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14th PAN ARAB TRANSFUSION MEDICINE CONFERENCE QATAR 2024
Inspiring Transfusion Excellence Across Arab Nations

TRANSFUSION STRATEGIES IN MALIGNANT HEMATOLOGY

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Disclosure Statement

I make the following declaration in relation to this CPD Activity :

- This complies with the Ministry of Public Health in Qatar Department of Healthcare Professions MoPH-DHP accreditation standards.
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- There is no plagiarism or copyright infringement.
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OUTLINE

- Transfusion practice in Hematology –Oncology:
  - Blood usage in malignant hematology
  - Restrictive vs Liberal strategies for RC Transfusion
    - Hemoglobin cutoff
    - Single vs double unit
- Platelet Transfusion
- PBM in Hematology Oncology
- Challenges in specific situations:
  - Transfusion support for patients with MDS
  - Mitigation of transfusion in MM patients treated with anti-CD38
- Future perspectives.

INTRODUCTION

- *Blood transfusion* is critical in managing patients with hematologic malignancies, as these patients often experience severe anemia and thrombocytopenia due to both disease and treatment.

- **Hematologic malignancies** create unique challenges for transfusion
  - a high transfusion dependence
  - susceptible to risks like iron overload, alloimmunization, and transfusion-related complications.

- **=> transfusion strategies need to be finely tuned to balance efficacy and minimize risks.**

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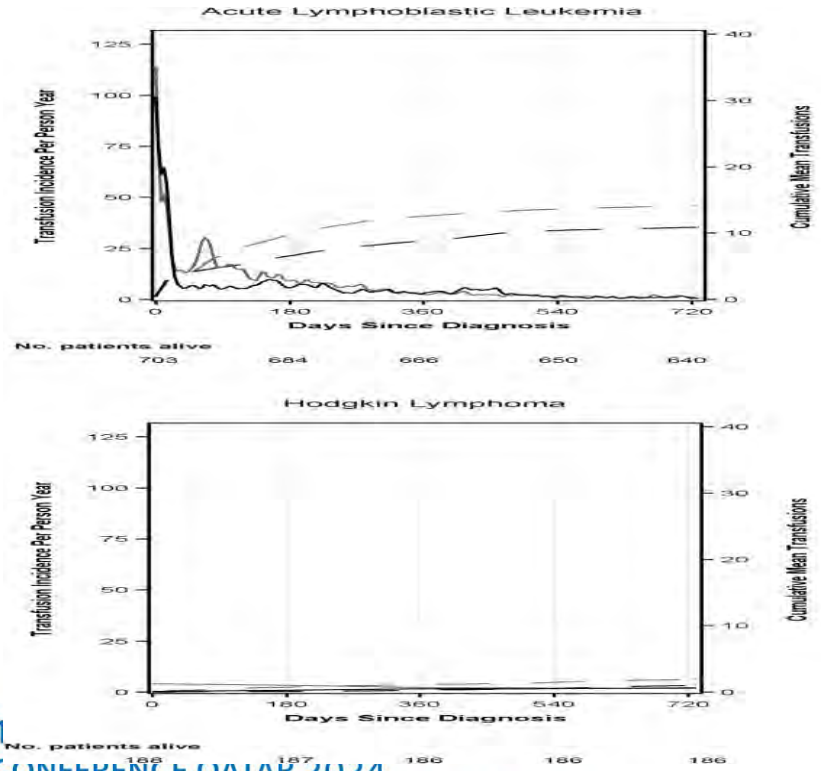
Blood use in hematologic malignancies: a nationwide overview in Sweden between 2000 and 2010

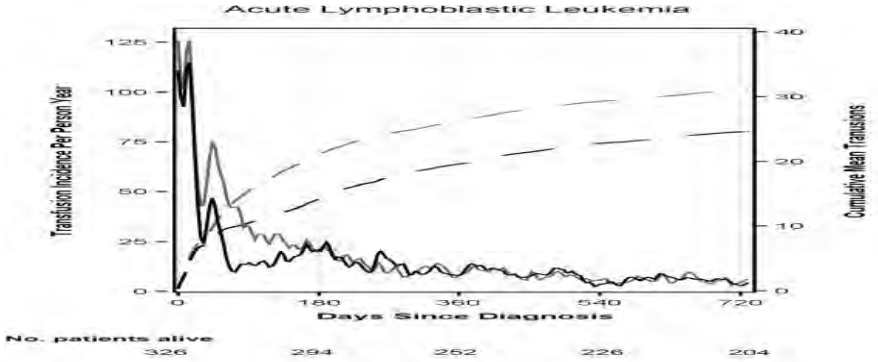
Transfusion incidence (—, RBCs; —, PLTs) and cumulative mean of PLTs (– – –) and RBCs (– – –) measured over time since diagnosis (0-18 years old at diagnosis).

