

Transfusion Guidelines: Less is Best (usually)

Nursing Transfusion Medicine
Boot Camp

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Conflicts of Interest

- No commercial conflicts to declare
- ORBCoN, for which I am a consultant, is funded by the Ministry of Health and Long Term Care
- I acknowledge a preference for a restrictive approach to transfusion whenever possible



Objectives

1. Explain the rationale for using restrictive transfusion practices.
2. Describe the recommendations for transfusing red cells, plasma, and platelets in the Choosing Wisely Canada statements.
3. List the Quality Indicators in the Ontario Transfusion Quality Improvement Plan.



Question 1

What is the recommended red cell transfusion threshold for stable adult inpatients, including patients in the ICU?

1. Hb 60 g/L
2. Hb 70 g/L
3. Hb 80 g/L
4. Hb 90 g/L
5. Hb 100 g/L



Question 2

What are the two quality indicators for red cell transfusion in the Ontario Transfusion Quality Improvement Plan?
(choose 2)

1. % transfusions with pre-transfusion Hb < 70 g/L
2. % transfusions with pre-transfusion Hb < 80 g/L
3. % single unit transfusions (1 unit ordered at a time)
4. % transfusions with documented consent on the chart
5. % RBC inventory wasted by the hospital for any reason



Transfusion Guidelines

Well-designed, appropriately powered randomised controlled trials



Systematic reviews



Clinical practice guideline (CPG)



**CPG endorsed by professional organisations
and/or health authorities**



Evidence-based medicine



Optimised patient care



Improved patient outcomes



Evaluating Evidence

- Grades of Recommendation Assessment, Development, and Evaluation (GRADE)
- Developed by an international working group starting in 2000, published in the BMJ in 2008
- A system for evaluating the **quality** of evidence supporting a recommendation, and the **strength** of the recommendation



GRADE System

Quality of evidence	Strength of recommendation
High (randomised controlled trial)	Strong
Moderate	
Low (observational study)	Weak
Very low	



Randomised Controlled Trial (RCT)

