

Transfusion of Fresh Frozen Plasma and Platelets in Critically Ill Adults



An American College of Chest Physicians Clinical Practice Guideline

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BACKGROUND: Platelets and fresh frozen plasma (FFP) are frequently administered to critically ill patients. Considering the variability in indications and thresholds guiding these transfusions, a comprehensive review of current evidence was conducted to provide guidance to critical care practitioners. This American College of Chest Physicians guideline examined the literature on platelet transfusions in critically ill patients with thrombocytopenia, with and without active bleeding, as well as data on prophylactic platelet and FFP transfusions for common procedures in the critical care setting.

METHODS: A panel of experts developed 7 Population, Intervention, Comparator, and Outcome questions addressing platelet and FFP transfusions in critically ill patients and performed a comprehensive evidence review. The panel applied the Grading of Recommendations, Assessment, Development, and Evaluations approach to assess the certainty of evidence, and to formulate and grade recommendations. A modified Delphi technique was used to reach consensus on the recommendations.

RESULTS: The initial search identified a total of 7,172 studies, and after the initial screening, 100 articles were reviewed. Sixteen studies met inclusion criteria, comprising 1 randomized controlled trial and 15 observational studies. Overall, the certainty of the evidence for all questions was very low. The panel formulated 7 conditional recommendations.

CONCLUSIONS: In critically ill patients with thrombocytopenia or coagulopathy, a risk/benefit assessment should be made by providers prior to transfusion of platelets or FFP. Given the known risks of blood product transfusion, and the limited data regarding the benefits from platelet or FFP transfusion, most patients will benefit from avoiding transfusion of these blood products. In patients at high risk of bleeding, or where the bleeding complication may be catastrophic, transfusion should be considered. CHEST 2025; 168(3):661-676

KEY WORDS: arterial line; bronchoscopy; central line; critically ill; fresh frozen plasma; lumbar puncture; paracentesis; platelets; thoracentesis; transfusion

ABBREVIATIONS: ASCO = American Society of Clinical Oncology; BSH = British Society for Haematology; CHEST = American College of Chest Physicians; CVC = central venous catheter; DIC = disseminated intravascular coagulation; ESICM = European Society of Intensive Care Medicine; FFP = fresh frozen plasma; GI = gastrointestinal; GRADE = Grading of Recommendations, Assessment, Development, and Evaluations; IMPROVE = International Medical Prevention Registry on Venous Thromboembolism; INR = international normalized ratio; LOS = length of stay; LP = lumbar puncture; PICO = Population, Intervention, Comparator, and Outcome; RCT = randomized

controlled trial; RR = risk ratio; SIR = Society of Interventional Radiology; WHO = World Health Organization

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Summary of Recommendations

The recommendations in this document apply to critically ill patients, excluding trauma and neuro-critical care populations. These recommendations should be implemented in a hierarchical fashion. Recommendations 1-3 should be applied first to critically ill patients with thrombocytopenia, while recommendations 4-7 provide additional guidance for specific situations involving invasive procedures.

1. In stable non-bleeding critically ill patients with thrombocytopenia and without high risk of spontaneous bleeding, we suggest transfusing platelets if platelet counts fall below $10 \times 10^9/L$ (Conditional Recommendation, Very Low Certainty of Evidence).

2. In stable non-bleeding critically ill patients with thrombocytopenia who are considered at high risk of spontaneous bleeding, we suggest transfusing platelets if platelet counts fall below $30-50 \times 10^9/L$ (Conditional Recommendation, Very Low Certainty of Evidence).

3. In critically ill patients with thrombocytopenia and serious active bleeding, we suggest transfusing platelets if platelet counts fall below $50 \times 10^9/L$ (Conditional Recommendation, Very Low Certainty of Evidence)

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4. Vascular procedures

4A. In critically ill patients at increased risk of bleeding due to thrombocytopenia undergoing a central venous catheter (CVC) or arterial line insertion, we suggest against routine prophylactic platelet transfusion (Conditional Recommendation, Very Low Certainty of Evidence).

4B. In critically ill patients at increased risk of bleeding due to coagulopathy undergoing a CVC or arterial line insertion, we suggest against routine prophylactic fresh frozen plasma (FFP) transfusion (Conditional Recommendation, Very Low Certainty of Evidence).

5. Bedside thoracic or abdominal procedure

5A. In critically ill patients with increased risk of bleeding due to thrombocytopenia undergoing a bedside thoracentesis or paracentesis, we suggest against routine prophylactic platelet transfusion (Conditional Recommendation, Very Low Certainty of Evidence).

5B. In critically ill patients with increased risk of bleeding due to coagulopathy undergoing a bedside thoracentesis or paracentesis, we suggest against routine prophylactic FFP transfusion (Conditional Recommendation, Very Low Certainty of Evidence).

6. Lumbar puncture

6A. In critically ill patients with increased risk of bleeding due to thrombocytopenia undergoing a bedside lumbar puncture, we suggest platelet transfusion if platelets counts are $40-50 \times 10^9/L$ or lower (Conditional Recommendation, Very Low Certainty of Evidence).

6B. In critically ill patients with increased risk of bleeding due to coagulopathy undergoing a bedside lumbar puncture, we suggest FFP transfusion to target international normalized ratio (INR) 1.5-2 before the procedure (Conditional Recommendation, Very Low Certainty of Evidence).

7. Bedside endoscopy

Bronchoscopy

7A. In critically ill patients with increased risk of bleeding due to thrombocytopenia undergoing routine flexible bronchoscopy without biopsy, we suggest against routine prophylactic platelet transfusion (Conditional Recommendation, Very Low Certainty of Evidence).

7B. In critically ill patients with increased risk of bleeding due to coagulopathy undergoing a routine bedside flexible bronchoscopy without biopsy, we suggest against routine prophylactic FFP transfusion (Conditional Recommendation, Very Low Certainty of Evidence).