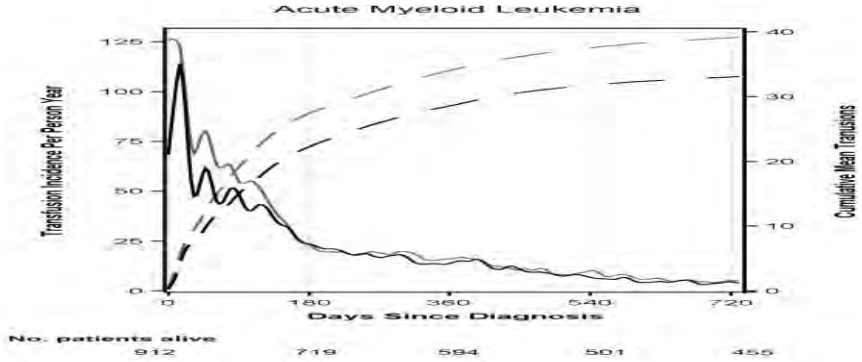


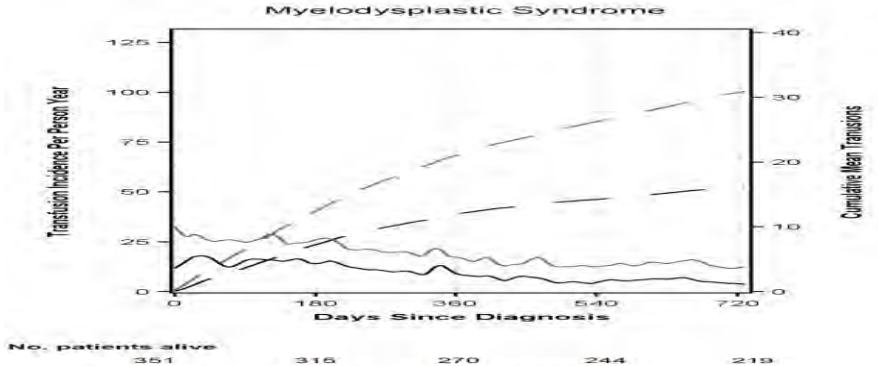
ZHAO et al. Transfusion 2018, Volume: 58, Issue: 2, Pages: 390-401

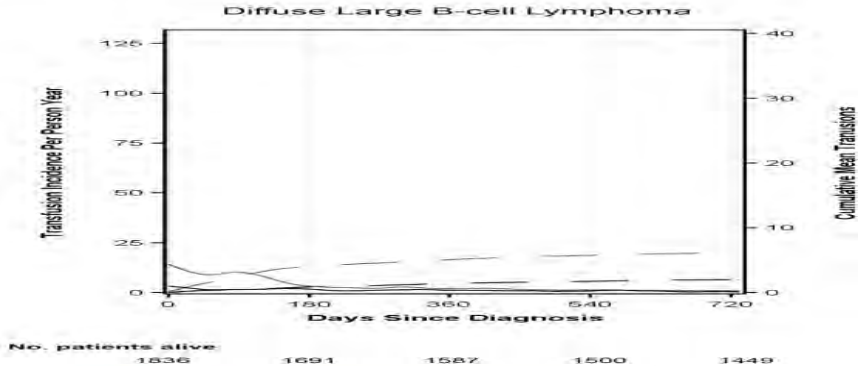
Blood use in hematologic malignancies: a nationwide overview in Sweden between 2000 and 2010

Transfusion incidence (—, RBCs; —, PLTs) and cumulative mean of PLTs (– – –) and RBCs (– – –) measured over time since diagnosis (19-65 years old at dx).





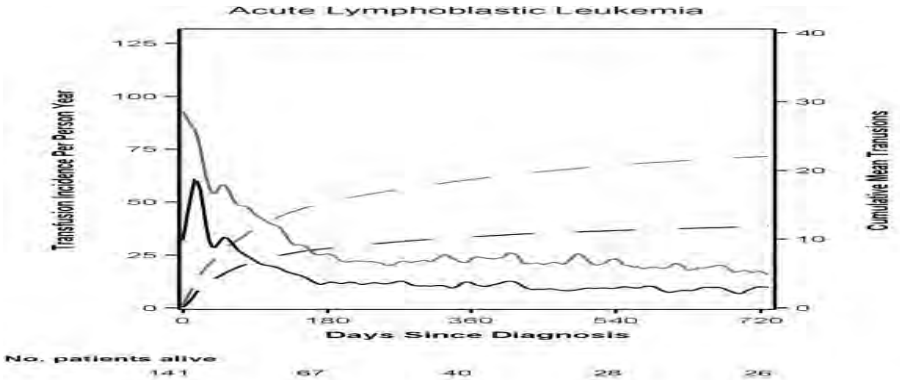


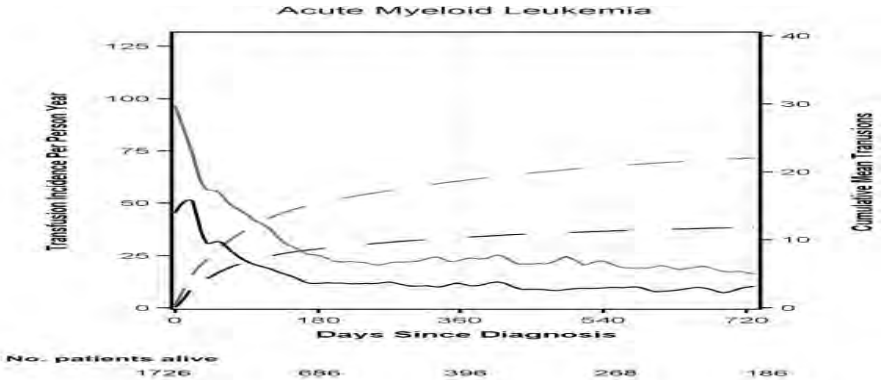


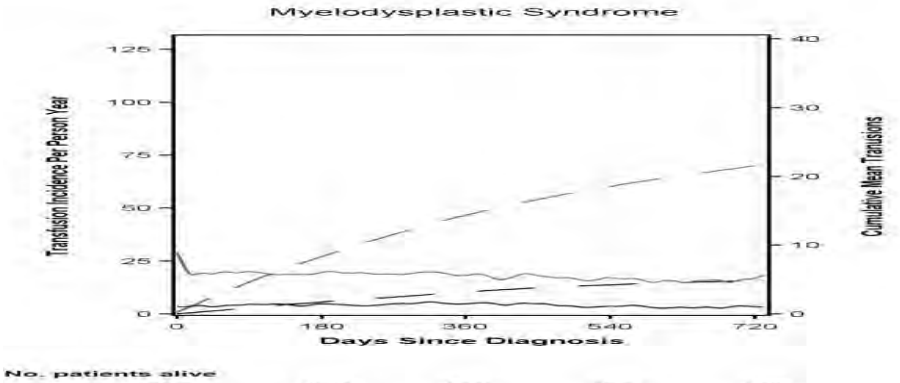
ZHAO et al. Transfusion 2018, Volume: 58, Issue: 2, Pages: 390-401