Transfusion Requirements in Critical Care (TRICC) Trial

829 ICU patients with Hb < 90



416 restrictive strategy
Transfused at Hb < 70
Hb maintained at 70-90

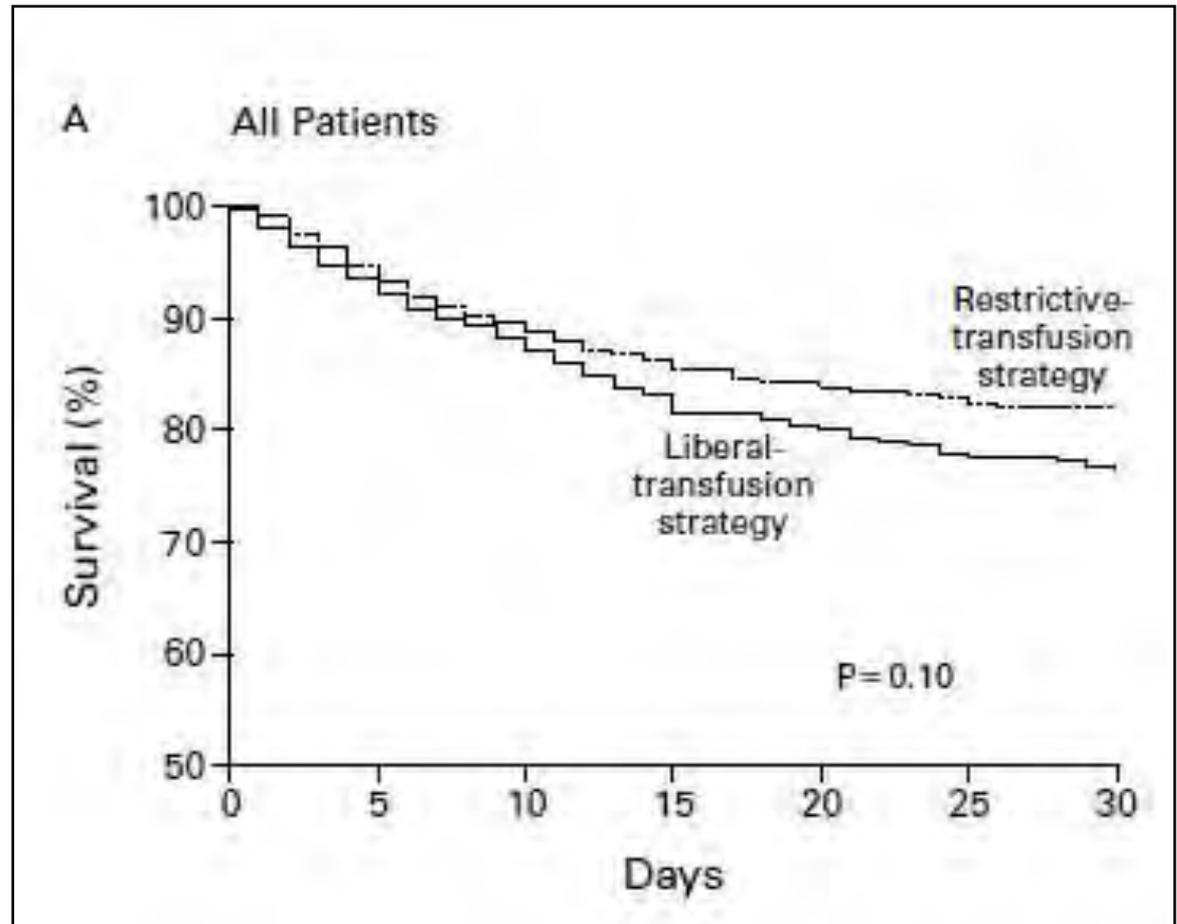
413 liberal strategy
Transfused at Hb < 100
Hb maintained at 100-120

Primary End points:
Death from all causes at 30 days
Severity of organ dysfunction