GI endoscopy

7C. In critically ill patients with suspected portal hypertension related gastrointestinal (GI) bleeding and increased risk of bleeding due to thrombocytopenia who are undergoing GI-endoscopy, we suggest against routine platelet transfusion (Conditional Recommendation, Very Low Certainty of Evidence)

7D. In critically ill patients with suspected portal hypertension related bleeding and increased risk of bleeding due to coagulopathy who are undergoing GI-endoscopy, we suggest against routine FFP transfusion (Conditional Recommendation, Very Low Certainty of Evidence)

Background

In the United States, 20% of platelets and fresh frozen plasma (FFP) are transfused to critically ill patients, totaling 2.2 million units of each annually.¹ The leading indications include mild abnormalities in platelet counts

and coagulation tests in non-bleeding patients and procedural prophylaxis.^{2,3} The lack of solid evidence has led to variability in the indications and thresholds guiding these transfusions.⁴⁻⁷

Coagulopathy is characterized by a disruption of coagulation factors and ineffective hemostasis, leading to impaired clot formation.⁸⁻¹⁰ Although definitions of coagulopathy vary, for the purpose of this document, a pragmatic definition of a prolonged INR was used. Thrombocytopenia and coagulopathy have been linked to increased bleeding risk and higher mortality.^{11,12} Despite the importance of platelet or FFP transfusions in managing these conditions, their use can result in severe and even life-threatening adverse effects.¹³ Hence, evidence weighing both the benefits and risks would be ideal to guide clinical decisions.

Platelets and FFP are scarce resources with variable costs and access globally.^{14,15} Therefore, judicious use is critical, preserving them for patients when the benefits outweigh the risks.¹⁶ The existing inconsistencies in transfusion practices underline the importance of evidence-based recommendations to optimize patient care and resource utilization.¹⁷ An expert panel identified, synthesized, and weighted the evidence to provide clinical recommendations for platelet and FFP transfusions in critically ill patients.

Methods

Expert Panel Composition

The co-chairs nominated a diverse and multidisciplinary panel based on their expertise encompassing critical care medicine, cardiology, hematology, and gastroenterology/hepatology. The final panel consisted of the 2 guideline co-chairs, 9 panelists, 2 methodologists, a medical librarian, and a liaison to the American College of Chest Physicians (CHEST) Guidelines Oversight Committee.

Conflicts of Interest

Financial relationships for each chair and panelists were reviewed by the CHEST Professional Standards Committee for potential conflicts of interest according to the CHEST Conflict of Interest Policy.¹⁸ None of the panel members had conflicts of interest to disclose.

Question Development

The panel developed 7 clinical questions using the Population, Intervention, Comparator, and Outcome

(PICO) format regarding platelet and FFP transfusions in different clinical scenarios. The panel ranked outcomes for each question to determine critical and important outcomes a priori (e-Table 1).

Literature Search

A comprehensive search of MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials using relevant key words was performed in May 2021 (e-Table 2), with an updated search performed in MEDLINE in January 2024. Searches were limited to English language, randomized controlled trials (RCTs), cohort studies, and case-control studies with at least 30 participants. Systematic reviews and prior guidelines were reviewed for context and completeness.

Study Selection and Data Extraction

Relevant citations identified during the literature search were reviewed in duplicate using predefined criteria over 2 rounds of study selection: the first reviewing titles and

abstracts and the second reviewing full texts (e-Figs 1-6). Data were extracted, analyzed, and summarized for each individual PICO question.

Assessment of the Certainty of Evidence

Risk of bias was assessed using the Cochrane Risk of Bias tool for RCTs (RoB 2) and Risk of Bias in Nonrandomized Studies of Intervention (ROBINS-I) based on study design.^{19,20} A meta-analysis was performed when possible using a random effects model. Results were reported as risk ratios (RRs) or ORs for dichotomous outcomes and mean difference for continuous outcomes with accompanying 95% CIs.

The overall certainty of the evidence was assessed for each outcome of interest using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach (e-Table 3).²¹

Results

Critically ill patients have complex problems that require a thoughtful and nuanced approach to medical care. The recommendations in this document apply to critically ill patients, excluding trauma and neuro-critical care populations, and should be implemented in a hierarchical fashion to optimize treatment. Recommendations 1-3

Development of Recommendations

The panel reviewed and discussed the evidence necessary to address each question. Recommendations were drafted using the GRADE approach, with strong recommendations using the wording “we recommend,” and conditional recommendations using the wording “we suggest.”²² Panel members voted individually via SurveyMonkey on the direction and strength of the recommendation.²³ Per CHEST policy, consensus was achieved with 80% agreement in directionality with at least 75% of the panel participating. Voting results per PICO question are provided in e-Appendix 1.

The guideline was reviewed and approved by the Guidelines Oversight Committee and CHEST presidential leadership.

should be applied initially to critically ill patients with thrombocytopenia, while the subsequent recommendations provide additional guidance for specific situations involving invasive procedures (Figs 1, 2). It is important to emphasize that conditional recommendations inherently require shared decision-making. Readers are encouraged to review the discussion

