ACCADEMIA di FORMAZIONE

SIMTI

Aggiornamenti in medicina trasfusionale: dalla produzione alla terapia con emocomponenti

Il supporto trasfusionale piastrinico nel paziente oncoematologico: aggiornamento ICTMG delle linee guida

Ursula La Rocca

Centro Nazionale Sangue

La sottoscritta La Rocca Ursula, in qualità di Relatrice dichiara che nell'esercizio della Sua funzione e per l'evento in oggetto, NON È in alcun modo portatrice di interessi commerciali propri o di terzi; e che gli eventuali rapporti avuti negli ultimi due anni con soggetti portatori di interessi commerciali non sono tali da permettere a tali soggetti di influenzare le mie funzioni al fine di trarne vantaggio.

Il supporto trasfusionale piastrinico

Le PLTS rappresentano il secondo **emocomponente più comunemente trasfuso** (Kaufmann et al. 2015)

In USA, **oltre 2 milioni di trasfusioni di PLTS e 300.000 nel Regno Unito** per anno a costi considerevoli, con difficoltà in termini di approvvigionamento.

La più **frequente indicazione resta la prevenzione ed il trattamento del sanguinamento nei pazienti ematologici ed oncologici.**

In 2023, 7,774 units of blood components were transfused per day. Compared to the previous year, there was a slight decrease (-0.10%) (Table 6).

Table 6. Transfused units of blood components (2022-2023)

Blood component	2022	2023	Δ%
Red Blood Cells	**2,393,798**	**2,392,289**	-0.06
Red Blood Cells from whole blood	*2,383,058*	*2,384,659*	-0.07
Red Blood Cells by apheresis	*10,740*	*7,630*	-28.96
Platelets from single donors	934	113	-87.90
Platelets Pools	193,041	201,316	4.29
Platelets by apheresis	47,305	47,292	-0.13
Plasma	**205,552**	**196,795**	-4.26
Recovered Plasma	*68,893*	*67,762*	-1.64
Source Plasma	*24,141*	*23,615*	-2.18
Source Plasma from multiple apheresis	*4,873*	*3,900*	-19.97
Plasma pooled and treated for virus inactivation	*107,645*	*101,518*	-5.69
Total	**2,840,630**	**2,837,805**	-0.10

Table 12. Transfused patients (2022-2023)

Patients* transfused with:	2022	2023	Δ%
Whole Blood^	32	23	-28.13
Red Blood Cells	604,761	603,125	-0.27
Plasma	46,426	43,415	-6.49
Platelets	54,512	55,431	1.69
Other	5,472	5,445	-0.49
Total**	**639,003**	**638,046**	-0.15

* Patients transfused once or more than once during the year under examination were counted only once.

** Patients transfused more than once during the year under examination with blood components of the same type were counted only once; patients transfused with more than one type of blood component were included in the count of each type.

^ Includes reconstituted whole blood.

RAPPORTI ISTISAN 24|26

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Italian Blood System 2023: activity data, haemovigilance and epidemiological surveillance

Il supporto trasfusionale piastrinico

TRANSFUSION PRACTICE

TRANSFUSION

Evaluating the appropriateness of platelet transfusions compared with evidence-based platelet guidelines: An audit of platelet transfusions at 57 hospitals

MaryJane Hill-Strathy[1,2] | Peter H. Pinkerton[1,3,4] | Troy A. Thompson[3] | Alison Wendt[3] | Allison Collins[3] | Robert Cohen[1] | Wendy Owens BComm[3] | Tracy Cameron[3] | Yulia Lin[1,4,5] | Wendy Lau[4,6] | Lani Lieberman[1,5] | Jeannie Callum[1,4,5]

- Richieste trasfusionali da oncologia/ematologia (38,9%), terapia intensiva (17%), chirurgia (12,5%) e medicina interna/pediatria (11,8%).

- Inappropriatezza nel 41,5% e 63,3% delle richieste in ambito adulto e pediatrico, rispettivamente.

Hill-Strathy M, et al. Transfusion. 2021

International Collaboration for Tranfusion Medicine Guidelines

ICTMG
International Collaboration for Transfusion Medicine Guidelines

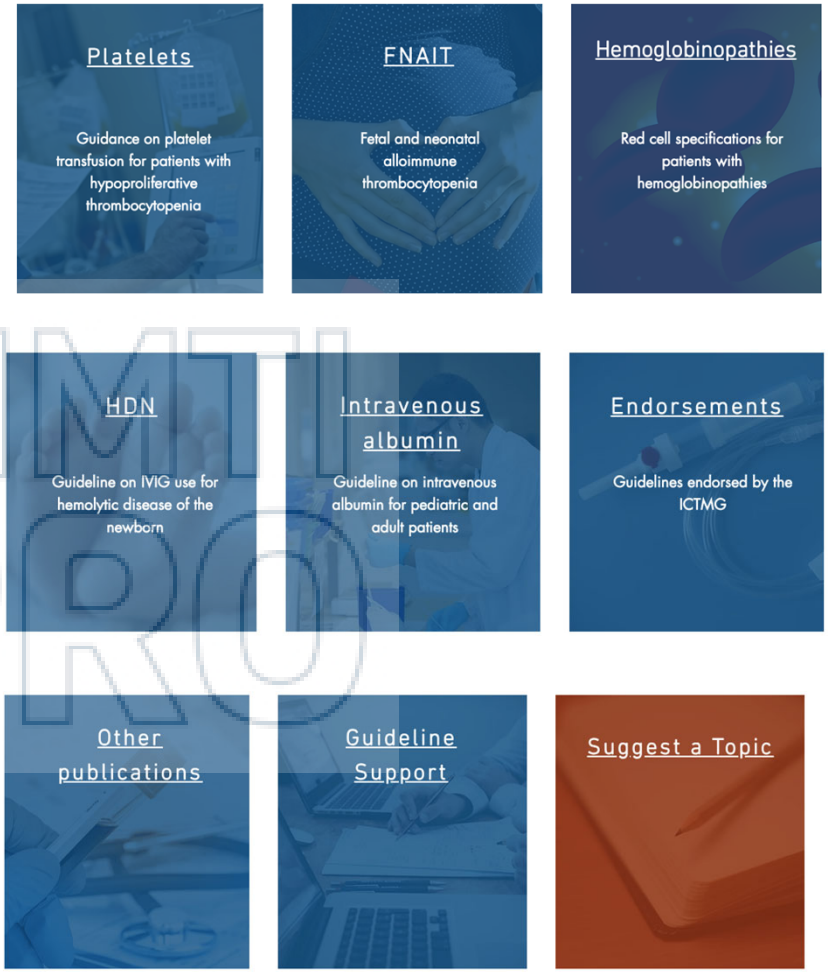
Our vision

The right transfusion, always, everywhere

Who we are

The ICTMG is an independent collaborative of volunteers with expertise in transfusion medicine and related clinical disciplines, guideline development methodology and implementation research. The ICTMG secretariat is hosted by Canadian Blood Services, the primary funder for ICTMG.

Our mission | **Our values**

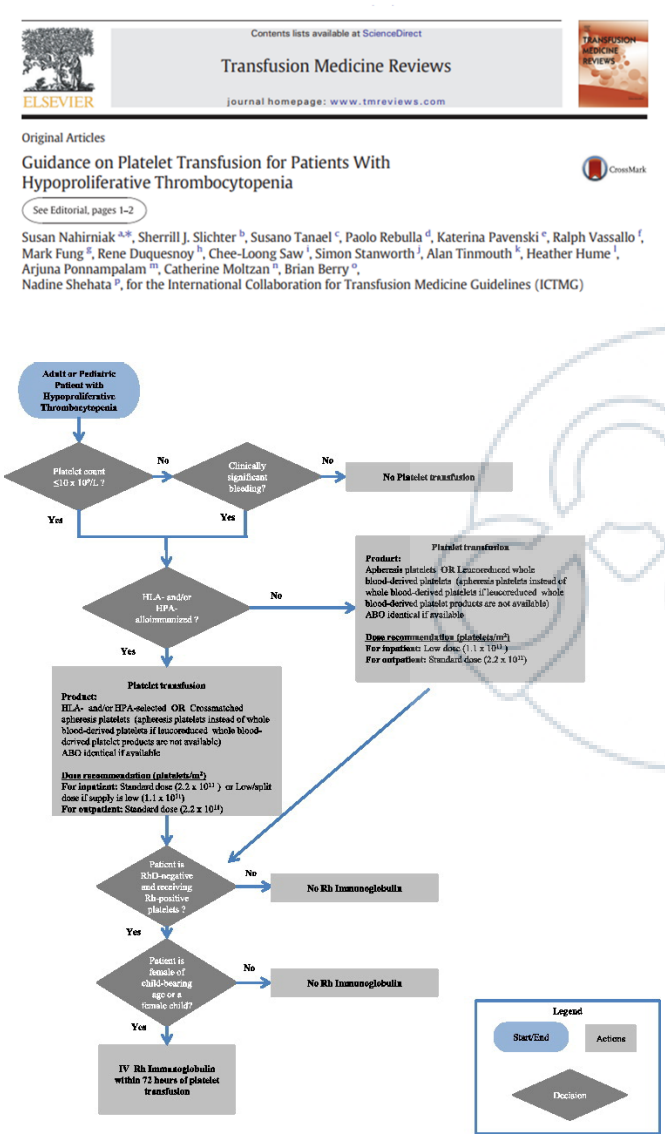


Gruppo di esperti nell'ambito della **medicina trasfusionale nato nel 2011.**

Obiettivo è **creare e promuovere linee guida cliniche basate sull'evidenza**, con il fine di **ottimizzare la pratica della medicina trasfusionale.**

L'ICTMG segue una rigorosa metodologia scientifica, basata su sistemi quali GRADE ed AGREE II.

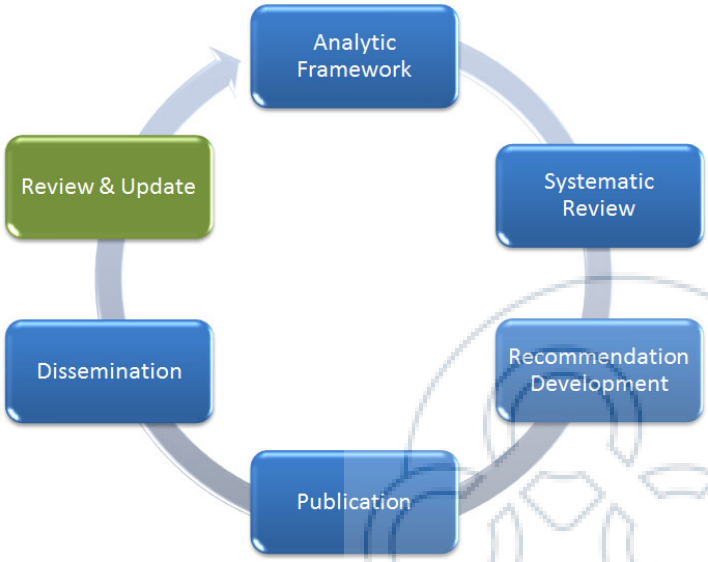
Guidance on Platelet Transfusion for Patients With Hypoproliferative Thrombocytopenia

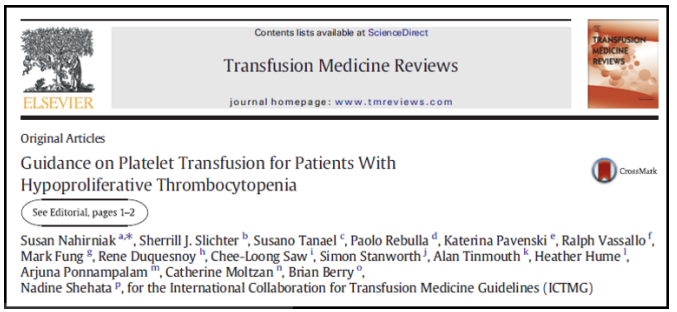


Nahirniak et al. 2015

- **Prophylactic transfusion for PLTS ≤ 10 × 10^9/L** optimal approach to **↓ risk of hemorrhage** for patients **requiring chemotherapy or undergoing allogeneic or autologous transplantation.**
- A **low dose of platelets (1.1×10^{11}/m^2)** is as effective **as higher dose of platelets** but requires **more frequent transfusions suggesting** that **low-dose platelets may be used in hospitalized patients.** For **outpatients, a median dose (2.2×10^{11}/m^2) may be more cost-effective** to prevent clinic visits only to receive a transfusion.
- Platelet products → **whole blood–derived platelet concentrates** used interchangeably with apheresis platelets; **ABO-compatible platelet** to improve platelet increments and decrease the rate of refractoriness to platelet transfusion.
- For **RhD-negative children/women** of child-bearing potential who have received RhD-positive PLTS, **Rh immunoglobulin should probably be given** to prevent immunization to the RhD antigen.
- Providing platelet support for the **alloimmunized refractory patients** with **ABO-matched and HLA-selected or crossmatched products** is of some benefit.

Percorso metodologico seguito dal gruppo di lavoro ICTMG





Contents lists available at ScienceDirect

Transfusion Medicine Reviews

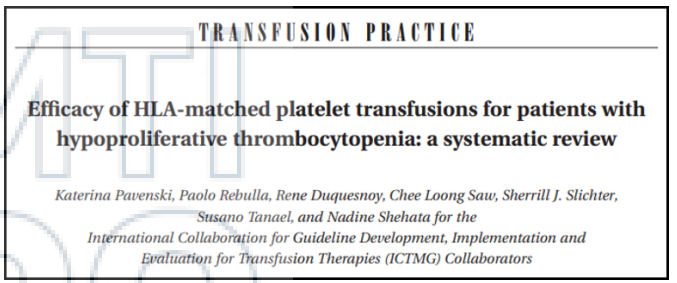
journal homepage: www.tmreviews.com

Original Articles

Guidance on Platelet Transfusion for Patients With Hypoproliferative Thrombocytopenia

See Editorial, pages 1–2

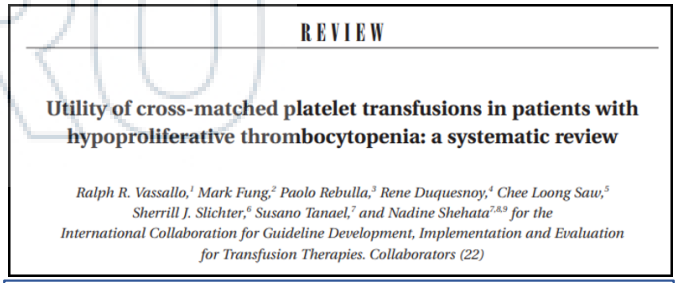
Susan Nahirniak [a,*], Sherrill J. Slichter [b], Susano Tanael [c], Paolo Rebulla [d], Katerina Pavenski [e], Ralph Vassallo [f], Mark Fung [g], Rene Duquesnoy [h], Chee-Loong Saw [i], Simon Stanworth [j], Alan Tinmouth [k], Heather Hume [l], Arjuna Ponnampalam [m], Catherine Moltzan [n], Brian Berry [o], Nadine Shehata [p], for the International Collaboration for Transfusion Medicine Guidelines (ICTMG)



TRANSFUSION PRACTICE

Efficacy of HLA-matched platelet transfusions for patients with hypoproliferative thrombocytopenia: a systematic review