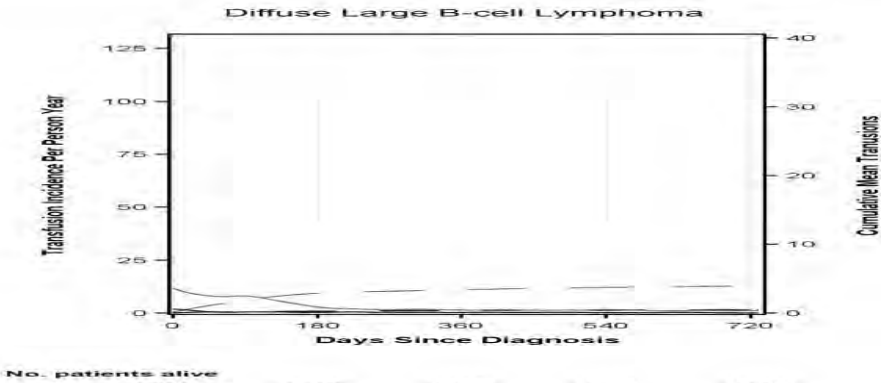
Blood use in hematologic malignancies: a nationwide overview in Sweden between 2000 and 2010

Transfusion incidence (—, RBCs; —, PLTs) and cumulative mean of PLTs (– – –) and RBCs (– – –) measured over time since diagnosis **(>65 years old at diagnosis).**









CONFERENCE QATAR 2024

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ZHAO et al. Transfusion 2018, Volume: 58, Issue: 2, Pages: 390-401

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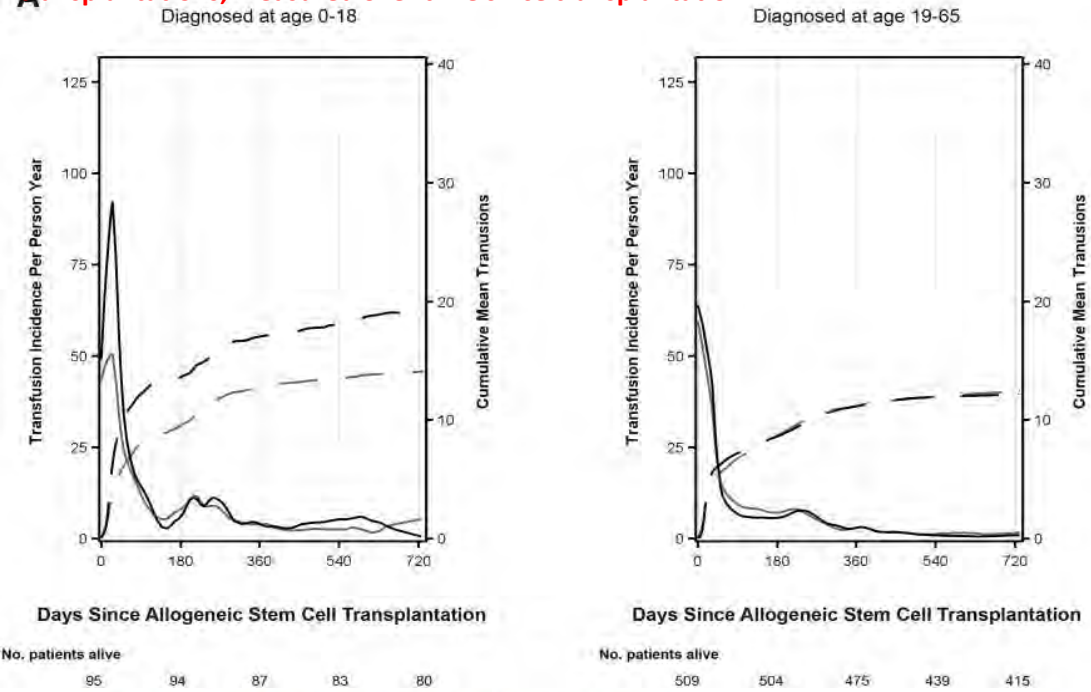
Blood use in hematologic malignancies: a nationwide overview in Sweden between 2000 and 2010

(A) Transfusion incidence (—, RBCs; —, PLTs) and cumulative mean of PLTs (– – –) and RBCs (– – –) in patients that have received allogeneic stem cell transplantations, measured over time since transplantation.

A



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RBC Transfusion Thresholds

- **Liberal Transfusion**: Triggered at Hb >9-10 g/dL.
  - Aims for a higher Hb level, but studies show no additional benefit in mortality or recovery in stable patients

- **Restrictive Transfusion**: Triggered at Hb 7-8 g/dL for stable patients.
  - Proven to reduce transfusion volume without increasing mortality or adverse events.
  - AABB's 2023 guidelines endorse this approach for stable patients, including those with hematologic malignancies.

JAMA | Special Communication

Red Blood Cell Transfusion
2023 AABB International Guidelines

Jeffrey L. Carson, MD; Simon J. Stanworth, MD, DPhil; Gordon Guyatt, MD; Stacey Valentine, MD, MPH; Jane Dennis, PhD; Sara Bakhtary, MD; Claudia S. Cohn, MD, PhD; Allan Dubon, MLS; Brenda J. Grossman, MD, MPH; Gaurav K. Gupta, MD, PhD; Aaron S. Hess, MD, PhD; Jessica L. Jacobson, MD; Lewis J. Kaplan, MD; Yulia Lin, MD; Ryan A. Metcalf, MD; Colin H. Murphy, MD; Katerina Pavenski, MD; Micah T. Prochaska, MD; Jay S. Raval, MD; Eric Salazar, MD, PhD; Nabiha H. Saifee, MD, PhD; Aaron A. R. Tobian, MD, PhD; Cynthia So-Osman, MD, PhD; Jonathan Waters, MD; Erica M. Wood, MD; Nicole D. Zantek, MD, PhD; Monica B. Pagano, MD

Hgb<7g/dL: stable hospitalized adults including ICU.