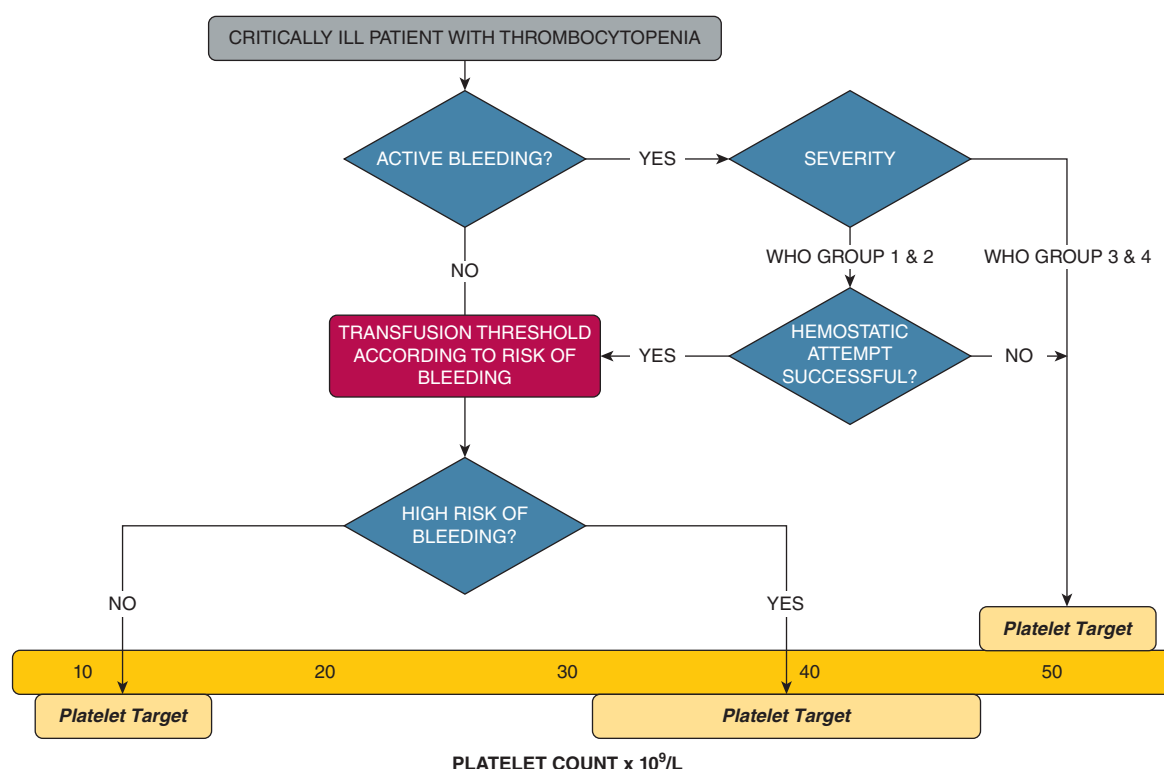


Figure 1 – Platelet transfusion thresholds in according bleeding risk and the presence of bleeding. WHO = World Health Organization.

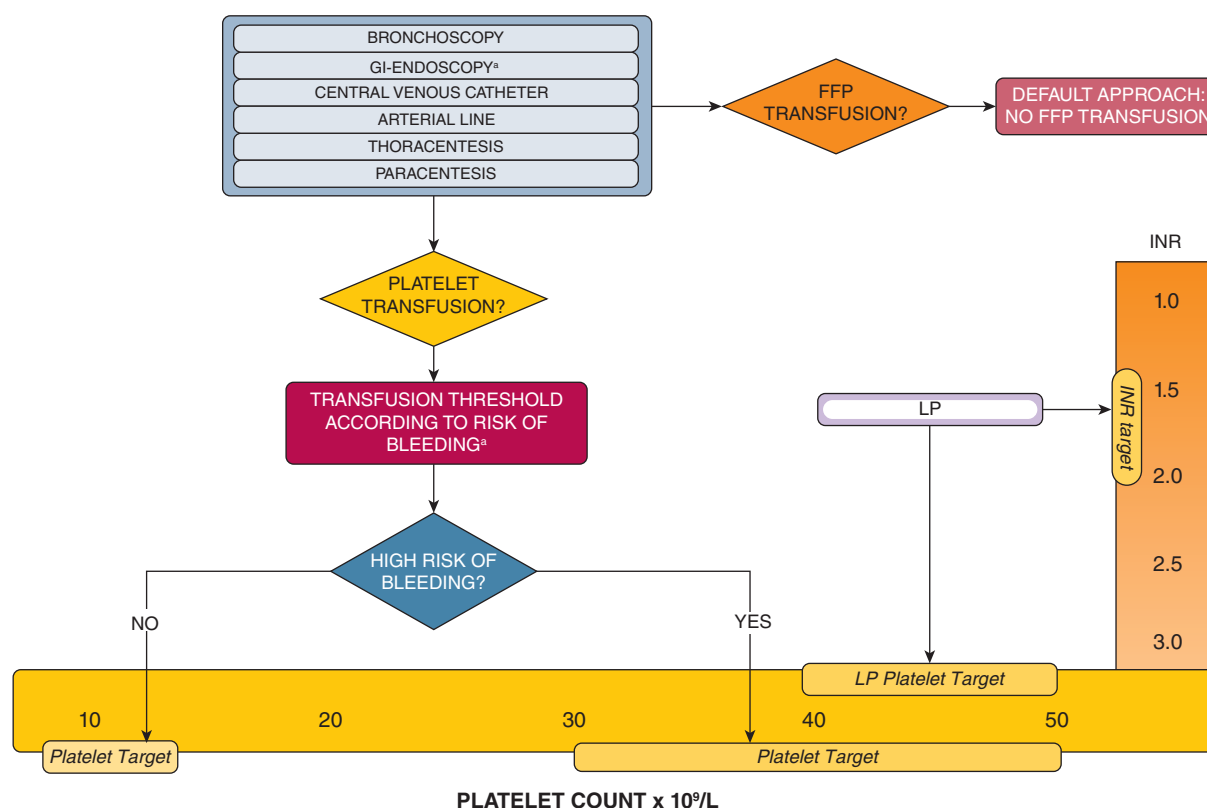


Figure 2 – Platelet and FFP transfusion thresholds for various ICU bedside procedures. The proposed strategy would be exemplified by a hypothetical critically ill patient with a platelet count of $20 \times 10^9/L$ who is at high risk of spontaneous bleeding and has indications for placement of a central venous catheter and performance of a thoracentesis. Recommendation 2 indicates that most practitioners would consider transfusing prophylactic platelets to this patient. When contemplating the placement of the central venous catheter, recommendation 4 would indicate that further platelet transfusions are not suggested prior to the catheter placement if the platelet level was above $30 \times 10^9/L$ after initial transfusion. In a similar fashion, prophylactic platelet transfusion is not suggested prior to the thoracentesis, in accordance with recommendation 6. ^aSuspected portal hypertension related bleed. FFP = fresh frozen plasma; GI = gastrointestinal; INR = international normalized ratio; LP = lumbar puncture.

to fully understand the nuances that informed these recommendations.

Question 1: Should critically ill patients with thrombocytopenia and without high risk of bleeding receive transfusion of platelets?

Recommendation: In stable non-bleeding critically ill patients with thrombocytopenia and without high risk of spontaneous bleeding, we suggest transfusing platelets if platelet counts fall below $10 \times 10^9/L$ (Conditional Recommendation, Very Low Certainty of Evidence).

Question 2: Should critically ill patients with thrombocytopenia and high risk of bleeding receive transfusion of platelets?

Recommendation: In stable non-bleeding critically ill patients with thrombocytopenia who are considered at high risk of spontaneous bleeding, we suggest transfusing platelets if platelet counts fall below $30\text{--}50 \times 10^9/L$ (Conditional Recommendation, Very Low Certainty of Evidence).