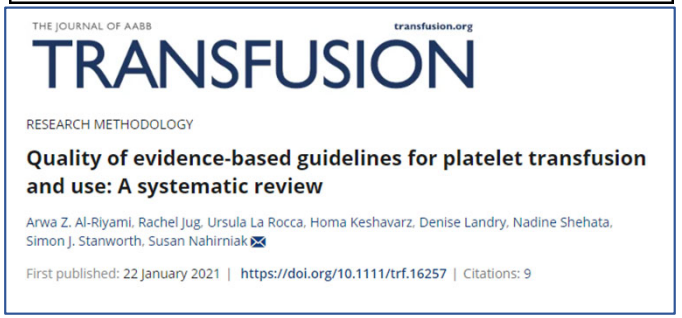
Katerina Pavenski, Paolo Rebulla, Rene Duquesnoy, Chee Loong Saw, Sherrill J. Slichter, Susano Tanael, and Nadine Shehata for the International Collaboration for Guideline Development, Implementation and Evaluation for Transfusion Therapies (ICTMG) Collaborators



REVIEW

Utility of cross-matched platelet transfusions in patients with hypoproliferative thrombocytopenia: a systematic review

Ralph R. Vassallo,[1] Mark Fung,[2] Paolo Rebulla,[3] Rene Duquesnoy,[4] Chee Loong Saw,[5] Sherrill J. Slichter,[6] Susano Tanael,[7] and Nadine Shehata[7,8,9] for the International Collaboration for Guideline Development, Implementation and Evaluation for Transfusion Therapies. Collaborators (22)



THE JOURNAL OF AABB

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TRANSFUSION

RESEARCH METHODOLOGY

Quality of evidence-based guidelines for platelet transfusion and use: A systematic review

Arwa Z. Al-Riyami, Rachel Jug, Ursula La Rocca, Homa Keshavarz, Denise Landry, Nadine Shehata, Simon J. Stanworth, Susan Nahirniak

First published: 22 January 2021 | https://doi.org/10.1111/trf.16257 | Citations: 9

Valutazione di tipo qualitativo delle LG utilizzando il metodo AGREE

ORIGINAL RESEARCH

TRANSFUSION

Quality of evidence-based guidelines for platelet transfusion and use: A systematic review

Arwa Z. Al-Riyami[1] | Rachel Jug[2,8] | Ursula La Rocca[3,4] | Homa Keshavarz[5] | Denise Landry[5] | Nadine Shehata[6,7,8] | Simon J. Stanworth[9,10,11] | Susan Nahirniak[12,13]

i) Rating Scale

All AGREE II items are rated on the following 7-point scale:

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

Domain	Scope (items)
1. Scope & purpose	Aim, including target population (1-3)
2. Stakeholder involvement	Development & representation by appropriate stakeholders (4-6)
3. Rigour of development	Methodology for data gathering, synthesis, recommendation formulation & updating (7-14)

Al-Riyami AZ, et al. Transfusion 2021; 61: 948-958.

- **Qualità molto variabile**; **molte LG non** basate su solide **evidenze.**
- La qualità delle linee guida per la pratica clinica deve essere valutata prima dell'**implementazione**.

Determinare **la qualità delle linee guida trasfusionali piastriniche** con lo strumento di valutazione delle linee guida *Appraisal of Guidelines for Reasearch and Evaluation (AGREE II)* e descrivere **la concordanza tra le raccomandazioni pubblicate.**

Domain	Scope (items)
4. Clarity of presentation	Language & formatting (15-17)
5. Applicability	Guideline implementation, uptake, and resource implications (18-21)
6. Editorial independence	Unbiased recommendations (22-23)

Global rating items:
+ overall rating of the quality of the guideline
+ whether the assessor would recommend the guideline for use

Guideline Appraisal AGREE II tool

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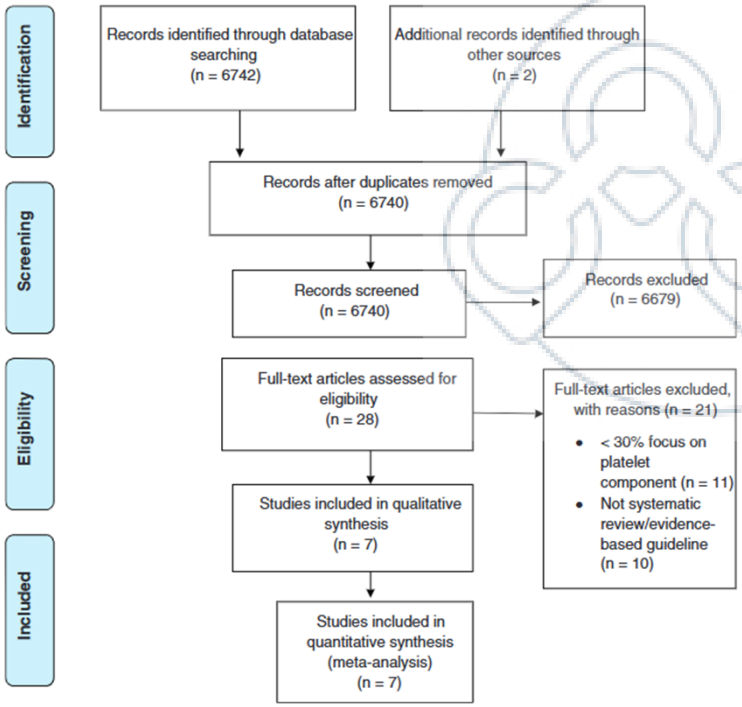

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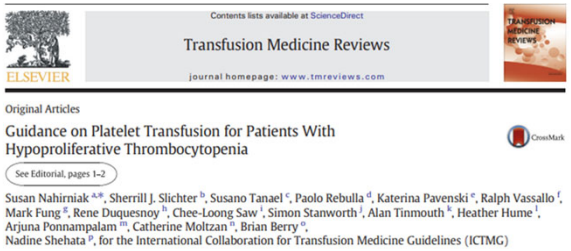
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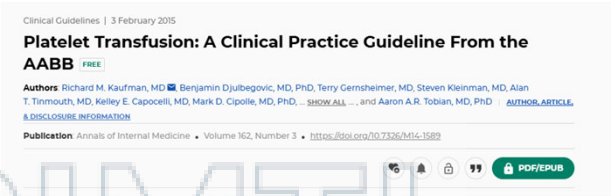
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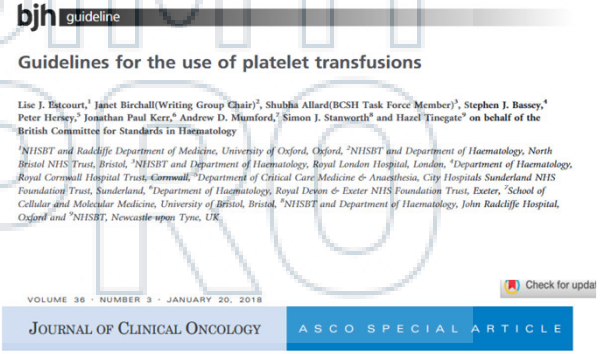
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Guideline Appraisal AGREE II tool

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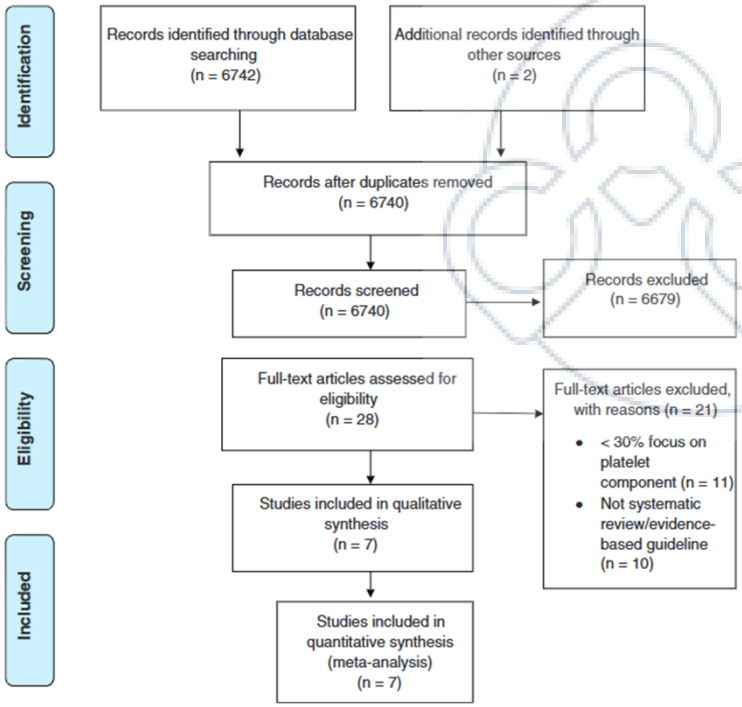

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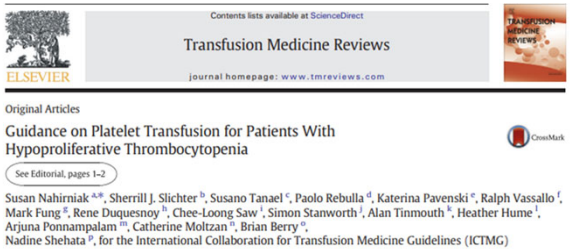
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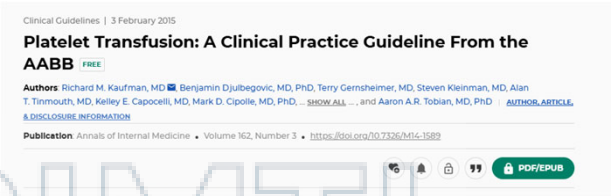
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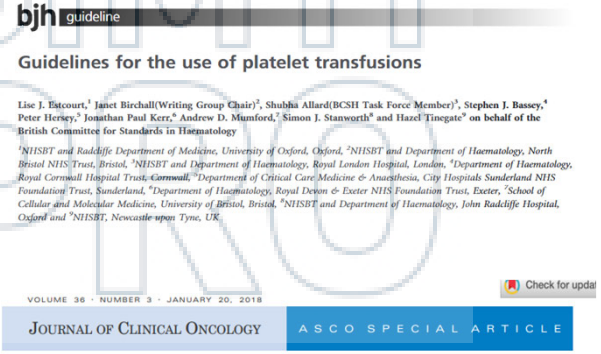
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ORIGINAL RESEARCH

TRANSFUSION

Quality of evidence-based guidelines for platelet transfusion and use: A systematic review

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Five guidelines addressed PLT transfusion for hypoproliferative thrombocytopenia.

Prophylactic PLT transfusion for patients with hypoproliferative thrombocytopenia if additional risk factors for bleeding exist; PLT threshold

Nahirniak, 2015[13]	ICTMG	• Patients with hypoproliferative thrombocytopenia with clinically significant bleeding attributed to thrombocytopenia should probably receive PLT transfusions even if the PLT count is $>10 \times 10^9$/L. (*Very weak level of evidence, weak recommendation*)
Killick, 2015[26]	BSCH	• In patients judged to have additional risk factors for bleeding, such as fever or sepsis, a higher prophylactic transfusion threshold of 20×10^9/L is recommended. *(2C)* • Patients with chronic bleeding of WHO grade 2 or above require individual management according to the severity of their symptoms and signs. *(2C)*
Estcourt, 2017[23]	BSCH	Reversible marrow failure, recovery anticipated • Consider increasing the threshold for prophylactic PLT transfusion to between 10×10^9–20×10^9/L in patients judged to have additional risk factors for bleeding. Individual review is required. *(2C)* Chronic marrow failure, recovery is not anticipated • Manage patients with chronic bleeding of WHO Grade 2 or above individually, according to the severity of their symptoms and signs. Consider a strategy of prophylaxis (eg, twice a week). *(2C)*
Schiffer, 2017[22]	ASCO	• Prophylactic PLT transfusion should be administered to patients with thrombocytopenia resulting from impaired marrow function to reduce the risk of hemorrhage when the PLT count falls below a predefined threshold level. This threshold level for transfusion varies according to the patient's diagnosis, clinical condition, and treatment modality. (*Evidence based, high evidence quality, strong recommendation*) • The Panel recommends a threshold of $<10 \times 10^9$/L for prophylactic PLT transfusion in patients receiving therapy for hematologic malignancies. Transfusion at higher levels may be advisable in patients with signs of hemorrhage, high fever, hyperleukocytosis, rapid decrease of PLT count, or coagulation abnormalities (eg, acute promyelocytic leukemia) and in those undergoing invasive procedures or in circumstances in which PLT transfusions may not be readily available in case of emergencies, as might be the case in outpatients who live at a distance from the treatment center. (*Evidence based, high evidence quality, strong recommendation*) • The risk of bleeding in patients with solid tumors during chemotherapy-induced thrombocytopenia is related to the depth and duration of the PLT nadir, although other factors contribute as well. The Panel recommends a threshold $<10 \times 10^9$/L for prophylactic PLT transfusion, based on extrapolation from studies in hematologic malignancies. PLT transfusion at higher levels is appropriate in patients with active localized bleeding which can sometimes be seen in patients with necrotic tumors. (*Informal consensus, low evidence quality, moderate recommendation*)

Prophylactic PLT transfusion for patients with hypoproliferative thrombocytopenia; PLT dose

Nahirniak, 2015[13]	ICTMG	• Patients with hypoproliferative thrombocytopenia with clinically significant bleeding attributed to thrombocytopenia should probably receive PLT transfusions even if the PLT count is $>10 \times 10^9$/L. (*Very weak level of evidence, weak recommendation*)
Killick, 2015[26]	BSCH	• In patients judged to have additional risk factors for bleeding, such as fever or sepsis, a higher prophylactic transfusion threshold of 20×10^9/L is recommended. *(2C)* • Patients with chronic bleeding of WHO grade 2 or above require individual management according to the severity of their symptoms and signs. *(2C)*
Estcourt, 2017[23]	BSCH	Reversible marrow failure, recovery anticipated • Consider increasing the threshold for prophylactic PLT transfusion to between 10×10^9–20×10^9/L in patients judged to have additional risk factors for bleeding. Individual review is required. *(2C)* Chronic marrow failure, recovery is not anticipated • Manage patients with chronic bleeding of WHO Grade 2 or above individually, according to the severity of their symptoms and signs. Consider a strategy of prophylaxis (eg, twice a week). *(2C)*
Schiffer, 2017[22]	ASCO	• Prophylactic PLT transfusion should be administered to patients with thrombocytopenia resulting from impaired marrow function to reduce the risk of hemorrhage when the PLT count falls below a predefined threshold level. This threshold level for transfusion varies according to the patient's diagnosis, clinical condition, and treatment modality. (*Evidence based, high evidence quality, strong recommendation*) • The Panel recommends a threshold of $<10 \times 10^9$/L for prophylactic PLT transfusion in patients receiving therapy for hematologic malignancies. Transfusion at higher levels may be advisable in patients with signs of hemorrhage, high fever, hyperleukocytosis, rapid decrease of PLT count, or coagulation abnormalities (eg, acute promyelocytic leukemia) and in those undergoing invasive procedures or in circumstances in which PLT transfusions may not be readily available in case of emergencies, as might be the case in outpatients who live at a distance from the treatment center. (*Evidence based, high evidence quality, strong recommendation*) • The risk of bleeding in patients with solid tumors during chemotherapy-induced thrombocytopenia is related to the depth and duration of the PLT nadir, although other factors contribute as well. The Panel recommends a threshold $<10 \times 10^9$/L for prophylactic PLT transfusion, based on extrapolation from studies in hematologic malignancies. PLT transfusion at higher levels is appropriate in patients with active localized bleeding which can sometimes be seen in patients with necrotic tumors. (*Informal consensus, low evidence quality, moderate recommendation*)

ORIGINAL RESEARCH

TRANSFUSION

Quality of evidence-based guidelines for platelet transfusion and use: A systematic review

Arwa Z. Al-Riyami[1] | Rachel Jug[2,8] | Ursula La Rocca[3,4] | Homa Keshavarz[5] | Denise Landry[5] | Nadine Shehata[6,7,8] | Simon J. Stanworth[9,10,11] | Susan Nahirniak[12,13]

Five guidelines addressed PLT transfusion for hypoproliferative thrombocytopenia.