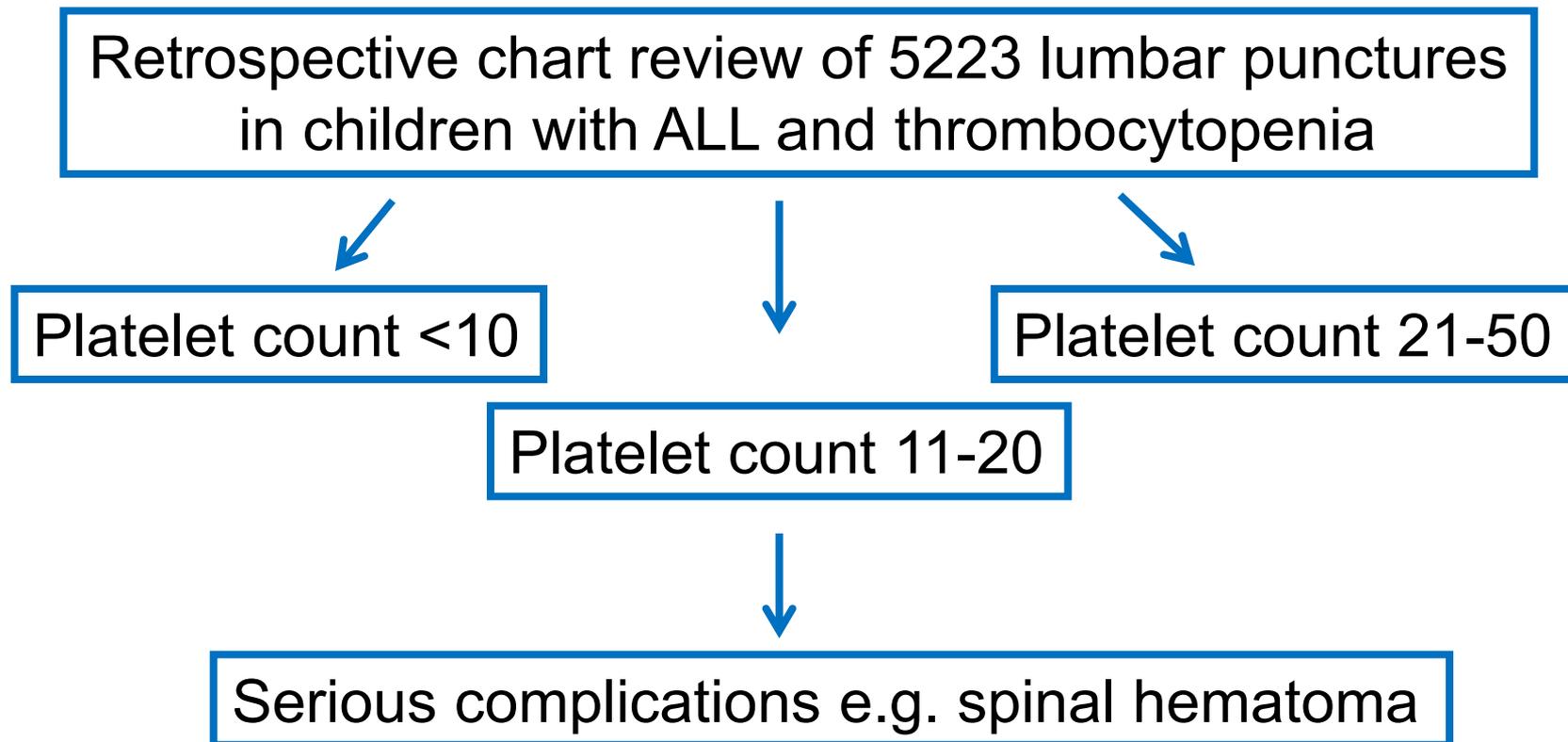
TRICC Trial: Results

- Overall 30-day mortality not significantly different



Observational Study

Safety of LP for Children with ALL and Thrombocytopenia



Prophylactic PLTs in LP

PLT	Number of LPs	95% CI for complications, %
1 – 5	6	0-40.19
6 – 10	23	0-13.21
11 – 20	170	0-2.05
21 – 30	234	0-1.49
31 – 40	235	0-1.48
41 – 50	273	0-1.27
51 – 100	858	0-0.40
> 100	3424	0-0.10
Total	5223	0-0.07

No serious complications at any platelet count.

Prophylactic transfusion is not necessary if platelet count >10 in this population.



Some Studies Are Not Done

Parachute use to prevent death and major trauma related to gravitational challenge: systematic review of randomised controlled trials



Problem – no control group



Evolution of Approach to Red Cell Transfusion

Liberal (pre-TRICC trial 1999)

- the transfusion threshold is **higher**; Hb 90 or 100
- routine order may be for **2 units**
- **MORE** blood is transfused



Restrictive

- the transfusion threshold is **lower**; Hb 70 or 80
- routine order is for **1 unit**
- **LESS** blood is transfused



Why Restrictive Transfusion?