Justification

The development of platelet transfusion guidelines for critically ill patients was hindered by the lack of randomized trials to fully test whether benefits exceed risks. The risks associated with platelet transfusion are generally higher than those of other blood products. These risks include both immunologically and nonimmunologically related complications, with the former category accounting for most adverse events. Approximately 1% of adverse reactions from platelet transfusion relate to transfusion-associated circulatory overload and transfusion-related acute lung injury.²⁴

Spontaneous bleeding in critically ill patients places the patient at risk for hemorrhagic shock or local effects from an expanding hematoma. Patients at high risk for spontaneous bleeding might be anticipated to benefit from platelet transfusions. However, a major challenge in this recommendation is defining “high risk of bleeding” as no universally accepted definition exists. Factors such as demographic characteristics,

TABLE 1] International Medical Prevention Registry on Venous Thromboembolism (IMPROVE) Bleeding Risk Score

Bleeding Risk Factor	Points
Moderate renal failure GFR 30-59 mL/min/m ²	1
Male vs female	1
Age 40-84 y	1.5
Current cancer	2
Rheumatic disease	2
Central venous catheter	2
ICU/CCU	2.5
Severe renal failure GFR < 30 mL/min/m ²	2.5
Hepatic failure (INR > 1.5)	2.5
Age ≥ 85 y	3.5
Platelet count < 50 × 10 ⁹ cells/L	4
Bleeding in 3 mo before admission	4
Active gastroduodenal ulcer	4.5

CCU = coronary care unit; GFR = glomerular filtration rate; INR = international normalized ratio.

thrombocytopenia, coagulopathy, and comorbidities can increase this risk.

The International Medical Prevention Registry on Venous Thromboembolism (IMPROVE) study assessed the risk of clinically significant bleeding in adults hospitalized for an acute medical illness and was later validated in a cohort comprising 22.4% ICU patients (Table 1).^{25,26} An IMPROVE score ≥ 7 correlated with higher rates of major bleeding (5.4% vs 1.6%) and non-major bleeding (6.5% vs 2.7%) compared with an IMPROVE score < 7.²⁶ The positive and negative predictive values for major bleeding of a IMPROVE score ≥ 7 are 3.4% and 99%, respectively.²⁷

While the IMPROVE score could be a useful tool for identifying patients at high risk of bleeding, no definition exists that can be easily applied at the bedside.

Therefore, clinician judgment and expertise are essential in evaluating a patient's bleeding risk, considering all available factors to determine the need for platelet transfusions.

The included studies varied significantly in patient characteristics, transfusion indications, and thresholds, preventing the differentiation between prophylactic and therapeutic transfusions (Table 2). An observational study reported no difference in ICU mortality between transfused and non-transfused patients (RR, 0.97; 95% CI, 0.64-1.47).²⁸ Similarly, the pooled comparison revealed no significant differences in 30-day mortality (RR, 1.07; 95% CI, 0.79-1.44)^{28,29} or ICU length of stay (LOS) (mean difference, +0.65 days; 95% CI, -0.25 to +1.56).^{30,31} The low incidence of adverse events and confounding by indication limited the assessment of the association between platelet transfusions and adverse outcomes in this setting.²⁸⁻³¹

Patients Without High Risk of Bleeding

Prophylactic transfusions at platelet counts < 10 × 10⁹/L in hematologic patients without acute myeloid leukemia reduced overall bleeding risk, defined as World Health Organization (WHO) grades 2-4 (Table 3).³² However, this reduction was mainly due to grade 2 bleeding, with grade 3 or 4 bleeding rates below 1%-2%.³³⁻³⁵ Despite the lack of direct evidence for critically ill patients, hematologic data were considered adequate for extrapolation to critically ill patients to prevent spontaneous bleeding.

Patients With High Risk of Bleeding

Given the absence of prospective studies and the heterogeneity of the critical care population, establishing a universal transfusion threshold to prevent spontaneous bleeding in critically ill patients at high risk of bleeding

TABLE 2] Studies Informing Recommendations 1 and 2

Study	Patient Type	Thrombocytopenia Definition ×10 ⁹ /L	Platelet-Transfused Group			Non-Platelet-Transfused Group		
			N	Platelet Count × 10 ⁹ /L	INR	N	Platelet Count × 10 ⁹ /L	INR
Warner et al ²⁸	ICU	Variable ^a	985	81.1 ± 50.1 ^b	1.4 ± 0.6 ^b	985	77.5 ± 60.1 ^b	1.3 ± 0.5 ^b
Salman et al ³⁰	ICU	< 50	90	23 (11-38) ^c	NR	27	33 (18-33) ^c	NR
He et al ²⁹	Sepsis	< 150	677	50.6 ± 31.5 ^b	2.15 ± 1.5 ^b	677	48.1 ± 32.2 ^b	2.05 ± 1.43 ^b
Wu et al ³¹	Sepsis	≤ 50	296	20 (11-33) ^c	NR	296	31 (19-41) ^c	NR

INR = international normalized ratio; NR = not reported.

^aPlatelet count ≤ 100 with active bleeding; ≤ 10 without active bleeding; ≤ 20 with fever, disseminated intravascular coagulation, sepsis, or other conditions associated with platelet destruction; ≤ 20 before central venous catheter insertion; ≤ 50 requiring surgery.

^bMean ± SD.

^cMedian (interquartile range).

TABLE 3] WHO Bleeding Scale

WHO Bleeding Grade	Examples
1	• Epistaxis $\leq$ 30 min in previous 24 h • Petechiae of oral mucosa or skin • Purpura $\leq$ 1 inch in diameter • Spontaneous hematoma in soft tissue or muscle • Positive stool occult blood test • Microscopic hematuria or hemoglobinuria • Abnormal vaginal bleeding (spotting)
2	• Epistaxis $>$ 30 min in 24 h • Purpura $>$ 1 inch in diameter • Joint bleeding • Melanotic stool • Hematemesis • Gross/visible hematuria • Abnormal vaginal bleeding (more than spotting) • Hemoptysis • Visible blood in body cavity fluid • Retinal bleeding without visual impairment • Bleeding at invasive sites
3	• Bleeding requiring RBC transfusion over routine transfusion needs. • Bleeding associated with moderate hemodynamic instability
4	• Bleeding associated with severe hemodynamic instability • Fatal bleeding • CNS bleeding on imaging study with or without dysfunction

CNS = central nervous system; WHO = World Health Organization.