Prophylactic PLT transfusion for patients with hypoproliferative thrombocytopenia if additional risk factors for bleeding exist; PLT threshold

Nahirniak, 2015[13]	ICTMG	• Patients with hypoproliferative thrombocytopenia with clinically significant bleeding attributed to thrombocytopenia should probably receive PLT transfusions even if the PLT count is $>10 \times 10^9$/L. (*Very weak level of evidence, weak recommendation*)
Killick, 2015[26]	BSCH	• In patients judged to have additional risk factors for bleeding, such as fever or sepsis, a higher prophylactic transfusion threshold of 20×10^9/L is recommended. *(2C)* • Patients with chronic bleeding of WHO grade 2 or above require individual management according to the severity of their symptoms and signs. *(2C)*

Prophylactic PLT transfusion for patients with hypoproliferative thrombocytopenia; PLT dose

Nahirniak, 2015[13]	ICTMG	• Patients with hypoproliferative thrombocytopenia with clinically significant bleeding attributed to thrombocytopenia should probably receive PLT transfusions even if the PLT count is $>10 \times 10^9$/L. (*Very weak level of evidence, weak recommendation*)
Killick, 2015[26]	BSCH	• In patients judged to have additional risk factors for bleeding, such as fever or sepsis, a higher prophylactic transfusion threshold of 20×10^9/L is recommended. *(2C)* • Patients with chronic bleeding of WHO grade 2 or above require individual management according to the severity of their symptoms and signs. *(2C)*

- **Incongruenze per la trasfusione piastrinica in profilassi** in presenza di **ulteriori fattori di rischio come sanguinamento e sepsi**.
  - Due LG raccomandavano **una soglia più elevata**, compresa tra **10×10^9/L e 20×10^9/L** (Estcourt et al) e **20×10^9/L** (Killick et al)**;**
  - Una LG raccomandava di trasfondere **in caso di conta piastrinica superiore a 10×10^9/L.**
  - Una LG raccomandava che la **soglia per la trasfusione dovesse variare in base alla diagnosi del paziente, alle condizioni cliniche e alla modalità di trattamento.**
  - Una LG non specificava una soglia specifica in questi contesti (Kaufman et al. 2015).

- **Ulteriore area di incongruenza** è risultata la **dose da somministrare.**

Guideline Appraisal AGREE II tool

A systematic search for evidence-based GL from January 1, 2013, to January 25, 2019.

Of 6744 citations, 6740 records were screened. Seven of 28 full-text studies met the inclusion criteria. The median scaled score (and the interquartile range of the scaled score) for the following items were as follows: scope and purpose, 94% (8%); stakeholder involvement, 63% (18%); rigor of development, 83% (14%); clarity of presentation, 94% (6%); applicability, 58% (20%); and editorial independence, 77% (4%). **Overall quality ranged from 4 to 7 (7 is the maximum score).**

Inconsistent recommendations were on prophylactic PLT transfusion in hypoproliferative thrombocytopenia in the presence of risk factors and dose recommendations.

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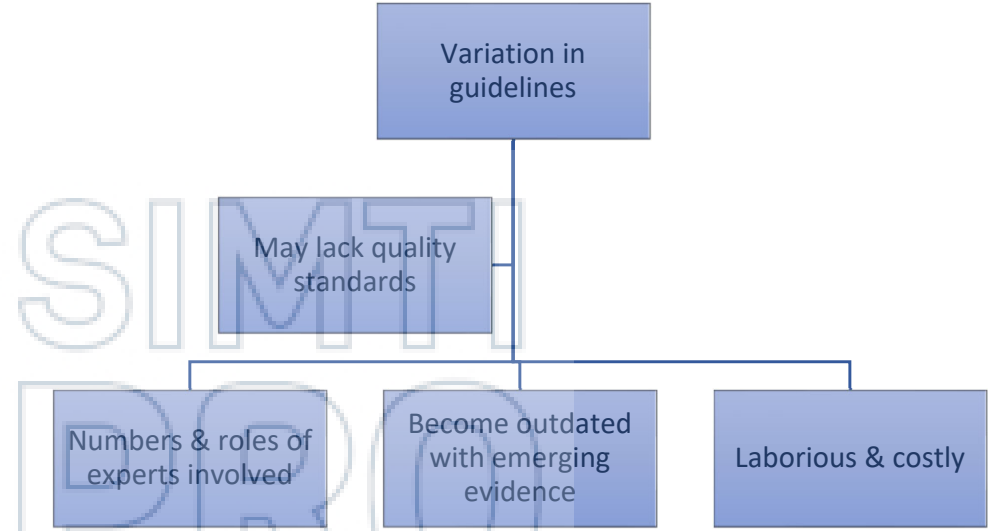

Al-Riyami AZ, Jug R, La Rocca U, Transfusion 2021; 61: 948-958.

Guideline Appraisal AGREE II tool

ORIGINAL RESEARCH

TRANSFUSION

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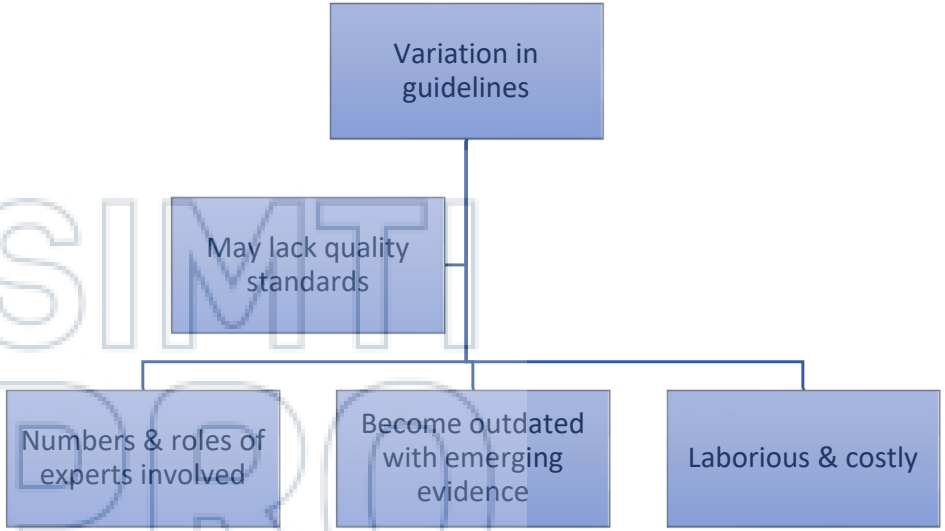


Qualità eterogenea delle linee guida:

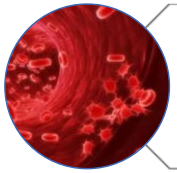
buoni punteggi per scopo e chiarezza, criticità per coinvolgimento degli stakeholder e applicabilità.

Le incongruenze e la variabilità qualitativa evidenziano la **necessità di miglioramenti nelle future LG**.

Al-Riyami AZ, Jug R, La Rocca U, Transfusion 2021; 61: 948-958.

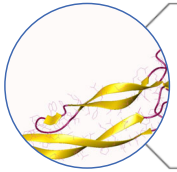
Supporto trasfusionale piastrinico: elementi decisionali

Quali sono i **fattori essenziali da considerare** nel valutare la **trasfusione di piastrine in ambito oncoematologico?**



TROMBOCITOPENIA E RISCHIO DI EMORRAGIA
alla luce del contesto clinico

TRASFUSIONE PIASTRINICA IN PROFILASSI/TRATTAMENTO



THRESHOLDS TRASFUSIONALI… Soglie basate sulle evidenze

SICUREZZA TRASFUSIONALE

STRATEGIE TRASFUSIONALI LIBERALI E RESTRITTIVE ED EFFICACIA CLINICA (outcomes: sanguinamento e mortalità)

Trasfusione piastrinica in profilassi e thresholds trasfusionali

Randomized Study of Prophylactic Platelet Transfusion Threshold During Induction Therapy for Adult Acute Leukemia: 10,000/μL Versus 20,000/μL

By Kevin D. Heckman, George J. Weiner, Charles S. Davis, Ronald G. Strauss, Michael P. Jones, and C. Patrick Burns

Purpose: **We designed and conducted a randomized single-institution trial comparing two common prophylactic platelet transfusion thresholds in patients undergoing induction therapy for acute leukemia.**

Patients and Methods: **Seventy-eight patients undergoing induction therapy for acute leukemia were randomized to receive prophylactic apheresis platelet concentrates when the platelet count was either ≤ 10,000/μL or ≤ 20,000/μL.**

Results: **There was no significant difference in the total number of bleeding episodes per patient with a median of four in the ≤ 10,000/μL arm and two in the ≤ 20,000/μL arm (25th to 75th percentiles of 2, 7 and 1, 5, respectively; *P* = .12). Patients randomized to the ≤ 10,000/μL arm received more platelet transfusions for bleeding [one (0, 2) *v* zero (0, 0); *P* = .0003]. In contrast, patients on the ≤ 20,000/μL arm received more platelet transfusions for prophylactic indications [10 (5, 14) *v* six (3, 8); *P* = 0.001], as would be expected, but less for bleeding. Nevertheless, the total number of platelet transfusions given to patients on the ≤ 20,000/μL arm was higher and nearly significant [11 (6, 15) *v* seven (5, 11); *P* = .07]. There were no statistically significant differences between the groups with regard to RBC transfusion requirements, febrile days, days hospitalized, days thrombocytopenic, need for HLA-matched platelets, remission rate, or death during induction chemotherapy. No patient in either group died from hemorrhage or underwent major surgery for bleeding complications.**

Conclusion: **Giving prophylactic platelets at a threshold of ≤ 10,000/μL compared with ≤ 20,000/μL can decrease the total utilization of platelets with only a small adverse effect on bleeding, and no statistically significant effect on morbidity.**

J Clin Oncol 15:1143-1149. © *1997 by American Society of Clinical Oncology.*

La **somministrazione profilattica di piastrine** a una **soglia ≤ 10.000/L** rispetto a ≤ 20.000/L può ridurre l'utilizzo totale di piastrine con minimo effetto avverso sul sanguinamento e **nessun effetto statisticamente significativo sulla morbilità**.

- British Committee for Standards in Hematology 1992
  10 x 10^9/L
- College of American Pathologists, 1994
  5 x 10^9/L
- Consensus Conference, Royal College of Physicians, 1998
  10 x 10^9/L
- American Society of Clinical Oncology, 2001
  10 x 10^9/L
- British Committee for Standards in Hematology, 2001
  10 x 10^9/L
- Italian Society for Transfusion Medicine and Immunohematology, 2009
  10 x 10^9/L

Heckman KD, et al. J Clin Oncol. 1997

Trasfusione piastrinica in profilassi: cosa sappiamo oggi?

🧪 Threshold trasfusionale

(Heckman et al, J Clin Oncol 1997)

<10 vs 20 ×10⁹/L

- Stessa efficacia nel prevenire sanguinamento
- ↓ utilizzo totale di piastrine
- Nessun impatto su mortalità

➞ 10 ×10⁹/L = soglia standard

💉 Dose di piastrine Studio PLADO

(Slichter et al, NEJM 2010)

1,1 – 2,2 – 4,4 ×10¹¹/m²

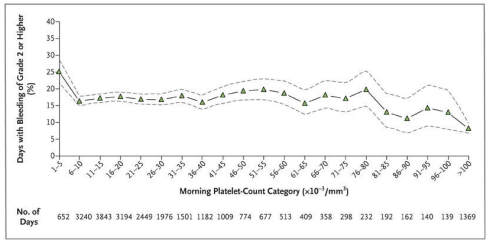
Sanguinamento ≈17% tutti

- Nessuna riduzione rischio di sanguinamento aumentando la conta (6→80 ×10⁹/L)
- Conta <5 ×10⁹/L → lieve ↑ (~25%)

Dose alta → ↑ eventi avversi

→ La dose standard è sufficiente

Sanguinamento ↑ nel HSCT allogenico e nei bambini: **altri fattori clinici**, oltre alla conta, determinano il rischio emorragico.



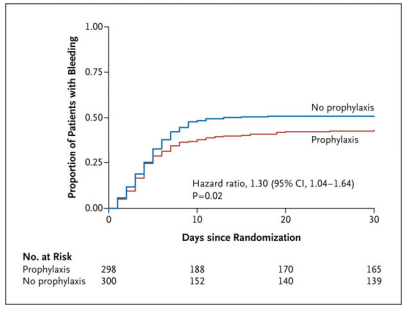
✓ No Profilassi vs profilassi – TOPPS

(Stanworth et al, NEJM 2013)

- PLT <10 ×10⁹/L
- Endpoint: sanguinamento WHO 2–4 (30 gg) **50% vs 43%**

- **Non inferiorità non dimostrata→ Riduce il rischio ma non lo elimina**

- Sottogruppo AutoHSCT: no differenze



⏳ Carico cumulativo Analisi secondaria TOPPS

(Stanworth et al. 2015)

- N. giorni con PLT <10 ×10⁹/L = predittore indipendente
- Più rilevante della singola conta
- Influenzato da trattamento, febbre, sanguinamento recente

→ Conta la durata della trombocitopenia

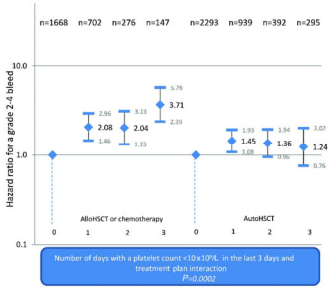
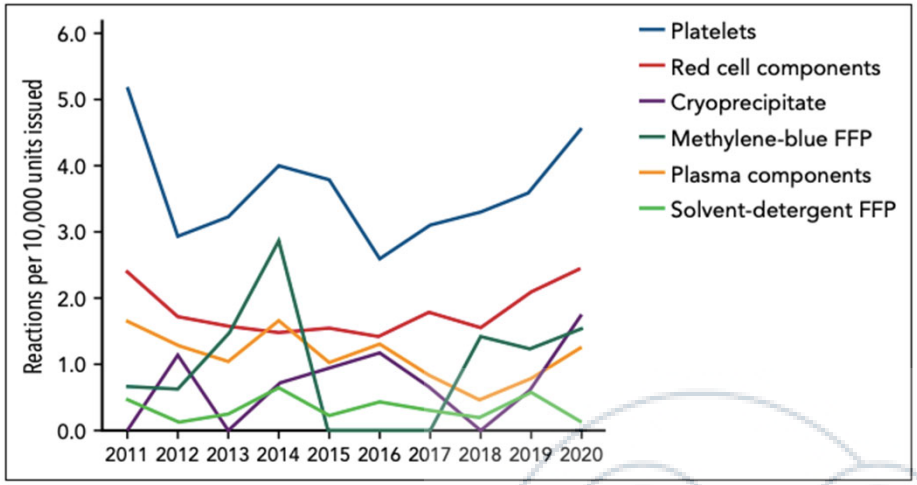


Figure 2. Risk-adjusted hazard ratios for grade 2-4 bleeds according to the number of days with a platelet count

Sicurezza trasfusionale



- La trasfusione piastrinica è più **comunemente implicata nelle reazioni trasfusionali.**
- **Reazioni trasfusionali febbrili** non emolitiche e **reazioni allergiche** possono verificarsi con una frequenza riportata rispettivamente di 1 su 14 e 1 su 50 per unità trasfusionale (Kauffman et al. 2015).
- Non vi sono prove che l'uso profilattico di antipiretici o antistaminici riduca l'incidenza di reazioni trasfusionali ma i dati suggeriscono meno reazioni per prodotti piastrinici conservati in soluzioni additive piastriniche, contenenti meno plasma.