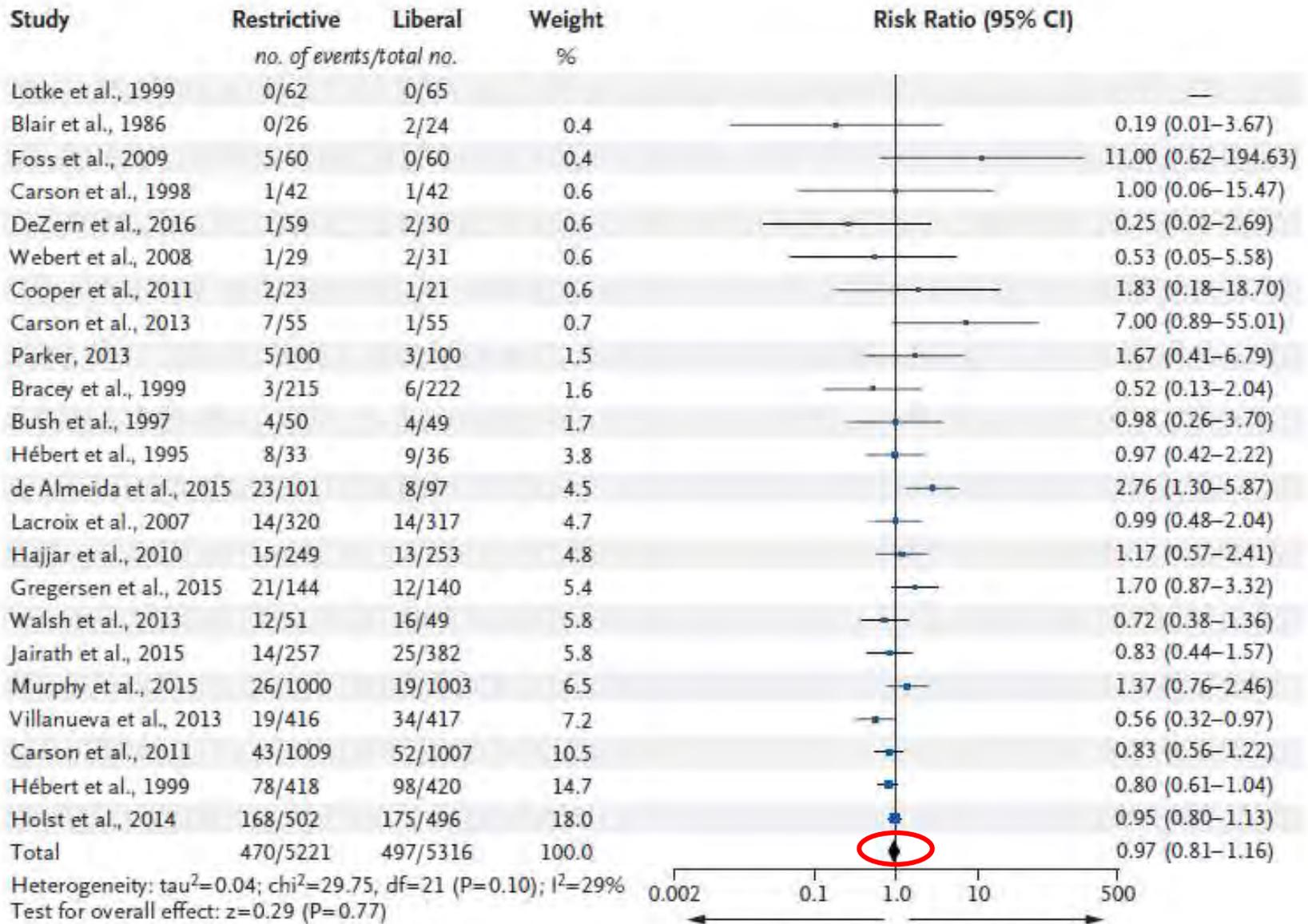
Evidence supports the safety of restrictive practice

Blood supply is limited (volunteer donors)