was challenging. Patients may be at high risk of bleeding due to factors that increase the likelihood of bleeding or because of critical anatomical sites where even minor bleeding could be catastrophic. Experts and guidelines recommend maintaining platelet counts $> 100 \times 10^9/L$ for patients undergoing neurosurgical procedures or those with intracranial hemorrhage to prevent catastrophic outcomes from intracranial bleeding.^{36,37} Similarly, platelet counts $> 50 \times 10^9/L$ are advised for patients with disseminated intravascular coagulation (DIC) at high risk of bleeding, and for those with thrombocytopenia experiencing acute venous thromboembolic disease before starting full-dose anticoagulation.³⁸⁻⁴⁰ Higher thresholds might also be considered for patients with tumors in critical areas (airway) or those on antiangiogenic medications that exacerbate bleeding risks. Consequently, given the heterogeneity of critically ill patients at high risk of bleeding, the panel recommended a platelet transfusion

threshold of $> 30-50 \times 10^9/L$ for patients with thrombocytopenia at high risk of bleeding.

Specific Populations

Platelet transfusions are not beneficial and can be harmful to certain patient groups, including those with thrombotic thrombocytopenic purpura, idiopathic thrombocytopenic purpura, alloimmunization, hyperleukocytosis, and leukostasis. Additionally, certain populations are at increased risk of transfusion-related acute lung injury and transfusion-associated circulatory overload such as congestive heart failure, chronic liver disease, shock, and current smoking.^{24,41} Clinicians might choose different transfusion thresholds for these patients.

What Others Are Saying

The recommendations for patients without high risk of bleeding align with those from the Association for the Advancement of Blood & Biotherapies, the American Society of Clinical Oncology (ASCO), the European Society of Intensive Care Medicine (ESICM), and the British Society for Haematology (BSH).⁴²⁻⁴⁵

For patients at high risk of bleeding, considering a higher platelet count threshold for transfusion is suggested.^{43,45} We believed that further defining this risk would offer more specific guidance to clinicians.

Research Priorities

Future research should aim to identify factors that increase bleeding risk, establish a clear definition of high risk of bleeding, and determine the optimal platelet transfusion thresholds for critically ill patients with thrombocytopenia.

Question 3: Should critically ill patients with thrombocytopenia and active bleeding receive transfusion of platelets?

Recommendation: In critically ill patients with thrombocytopenia and serious active bleeding, we suggest transfusing platelets if platelet counts fall below $50 \times 10^9/L$ (Conditional Recommendation, Very Low Certainty of Evidence)

Justification

The effectiveness of transfusing platelets to critically ill medical patients with active bleeding remains unclear. Moreover, there is significant variability in what clinicians consider serious active bleeding. The panel considered WHO grades 3 and 4 as serious active bleeding.

TABLE 4] Suggested Approach for Platelet Transfusions

Bleeding Severity (WHO Group)	Suggested Approach
1	• The intervention should focus on addressing the cause of bleeding and not on platelet transfusions • Use thresholds recommended for non-bleeding patients
2	• Hemostatic approaches such as tamponade/pressure, topical hemostatic agents, and therapeutic procedures should be considered if they might obviate the need for platelet transfusion • Platelet transfusions can be considered if attempts to control bleeding are unsuccessful or if bleeding site is not suitable for compression^a
3 and 4	• Platelet transfusion threshold of $50 \times 10^9/L$ is recommended^a

WHO = World Health Organization.

^aIn high-risk situations where further bleeding would not be tolerated (eg, diffuse alveolar hemorrhage, ocular hemorrhage, compartment syndrome), a higher threshold might be considered. Central nervous system bleeding is not included in these recommendations.

The literature search excluded patients with trauma and those with intracranial hemorrhage, resulting in the identification of 1 relevant study. An observational examination of platelet transfusions in adults with cirrhosis and esophageal variceal bleeding showed no significant difference in mortality rates between transfused and non-transfused individuals (25.3% vs 17.4%; $P = .074$). Moreover, stratification by platelet counts did not affect the results. Rebleeding rates were higher in those who received platelets, especially with pre-transfusion platelet counts $> 20 \times 10^9/L$, but not below this threshold.⁴⁶ The relevance of these findings to other critically ill groups remains uncertain due to varying transfusion thresholds and potential selection and confounding bias.

In patients with thrombocytopenia and clinically significant active bleeding, platelet transfusion is the standard treatment. Strong evidence of net harm would be required to deviate from this practice, but the current evidence was insufficient to justify change. While a framework is suggested (Table 4), clinical judgment should guide platelet transfusion decisions, considering the bleeding site, severity, and coexisting factors that influence the patient's ability to tolerate bleeding.

What Others Are Saying

Our recommendation aligns with those from other organizations. The BSH advises that for patients with WHO grade ≥ 2 bleeding, platelet counts should be maintained $> 50 \times 10^9/L$ if the clinician considered the bleeding severe and $> 30 \times 10^9/L$ if considered not severe.⁴⁵ Moreover, they suggest considering empirical transfusion in initial management of major hemorrhage (causing heart rate > 110 beats/min and/or systolic

BP < 90 mm Hg). The International Society on Thrombosis and Haemostasis advocates for transfusions to achieve $> 50 \times 10^9/L$ in patients with DIC and active bleeding.⁴⁷ The ASCO suggests transfusing platelets above prophylactic levels for active localized bleeding associated with necrotic tumors.⁴³ ESICM guidelines made no recommendation regarding platelet transfusions in patients with massive or non-massive bleeding.⁴⁸ Meanwhile, recommendations to transfuse platelets above $50 \times 10^9/L$ for bleeding patients with cirrhosis are controversial.^{49,50}

Research Priorities

Future research should focus on identifying measurable factors that correlate with bleeding risk and on evaluating the utility of functional platelet assessments for guiding transfusion practices.

Question 4: Should critically ill patients with increased risk of bleeding due to thrombocytopenia or coagulopathy undergoing a bedside CVC or arterial line insertion receive blood products to reverse thrombocytopenia or coagulopathy?