Approximate risks of transfusion-related adverse events

Stanworth SJ, Shah A. Blood. 2022

Table 1. Approximate Risks of Transfusion-Related Adverse Events

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

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

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

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

Platelet Transfusion: 2025 AABB and ICTMG International Clinical Practice Guidelines

Alcune considerazioni

- Le evidenze da **RCT e metanalisi supportano la strategia profilattica nei pazienti con neoplasie ematologiche in chemioterapia o HSCT allogenico.** La soglia di **10 $\times 10^9$/L è appropriata**.
- **Aumentare la dose** di piastrine **non riduce il rischio emorragico**.
- La profilassi riduce il sanguinamento clinicamente significativo, ma non lo elimina.
- Il **rischio emorragico è multifattoriale**: durata della trombocitopenia e fattori clinici sono determinanti.
- Alcuni **sottogruppi (auto-HSCT)** potrebbero **non richiedere profilassi** sistematica.
- Alla luce di queste evidenze, diventa centrale identificare **quali pazienti possano beneficiare di strategie differenziate**.

Dalle evidenze alle Linee Guida ICTMG–AABB

REVIEW ARTICLE

TRANSFUSION

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

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

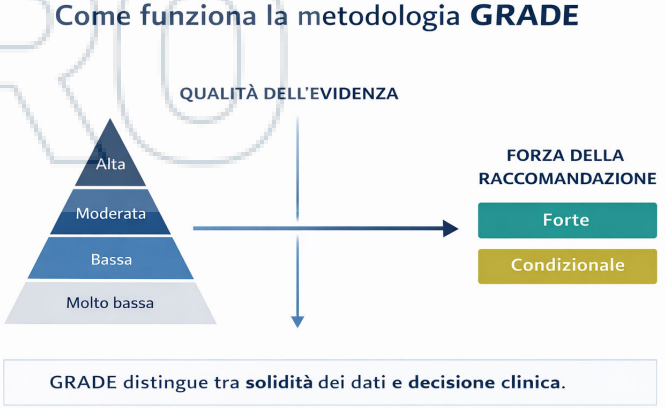
[1]Department of Pathology, University of Cincinnati, Cincinnati, Ohio, USA
[2]Italian National Blood Center, National Institute of Health, Sapienza University of Rome, Rome, Italy
[3]Department of Hematology, Sultan Qaboos University Hospital, University Medical City, Muscat, Oman
[4]College of Medicine and Health Sciences, Sultan Qaboos University, Muscat, Oman
[5]Canadian Blood Services, Toronto, Canada
[6]Department of Pathology, University of Utah, Salt Lake City, Utah, USA
[7]NHS Blood and Transplant, University of Oxford, Oxford, UK
[8]Oxford University Hospitals NHS Trust, University of Oxford, Oxford, UK
[9]Radcliffe Department of Medicine, University of Oxford, Oxford, UK
[10]Department of Laboratory Medicine and Pathology, University of Alberta, Edmonton, Alberta, Canada
[11]Alberta Precision Laboratories, Edmonton, Alberta, Canada

Transfusion. 2025 Jun;65(6):1155-1169.

SCENARI

- Trombocitopenia ipoproliferativa
- Trombocitopenia da consumo
- Trombocitopenia e procedure invasive
- Chirurgia cardiovascolare (± bypass cardiopolmonare)
- Emorragia intracranica

- **Base scientifica**
  Systematic review e meta-analisi ICTMG su trasfusione piastrinica
- **Metodo**
  Valutazione delle evidenze
  Metodologia GRADE
- **Output**
  Linee guida AABB–ICTMG 2025
  11 raccomandazioni cliniche



JAMA. 2025 Aug 19;334(7):606-617.

Le raccomandazioni attuali derivano da una sintesi sistematica e metodologicamente strutturata delle evidenze.

ICTMG Systematic Literature Review and Meta-analysis

PRISMA Diagram (1946- 2024)

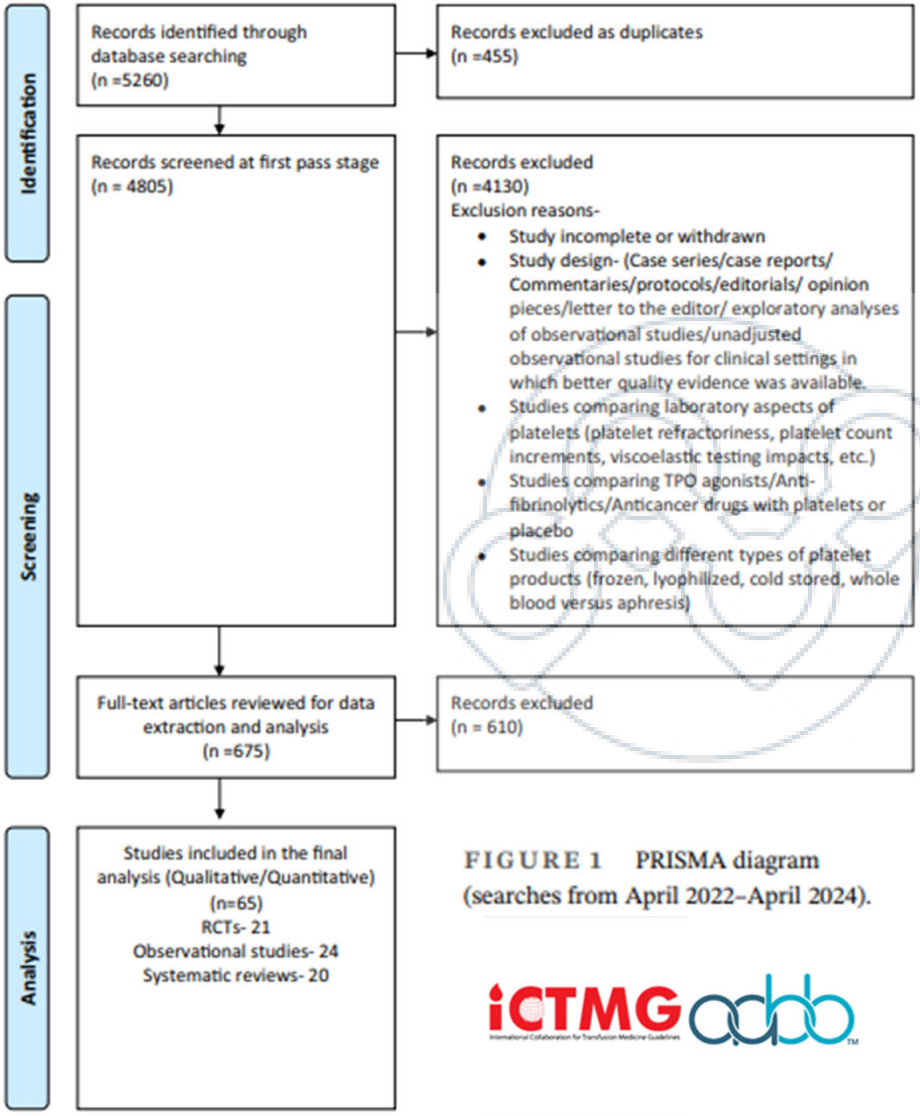


FIGURE 1 PRISMA diagram (searches from April 2022–April 2024).

RICERCA DELLA LETTERATURA

- RCTs
- In caso di basso grado di evidenza, SR o studi osservazionali

65 studi

- 21 RCT
- 24 osservazionali
- 20 SR

La certezza delle evidenze è stata valutata in relazione a soglie predefinite di **differenza minima** clinicamente **importante (MID):**

- 2% per la mortalità,
- 20% per il sanguinamento di grado 2–4 (o equivalente)
- 5% per il sanguinamento di grado 3–4 (o equivalente).

Level of evidence	Explanation
High	Further research is very unlikely to change our confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Weak	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very weak	Any estimate of effect is very uncertain.

ICTMG Systematic Literature Review and Meta-analysis

P

- TROMBOCITOPENIA IPOPROLIFERATIVA
- PROFILASSI PRE-PERIPROCEDURALE
- CHIRURGIA CARDIOVASCOLARE
- TROMBOCITOPENIA DA CONSUMO
- EMORRAGIA INTRACRANICA

Per pazienti per cui la trasfusione piastrinica può ridurre il rischio di sanguinamento, qual è l'impatto di una strategia trasfusionale restrittiva rispetto ad una liberale?

I STRATEGIE RESTRITTIVE

C STRATEGIE LIBERALI

CONFRONTO TRA:

- strategie terapeutiche vs profilattiche
- diverse dosi piastriniche
- diverse soglie trasfusionali per la trasfusione profilattica.

O MORTALITA'
EMORRAGIA (WHO)

SURVEY ICTMG

REVIEW ARTICLE

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Transfusion. 2025 Jun;65(6):1155-1169.

STRATEGIE LIBERALI VS RESTRITTIVE

Randomized Trial	Intervention		Population
Platelet threshold			
	Restrictive	Liberal	
Solomon 1978	No platelet	20 x 10^3/µl	Hypoproliferative
Murphy 1982	No platelet	20 x 10^3/µl	Hypoproliferative
Andrew 1993	25 x 10^3/µl	50 x 10^3/µl	Consumptive
Heckman 1997	10 x 10^3/µl	20 x 10^3/µl	Hypoproliferative
Rebulla 1997	10 x 10^3/µl	20 x 10^3/µl	Hypoproliferative
Zumberg 2002	10 x 10^3/µl	20 x 10^3/µl	Hypoproliferative
Diedrich 2005	10 x 10^3/µl	30 x 10^3/µl	Hypoproliferative
Wandt 2012	No platelet	10 x 10^3/µl	Hypoproliferative
Assir 2013	No platelet	30 x 10^3/µl	Consumptive
Stanworth 2013	No platelet	10 x 10^3/µl	Hypoproliferative
Baharoglu 2016	No platelet	Platelet transfusion	Spontaneous ICH with platelet counts >100,000/µl
Lye 2017	No platelet	20 x 10^3/µl	Consumptive
Curley 2019	25 x 10^3/µl	50 x 10^3/µl	Consumptive
Kumar 2020	20 x 10^3/µl	100 x 10^3/µl	Consumptive
Van Baarle 2023	No platelet	Platelet transfusion	Peri-procedural states with platelet counts 10,000-50,000/µl
Platelet dose			
	Restrictive	Liberal	
Tinmouth 2004	Low dose (3 platelet units)	Standard dose (5 platelet units)	Hypoproliferative
Sensebe 2005	Standard dose (0.5 x 10(11)/10 kg)	High dose (1 x 10(11)/10 kg)	Hypoproliferative
Heddle 2009	Low-dose 1.5-3.0x10^{11} platelets	Standard dose 3.0-6.0x10^{11} platelets	Hypoproliferative
Slichter 2010	Low dose (1.1 x 10^{11} platelets/M^2 BSA)	Standard dose, high dose (2.2 x 10^{11}, 4.4 x 10^{11} platelets/M^2 BSA)	Hypoproliferative
Early platelet transfusion			
	Restrictive	Liberal	
Lunen 2018	No early platelet transfusion	Early platelet transfusion	Cardiovascular surgery
Gautman 2019	No early platelet transfusion	Early platelet transfusion	Cardiovascular surgery

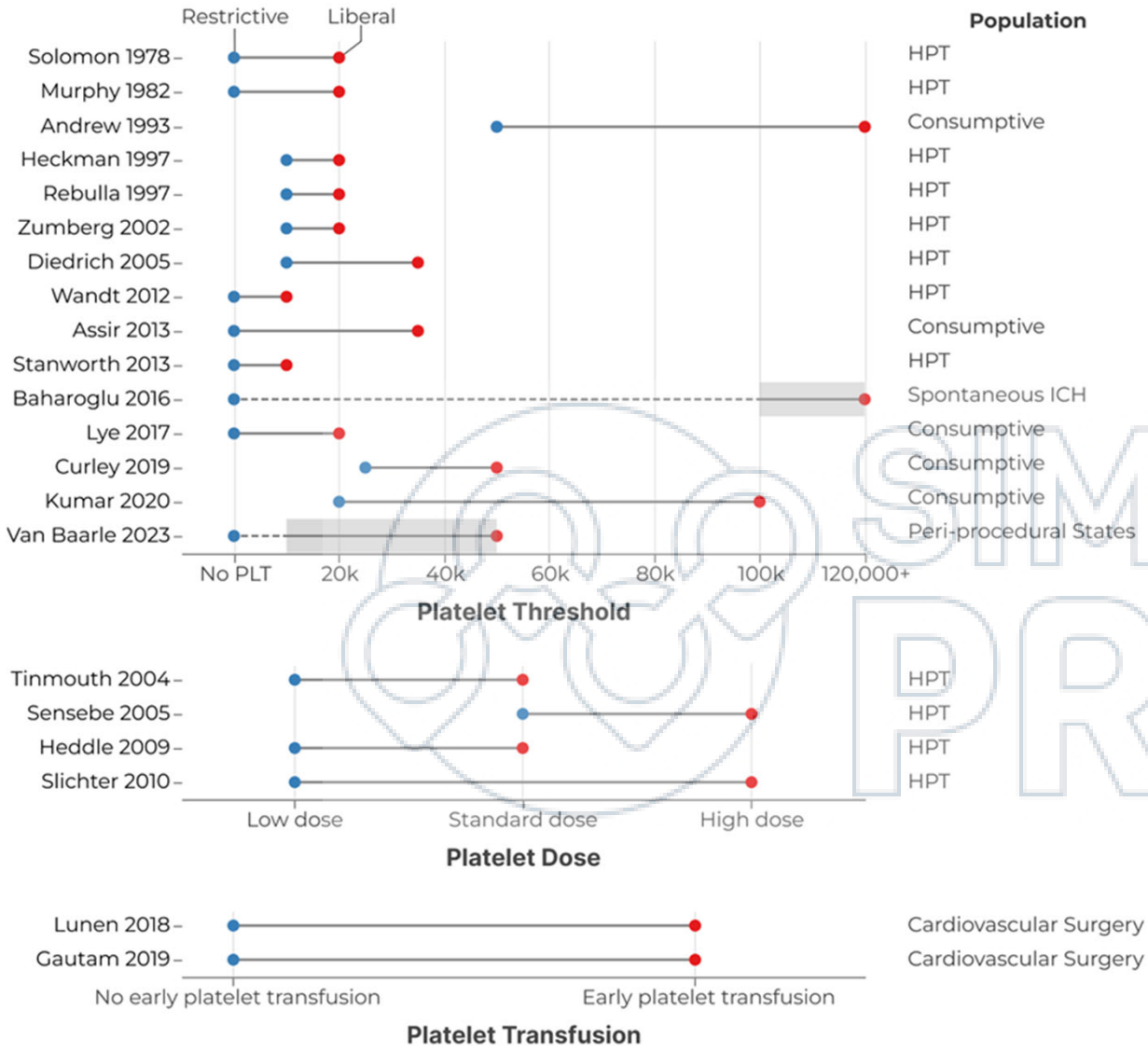
Strategie interventistiche

•Definite come **liberali** vs **restrittive:**
intese come uso di **maggiore** vs **minore** quantità di trasfusioni piastriniche

•Definizione ampia per includere studi con:

- Soglie trasfusionali differenti
- Dosaggi diversi
- Tempistiche variabili, incluso no profilassi

STRATEGIE LIBERALI VS RESTRITTIVE



Nel grafico:

- L'**area grigia** indica gli intervalli di conta piastrinica dei pazienti realmente inclusi in due studi.
- Le **linee tratteggiate** indicano intervalli non inclusi.