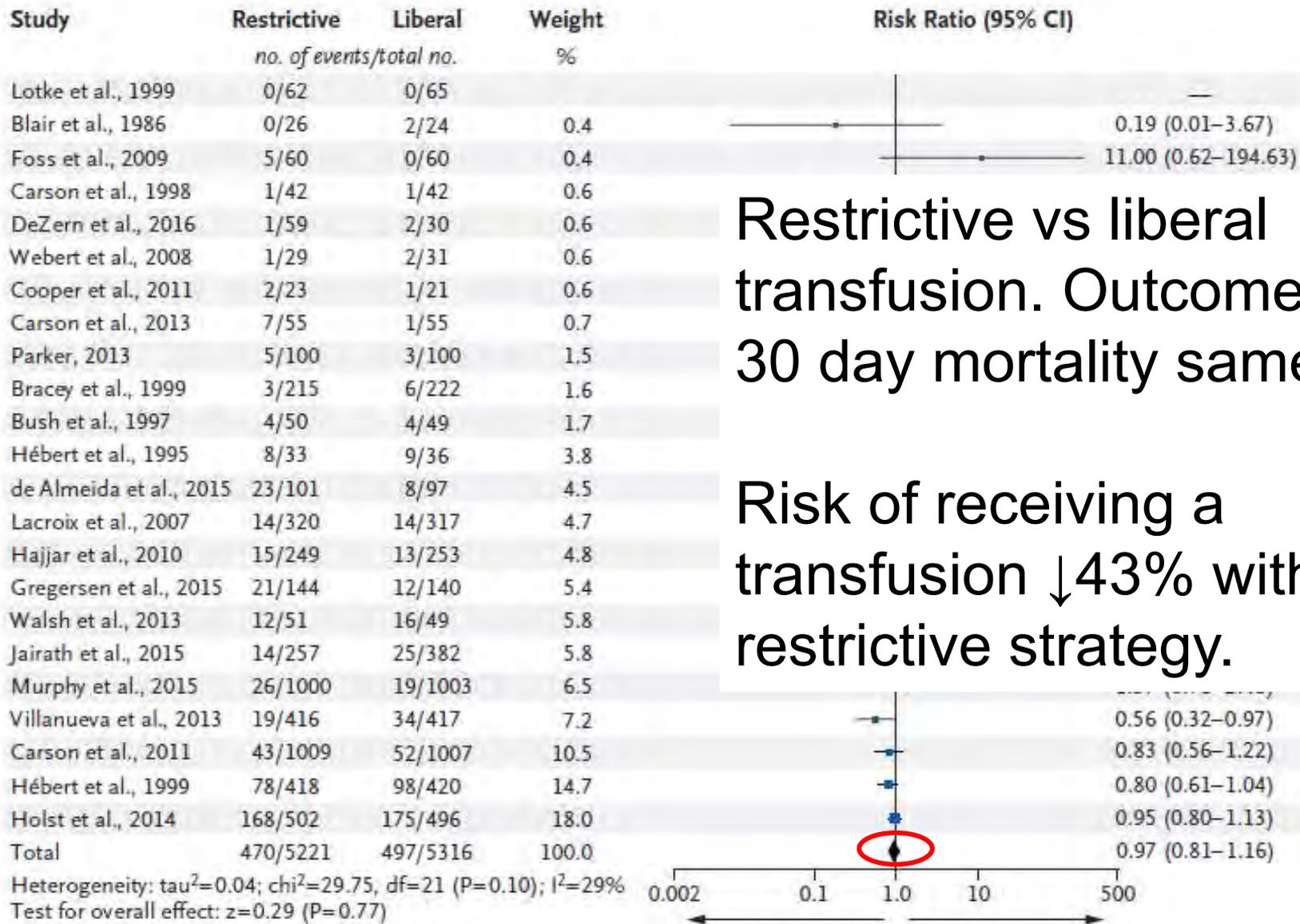
Risk of adverse events is often dose dependent

- Costs:
- blood products
 - transfusing them
 - adverse events





restrictive better **liberal better**



Restrictive vs liberal transfusion. Outcome: 30 day mortality same.

Risk of receiving a transfusion ↓43% with restrictive strategy.

AABB Red Cell Recommendations 2016

1. Hb threshold **70g/L** for:
 - hospitalized adult patients
 - hemodynamically stable
 - including critically ill patients
2. Hb threshold **80 g/L** for:
 - cardiac surgery
 - orthopedic surgery
 - pre-existing cardiovascular disease
3. Excluded conditions:
 - acute coronary syndrome
 - severe thrombocytopenia
 - chronic transfusion-dependent anemia
 - insufficient evidence



“...standard practice should be to initiate a transfusion with 1 unit of blood rather than 2 units”.