Recommendation 4A: In critically ill patients at increased risk of bleeding due to thrombocytopenia undergoing a CVC or arterial line insertion, we suggest against routine prophylactic platelet transfusion. (Conditional Recommendation, Very Low Certainty of Evidence)

Recommendation 4B: In critically ill patients at increased risk of bleeding due to coagulopathy undergoing a CVC or arterial line insertion, we suggest against routine prophylactic FFP transfusion. (Conditional Recommendation, Very Low Certainty of Evidence)

Justification

The scarce data on platelet or FFP transfusions for bedside vascular procedures was limited to CVC placement.⁵¹⁻⁵³ Platelet transfusion practices prior to CVC placement are variable, with general acceptance that prophylactic transfusions are unnecessary when counts are $\geq 50 \times 10^9/L$.^{54,55}

van Baarle et al⁵¹ evaluated prophylactic platelet transfusions for ultrasound-guided CVC placement in hematology ward and ICU patients with counts $10-50 \times 10^9/L$. No differences in mortality or episodes of bleeding-related hemodynamic instability were observed between groups. Bleeding events were influenced by hematologic disorders, tunneled CVCs, and placement in non-compressible sites. Patients with platelet counts $10-20 \times 10^9/L$ experienced more frequent bleeding, with platelet transfusions reducing the bleeding rate from 22% to 15.6%, a nonsignificant difference (RR, 1.30; 95% CI, 0.48-3.55). However, this was a subgroup analysis and might not have been adequately powered to detect a significant difference. The low incidence of severe bleeding, variability in platelet component availability, and high costs associated with platelet transfusions (\$410 per catheter placement) favor a therapeutic strategy over routine prophylactic transfusion.

A small RCT and a retrospective study assessed FFP transfusions, excluding individuals with $INR > 3$ and noting an imbalance of patients with liver disease across comparison groups. Clinically significant bleeding was rare and unaffected by FFP transfusions. No differences were observed in mortality, ICU LOS, or complication rates.^{52,53} Previous data suggest that coexisting coagulopathy ($INR > 1.5$ and/or activated partial thromboplastin time > 45 s) does not elevate bleeding risk in patients with platelets $< 50 \times 10^9/L$.⁵⁶

Establishing a transfusion threshold based on the number and combination of factors is challenging. The recommended approach includes avoiding routine platelet transfusion for patients with platelet counts $10-50 \times 10^9/L$ and avoiding routine FFP transfusion for patients with coagulopathy. However, platelet transfusions may be appropriate before tunneled CVC placement or when non-compressible sites are unavoidable. Additionally, clinicians might consider specific factors such as catheter size, degree of thrombocytopenia, degree of INR elevation (patients with $INR > 3$ are largely unstudied), coexisting thrombocytopenia with coagulopathy, ultrasound

availability, and operator experience to decide on transfusions. Although specific data on platelet or FFP transfusions for arterial catheters are lacking, recommendations for CVC could be extrapolated to arterial lines.

What Others Are Saying

Prophylactic platelet transfusions have been recommended prior to vascular catheter placement for counts $< 20 \times 10^9/L$ by the Society of Interventional Radiology (SIR), the Association for the Advancement of Blood & Biotherapies, ASCO, and BSH.^{42,43,45,57} ESICM guidelines recommended against prophylactic platelet transfusions for counts $> 50-100 \times 10^9/L$ but no recommendation was issued for counts $10-50 \times 10^9/L$.⁴⁴ However, these preceded the RCT by van Baarle et al.⁵¹ ESICM and BSH recommend withholding prophylactic FFP transfusions in patients with coagulopathy.^{44,58} However, SIR recommends correcting INR to within range of 2-3.⁵⁷

Research Priorities

Research assessing bleeding risk in settings with $INR > 3$, mixed coagulopathies, and various degrees and etiologies of thrombocytopenia is necessary. Furthermore, alternative methods for assessing bleeding risk and coagulation abnormalities (ie, viscoelastic monitoring) should be studied.

Question 5: Should critically ill patients with increased risk of bleeding due to thrombocytopenia or coagulopathy undergoing a bedside thoracentesis or paracentesis receive blood products to reverse thrombocytopenia or coagulopathy?

Recommendation 5A: In critically ill patients with increased risk of bleeding due to thrombocytopenia undergoing a bedside thoracentesis or paracentesis, we suggest against routine prophylactic platelet transfusion (Conditional Recommendation, Very Low Certainty of Evidence).

Recommendation 5B: In critically ill patients with increased risk of bleeding due to coagulopathy undergoing a bedside thoracentesis or paracentesis, we suggest against routine prophylactic FFP transfusion (Conditional Recommendation, Very Low Certainty of Evidence).

Justification

Three studies eligible for analysis varied in population characteristics, blood product use, definitions of bleeding, and outcomes (Table 5).

TABLE 5] Studies Informing Recommendation 5

Study	Patients	Procedure	Product Transfused	Bleeding Definition	Major Bleeding Relative Risk Transfused vs Nontransfused
Hibbert ⁶⁰	Patients with platelets $< 50 \times 10^9/L$ and/or INR > 1.6	Thoracentesis	FFP or platelets	WHO grade 2-4	6.75 (95% CI, 0.37-124.11)
Faiz ⁵⁹	Hematologic patients	Thoracentesis, chest tube insertion, and pleural catheter	Platelets	Hemothorax or bleeding requiring transfusion and/or surgical intervention	0.74 (95% CI, 0.10-5.43)
McVay ⁶¹	Patients with PT, PTT, and platelets measured within 10 days of procedure	Thoracentesis or paracentesis	FFP	Decrease in hemoglobin > 2 g/dL after procedure	20.93 (95% CI, 1.13-387.56)

FFP = fresh frozen plasma; INR = international normalized ratio; PT = prothrombin time; PTT = partial thromboplastin time; WHO = World Health Organization.

Each study encountered issues such as bias, noninclusion of critically ill patients, unreported transfusion indications, and the use of antiplatelets or anticoagulants.⁵⁹⁻⁶¹ Two studies reported no major bleeding in non-transfused groups,^{59,60} while a third noted that 0.2% of patients received RBC transfusions despite no clinical hypovolemia.⁶¹ Overall, major bleeding and the need for surgical interventions were rare.

Given the risks of blood product transfusions and the unclear impact of transfusions, including thresholds, dose, and timing on bleeding, the evidence favors withholding transfusions. Clinical decisions on transfusions should weigh factors such as ultrasound availability, operator experience, anticoagulant use, platelet function disorders, concomitant thrombocytopenia and coagulopathy, and technical or anatomical challenges.