Hgb<8g/dL: prior cardiovascular disease, cardiac & orthopedic surgery

These recommendations do not apply to:

- **Severe thrombocytopenia, hematology-oncology treatment and risk of bleeding**
- **Chronic transfusion Dependent anemia.**

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[Intervention Review]

Restrictive versus liberal red blood cell transfusion strategies for people with haematological malignancies treated with intensive chemotherapy or radiotherapy, or both, with or without haematopoietic stem cell support

Michael Radford[1,2], Lise J Estcourt[3,4], Emily Sirotich[5], Tyler Pitre[6], Joanne Britto[7], Megan Watson[6], Susan J Brunskill[4,8], Dean A Fergusson[9], Carolyn Dorée[4,8], Donald M Arnold[10,11]

2024: Nine studies were included: eight RCTs and one NRS. 644 participants were included in analysis from six completed RCTs (n=560) and one completed NRS (n=84).

A restrictive transfusion strategy demonstrated a reduction in RBC usage, while there may be no impact on mortality. Definite conclusions are challenging

There is a need for larger and methodologically better designed and executed studies.

There is insufficient evidence to answer this review's primary outcome.

Further RCTs are required overall, particularly trials inclusive of pediatric participants.

Restrictive compared with liberal for adults with haematological malignancies treated with intensive chemotherapy or radiotherapy, or both, with or without haematopoietic stem cell support

Patient or population: Adults with haematological malignancies treated with intensive chemotherapy or radiotherapy, or both, with or without haematopoietic stem cell support
Setting: Hospitals, haematology centres
Intervention: Restrictive RBC transfusion RCTs
Comparison: Liberal RBC transfusion RCTs

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with liberal RBC transfusion RCTs	Risk with restrictive RBC transfusion RCTs				
All-cause mortality at 31 to 100 days	19 per 1000	**19 per 1000** (5 to 70)	**RR 1.00** (0.27 to 3.70)	451 (3 RCTs)	⊕⊖⊖⊖ VERY LOW[a,b]	
Quality of life (0 to 3 months)	No appreciable difference seen in QOL between a restrictive and liberal transfusion policy. See Table 1			431 (3 RCTs)	⊕⊖⊖⊖ VERY LOW[c,d]	QOL was heterogeneously reported and the summary calculation was unable to be completed. QOL was the primary outcome in Tay 2020.
Number of participants with any bleeding (0 to 3 months)	483 per 1000	**440 per 1000** (377 to 512)	**RR 0.91** (0.78 to 1.06)	448 (3 RCTs)	⊕⊕⊖⊖ LOW[c,e]	Unpublished data provided by authors for Tay 2020
Number of participants with clinically significant bleeding (0 to 3 months)	282 per 1000	**265 per 1000** (208 to 335)	**RR 0.94** (0.74 to 1.19)	511 (4 RCTs)	⊕⊕⊖⊖ LOW[c,e]	Unpublished data provided by authors for Tay 2020 and Byun 2023 (D), Byun 2023 (S)
Serious infections (0 to 3 months)	192 per 1000	**230 per 1000** (178 to 297)	**RR 1.20** (0.93 to 1.55)	451 (3 RCTs)	⊕⊕⊖⊖ LOW[a,c]	Unpublished data provided by authors for all included RCTs
Length of hospital admission (days) (0 to 3 months)	No difference seen in length of admission between a restrictive and liberal transfusion policy. See Table 2			388 (2 RCTs)	⊕⊕⊕⊖ MODERATE[c,f]	Length of hospital admission heterogeneously reported and summary calculation was unable to be completed.
Hospital readmission (0 to 3 months)	Study population 167 per 1000	**148 per 1000** (87 to 250)	**RR 0.89** (0.52 to 1.50)	299 (1 RCT)	⊕⊕⊖⊖ LOW[c,f,g]	

***The risk in the intervention group** (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **IQR:** Interquartile range; **OR:** Odds ratio; **QOL:** Quality of life; **RR:** Risk ratio; **SOF:** Summary of findings;

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Single vs Double-Unit Transfusion in Patients With Hematological Disorders Undergoing Chemotherapy or Stem Cell Transplantation: A Systematic Review And Meta-Analysis

Catalina Herrán-Fonseca[a,*], Laura Jekov[b], Carlotta Persaud[c], Fahad Alabbas[d]

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[c] University Hospital of the West Indies, Internal Medicine, Faculty of Medical Sciences, Mona, Kingston, Jamaica
[d] Scientific Research Center and Department of Pediatric Hematology and Oncology, Prince Sultan Medical, Military City, Riyadh, Saudi Arabia

Table 1
Baseline characteristics of included studies.

Study	Design	Patients, n DB/ SN	Male, % DB/ SN	Age[b], y DB/SN	AML, % DB/SN	ALL, % DB/SN	LYM, % DB/SN	Others, % DB/SN	BS Hb[b], g/dL DB/SN	Transfusion trigger, g/dL
Avdic et al.[22]	Non-RCT	166/193	60/58	51/56	NA	NA	NA	100/100	NA	NA
Berger et al.[23]	Non-RCT	77/62	54/48	51/47	73/74	8/18	10/6	9/2	8.9/8.9	≤ 6
Bowman et al.[24]	Non-RCT	147/126	61/52	55/53	40/40	8/4	37/40	15/15.9	9.5/9.7	< 8
Chantepie et al.[25]	Non-RCT	186/126[c]	60/56	54/53	53.8/61.1	11.8/12.7	20.4/15.9	14/10.3	10.3/10.3	< 8[c]
Lamarche et al.[26]	Non-RCT	65/69	60/51	62/56	30.8/30.4	4.61/13	18.5/20.2	44.6/30.4	8.2/8.3	≤ 7[c] vs ≤ 8[c]
Solves et al.[a,27]	Non-RCT	60/60	NA	NA	NA	NA	NA	100/100	NA	NA
Chantepie et al.[28]	RCT	120/125	46/55	56/54	60/58.1	12/14.5	18.3/14.5	10/12.9	7.92/7.89	≤ 8
Byun et al.[f,29]	RCT	45/46	64/58	54/52	100/100	-	-	-	10.1/10.7	≤ 7 vs ≤ 8

[a] conference abstract
[b] mean or median
[c] trigger was that morning Hb level OR the presence of symptoms of anemia
[d] received DB
[e] received SN
[f] patients were randomized into 4 groups by transfusion trigger and units/transfusion; DB: double-unit transfusion; SN: single-unit transfusion; AML: acute myeloid leukemia; ALL: acute lymphoblastic leukemia; LYM: lymphoma; BS Hb: baseline hemoglobin; NA: not available; RCT: randomized controlled trial.

