr>
<th>Studies by Subgroup, n</th>
<th>Quality Assessment*</th>
<th>Patients, n/N (%)</th>
<th>Effect</th>
<th>Quality</th>
<th>Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Design</td>
<td>Risk of Bias</td>
<td>Inconsistency</td>
<td>Indirectness</td>
<td>Imprecision</td>
</tr>
<tr>
<td>Grade 2 or greater bleeding: 4 (15, 26-28)</td>
<td>Randomized trials</td>
<td>No serious risk</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Serious†</td>
</tr>
<tr>
<td>All-cause mortality: 3 (26-28)</td>
<td>Randomized trials</td>
<td>No serious risk</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Serious†</td>
</tr>
<tr>
<td>Bleeding-related mortality: 4 (15, 26-28)</td>
<td>Randomized trials</td>
<td>No serious risk</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Serious†</td>
</tr>
</tbody>
</table>

* Quality assessment evaluated risk of bias, inconsistency (based on heterogeneity among trials), indirectness (based on assessment of generalizability of results), and imprecision (based on width of CIs).† Wide CIs.

### Appendix Table 5. Standard-Dose Versus Low-Dose Prophylactic Platelet Transfusions in Therapy-Induced Hypoproliferative Thrombocytopenia

<table>
<thead>
<tr>
<th>Studies by Subgroup, n</th>
<th>Quality Assessment*</th>
<th>Patients, n/N (%)</th>
<th>Effect</th>
<th>Quality</th>
<th>Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Design</td>
<td>Risk of Bias</td>
<td>Inconsistency</td>
<td>Indirectness</td>
<td>Imprecision</td>
</tr>
<tr>
<td>Grade 2 or greater bleeding: 4 (16, 18, 20, 29)</td>
<td>Randomized trials</td>
<td>No serious risk</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Serious†</td>
</tr>
<tr>
<td>All-cause mortality: 3 (16, 18, 20)</td>
<td>Randomized trials</td>
<td>No serious risk</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Serious†</td>
</tr>
<tr>
<td>Bleeding-related mortality: 3 (14, 18, 20)</td>
<td>Randomized trials</td>
<td>No serious risk</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Serious†</td>
</tr>
</tbody>
</table>

* Quality assessment evaluated risk of bias, inconsistency (based on heterogeneity among trials), indirectness (based on assessment of generalizability of results), and imprecision (based on width of CIs).† Wide CIs.
‡ 3/7 trials reported this outcome.
§ 4/7 trials reported this outcome.
### Appendix Table 6. High-Dose Versus Standard-Dose Prophylactic Platelet Transfusions in Therapy-Induced Hypoproliferative Thrombocytopenia

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Design</th>
<th>Risk of Bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other Considerations</th>
<th>Patients, n/N (%)</th>
<th>Effect</th>
<th>Quality</th>
<th>Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 2 or greater bleeding: 2 (17, 18)</td>
<td>Randomized trials</td>
<td>No serious risk</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Serious†</td>
<td>None</td>
<td>305/480 (63.5)</td>
<td>294/471 (62.4)</td>
<td>1.05 (0.79–1.40)</td>
<td>11 more bleeding events per 1000 (from 75 more bleeding events)</td>
</tr>
<tr>
<td>All-cause mortality: 1 (18)</td>
<td>Randomized trials</td>
<td>No serious risk</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Serious†</td>
<td>Reporting bias‡</td>
<td>7/432 (1.6)</td>
<td>4/423 (0.9)</td>
<td>1.73 (0.5–5.94)</td>
<td>7 fewer deaths per 1000 (from 5 fewer to 44 more deaths)</td>
</tr>
<tr>
<td>Bleeding-related mortality: 2 (17, 18)</td>
<td>Randomized trials</td>
<td>No serious risk</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Serious†</td>
<td>Reporting bias§</td>
<td>1/480 (0.2)</td>
<td>0/471 (0)</td>
<td>2.94 (0.12–72.48)</td>
<td>–</td>
</tr>
</tbody>
</table>

* Quality assessment evaluated risk of bias, inconsistency (based on heterogeneity among trials), indirectness (based on assessment of generalizability of results), and imprecision (based on width of CIs).
† Wide CIs.
‡ 3/7 trials reported this outcome.
§ 4/7 trials reported this outcome.