What Others Are Saying

Several professional societies classify thoracentesis and paracentesis as low-risk procedures. Consequently, they do not recommend routine preprocedural transfusions for thrombocytopenia or coagulopathy.^{57,62-64}

Research Priorities

High-quality data acquisition necessitates large-scale enrollment given the low frequency of complications.

Question 6: Should critically ill patients with increased risk of bleeding due to thrombocytopenia or coagulopathy undergoing a bedside lumbar puncture

(LP) receive blood products to reverse thrombocytopenia or coagulopathy?

Recommendation 6A: In critically ill patients with increased risk of bleeding due to thrombocytopenia undergoing a bedside LP, we suggest platelet transfusion if platelets counts are $40-50 \times 10^9/L$ or lower (Conditional Recommendation, Very Low Certainty of Evidence)

Recommendation 6B: In critically ill patients with increased risk of bleeding due to coagulopathy undergoing a bedside lumbar puncture, we suggest FFP transfusion to target INR 1.5-2 before the procedure (Conditional recommendation, very low certainty of evidence)

Justification

Two articles met the inclusion criteria, allowing the assessment of the safety of LP at different INR and platelet count levels. The search excluded obstetric and oncologic populations and epidural catheter use.^{65,66}

The risk of a traumatic LP was higher in patients with elevated INR. Platelet counts ranging from 50 to $150 \times 10^9/L$ did not increase this risk, but platelet counts $< 50 \times 10^9/L$ did, although this risk was dependent on operator experience.^{65,66} The risk of spinal hematoma in patients with platelet counts $< 150 \times 10^9/L$, INR > 1.4 and/or activated partial thromboplastin time > 39 seconds was 0.2%, irrespective of the severity of the abnormality.⁶⁵ A strategy decreasing the platelet transfusion threshold from 50 to $40 \times 10^9/L$, significantly reduced the number

of platelet transfusions without increasing the risk of complications.⁶⁷ However, the effectiveness of transfusions in preventing spinal hematomas and the optimal transfusion thresholds remain unknown. In patients with platelet counts $< 40\text{--}50 \times 10^9/\text{L}$, platelet transfusion is the standard treatment. Despite the extremely low risk of LP-related spinal hematoma, the consequences could be devastating.⁶⁸ Therefore, strong evidence of net harm would be required to deviate from this practice. Given the rarity of spinal hematoma, the panel deemed that a sufficiently large study to answer this question was unlikely. FFP transfusion to patients with an INR > 2.0 is suggested to represent safe and prudent practice. While prolonged INR indicates a deficiency or decreased activity in 1 or more coagulation factors, it does not necessarily correlate with bleeding risk. Further, the INR was developed to monitor warfarin therapy and clinicians should consider the distinction between patients with liver dysfunction and hypercoagulability vs those on anticoagulation therapy.^{69,70} Clinicians should individualize patient factors to decide on whether or not to administer transfusions.

What Others Are Saying

The SIR categorized LP as low bleeding risk procedure with platelet transfusions recommended for counts $< 20 \times 10^9/\text{L}$ and FFP administration to correct INR to within range of $\leq 2\text{--}3$.⁵⁷ However, several other guidelines suggest targeting platelet counts $> 40\text{--}50 \times 10^9/\text{L}$ for elective LP and maintaining INR < 1.5 for neurologic patients and those undergoing interventional radiology procedures.^{42,45,57,71}

Research Priorities

While registry data could provide insight into the incidence, evaluating the effectiveness of transfusions might be challenging because most patients are transfused in current practice. Future research exploring viscoelastic testing to guide transfusions, evaluating complication reduction through image guidance, and exploring alternative diagnostic modalities for high-risk LP might prove useful.

Question 7: Should critically ill patients with increased risk of bleeding due to thrombocytopenia or coagulopathy undergoing a bedside endoscopic procedure receive blood products to reverse thrombocytopenia or coagulopathy?

Recommendation 7A: In critically ill patients with increased risk of bleeding due to thrombocytopenia

undergoing routine flexible bronchoscopy without biopsy, we suggest against routine prophylactic platelet transfusion (Conditional Recommendation, Very Low Certainty of Evidence).

Recommendation 7B: In critically ill patients with increased risk of bleeding due to coagulopathy undergoing a routine bedside flexible bronchoscopy without biopsy, we suggest against routine prophylactic FFP transfusion (Conditional Recommendation, Very Low Certainty of Evidence).

Justification

To our knowledge, no RCT data exist to inform this recommendation. Two retrospective studies examined platelet transfusions prior to bronchoscopy in ICU and oncologic patients with varying transfusion thresholds.^{72,73} Kim et al⁷² studied 37 ICU patients with platelet counts $< 50 \times 10^9/\text{L}$ (mean $27.3 \pm 12.5 \times 10^9/\text{L}$). Faiz et al⁷³ reviewed 2,053 bronchoscopies in 1,711 thrombocytopenic oncology patients (criteria for inclusion: $< 100 \times 10^9/\text{L}$ with 14.7% of the population $< 20 \times 10^9/\text{L}$). To our knowledge, no studies have evaluated FFP transfusions in this context. Among oncologic patients undergoing trans-nasal bronchoalveolar lavage, no procedure-related deaths occurred, regardless of transfusion status.⁷³ Though more bleeding episodes were reported in non-transfused oncologic patients, the opposite was described in ICU patients.^{72,73} Routine bronchoscopy and bronchoalveolar lavage are considered low risk, and the existing data on prophylactic transfusions, primarily extrapolated from non-ICU patients, are of low quality.^{74–76}

The effects of platelet transfusion on procedural mortality and transfusion-related adverse events are unclear. Given the low risks of death or bleeding and the unlikely influence of transfusions on these outcomes, evidence supports a default no transfusion approach. Advanced bronchoscopy procedures are beyond the scope of this document.