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JID: YTMRV [mNS;November 13, 2024;3:23]
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Single vs Double-Unit Transfusion in Patients With Hematological Disorders Undergoing Chemotherapy or Stem Cell Transplantation: A Systematic Review And Meta-Analysis

Catalina Herrán-Fonseca[a,*], Laura Jekov[b], Carlotta Persaud[c], Fahad Alabbas[d]

[a] Department of Medicine, Faculty of Health Sciences, Universidad Autónoma de Bucaramanga, Floridablanca, Colombia
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Single unit transfusion is associated with lower hemoglobin levels at discharge.
Single unit transfusion is associated with less RBC units used per admission.
No significant difference in hospital stay, bleeding, adverse events, or mortality.
Future studies should assess transfusions in transplant subgroups.
these studies should evaluate key transfusion-related endpoints, such as quality of life and the number of concurrent transfusions during hospitalization

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DOI: 10.1111/trf.16257

RESEARCH METHODOLOGY

TRANSFUSION

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

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FULL TEXT ARTICLE

Platelet Transfusion

Shan Yuan MD and Zaher K. Otrock MD

Clinics in Laboratory Medicine, 2021-12-01, Volume 41, Issue 4, Pages 621-634, Copyright © 2021 Elsevier Inc.

An Update on Indications and Guidelines

- Published platelet transfusion guidelines partly lack recommendations or differ in the platelet threshold recommendations in some clinical situations.
- Platelet transfusion guidelines concur with strongly recommending prophylactic platelet transfusion for severe hypoproliferative thrombocytopenia (10,000/mL) following chemotherapy or allogeneic bone marrow transplantation.
- Platelet transfusion decisions should be weighed against the risks of transfusions and the availability of platelet products.

Prophylactic platelet transfusion thresholds according to different guidelines

Indication/Procedure	Platelet Transfusion Threshold (Level of Evidence) AABB[6]	ASCO[8]	BSH[7]
Major surgery	<50,000/μL (WR)	<40,000–50,000/μL (WR)	<50,000/μL (WR)
CNS or ophthalmic surgery	NR	NR	<100,000/μL (WR)
Central venous catheter placement	<20,000/μL (WR)	NR	<20,000/μL (SR)
Lumbar puncture	<50,000/μL (WR)	NR	<40,000/μL (WR)
Epidural or spinal anesthesia	NR	NR	<80,000/μL (WR)
Bone marrow aspirate or trephine biopsy	NR	NR	Platelet transfusion not indicated (SR)
Percutaneous liver biopsy	NR	NR	<50,000/μL (MR)
Hypoproliferative thrombocytopenia following chemotherapy or allogeneic BMT	≤10,000/μL (SR)	<10,000/μL (SR)	<10,000/μL (SR)
Hypoproliferative thrombocytopenia following autologous BMT	NR	Platelet transfusion not indicated (MR)	Platelet transfusion not indicated (MR)
Chronic bone marrow failure (including patients on low-dose oral chemotherapy or azacitidine)	NR	NR	Platelet transfusion not indicated (MR)
Chronic bone marrow failure on intensive chemotherapy	NR	NR	<10,000/μL (SR)

Abbreviations: AABB, American Association of Blood Banks (former name); ASCO, American Society of Clinical Oncology; BMT, bone marrow transplant; BSH, British Society for Haematology; CNS, central nervous system; NR, no recommendation is provided; MR, moderate recommendation; SR, strong recommendation; WR, weak recommendation.

VoxSanguinis
The International Journal of Transfusion Medicine
ISBT International Society of Blood Transfusion
Vox Sanguinis (2019) **114**, 517–522

DOI: 10.1111/vox.12785

ORIGINAL PAPER

One-unit compared to two-unit platelet transfusions for adult oncology outpatients

Eric A. Gehrie,[1,2] Steven M. Frank,[3,4] Mereze Visagie,[3] Mary K. Grabowski,[1] Aaron A. R. Tobian,[1] Valerie L. Strockbine,[1] Vincent M. DeMario,[3] Courtney E. Lawrence,[1] Bryan C. Hambley,[5] Kristin Uglik,[1] Paul M. Ness,[1] Amy E. DeZern[5] & Evan M. Bloch[1]

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A retrospective chart review was conducted of all adult oncology patients who received an outpatient platelet transfusion over a 16-month period (July 2016–November 2017). A total of 8467 platelet transfusions were administered to 602 patients during the study period.

Conclusion:

Among adult, oncology outpatients that were transfused interchangeably with one or two units of platelets, transfusion with two platelets did not offer a durable improvement in platelet count or impact the subsequent transfusion schedule.

Note: Low content platelet likely in pathogen reduced products

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PBM in Hematology Oncology: Causes of Anemia

JULY 2020

PATIENT BLOOD MANAGEMENT IN HEMATOLOGY AND ONCOLOGY
By Mark T. Friedman, DO
Icahn School of Medicine, Mt. Sinai

- Anemia is frequently induced via
  - direct deficiency: marrow infiltration/ coagulopathy-related bleeding
  - indirect (e.g., anemia of chronic disease related to inflammation and autoimmune hemolytic anemia) effects.

- Anemia and thrombocytopenia are two common side effects of cancer treatment (chemotherapy and radiation therapy).