- Strategia **restrittiva** = minore quantità di piastrine trasfuse.
- Strategia **liberale** = maggiore quantità di piastrine trasfuse.

Metcalf RA, Nahirniak S, Guyatt G, et al. Platelet Transfusion: 2025 AABB and ICTMG International Clinical Practice Guidelines. JAMA. 2025 Aug 19;334(7):606-617.

La maggior parte degli studi ha valutato le strategie di trasfusione piastrinica basandosi su **soglie di conta piastrinica**; meno studi hanno confrontato **diverse dosi di piastrine** o il **timing della trasfusione**.

Le definizioni di "bassa" o "alta" dose variavano per peso, superficie corporea o numero di trasfusioni, ma in generale confrontavano quantità inferiori vs superiori di piastrine.

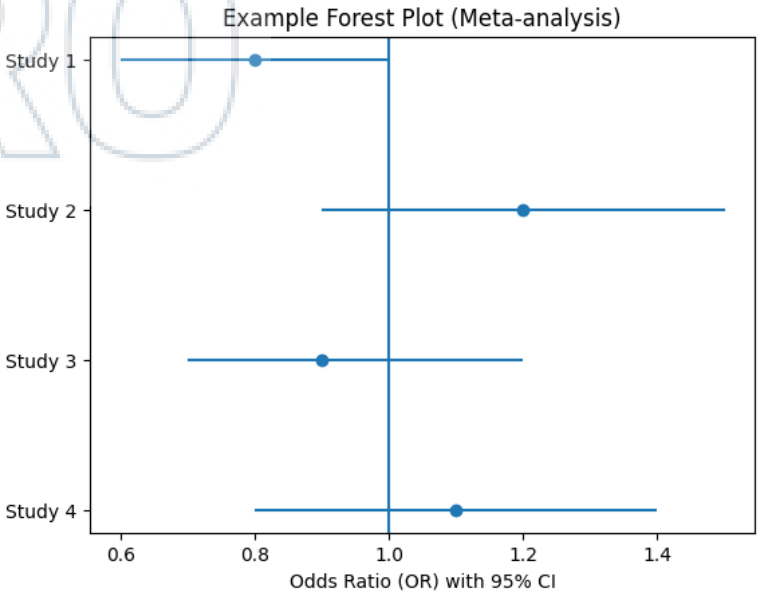
2.5 | Analisi e Sintesi

Le analisi sono state condotte con un approccio qualitativo e quantitativo, includendo prioritariamente RCT e, in assenza di questi, studi osservazionali (MCOS). Quando possibile, sono state combinate misure di effetti compariparabili tra studi.

Le stime sono state espresse come Odds Ratio (OR) con il IC 95% utilizzando RevMan (v8.14.0) e applicando un modello a effetti casuali (Mantel-Haenszlel), considerando le differenze tra popolazioni e contesti geografici.

L'eterogeneità è stata valutata mediante test X^2 e indice I^2 di Higgins, definendo elevata eterogeneità per $I^2 > 50\%$. La significatività statistica è stata fissata a $p < 0,005$ (due code).

Quando i dati non consentivano meta-analisi, i risultati sono stati sintetizzati in forma narrativa strutturata.



Clinical Review & Education

JAMA | Special Communication

Platelet Transfusion
2025 AABB and ICTMG International Clinical Practice Guidelines

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Platelet Transfusion: 2025
AABB and ICTMG Guideline
R. Metcalf et al. JAMA

LINEA GUIDA AABB–ICTMG 2025
Finalità e rilevanza clinica

Basata sui risultati della revisione sistematica e meta-analisi

Finalità
- Raccomandazioni aggiornate e basate su evidenze
- Supporto al processo decisionale
- Uso appropriato della trasfusione piastrinica
- Riduzione della sovra-trasfusione

Ambiti applicativi
- Neoplasie ematologiche
- Trombocitopenia da chemioterapia
- Procedure chirurgiche e invasive
- Terapia intensiva
- Sanguinamento attivo

Implicazioni per la pratica
- Standardizzazione della gestione
- Riduzione della sovra-trasfusione
- Decisione condivisa
- Ottimizzazione degli outcome

LINEA GUIDA AABB–ICTMG 2025
Struttura dell'analisi e ambito delle raccomandazioni

1. Interventi confrontati
- Strategie restrittive vs liberali
  - Profilassi vs assenza di profilassi
  - Evidenze provenienti da:
    - RCT
    - Studi osservazionali

2. Outcome primari
- Mortalità
- Sanguinamento WHO grado 2-4
- Sanguinamento WHO grado 3-4

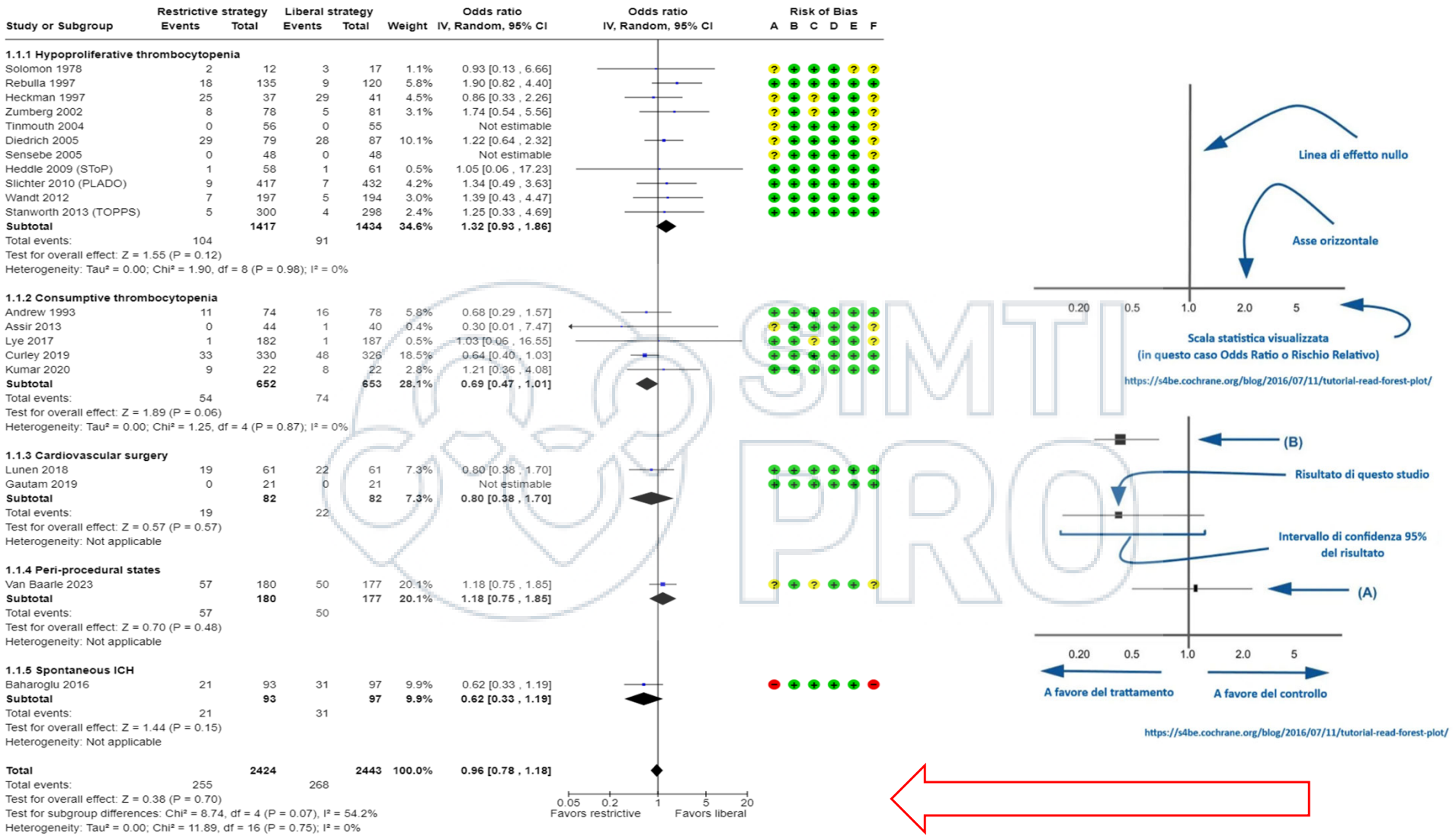
(Valutazione tramite differenza assoluta di rischio e IC 95%)

3. Metodologia
- Revisione sistematica della letteratura
- Valutazione della qualità dell'evidenza con metod GRADE
- Panel multidisciplinare internazionale

4. Prospettiva dell'analisi
- Paziente e famiglia
- Sistema sanitario

5. Fuori dallo scopo
- Tipologia di prodotto
- Refrattarietà piastrinica
- Protocolli di emorragia massiva
- Test viscoelastici
- Strategie alternative

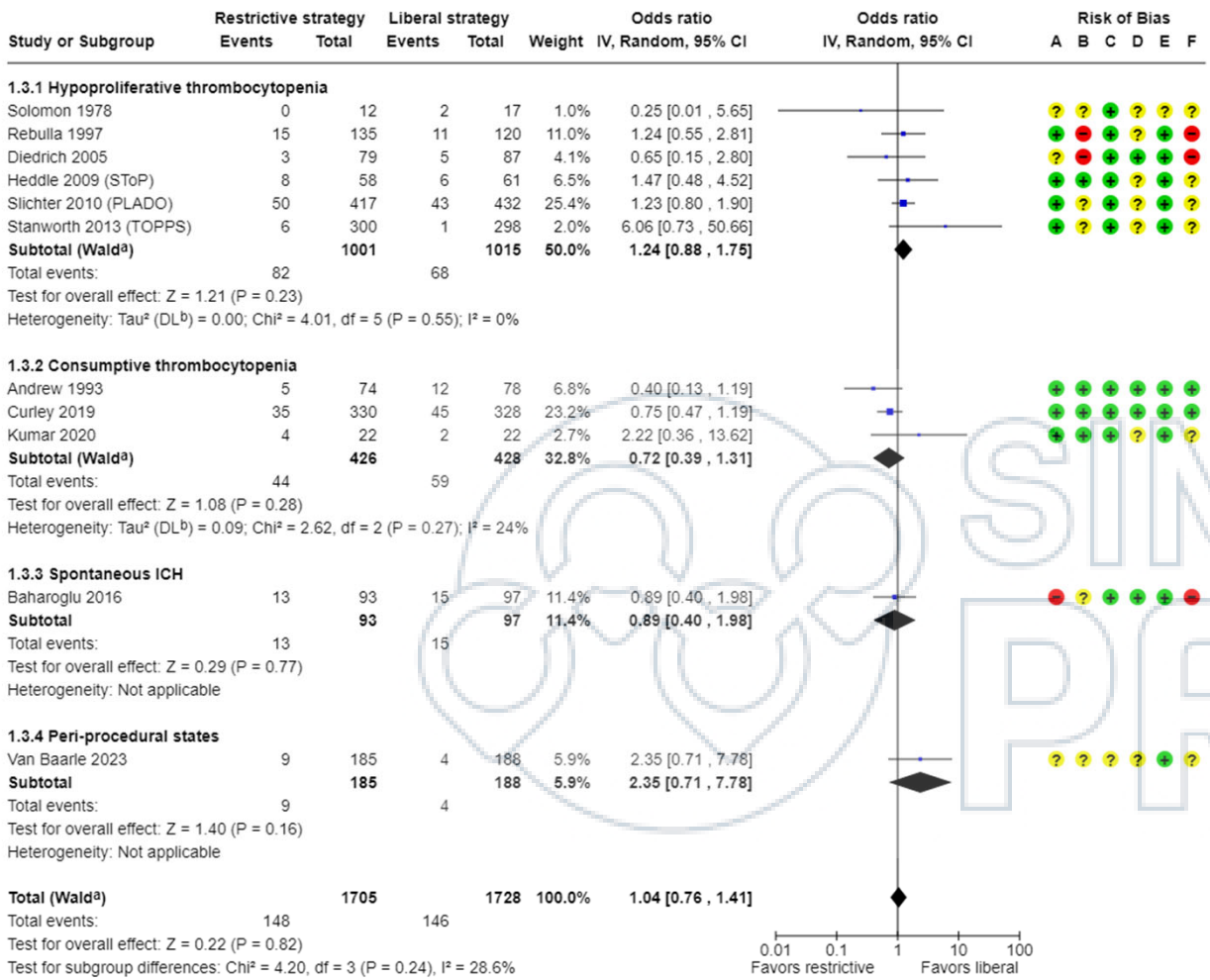
Mortalità per tutte le cause negli studi randomizzati che confrontano strategie trasfusionali restrittive rispetto a quelle liberali in tutti i contesti clinici



Metcalf RA, Nahirniak S, Guyatt G, et al. Platelet Transfusion: 2025 AABB and ICTMG International Clinical Practice Guidelines. JAMA. 2025 Aug 19;334(7):606-617.

Sanguinamento negli studi randomizzati che confrontano strategie di trasfusione piastrinica restrittive rispetto a quelle liberali in diversi contesti clinici.