Red Cells

1. Don't transfuse blood if other non-transfusion therapies or observation would be just as effective.
 - e.g. hemodynamically stable patients with iron deficiency anemia should be treated with iron therapy
2. Don't transfuse more than one red cell unit at a time when transfusion is required in stable, non-bleeding patients.
 - 1U RBC raises the Hb by about 10 g/L in the non-bleeding patient



Ontario Transfusion Quality Improvement Plan (launched April 2016)

- Narrative template
- Quality improvement plan template (spreadsheet)
- Clinical Practice Recommendations for Blood Component Use in Adult Inpatients
 - red cells, plasma, platelets
- Order Set template
- Technologist Screening Tools
- Tracker Tool for reporting audit results



Ontario RBC Recommendations: Adult Inpatient

Clinical Setting	Recommendation and dose
Hb <60 g/L	Transfusion likely appropriate. 1 unit and re-check patient and Hb (healthy/younger patients may tolerate lower Hb)
Hb <70 g/L	Consider transfusion. 1 unit and re-check patient and Hb
Hb <80 g/L	Consider transfusion if pre-existing cardiovascular disease or evidence of impaired tissue oxygenation. 1 unit and re-check patient and Hb
Hb 80-90 g/L	Likely inappropriate unless evidence of impaired tissue oxygenation.
Hb >90 g/L	Likely inappropriate. Clearly document rationale for transfusion and discuss with patient.
Bleeding patient	<ul style="list-style-type: none">• Maintain Hb >70 g/L• If pre-existing cardiovascular disease maintain Hb >80 g/L



Blood Product Order Set Template RBC/PLT/ FP - Adult

Allergies/Sensitivities <input type="checkbox"/> none known <input type="checkbox"/> yes (specify) _____
Admitting Diagnosis: _____
<input type="checkbox"/> informed consent completed as per institutional guidelines
Date of transfusion: <input type="checkbox"/> today <input type="checkbox"/> other (DD/MM/YYYY) _____ <input type="checkbox"/> STAT (call blood bank at XXXXX)
Pre-transfusion laboratory tests <input type="checkbox"/> group and screen Previous transfusion within 3 months <input type="checkbox"/> yes <input type="checkbox"/> no Previous pregnancy within 3 months <input type="checkbox"/> yes <input type="checkbox"/> no Previous transplant <input type="checkbox"/> yes <input type="checkbox"/> no
<input type="checkbox"/> if no existing IV initiate IV 0.9% NaCl to keep vein open <input type="checkbox"/> discontinue peripheral IV after transfusion complete
Pre-transfusion medications

Red Blood Cells

Pre-transfusion Hb: _____ g/L

Indication: low Hb significant bleeding symptomatic other

Transfuse 1 unit, over _____ hours (e.g. 1 unit over 2-3 hours, maximum 4 hrs)

Pre-transfusion Hb: _____ g/L

Indication: low Hb significant bleeding symptomatic other

Transfuse 1 unit, over _____ hours (e.g. 1 unit over 2-3 hours, maximum 4 hrs)

Transfuse ___ units, each over _____ hours

Note: consider IV iron instead of red blood cells for patients with stable iron deficiency anemia

Blood Order Screening

- Orders screened by the blood bank technologists
- Similar to pharmacy screening of drug orders
- To ensure that orders comply with institutional guidelines
- To clarify the reason for the order e.g. patient has signs or symptoms of impaired tissue oxygenation or a relevant clinical history that would justify transfusion
- To enable a discussion between the ordering physician and the blood bank physician if necessary