PBM in Hematology Oncology: Strategies

JULY 2020

PATIENT BLOOD MANAGEMENT IN HEMATOLOGY AND ONCOLOGY

By Mark T. Friedman, DO
Icahn School of Medicine, Mt. Sinai

- Strategies to minimize exposure to blood products should be considered in light of the risks and complications of blood transfusion.
- Long-term risks of alloimmunization, iron overload and transfusion-related immunomodulation (TRIM)
- Patient blood management (PBM) strategies that may be employed to reduce transfusions in cancer patients in both the inpatient and outpatient settings

PBM in Hematology Oncology: Strategies

JULY 2020

PATIENT BLOOD MANAGEMENT IN HEMATOLOGY AND ONCOLOGY

By Mark T. Friedman, DO

Icahn School of Medicine, Mt. Sinai

- Adherence to stricter transfusion guidelines:
  - use of a hemoglobin level closer to 7.0 g/dL as the transfusion trigger for stable patients with anemia
  - transfusion of single rather than multiple RBC units in nonbleeding patients.
- A computer-physician-order-entry (CPOE) system with clinical-decision support (CDS)
- Identification of “PBM champions” to serve as role
- Important role of data collection and analysis in the development of a PBM program.

PBM in Hematology Oncology: specific Strategies

JULY 2020

PATIENT BLOOD MANAGEMENT IN HEMATOLOGY AND ONCOLOGY

By Mark T. Friedman, DO
Icahn School of Medicine, Mt. Sinai

- **Erythropoiesis-Stimulating Agents (ESAs)**:
  - Used to raise hemoglobin minimally to avoid transfusions; discontinued if ineffective in 6–8 weeks.
  - reduce transfusion dependence for chemotherapy-induced anemia when cancer treatment is not curative (ASCO and ASH guidelines).
  - Not recommended for most nonchemotherapy-induced anemias
  - May be offered to selected patients with myelodysplastic syndromes (MDS).
  - Associated Risks of thromboembolism; to be used cautiously, aiming to achieve the lowest effective Hb level.

- **Iron Therapy:** IV iron, often combined with ESAs, enhances Hb response, reducing the need for RBC transfusions even if iron deficiency is not present.

PBM in Hematology Oncology: specific Strategies

JULY 2020

PATIENT BLOOD MANAGEMENT IN HEMATOLOGY AND ONCOLOGY

By Mark T. Friedman, DO
Icahn School of Medicine, Mt. Sinai

Thrombopoiesis-Stimulating Agents (TSAs):
Effective in some chemotherapy-induced thrombocytopenia cases but carry risks such as disease progression in MDS.

Future Directions:

- Targeted therapies like immunotherapy and CAR-T may reduce the need for transfusions by minimizing marrow suppression.
- *Luspatercept is a transforming growth factor β (TGF-β) ligand trap, which neutralizes TGF-β to suppress SMAD 2/3 signaling and promote terminal erythroid differentiation.*

PBM in Hematology Oncology: specific Strategies

Prioritization of PBM during the pandemic or a blood shortage
help sustain the blood supply and lead to improved patient outcomes

frontiers in Oncology

PERSPECTIVE
published: 15 March 2021
doi: 10.3389/fonc.2021.564383

Changing Management of Hematological Malignancies With COVID-19: Statement and Recommendations of the Lebanese Society of Hematology and Blood Transfusion

Ahmad Ibrahim [1,2,3,4*], *Peter Noun* [5,6], *Charbel Khalil* [7,8] *and Ali Taher* [4,9,10]

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FOCUS ON QUALITY

Optimizing Utilization of Blood Products in the Hematologic Malignancy Clinic: Less Is More

Adam F. Binder, MD[1]; Katy Loos[2]; Alexander Xu, BA[3]; Alexis R. Peedin, MD[2]; Usama Gergis, MD[1]; Julie Katz Karp, MD[2]; and Lindsay Wilde, MD[1]

Interventions in sequence to allow for appropriate analysis of each:

- **March2020:**
  - **transfusion medicine physicians reviewing all RBC orders for patients with hemoglobin>8g/dL and all multiunit orders for platelet and RBCs in real time & discussion with ordering physicians**
- **May 2020**
  - **Updated wording of blood product orders in the electronic health record system**
    - Including the expected post-transfusion increment for one unit of platelet or RBC administered and recommendation for single unit and threshold
- **October2020**
  - **Updated blood product transfusion guidelines for patients with HMs were approved and posted on the HM intranet page.**