WHO Grade 3-4



Study or Subgroup	Restrictive strategy Events	Total	Liberal strategy Events	Total	Weight	Odds ratio IV, Random, 95% CI	Risk of Bias A B C D E F
1.3.1 Hypoproliferative thrombocytopenia							
Solomon 1978	0	12	2	17	1.0%	0.25 [0.01 , 5.65]	? ? + ? ? ?
Rebulla 1997	15	135	11	120	11.0%	1.24 [0.55 , 2.81]	+ - + ? + -
Diedrich 2005	3	79	5	87	4.1%	0.65 [0.15 , 2.80]	? - + + + -
Heddle 2009 (SToP)	8	58	6	61	6.5%	1.47 [0.48 , 4.52]	+ + + ? + ?
Slichter 2010 (PLADO)	50	417	43	432	25.4%	1.23 [0.80 , 1.90]	+ ? + ? + ?
Stanworth 2013 (TOPPS)	6	300	1	298	2.0%	6.06 [0.73 , 50.66]	+ ? + ? + ?
Subtotal (Wald[a])		**1001**		**1015**	**50.0%**	**1.24 [0.88 , 1.75]**	
Total events:	82		68				
Test for overall effect: Z = 1.21 (P = 0.23)							
Heterogeneity: Tau² (DL[b]) = 0.00; Chi² = 4.01, df = 5 (P = 0.55); I² = 0%							
1.3.2 Consumptive thrombocytopenia							
Andrew 1993	5	74	12	78	6.8%	0.40 [0.13 , 1.19]	+ + + + + +
Curley 2019	35	330	45	328	23.2%	0.75 [0.47 , 1.19]	+ + + + + +
Kumar 2020	4	22	2	22	2.7%	2.22 [0.36 , 13.62]	+ + + ? + ?
Subtotal (Wald[a])		**426**		**428**	**32.8%**	**0.72 [0.39 , 1.31]**	
Total events:	44		59				
Test for overall effect: Z = 1.08 (P = 0.28)							
Heterogeneity: Tau² (DL[b]) = 0.09; Chi² = 2.62, df = 2 (P = 0.27); I² = 24%							
1.3.3 Spontaneous ICH							
Baharoglu 2016	13	93	15	97	11.4%	0.89 [0.40 , 1.98]	- ? + + + -
Subtotal		**93**		**97**	**11.4%**	**0.89 [0.40 , 1.98]**	
Total events:	13		15				
Test for overall effect: Z = 0.29 (P = 0.77)							
Heterogeneity: Not applicable							
1.3.4 Peri-procedural states							
Van Baarle 2023	9	185	4	188	5.9%	2.35 [0.71 , 7.78]	? ? ? ? + ?
Subtotal		**185**		**188**	**5.9%**	**2.35 [0.71 , 7.78]**	
Total events:	9		4				
Test for overall effect: Z = 1.40 (P = 0.16)							
Heterogeneity: Not applicable							
Total (Wald[a])		**1705**		**1728**	**100.0%**	**1.04 [0.76 , 1.41]**	
Total events:	148		146				
Test for overall effect: Z = 0.22 (P = 0.82)							
Test for subgroup differences: Chi² = 4.20, df = 3 (P = 0.24), I² = 28.6%							
Heterogeneity: Tau² (DL[b]) = 0.05; Chi² = 12.43, df = 10 (P = 0.26); I² = 20%							

Footnotes

[a]CI calculated by Wald-type method.

[b]Tau² calculated by DerSimonian and Laird method.

Risk of bias legend

(A) Bias arising from the randomization process
(B) Bias due to deviations from intended interventions
(C) Bias due to missing outcome data
(D) Bias in measurement of the outcome
(E) Bias in selection of the reported result
(F) Overall bias

Metcalf RA, Nahirniak S, Guyatt G, et al. Platelet Transfusion: 2025 AABB and ICTMG International Clinical Practice Guidelines. JAMA. 2025 Aug 19;334(7):606-617.

Dalle evidenze alle Linee Guida ICTMG–AABB

SCENARI

Trombocitopenia ipoproliferativa

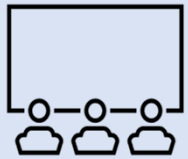
Trombocitopenia da consumo

Trombocitopenia e procedure invasive

Chirurgia cardiovascolare (± bypass cardiopolmonare)

Emorragia intracranica

Scenario clinico 1: Trombocitopenia ipoproliferativa in assenza di emorragia



Nei pazienti non sanguinanti con trombocitopenia ipoproliferativa qual è l'impatto di strategie trasfusionali piastriniche restrittive rispetto a liberali su mortalità e sanguinamento?

Un sottogruppo predefinito era rappresentato dai pazienti sottoposti a trapianto autologo di cellule staminali (SCT).

11 RCTs (2860 pazienti) analizzati:

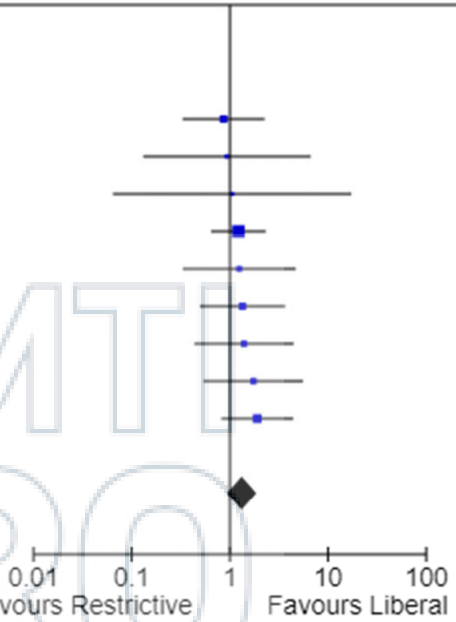
- **3 RCTs:** confronto tra **strategie profilattiche vs quelle terapeutiche** (Solomon et al. 1978, Stanworth et al. 2013; Wandt et al. 2012)
- **4 RCTs:** confronto tra **diverse dosi piastriniche** (Heddle et al. 2009; Slichter et al. 2010; Sensebe et al. 2005; Tinmouth et al. 2004)
- **4 RCTs:** confronto tra **diverse soglie trasfusionali** (Heckman et al. 1997; Rebulla et al 1997; Zumberg et al. 2002; Dietrich et al. 2005) per la trasfusione profilattica.

Scenario clinico 1: Trombocitopenia ipoproliferativa in assenza di emorragia

Mortalità per tutte le cause

Study or Subgroup	Restrictive Events	Restrictive Total	Liberal Events	Liberal Total	Weight	Odds ratio M-H, Random, 95% CI	Risk of Bias A	B	C	D	E	F
Tinmouth 2004_Mortality[a]	0	56	0	55		Not estimable	?	+	+		+	?
Sensebe 2005_Mortality	0	48	0	48		Not estimable	?	+	+		+	?
Heckman 1997_Mortality	25	37	29	41	12.9%	0.86 [0.33 , 2.26]	?	?	+		+	?
Solomon 1978_Mortality	2	12	3	17	3.1%	0.93 [0.13 , 6.66]	?	+	?		?	?
Heddle 2009 (SToP)_Mortality	1	58	1	61	1.5%	1.05 [0.06 , 17.23]	+	+	+		+	+
Diedrich 2005_Mortality	29	79	28	87	29.1%	1.22 [0.64 , 2.32]	?	+	+		+	?
Stanworth 2014 (TOPPS)_Mortality	5	300	4	298	6.8%	1.25 [0.33 , 4.69]	+	+	+		+	+
Slichter 2010 (PLADO)_Mortality	9	417	7	432	12.0%	1.34 [0.49 , 3.63]	+	+	+		+	+
Wandt 2012_Mortality	7	197	5	194	8.8%	1.39 [0.43 , 4.47]	+	+	+		+	+
Zumberg 2002_Mortality	8	78	5	81	8.8%	1.74 [0.54 , 5.56]	?	?	+		+	?
Rebulla 1997_Mortality	18	135	9	120	16.9%	1.90 [0.82 , 4.40]	+	+	+		+	+
Total		**1417**		**1434**	**100.0%**	**1.32 [0.93 , 1.86]**						
Total events:	104		91									

Test for overall effect: Z = 1.55 (P = 0.12)
Test for subgroup differences: Not applicable
Heterogeneity: Tau² = 0.00; Chi² = 1.90, df = 8 (P = 0.98); I² = 0%



Footnotes

[a]Blinding assessment is not applicable as outcome assessors cannot be blinded to a binary outcome like mortality.

Risk of bias legend

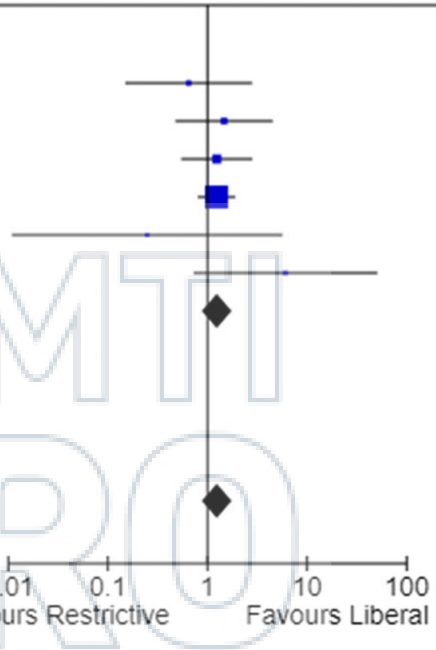
(A) Randomization
(B) Deviations from intended interventions
(C) Missing outcome data
(D) Measurement of the outcome
(E) Selection of the reported result
(F) Overall risk of bias

Mortalità per tutte le cause: il confronto ha consentito di evidenziare un OR di 1,32, con un IC 95% di 0.93-1.86, dunque non significativo

Trombocitopenia ipoproliferativa

Sanguinamento di grado 3–4 (WHO) o equivalente

Study or Subgroup	Restrictive Events	Restrictive Total	Liberal Events	Liberal Total	Weight	Odds ratio M-H, Random, 95% CI
4.4.1 Hypoproliferative thrombocytopenia						
Diedrich 2005_Bleeding	3	79	5	87	5.5%	0.65 [0.15 , 2.80]
Heddle 2009_Bleeding	8	58	6	61	9.4%	1.47 [0.48 , 4.52]
Rebulla 1997_Bleeding	15	135	11	120	17.6%	1.24 [0.55 , 2.81]
Slichter 2010_Bleeding	50	417	43	432	63.6%	1.23 [0.80 , 1.90]
Solomon 1978_Bleeding	0	12	2	17	1.2%	0.25 [0.01 , 5.65]
Stanworth 2014_Bleeding	6	300	1	298	2.6%	6.06 [0.73 , 50.66]
Subtotal		**1001**		**1015**	**100.0%**	**1.24 [0.88 , 1.75]**
Total events:	82		68			
Test for overall effect: Z = 1.21 (P = 0.23)						
Heterogeneity: Tau² = 0.00; Chi² = 4.01, df = 5 (P = 0.55); I² = 0%						
Total		**1001**		**1015**	**100.0%**	**1.24 [0.88 , 1.75]**
Total events:	82		68			
Test for overall effect: Z = 1.21 (P = 0.23)						
Test for subgroup differences: Not applicable						
Heterogeneity: Tau² = 0.00; Chi² = 4.01, df = 5 (P = 0.55); I² = 0%						

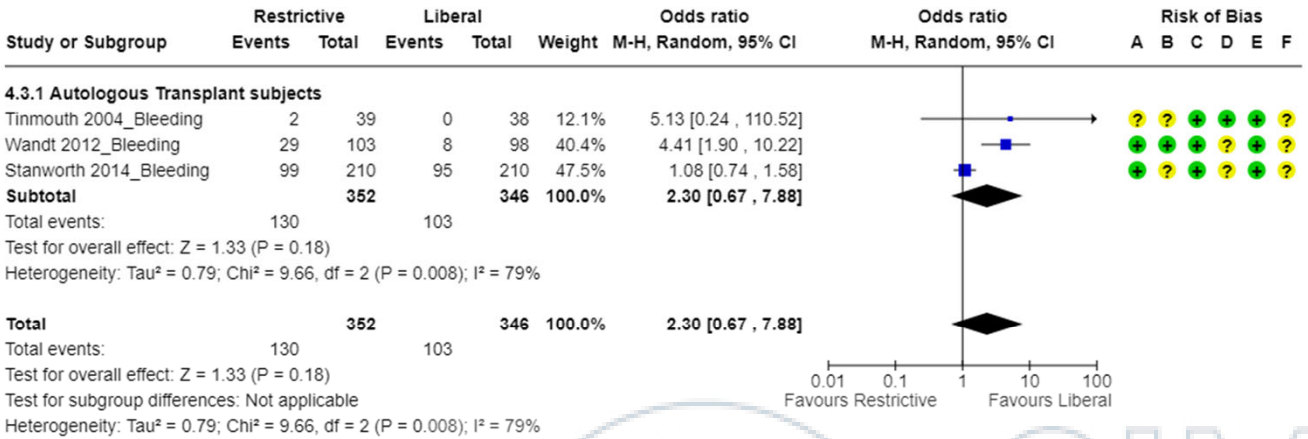


Risk of bias legend

(A) Randomization
(B) Deviations from intended interventions
(C) Missing outcome data
(D) Measurement of the outcome
(E) Selection of the reported result
(F) Overall risk of bias

Per emorragia grado 3 e 4 WHO (o equivalente), i dati di 6 studi randomizzati hanno mostrato un OR di 1,24 [da 0,88 a 1,75]

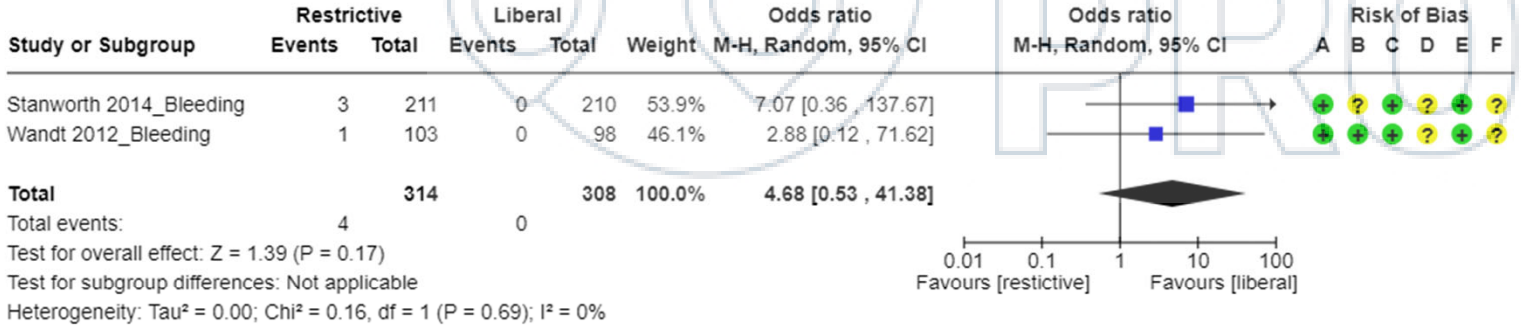
Sanguinamento: trombocitopenia ipoproliferativa – trapianto autologo