Recommendation 7C: In critically ill patients with suspected portal hypertension related GI bleeding and increased risk of bleeding due to thrombocytopenia who are undergoing GI-endoscopy, we suggest against routine platelet transfusion. (Conditional Recommendation, Very Low Certainty of Evidence)

Recommendation 7D: In critically ill patients with suspected portal hypertension related bleeding at increased risk of bleeding due to coagulopathy who

are undergoing GI-endoscopy, we suggest against routine FFP transfusion (Conditional recommendation, very low certainty of evidence)

Justification

No RCT data were found on the prophylactic use of blood products prior to endoscopy. Two retrospective studies explored the effects of platelet transfusion or INR correction before GI-endoscopy in patients with active variceal bleeding.^{46,77} Biswas et al⁴⁶ studied 913 patients by developing cohorts based on platelet levels (< 20 , 20 – 50 , and $> 50 \times 10^9/L$) and examining whether or not patients received platelet transfusions. Mohanty et al⁷⁷ retrospectively assessed 244 patients with variceal bleeding comparing those treated with FFP with those who were not. Patients receiving FFP had a significantly higher INR than those who did not receive treatment (1.97 vs 1.45 ; $P < .0001$). Higher mortality and rebleeding rates were noted in those transfused with platelets or FFP.^{46,77} Moreover, rescue transjugular intrahepatic portosystemic shunt occurred more frequently in patients who received FFP.⁷⁷ However, transfused patients generally were older and had higher rates of hemodynamic instability, renal dysfunction, and more severe liver disease at baseline. The unfavorable clinical outcomes were likely related to the severity of illness rather than adverse transfusion effects.^{46,77} No data exist on the impact of prophylactic transfusion on 30-day mortality, major bleeding, and ICU LOS.

Given the low risk of GI-endoscopy without biopsy causing further bleeding, the multiple confounders, and the uncertain risk attributable to transfusions, the evidence suggests not routinely transfusing platelets or FFP.

In the ICU, endoscopy is primarily performed for active hemorrhage, focusing on hemostatic interventions. Therefore, the decision to transfuse patients with active GI bleeding undergoing endoscopy should rely on clinical need rather than procedural risk. For instance, post-polypectomy bleeding rates are $< 1\%$.⁷⁸ Even in severe cases such as variceal bleeding, endoscopy is unlikely to worsen bleeding, making transfusion generally unnecessary for improving the safety of the procedure.

What Others Are Saying

Our recommendations for GI-endoscopy align with other societies that advise against INR correction in variceal hemorrhage and deem it reasonable to perform GI-endoscopy without prophylactic platelet transfusion.

These statements consider the risks, lack of benefit from prophylactic FFP transfusions, and the weak evidence supporting platelet transfusions.^{43,64,79,80} An individualized approach is recommended for patients with severe thrombocytopenia.

Research Priorities

Studies evaluating viscoelastic blood testing to guide product administration are underway.

Additional Considerations

Statements on cost, equity, acceptability, feasibility, and implementation were consolidated given the significant overlap across various PICO questions.

Cost

Blood products are scarce and costly, with the entire process from collection to administration incurring substantial costs with global variability.^{14,81} The cost of an apheresis leukoreduced platelet unit in the United States is approximately \$1,400,^{15,82} whereas the total platelet cost for patients with chronic liver disease and thrombocytopenia before elective procedures has been estimated at \$4,000.⁸³ Costs vary regionally within the United States, and costs have high variability worldwide. Given the absence of cost-effectiveness studies, cost minimization and efficient resource utilization should be the priority, especially in settings where transfusions are not clearly beneficial.

Equity

Structural inequities affect access to blood products, likely influenced by hospital policies and clinician practices. Factors such as race, comorbidities, and socioeconomic status contribute to disparities in access to blood products. For instance, Black patients often face challenges finding compatible donors for human leukocyte antigen-matched transfusions, and alloimmunization further impacts supply.⁸⁴ Patients in underresourced and rural areas may experience delays in accessing blood products.^{85–87} While liberal transfusion policies may exacerbate equity issues, the extent of inequitable access to blood products and their impact on patient care remains unknown. Uniform transfusion policies by institutions could alleviate these inequities. Additionally, exploring the role of social determinants of health is crucial in understanding and addressing barriers to accessing blood products.

Acceptability and Feasibility

The acceptability and feasibility of blood product transfusions vary widely depending on the clinical scenarios, clinician practice patterns, patient comorbidities, patient perspectives, and stakeholder resistance to changing established practices despite the lack of evidence. For example, during active bleeding or prior to an LP, most clinicians favor platelet transfusions in patients with thrombocytopenia.⁸⁸ However, greater practice variability exists before procedures like bedside endoscopy, paracentesis, and thoracentesis, depending on the perceived risk and severity of complications. Clinicians may prioritize transfusion over potential complications and subsequent liability. Some patients may reject transfusions based on personal values or religious beliefs, while those accustomed to receiving periprocedural transfusions may resist change.

Implementation

Decisions about platelet or FFP transfusions in critically ill patients should consider factors such as worsening alloimmunization in highly alloimmunized patients. Patients at high risk of bleeding due to coagulopathy, endotheliopathy, hematologic malignancy, or antiplatelet medications may require different thresholds. Conditions such as massive splenomegaly, von Willebrand disease, or presence of antiplatelet antibodies can affect the accuracy of circulating platelet levels as indicators of bleeding risk. For patients who decline transfusions based on personal or religious beliefs, clinicians should align the medical plan with patient values after thorough discussion.

Initiatives to unify institutional practices and reduce unnecessary platelet transfusions have shown success. These initiatives resulted in a 25% reduction in units transfused, decreasing platelet wastage, and significantly reducing costs, demonstrating the potential for sustainable, impactful changes.^{89,90}

Summary

For all recommendations, high-certainty evidence directly addressing each recommendation was either absent or insufficient. Therefore, our recommendations were primarily based upon expert opinion. This document provides recommendations for platelet transfusion thresholds in non-bleeding patients stratified by risk of bleeding and those with active bleeding. In the procedural setting, the evidence for platelets and FFP is limited but favors a first-line no transfusion approach for vascular, bedside thoracic or abdominal, and

endoscopic procedures without biopsy. For LP, given the potentially catastrophic complications, a less restrictive approach is suggested. Despite the lack of high-certainty evidence, these guidelines provide a framework for managing critically ill patients with thrombocytopenia and coagulopathy. Shared decision-making and the implementation of institutional guidelines to standardize transfusion practices could optimize patient care, improve equity in access to blood products and reduce costs. On a large scale, this could amount to approximately half a million less units of platelets and FFP transfused annually. These guidelines should be an opportunity for institutions to develop local policies, monitor their impact on transfusion practices, and provide a framework to longitudinally optimize platelet and FFP use.

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Additional information: The e-Appendixes, e-Figure, and e-Tables are available online under “Supplementary Data.”

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