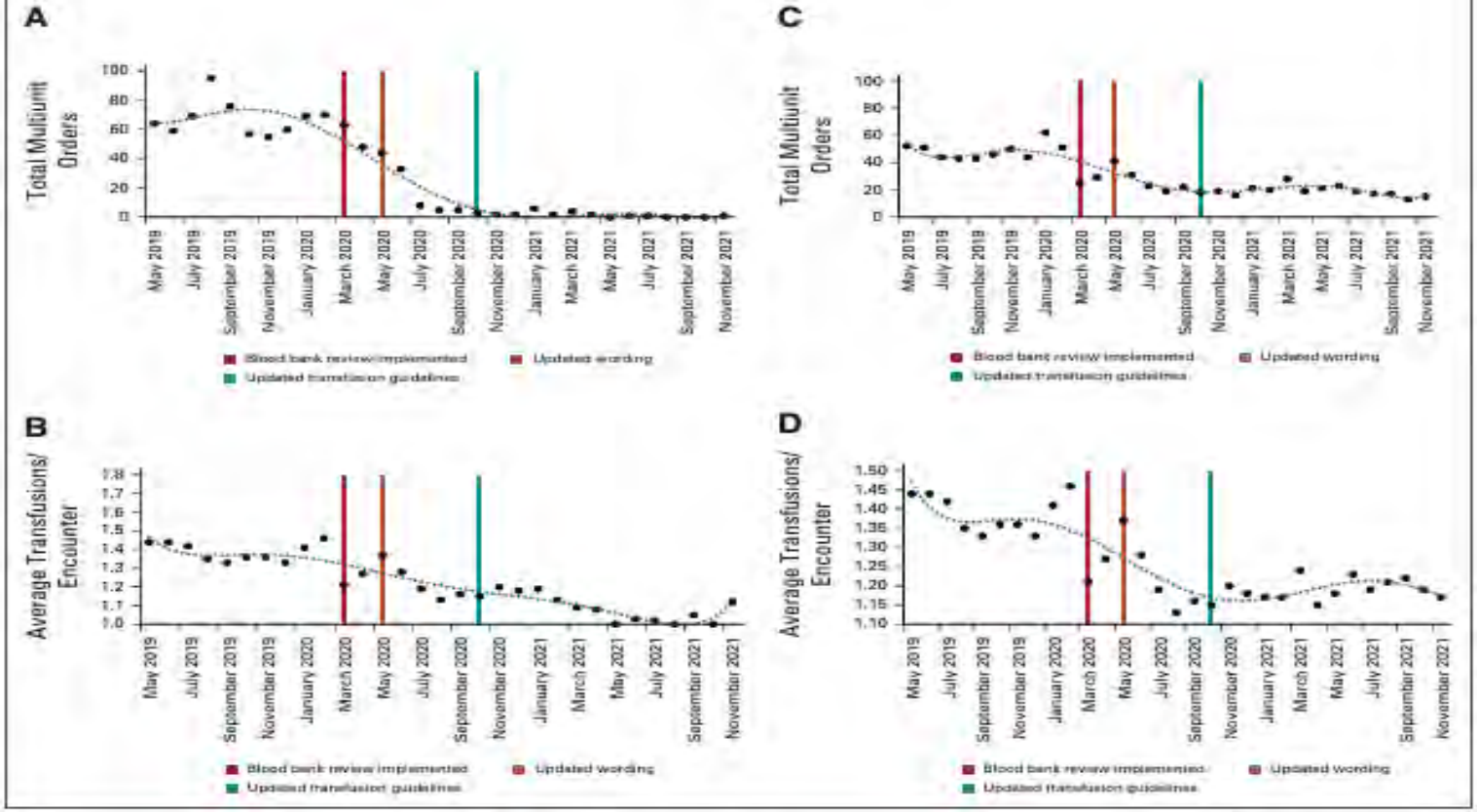

FIG 1. Outpatient transfusion metrics for platelets and RBCs: (A) total multiunit transfusion orders for platelets, (B) average platelet transfusions per encounter, (C) total multiunit transfusion order for RBC, and (D) average RBC transfusions per encounter. pRBC, packed RBC.

Adam F et al. JCO Oncol Pract 2022 02-22

FOCUS ON QUALITY

Optimizing Utilization of Blood Products in the Hematologic Malignancy Clinic: Less Is More

Adam F. Binder, MD[1]; Katy Loos[2]; Alexander Xu, BA[2]; Alexis R. Peedin, MD[2]; Usama Gergis, MD[1]; Julie Katz Karp, MD[2]; and Lindsay Wilde, MD[1]

TABLE 1. Outcomes of RBC and Platelet Transfusion Orders for Patients With Cancer at Preperiods and Postperiods

Outcome	Preperiod[a]	Postperiod[b]	P[c]
Platelets			
Total number of transfusions	1,665	1,152	
Total transfusions monthly, mean (SD)	166.5 (26.5)	115.2 (26.1)	.0014[d]
Multiunit orders monthly, mean (SD)	67.4 (11.8)	21.3 (23.3)	.00023[e]
Average orders per encounter, mean (SD)	1.68 (0.073)	1.264 (0.273)	.00021[f]
pRBC			
Total number of transfusions	1,685	1,542	
Total transfusions monthly, mean (SD)	168.5 (16.6)	154.2 (16.4)	.145
Multiunit orders monthly, mean (SD)	48.6 (5.9)	24.3 (7.6)	.00007[g]
Average orders per encounter, mean (SD)	1.39 (0.049)	1.21 (0.073)	.00002[d]
HgB content, g/dL			
< 7	367	533	
7-8	975	810	
> 8	341	197	
Average, g/dL	7.47	7.22	

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OUTLINE

- Transfusion practice in Hematology –Oncology:
  - Blood usage in malignant hematology
  - Restrictive vs Liberal strategies
    - Hemoglobin cutoff
    - Single vs double unit
- PBM in Hematology Oncology
- Challenges in specific situations:
  - Transfusion support for patients with MDS
  - Mitigation of transfusion in MM patients treated with anti-CD38
- Future perspectives.

Transfusion support for patients with MDS

Anemia and Thrombocytopenia in MDS:

- Anemia is universal in MDS and associated with poor QoL and cardiac complications.
- Thrombocytopenia, common in MDS, increases bleeding risk and worsens prognosis.

Goals of Transfusion Support:

- Alleviate anemia and thrombocytopenia symptoms.
- Prevent complications like bleeding and cardiac stress.
- Improve functional outcomes and QoL.

Optimal Transfusion Practices:

- Tailored strategies rather than one-size-fits-all approaches.
- Questions remain about ideal hemoglobin thresholds and transfusion schedules.
- Emerging evidence suggests a liberal transfusion policy may benefit QoL.

Transfusion support for patients with MDS

Hemoglobin Thresholds for Transfusion:

- Lack of data on chronic anemia in MDS patients.
- REDDS and RBC-ENHANCE Studies indicate that liberal thresholds improve QoL but require more frequent transfusion

  restrictive transfusion threshold *(maintaining hemoglobin levels of 85–100 g/L) or a* ***liberal transfusion threshold*** *(maintaining hemoglobin levels of 110–125 g/L).*

Challenges in Transfusion:

- Complications include transfusion reactions, alloimmunization, and iron overload.
- Iron chelation may improve outcomes but is underutilized due to cost and side effects.

Stanworth SJ et al. Br J Haematol, 189: 279-290. Buckstein et al. Transfusion. 2024;64:223–235.

Transfusion support for patients with MDS

Therapeutic Options for MDS:

- Treatments include erythropoiesis-stimulating agents (ESAs), hypomethylating agents, and stem cell transplantation.

- Transfusions remain central, especially for lower-risk patients.

- Current standard of transfusion care in transfusion-dependent MDS : regular red blood cell transfusions (2–4) units every 3–4 weeks.

Mo A, Wood E. Shortt J. Transfusion. 2024; 64(2): 236–247.

Transfusion support for patients with MDS

Therapeutic Options for MDS:

- The REDDS-2 Study is a randomized clinical trial that will assess the feasibility of a weekly red cell transfusion schedule (using matched red cells) and its impact on quality of life and physical function outcomes in patients with transfusion-dependent MDS.