Study or Subgroup	Restrictive Events	Restrictive Total	Liberal Events	Liberal Total	Weight	Odds ratio M-H, Random, 95% CI
4.3.1 Autologous Transplant subjects						
Tinmouth 2004_Bleeding	2	39	0	38	12.1%	5.13 [0.24 , 110.52]
Wandt 2012_Bleeding	29	103	8	98	40.4%	4.41 [1.90 , 10.22]
Stanworth 2014_Bleeding	99	210	95	210	47.5%	1.08 [0.74 , 1.58]
Subtotal		**352**		**346**	**100.0%**	**2.30 [0.67 , 7.88]**
Total events:	130		103			
Test for overall effect: Z = 1.33 (P = 0.18)						
Heterogeneity: Tau² = 0.79; Chi² = 9.66, df = 2 (P = 0.008); I² = 79%						
Total		**352**		**346**	**100.0%**	**2.30 [0.67 , 7.88]**
Total events:	130		103			
Test for overall effect: Z = 1.33 (P = 0.18)						
Test for subgroup differences: Not applicable						
Heterogeneity: Tau² = 0.79; Chi² = 9.66, df = 2 (P = 0.008); I² = 79%						

Risk of bias legend
(A) Randomization
(B) Deviations from intended interventions
(C) Missing outcome data
(D) Measurement of the outcome
(E) Selection of the reported result
(F) Overall risk of bias

Tre studi randomizzati con un OR di 2,30 [0,67- 7,88] suggeriscono **assenza di riduzione del rischio di sanguinamento**



Study or Subgroup	Restrictive Events	Restrictive Total	Liberal Events	Liberal Total	Weight	Odds ratio M-H, Random, 95% CI
Stanworth 2014_Bleeding	3	211	0	210	53.9%	7.07 [0.36 , 137.67]
Wandt 2012_Bleeding	1	103	0	98	46.1%	2.88 [0.12 , 71.62]
Total		**314**		**308**	**100.0%**	**4.68 [0.53 , 41.38]**
Total events:	4		0			
Test for overall effect: Z = 1.39 (P = 0.17)						
Test for subgroup differences: Not applicable						
Heterogeneity: Tau² = 0.00; Chi² = 0.16, df = 1 (P = 0.69); I² = 0%						

Risk of bias legend
(A) Randomization
(B) Deviations from intended interventions
(C) Missing outcome data
(D) Measurement of the outcome
(E) Selection of the reported result
(F) Overall risk of bias

…dato confermato per **emorragia di grado 3 e 4 sec WHO (o equivalente),** i dati sono stati ottenuti **da 2 RCT con un OR di 4,68 [0,53 - 41,38]**

Raccomandazioni

Clinical Review & Education
JAMA | Special Communication
Platelet Transfusion
2025 AABB and ICTMG International Clinical Practice Guidelines

1.1 La trasfusione piastrinica è oggetto di raccomandazione forte nella trombocitopenia ipoproliferativa in assenza di sanguinamento, in caso di chemioterapia o trapianto allogenico con conta piastrinica (PLT) < 10 × 10^3/µL;

Popolazione	Raccomandazione	Certezza evidenze	Sintesi della giustificazione
Pazienti non sanguinanti con trombocitopenia ipoproliferativa in chemioterapia o sottoposti a trapianto allogenico di cellule staminali	Trasfondere piastrine se PLT <10 × 10^3/µL	Moderata	Nessun beneficio con strategie più liberali; soglia pratica e implementabile.

2.1 Tra le raccomandazioni condizionali, non è raccomandata la profilassi piastrinica nel trapianto autologo o nell'anemia aplastica, in assenza di sanguinamento.

Popolazione	Raccomandazione	Certezza evidenze	Sintesi della giustificazione
Pazienti adulti non sanguinanti con trombocitopenia ipoproliferativa sottoposti a trapianto autologo di cellule staminali (SCT) o con anemia aplastica	Strategia senza profilassi piastrinica	Bassa – Molto bassa	Le evidenze derivano da analisi per sottogruppi degli esiti emorragici nei trial clinici.

Raccomandazioni del panel:

- **HSCT autologo →** Trombocitopenia generalmente di breve durata→ Beneficio atteso della trasfusione profilattica ridotto rispetto ad altri sottogruppi
- **Anemia aplastica →** Nonostante la trombocitopenia prolungata→ Maggiore peso attribuito alla qualità di vita

Scenario clinico 2: Trombocitopenia e procedure invasive

- Nei **pazienti con trombocitopenia** che necessitano di **procedure invasive,** qual è **l'impatto delle strategie trasfusionali restrittive** rispetto a **quelle liberali** su **mortalità e sanguinamento grave** correlato alla procedura?

- I sottogruppi predefiniti includevano pazienti sottoposti a:posizionamento di **catetere venoso centrale (CVC),puntura lombare (LP),procedure di radiologia interventistica**.

CVC:

- **1 solo RCT (Van Baarle) in pazienti trombocitopenici sottoposti a posizionamento di CVC: pazienti con PLTS tra 10.000 e 50.000/µL sottoposti a CVC ecoguidato in reparto a trasfusione vs nessuna trasfusione. Maggiore incidenza di sanguinamento grado 2-4 nel braccio restrittivo** con variazioni in base al sito anatomico: **no differenze nei siti comprimibili (giugulare interna/femorale).** L'ematoma medio risultava più grande nel gruppo liberale. **Mortalità per tutte le cause: OR di 1,18, con un IC 95% di 0.75, 1.85, dunque non significativo**
- **1 studio prospettico** → nessuna differenza in mortalità o sanguinamento maggiore.

Radiologia interventistica: 1 MCOS (2060 pazienti) → nessuna differenza in mortalità o trasfusione RBC, anche per soglie ≤50.000/µL.

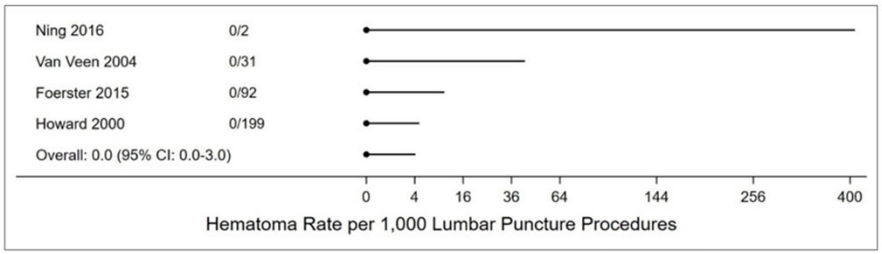
Puntura lombare (ematoma spinale): 6 MCOS (PLT <50.000/µL) di cui 4 riportavano anche dati per PLT <20.000/µL → **incidenza estremamente bassa.**

Meta-analisi: mortalità (CVC, 1 RCT) RR 1,18 [0,75–1,85]; sanguinamento WHO 2–4 aumentato nel braccio restrittivo in ematologia (OR 3,56), non in ICU; radiologia interventistica: minori ricoveri in ICU (OR 0,64), nessuna chiara riduzione delle trasfusioni di emazie; ematoma spinale raro (<1/1000).

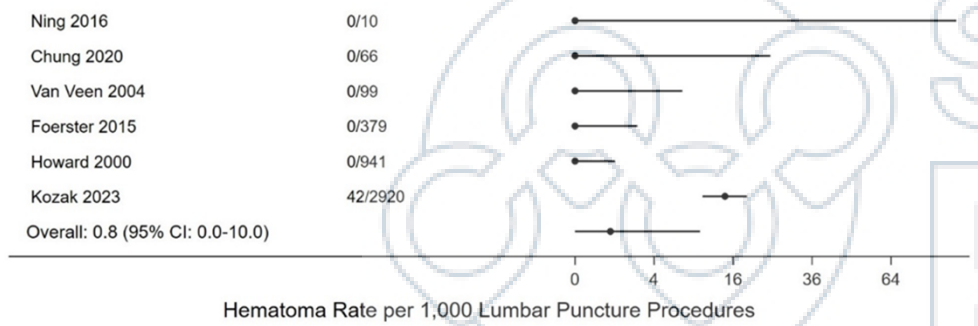
Scenario clinico 2: Trombocitopenia e procedure invasive

Figure S9: Spinal Hematoma incidence in Lumbar Punctures

a. Platelet counts <20,000/ul



b. Platelet counts <50,000/ul



Per quanto riguarda **l'ematoma spinale dopo PL, la meta-analisi mostra un'incidenza estremamente bassa.**

- Nei pazienti con conta piastrinica inferiore a 20.000/µL, su quattro studi e 324 pazienti, non sono stati osservati casi di ematoma spinale, con un tasso stimato pari a 0 per 1000 procedure.
- Nei pazienti con conta inferiore a 50.000/µL, su sei studi e oltre 4400 pazienti, l'incidenza stimata è stata di 0,78 per 1000 procedure.
- Evento raro, anche in presenza di trombocitopenia.

Ematoma spinale — Meta-analisi:

•**0/1000 punture lombari** [0–2,96] nei pazienti con conta piastrinica <20.000/µL (4 studi, 324 pazienti)

•**0,78/1000 punture lombari** [0–10,02] nei pazienti con conta piastrinica <50.000/µL (6 studi, 4418 pazienti)

Evento complessivamente molto raro.

Scenario clinico 2: Trombocitopenia e procedure invasive

Raccomandazione Forte

1.3 La trasfusione piastrinica è oggetto di raccomandazione forte in pazienti candidati a puntura lombare con PLT < 20 × 10^3/µL.

Popolazione	Raccomandazione	Certezza delle evidenze	Sintesi della giustificazione
Pazienti sottoposti a puntura lombare	Trasfondere piastrine se PLT <20 × 10^3/µL	Moderata	Riduce trasfusioni inutili mantenendo sicurezza clinica.

Raccomandazioni Condizionali

2.3 La trasfusione è raccomandata per PLT <10 × 10^3/µL, in caso di pazienti adulti sottoposti a posizionamento di catetere venoso centrale (CVC) in sedi comprimibili manualmente;
2.4 La trasfusione è raccomandata nelle procedure di radiologia interventistica, in caso di PLT <20 × 10^3/µL (procedure a basso rischio) o <50 × 10^3/µL (procedure ad alto rischio);
2.5 La trasfusione è raccomandata nella chirurgia maggiore non neuroassiale, in caso di PLT <50 × 10^3/µL.

Popolazione	Raccomandazione	Certezza delle evidenze	Sintesi della giustificazione
Pazienti adulti sottoposti a posizionamento di catetere venoso centrale (CVC) in sedi comprimibili manualmente	Trasfusione piastrinica se PLT ≤10 × 10^3/µL	Moderata – Molto bassa	Soglia pratica che riduce trasfusioni non necessarie.
Pazienti adulti sottoposti a procedure di radiologia interventistica	Trasfusione piastrinica se PLT <20 × 10^3/µL (basso rischio) o <50 × 10^3/µL (alto rischio)	Molto bassa	Le soglie proposte tengono conto del diverso rischio emorragico delle procedure.
Pazienti adulti sottoposti a chirurgia maggiore non neuroassiale	Trasfusione piastrinica se PLT <50 × 10^3/µL	Molto bassa	Soglia pragmatica che considera il potenziale rischio di sanguinamento severo.

Table 3. Recommendations for Platelet Transfusion

Population	Recommendation and guidance	Certainty of the evidence[a]	Summary justification
1. Strong recommendations			
1.1: Nonbleeding patients with hypoproliferative thrombocytopenia actively receiving chemotherapy or undergoing allogeneic stem cell transplant (SCT)	Platelet transfusion should be administered when the platelet count is <10 × 10^3/μL	Moderate	The data support no benefit with liberal strategies and a platelet count threshold <10 × 10^3/μL is practical for implementation
1.2: Preterm neonates without major bleeding	Platelet transfusion should be administered when the platelet count is <25 × 10^3/μL	High	The data support no benefits with liberal policies of <50 × 10^3/μL and the possibility of harm.
1.3: Patients undergoing lumbar puncture	Platelet transfusion should be administered when the platelet count is <20 × 10^3/μL	Moderate	A platelet count threshold <20 × 10^3/μL is practical for implementation, and minimizes need for platelet transfusion, while recognizing the extremely low event rate estimate
1.4: Patients with Dengue-related consumptive thrombocytopenia in the absence of major bleeding	No platelet transfusion	Moderate	The data support no benefits with use of platelets as prophylaxis and possibility of harm
2. Conditional recommendations			
2.1: Nonbleeding adult patients with hypoproliferative thrombocytopenia undergoing autologous SCT or with aplastic anemia	No-prophylaxis strategy	Low to very low	The evidence includes subgroup analyses of bleeding outcomes in trials
2.2: Adult patients with consumptive thrombocytopenia due to critical illness (non-Dengue) and without major bleeding	Platelet transfusion should be administered when the platelet count is <10 × 10^3/μL	Very low	Lack of direct randomized trial data; a platelet count threshold <10 × 10^3/μL is practical for implementation and minimizes requirements for platelet transfusions with attendant risks
2.3: Adult patients undergoing central venous catheter (CVC) placement at anatomic sites amenable to manual compression	Platelet transfusion should be administered when the platelet count is <10 × 10^3/μL	Moderate to very low	A platelet count threshold <10 × 10^3/μL is practical for implementation and minimizes need for platelet transfusion
2.4: Adult patients undergoing interventional radiology procedures	Platelet transfusion should be administered when the platelet count is <20 × 10^3/μL for low-risk procedures and <50 × 10^3/μL for high-risk procedures[7]	Very low	A platelet count threshold <20 × 10^3/μL or <50 × 10^3/μL is practical for implementation; recognizes the varying degrees of bleeding risk by procedure
2.5: Adult patients undergoing major nonneuraxial surgery	Platelet transfusion should be administered when the platelet count is <50 × 10^3/μL	Very low	A platelet count threshold <50 × 10^3/μL is practical for implementation; recognizes the degree of potential risk of severe bleeding for these procedures
2.6: Nonthrombocytopenic patients undergoing cardiovascular surgery in the absence of major hemorrhage, including those receiving cardiopulmonary bypass	No platelet transfusion	Very low	The limited data available support no benefit with use of platelets
2.7: Adult patients with spontaneous or traumatic, nonoperative intracranial hemorrhage with platelet counts >100 × 10^3/μL, including those receiving antiplatelet agents	No platelet transfusion	Low to very low	The limited data available support no benefit with use of platelets and the possibility of harm

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

Metcalf RA, et al. Platelet Transfusion: 2025 AABB and ICTMG International Clinical Practice Guidelines. JAMA. 2025

Clinical Review & Education

JAMA | Special Communication

Platelet Transfusion
2025 AABB and ICTMG International Clinical Practice Guidelines

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Members of the platelet guideline development team from ICTMG and AABB are pictured in Bethesda, Maryland in May 2024.

Le raccomandazioni sono state suddivise in forti, in presenza di evidenze di alta o moderata certezza, e condizionali, per evidenze di grado basso o molto basso.