### Appendix Table 7. Prophylactic Platelet Transfusion for Central Venous Catheter Placement

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Design</th>
<th>Risk of Bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other Considerations</th>
<th>Patients, n/N (%)</th>
<th>Effect</th>
<th>Quality</th>
<th>Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding: 1 (40)</td>
<td>Observational study</td>
<td>Serious†</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Serious‡</td>
<td>Reporting bias§</td>
<td>0/37 (0)</td>
<td>4/68 (5.9)</td>
<td>0.19 (0.01–3.65)</td>
<td>47 fewer bleeding events per 1000 (from 58 fewer to 156 more bleeding events)</td>
</tr>
<tr>
<td>All-cause mortality: 1 (40)</td>
<td>Observational study</td>
<td>Serious†</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>Serious‡</td>
<td>Reporting bias§</td>
<td>10/37 (27.0)</td>
<td>9/68 (13.2)</td>
<td>2.43 (0.89–6.66)</td>
<td>138 more deaths per 1000 (from 12 fewer to 472 more deaths)</td>
</tr>
</tbody>
</table>

* Quality assessment evaluated risk of bias, inconsistency (based on heterogeneity among trials), indirectness (based on assessment of generalizability of results), and imprecision (based on width of CIs).
† The authors did not provide details on co-interventions.
‡ Wide CIs.
§ Only 1 study (36) reported a comparison of platelet transfusion vs. no platelet transfusion in patients having central venous catheter placement. Six additional observational studies (969 cannulations) without a comparison group (35, 37–41) were identified in the original literature search to April 2013. One additional observational study without a comparison group (57 apheresis catheter placements in patients with thrombotic thrombocytopenic purpura) (12) was identified in the updated literature search to September 2014. These 7 studies reported overall bleeding rates of 0%–9% in thrombocytopenic patients having central venous catheter placement.
### Appendix Table 8. Prophylactic Platelet Transfusion Versus No Prophylactic Platelet Transfusion for Lumbar Puncture

<table>
<thead>
<tr>
<th>Study Subgroup</th>
<th>Quality Assessment*</th>
<th>Events/Patients, n/N (%)</th>
<th>Effect</th>
<th>Quality</th>
<th>Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spinal hematoma (pediatric patients): 5 (44-48)</td>
<td>Observational study</td>
<td>Serious‡</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
</tr>
<tr>
<td>Spinal hematoma (adult patients): 2 (42, 49)</td>
<td>Observational study</td>
<td>Serious§</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
</tr>
</tbody>
</table>

NA = not applicable.
* Quality assessment evaluated risk of bias, inconsistency (based on heterogeneity among trials), indirectness (based on assessment of generalizability of results), and imprecision (based on width of CIs).
† Some authors did not report the number of lumbar puncture procedures done but report only the total number of patients; therefore, the denominator is the number of patients.
‡ Only 2/5 studies reported data from consecutive patients.
§ Neither of the 2 studies reported data from consecutive patients.

### Appendix Table 9. Prophylactic Platelet Transfusion Versus No Prophylactic Platelet Transfusion for Surgery

<table>
<thead>
<tr>
<th>Study Subgroup</th>
<th>Quality Assessment*</th>
<th>Patients, n/N (%)</th>
<th>Effect</th>
<th>Quality</th>
<th>Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortality: 1 (52)</td>
<td>Observation study</td>
<td>Serious†</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
</tr>
<tr>
<td>Bleeding-related mortality: 1 (52)</td>
<td>Observation study</td>
<td>Serious†</td>
<td>No serious inconsistency</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
</tr>
</tbody>
</table>

NA = not applicable.
* Quality assessment evaluated risk of bias, inconsistency (based on heterogeneity among trials), indirectness (based on assessment of generalizability of results), and imprecision (based on width of CIs).
† The study included 435 consecutive patients with acute leukemia, and 95 patients had 167 operations with a platelet count <100 × 10⁹ cells/L and 130 operations with platelet counts <50 × 10⁹ cells/L. Only 7% of operations had intraoperative blood loss >500 mL, and 7% required >4 units of red blood cells transfused in the perioperative period.
‡ Only 2 studies reported data on the effect of platelet transfusion on clinical outcomes in patients having surgical procedures.
### Appendix Table 10. Platelet Transfusion Versus No Platelet Transfusion for Coronary Artery Bypass Graft Surgery