- Luspatercept: 58.5% achieved transfusion independence for at least a 12-week consecutive period within the first 24 weeks, along with an increase in hemoglobin of at least 1.5 g/dL. This contrasted with only 31.2% of patients receiving epoetin alpha (phase 3 COMMANDS trial)

Mo A, Wood E. Shortt J. Transfusion. 2024; 64(2): 236–247.
https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-luspatercept-aamt-anemia-adults-mds

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Mitigation of transfusion in MM patients treated with anti-CD38

- **Background**: Monoclonal antibodies (mAbs) like **Daratumumab (anti-CD38)** are used in treating multiple myeloma.

- They may interfere with pre-transfusion blood compatibility testing=> challenging transfusion scenarios.
  - Binds CD38 on both myeloma cells **and red blood cells** (RBCs).
  - Anti-CD38 drugs may lead to positive antibody screens unrelated to the patient's condition.
  - Causes **false-positive antibody screens**, masking alloantibodies in blood tests.
  - Effect on testing persists **up to 6 months after treatment**.

Mitigation of transfusion in MM patients treated with anti-CD38

I. RBCs with lacking, diminished or destroyed CD38 antigens used in pre-transfusion testing

Long standing technique

Highly reliable as a blood bank procedure

Training and competency of technologists well established

- **Dithiothreitol (DTT)**
  Denatures CD38 antigen
  DTT treated donor cells can be used for a crossmatch
  Caution needed as DTT denatures Kell and other clinically significant antigens
- **Trypsin/Papain**
  Cleaves CD38 antigen
  Destroys many other significant RBC antigens
  Less reliable than DTT
- **Cord blood cells**
  Lacking CD38 antigen
  Cord blood cell antigen panels reagent are not routinely available
- **In (Lu) RBCs**
  Lacking CD38 antigen
  Rare and not routinely available reagent cells
- **Panels from RBC of Daratumumab treated Patients**
  Not standardized

II. Blocking CD38 antigens on reagent and donor cells

Not recognized by antihuman globulin (AHG)

- **Anti-CD38 F(ab')2 fragments**
  Bind and mask CD38 on reagent cells
  Not commercially available.
- **Anti-CD38 + monospecific anti-human IgG**
  Pre-Adsorbed RBCs with Daratumumab blocked with mono-specific anti-human IgG competing out AHG
- **Non-human anti-CD38**
  Not recognized by AHG

III. Neutralization of anti-CD38 antibody in patient plasma prior to IAT testing

Routine blood bank testing providing adequate anti-CD38 antibody neutralization with:

- **Anti-idiotype antibody**
  Commercially available
  Not typically available in standard blood bank inventory
- **Soluble CD38 antigen**
  Requires large amounts of soluble CD38 required for neutralization of therapeutic daratumumab levels
  Less efficacious than anti-idiotype
  Method not standardized
- **CD38 antigen from myeloma lines lysate/stroma**
  Difficult to standardize methodology
- **Anti-CD38 aptamers**

IV. Extended patient antigen typing with phenotypical matching of RBC units

Delays in transfusion if extended-match units difficult to acquire

Historically a method of choice for patients with known auto- and allo-antibodies

Antibody identification testing not required when matched units available

Serologic Crossmatch will be incompatible due to presence of Anti-CD38

- **Extended RBC phenotype of recipients**
  To be performed prior initiating daratumumab therapy
- **RBC genotyping**
  Can be performed at any time
  Universal genotyping is expensive
  Extended matching not necessary if:
  negative antibody screen and no prior history of auto- and allo-antibodies

Abbreviations: AHG, antihuman globulin; DTT, dithiothreitol; IAT, indirect antiglobulin test; RBC, red blood cells.

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Nedumcheril et al. *Journal of Blood Medicine 2021:12 327–336*

Mitigation of transfusion in MM patients treated with anti-CD38

- **Recommended Testing Before Therapy**:
  - Baseline ABO/D typing, antibody screening, direct antiglobulin test (DAT), and phenotype/genotype for key antigens (Rh, Kell, MNS, etc.).

- **During Therapy**:
  - Treat reagent RBCs with **dithiothreitol (DTT)** to bypass Daratumumab interference.
  - Use DTT-treated RBCs for antibody screening and **ensure Kell antigen-matched** units for transfusion.
  - Grifols sCD38 has received the CE mark November 2023

Mitigation of transfusion in MM patients treated with anti-CD38

- **Transfusion Management Recommendations:**
  - **Elective and Non-Urgent Transfusions**:
    - Use ABO, Rh, and K-compatible blood after antibody testing.
    - Provide irradiated blood if required.
  - **Emergency Situations**:
    - Administer uncrossmatched ABO and D-compatible blood if needed.

- Effective communication and preemptive testing

- Close collaboration among healthcare providers and adherence to specific testing protocols

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Hemasphere (2022) 6:2

EHA Aims to highlight achievements in the diagnostics and treatment of blood disorders to better inform European policy makers and other stakeholders about the urgent clinical and scientific needs and priorities in the field of hematology.

Summary of main research and policy priorities:

- Continued need for evidence for safe and effective use of blood components, including how donor/donation characteristics impact on outcomes after transfusion. E.g. Better **diagnostic tests and biomarkers** identifying transfusion needs remain an area of research need.
- Strategies for addressing **prevention and management of alloimmunization**, and the role **of genotyping** of donors and patients for matching.
- Defining evidence-informed indications for **therapeutic apheresis** and use of immunoglobulins, including dose and formulations alongside addressing self-sufficiency at a European level.
- Initiatives on safety and hemovigilance should specifically include donor vigilance of blood, plasma, and cell donation.
- Research in new areas of **cellular therapies** and the place of **ex vivo generation** and **storage** of blood cells.

Anticipated impact of the research

- New methodological approaches to trial design, incorporating routine data
- Big Data, AI: access and analyze comprehensive real-world data through electronic medical record systems
- Cost-effectiveness is an increasingly important objective for research given the costs (alongside unwanted effects) of unnecessary transfusions.

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