Good Practice Statement

Good Practice Statement

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

Il panel ha sottolineato che la **decisione di eseguire una trasfusione di piastrine non dovrebbe basarsi esclusivamente sul valore della conta piastrinica**. Una buona pratica clinica richiede di **considerare l'intero quadro clinico,** inclusi:

- I sintomi e i segni clinici del paziente
- Altri parametri di laboratorio
- La storia di sanguinamento
- I farmaci assunti
- I valori e le preferenze del paziente
- Eventuali terapie alternative
- Il contesto clinico generale

Questa raccomandazione è intesa come guida per la cura del paziente, non per finalità legali. Tuttavia, **può rassicurare i clinici che stanno valutando di non somministrare trasfusioni di piastrine non necessarie, soprattutto quando il loro comportamento potrebbe essere influenzato dal timore di contenziosi legali.**

Il supporto trasfusionale piastrinico nel paziente oncoematologico: aggiornamento dei livelli di evidenza

- E' essenziale promuovere un **uso appropriato della trasfusione piastrinica** basato su **raccomandazioni evidence-based,** in relazione al **contesto clinico complessivo** ed alla luce di eventuale disponibilità di terapie alternative

- Estensione **dell'opportunità di adozione di strategie restrittive alla trasfusione piastrinica**, contribuendo ad una visione volta all'ottimizzazione delle risorse ed alla sicurezza trasfusionale in **assenza di evidenze che mostrino superiorità delle strategie trasfusionali liberali** nel ridurre mortalità o emorragia nei contesti clinici valutati. Ciò è sostenuto anche dall'evidenza di un **numero maggiore di eventi avversi emersi in RCT selezionati nei bracci di trattamento liberali rispetto a quelli restrittivi in diversi contesti**.

- In generale, il panel di esperti ha evidenziato l'importanza di considerare oltre alla conta piastrinica, altri elementi quali sintomi, segni, parametri di laboratorio, anamnesi, ma anche il **punto di vista del paziente n**el decidere se somministrare una trasfusione.

Il supporto trasfusionale piastrinico nel paziente oncoematologico: aggiornamento ICTMG delle linee guida

- ***Aree per attuali e futuri sviluppi di ricerca:***

- Uso ottimale delle piastrine nei pazienti che assumono agenti anticoagulanti e antiaggreganti.
- Impatto delle trasfusioni di piastrine sui processi immunologici e infiammatori, migliore comprensione degli effetti immunomodulatori della trasfusione di piastrine nell'uomo.
- Alternative alla trasfusione piastrinica.
- Caratteristiche del donatore che possono impattare sulla resa trasfusionale: caratteristiche biologiche, età, sesso del donatore (sesso F e citochine infiammatorie).

Il supporto trasfusionale piastrinico nel paziente oncoematologico: aggiornamento ICTMG delle linee guida

ORIGINAL RESEARCH

TRANSFUSION

An audit of platelet transfusions at a tertiary care center: New opportunities for patient blood management with the 2025 AABB/ICTMG platelet guidelines

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Abstract

Background: Platelet transfusions are an important tool to prevent and stop bleeding. Thresholds for pretransfusion platelet counts have been studied in various patient populations, yielding evidence-based guidelines. The Association for the Advancement of Blood and Biotherapies (AABB) collaborated with the International Collaboration for Transfusion Medicine Guidelines (ICTMG) to develop a platelet guideline with new and updated recommendations for different patient populations. The goal of this study was to determine platelet transfusion appropriateness in a large tertiary care hospital, identify common scenarios with deviations from guidelines, and assess the effect that the new AABB/ICTMG guidelines could have on platelet utilization.

Study Design and Methods: A retrospective 8-week audit of platelet transfusions at a university hospital was conducted using institution-specific adjudication criteria. A second audit applied the AABB/ICTMG recommendations. Patient demographics, laboratory values, and transfusion details were collected with an electronic audit tool. Each platelet (PLT) order was adjudicated through manual record review.

Results: A total of 1667 units of apheresis PLT were transfused to 312 patients. Using current hospital guidelines, 163 of 1288 adult (12.7%) and 44 of 379 pediatric orders (11.6%) were deemed inappropriate and 119 adult (9.2%) and 24 pediatric (6.3%) orders were indeterminate. The second audit, which applied recommendations from the 2025 AABB/ICTMG platelet guideline, found multiple PLT transfusions that would be newly noncompliant.

Discussion: There is an incongruency between clinical practice across various specialties and evidence-based platelet guidelines for platelet transfusions. The

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ORIGINAL PAPER

Platelets, Haemostasis and Thrombosis

Opportunities for improving platelet transfusion practice: A large retrospective audit across 22 hospitals

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Summary

Despite evidence-based guidelines to inform platelet transfusion practice, unnecessary platelet transfusion persists. We performed a multicentre retrospective analysis of adults admitted to general medicine, subspecialty medicine and critical care from 1 January 2017 to 30 June 2022. Platelet transfusion guideline compliance was defined as platelet transfusion below 100×10^9/L for neurosurgical, cardiac surgery or extracorporeal membrane oxygenation indications, below 50×10^9/L for invasive procedures, bleeding or therapeutic anticoagulation, and below 10×10^9/L if the patient did not have an immune-mediated thrombocytopenia. We analysed 821 950 patient admissions at 22 hospital sites, identifying 56 825 platelet transfusion events. Overall, 13 199 (23.2%) platelet transfusion events were guideline-non-compliant. High rates of non-compliant transfusions were observed in the context of anti-platelet therapy (n = 1515, 48.5% non-compliant), cardiac surgery (n = 1935, 49.7%), invasive procedures (n = 4648, 29.2%), immune-mediated thrombocytopenia (n = 596, 32.9%) and primary prophylaxis (n = 7370, 47.2%). After adjusting for physician characteristics, there was a lower risk of guideline-non-compliant platelet transfusions at academic than at community hospitals (odds ratio [OR] 0.768, 95% confidence interval [CI] 0.678–0.871, $p < 0.001$). Physician specialty, but not physician gender or years in practice, influenced guideline compliance. These findings underscore the need for targeted intervention to optimize platelet transfusion practices, minimize avoidable transfusion reactions, reduce costs and mitigate platelet shortages.

KEYWORDS
guideline compliance, platelet transfusion, practice audit, quality improvement

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Thank you!

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Scenario clinico 3: Chirurgia cardiovascolare

Nei pazienti sottoposti a chirurgia cardiovascolare (CVS), inclusi quelli in circolazione extracorporea (CPB), qual è l'impatto delle strategie trasfusionali piastriniche restrittive rispetto a quelle liberali su mortalità e sanguinamento?

3 RCT (due in adulti e uno in neonati; Lunen et al. 2018, Simon et al. 1984; Gautam et al. 2020) hanno valutato la trasfusione piastrinica in CVS. Negli adulti, la somministrazione preoperatoria di piastrine **non ha mostrato benefici significativi su complicanze, durata della degenza o mortalità** (ROB basso). Nei neonati sottoposti a cardiochirurgia con CPB, **la tempistica della trasfusione non ha evidenziato differenze in mortalità (ROB basso per mortalità, moderato per sanguinamento). Non sono disponibili RCT in pazienti in ECMO.**

Quattro studi osservazionali aggiustati in CVS non hanno mostrato differenze significative di mortalità tra strategie restrittive e liberali.

La meta-analisi evidenzia assenza di differenze significative nella mortalità negli adulti (OR 0,80 [0,38–1,70]) sia nell'analisi complessiva CVS (OR 0,79 [0,37–1,72]).
Nei neonati l'OR non è stimabile (0 eventi). Complessivamente, le evidenze non dimostrano un chiaro beneficio di una strategia trasfusionale liberale rispetto a una restrittiva in CVS.

Scenario clinico 4: Trombocitopenia da consumo in malattia critica

- **Per i pazienti con trombocitopenia da consumo associata a malattia critica, qual è l'impatto di strategie trasfusionali piastriniche restrittive rispetto a quelle liberali su mortalità e sanguinamento?**
- **I sottogruppi predefiniti erano neonati e adulti.**

- **RCT Negli adulti con dengue, due RCT (Lye et al. 2017; Assir et al. 2013)** non hanno dimostrato **un chiaro beneficio** della trasfusione piastrinica sulla **mortalità per tutte le cause (OR 0,30 [0,01–7,47]).**
- **Nei neonati critici, tre RCT (Curley et al. 2019; Andrew et al. 1993; Kumar et al. 2019;)** hanno valutato **strategie liberali vs restrittive.** Il trial Planet-2/MATISSE (660 neonati) ha evidenziato un aumento di morte o sanguinamento maggiore entro 28 giorni nel braccio liberale (soglia 50×10^9/L vs 25×10^9/L), effetto indipendente dal rischio basale. Studi successivi hanno confermato assenza di beneficio in mortalità con strategie liberali e possibile segnale di eventi avversi in sottogruppi (es. dotto arterioso pervio). **La meta-analisi nei neonati mostra OR 0,69 [0,47–1,03],** suggerendo una **possibile tendenza favorevole alla strategia restrittiva.**
- **Studi osservazionali (adulti ICU non dengue)** In assenza di RCT, **tre studi osservazionali multicentrici** (Warner et al. 2019; He et al. 2022 Xiao et al. 2024) con propensity score (ROB basso) non mostrano un beneficio chiaro della strategia liberale; l'OR combinato per la mortalità **è 0,80 [0,68–0,94].**
- **Conclusione complessiva: Le evidenze disponibili non dimostrano un vantaggio della strategia trasfusionale liberale nei pazienti critici. Nei neonati, dati di buona qualità suggeriscono potenziale danno con soglie più alte; negli adulti, le prove sono limitate e imprecise, ma non indicano un beneficio clinicamente rilevante della trasfusione profilattica più liberale.**

Scenario clinico 5: Emorragia intracranica

- **Nei pazienti con emorragia intracranica (ICH), qual è l'impatto delle strategie trasfusionali piastriniche restrittive rispetto a quelle liberali su mortalità ed emostasi?**
- **I sottogruppi predefiniti includevano pazienti con ICH spontanea e ICH traumatica.**

Il trial PATCH (Baharanglu et al. 2016) ha randomizzato 190 pazienti **con ICH spontanea (S-ICH) in terapia antiaggregante da ≥7 giorni, GCS 8–15**, non candidati a evacuazione chirurgica, **a trasfusione piastrinica entro 6 ore dall'esordio** vs **standard care.** La **mortalità a 3 mesi** è risultata **più elevata nel gruppo piastrine (32% vs 22,6%), con OR 0,62 [0,33–1,19]** (dato espresso come controllo vs piastrine). Il rischio di bias è stato giudicato elevato.

Studi osservazionali: Un solo studio osservazionale multicentrico aggiustato in pazienti con S-ICH in **terapia antiaggregante** non ha evidenziato associazione significativa tra trasfusione piastrinica e mortalità (OR 1,00 [0,13–7,59]), con basso rischio di bias.
Quindici studi osservazionali (n=1745) hanno valutato la **trasfusione piastrinica nell'ICH traumatico associato ad antiaggreganti**; la maggior parte presenta importanti limiti metodologici e problemi di confondimento, con **qualità complessiva bassa e alto rischio di bias**.

Conclusione **Le evidenze disponibili non supportano un beneficio della trasfusione piastrinica nell'ICH associata ad antiaggreganti** e, nel trial PATCH, è emerso un **possibile segnale di danno**. I dati **osservazionali, soprattutto nel trauma, sono di bassa qualità** e **non consentono conclusioni definitive.**

Raccomandazioni Forti

Clinical Review & Education

JAMA | Special Communication

Platelet Transfusion

2025 AABB and ICTMG International Clinical Practice Guidelines

Popolazione	Raccomandazione	Certezza delle evidenze	Sintesi della giustificazione
Pazienti non sanguinanti con trombocitopenia ipoproliferativa in chemioterapia o sottoposti a trapianto allogenico di cellule staminali	Trasfondere piastrine se PLT <10 × 10^3/µL	Moderata	Nessun beneficio con strategie più liberali; soglia pratica e implementabile.
Neonati pretermine senza sanguinamento maggiore	Trasfondere piastrine se PLT <25 × 10^3/µL	Alta	Nessun beneficio con soglia <50 × 10^3/µL; possibile aumento del rischio di effetti collaterali.
Pazienti sottoposti a puntura lombare	Trasfondere piastrine se PLT <20 × 10^3/µL	Moderata	Riduce trasfusioni inutili mantenendo sicurezza clinica.
Pazienti con trombocitopenia da consumo dovuta a dengue senza sanguinamento maggiore	Non trasfondere piastrine	Moderata	Nessun beneficio profilattico e possibile rischio di effetti collaterali.

Raccomandazioni Condizionali

Clinical Review & Education
JAMA | Special Communication
Platelet Transfusion
2025 AABB and ICTMG International Clinical Practice Guidelines

Popolazione	Raccomandazione	Certezza delle evidenze	Sintesi della giustificazione
Pazienti adulti non sanguinanti con trombocitopenia ipoproliferativa sottoposti a trapianto autologo di cellule staminali (SCT) o con anemia aplastica	Strategia senza profilassi piastrinica	Bassa – Molto bassa	Le evidenze derivano da analisi per sottogruppi degli esiti emorragici nei trial clinici.
Pazienti adulti con trombocitopenia da consumo dovuta a malattia critica (non dengue)	Trasfusione piastrinica se PLT <10 × 10^3/µL	Molto bassa	Mancano trial randomizzati diretti; la soglia <10 × 10^3/µL è pragmatica e riduce esposizione a rischi trasfusionali.
Pazienti adulti sottoposti a posizionamento di catetere venoso centrale (CVC) in sedi comprimibili manualmente	Trasfusione piastrinica se PLT ≤10 × 10^3/µL	Moderata – Molto bassa	Soglia pratica che riduce trasfusioni non necessarie.
Pazienti adulti sottoposti a procedure di radiologia interventistica	Trasfusione piastrinica se PLT <20 × 10^3/µL (basso rischio) o <50 × 10^3/µL (alto rischio)	Molto bassa	Le soglie proposte tengono conto del diverso rischio emorragico delle procedure.
Pazienti adulti sottoposti a chirurgia maggiore non neuroassiale	Trasfusione piastrinica se PLT <50 × 10^3/µL	Molto bassa	Soglia pragmatica che considera il potenziale rischio di sanguinamento severo.
Pazienti non trombocitopenici sottoposti a chirurgia cardiovascolare in assenza di emorragia maggiore (incluso bypass cardiopolmonare)	Non trasfondere piastrine	Molto bassa	Le evidenze disponibili non dimostrano beneficio dall'uso profilattico.
Pazienti adulti con emorragia intracranica spontanea o traumatica non operativa con PLT >100 × 10^3/µL (inclusi pazienti in terapia antiaggregante)	Non trasfondere piastrine	Bassa – Molto bassa	I dati disponibili non mostrano beneficio e suggeriscono possibile danno.

La certezza delle evidenze è stata valutata in relazione a soglie predefinite di differenza minima clinicamente importante (MID):

- 2% per la mortalità,
- 20% per il sanguinamento di grado 2–4 (o equivalente)
- 5% per il sanguinamento di grado 3–4 (o equivalente).

Utilizzando il Summary of Findings del metodo GRADE, il panel ha formulato le raccomandazioni secondo il framework GRADE Evidence-to-Decision.

In assenza di accordo unanime, è stata effettuata una votazione del panel, con una soglia di approvazione superiore al 50% per assumere una decisione.

Come sono state formulate le raccomandazioni cliniche in modo metodologicamente rigoroso.
Cosa sono le MID (Minimal Important Differences)?
Sono le differenze minime considerate clinicamente rilevanti.

In pratica: quanto deve cambiare un esito perché il cambiamento sia davvero importante per il paziente.

•Mortalità: una differenza del 2% è considerata clinicamente importante.
•Sanguinamento grado 2–4: differenza del 20%.
•Sanguinamento grado 3–4: differenza del 5%.

Queste soglie aiutano a stabilire se un trattamento produce un beneficio (o danno) significativo.