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Patients, n</th>
<th>Effect</th>
<th>Quality</th>
<th>Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelet Transfusion</td>
<td>284</td>
<td>4.76 (1.65–13.73)</td>
<td>NA</td>
<td>Very low</td>
</tr>
<tr>
<td>No Platelet Transfusion</td>
<td>1436</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Studies by Subgroup, n**

<table>
<thead>
<tr>
<th>Design</th>
<th>Risk of Bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 randomized trials, 1 observational study</td>
<td>Serious†</td>
<td>Serious ‡</td>
<td>No serious indirectness</td>
<td>No serious imprecision</td>
<td>Serious reporting bias§</td>
</tr>
</tbody>
</table>

Mortality: 1 (53)

- Quality assessment evaluated risk of bias, inconsistency (based on heterogeneity among trials), indirectness (based on assessment of generalizability of results), and imprecision (based on width of CIs).
- Individual-patient data from 6 randomized, double-blinded, phase III, placebo-controlled trials evaluating aprotinin use in coronary artery bypass graft surgery were pooled together in this analysis. Data from 37 patients participating in a pilot study were also included in the analysis. The distribution of the quantity of platelets transfused was highly skewed between 2 groups. The data-recording tool did not always delineate single-donor plateletpheresis units (presumably those with <5–6 units) vs. pooled random donor units (those with ≥5–24 units). The patients receiving platelets were not similar to patients who did not receive platelets (potential confounding by indication). Transfusion was not randomly assigned in this patient population, and there is a concern that multivariate analysis may not accurately control for confounding and bias. To address this issue, authors used propensity score matching for analysis. The risk estimates reported here are derived from the propensity score analysis.
- The 6 randomized, controlled trials were originally designed to evaluate aprotinin and not prophylactic use of platelets among patients having coronary artery bypass graft surgery.
- The study did not report comprehensive bleeding outcomes and may be limited by outcome reporting bias.

### Appendix Table 11. Platelet Transfusion Versus No Platelet Transfusion in Patients Who Were Thrombocytopenic and Had a Traumatic Brain Injury

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Patients, n/N (%</th>
<th>Effect</th>
<th>Quality</th>
<th>Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelet Transfusion</td>
<td>67/375 (17.9)</td>
<td>1.11 (0.51–2.46)</td>
<td>17 more deaths per 1000 (from 86 fewer to 180 more deaths)</td>
<td>Very low</td>
</tr>
<tr>
<td>No Platelet Transfusion</td>
<td>76/384 (19.8)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Mortality (on antiplatelet therapy): 5 (43, 57-60)

- Observational studies
- Serious†
- No serious inconsistency
- No serious indirectness
- Reduced effect for RR >1 or <1†

Mortality (no antiplatelet therapy): 1 (62)

- Observational studies
- Serious§
- No serious inconsistency
- No serious indirectness
- Reduced effect for RR >1 or <1†

### RR = relative risk.

- Quality assessment evaluated risk of bias, inconsistency (based on heterogeneity among trials), indirectness (based on assessment of generalizability of results), and imprecision (based on width of CIs).
- All included studies were based on registry data; thus, they experienced limitations inherent to retrospective analysis of a secondary data set. Most of these studies did not adequately control for confounding factors (e.g., concomitant warfarin use). Even with attempts to adjust for differences in baseline prognostic variables, it is probable that significant bias existed in the decision about whether to transfuse platelets. The included studies provided limited information about the timing of transfusion after injury, which may affect outcomes.
- Wide CIs.
- Experienced from limitations inherent to retrospective analysis of a secondary data set. Inclusion criteria were brain injuries confirmed by the presence of abnormal neuroimaging or a Glasgow Coma Scale score <13 after resuscitation. Instead of randomization, the study relied on variation in clinical practice to elucidate differences in outcome between patients who did and did not receive a transfusion. Of the 480 patients included in this study, mortality data were available for patients with moderate thrombocytopenia, defined as a platelet count of 50 to 107 × 10⁹ cells/L (n = 88).