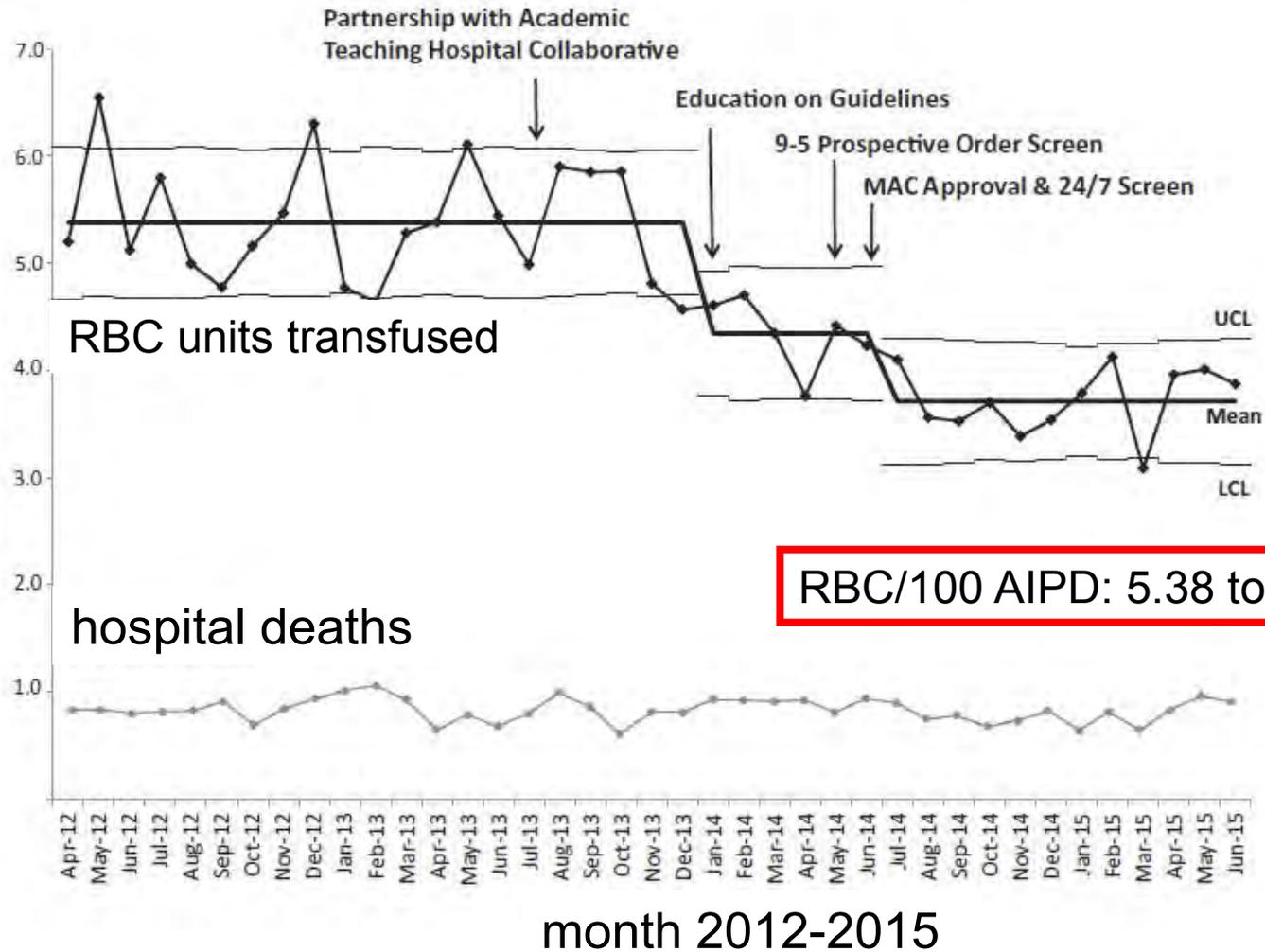
Significant Signs and Symptoms of Anemia?

- Dyspnea, chest pain
- Syncope, presyncope
- Dizziness upon walking/standing
- HR >100 bpm, systolic BP < 90 mmHg
 - unresponsive to fluid challenge
- ST changes on ECG, positive troponin
- not fatigue, pallor or decreased exercise tolerance alone



Technologist Screening in an Ontario Community Hospital

Events per 100 acute inpatient days (AIPD)

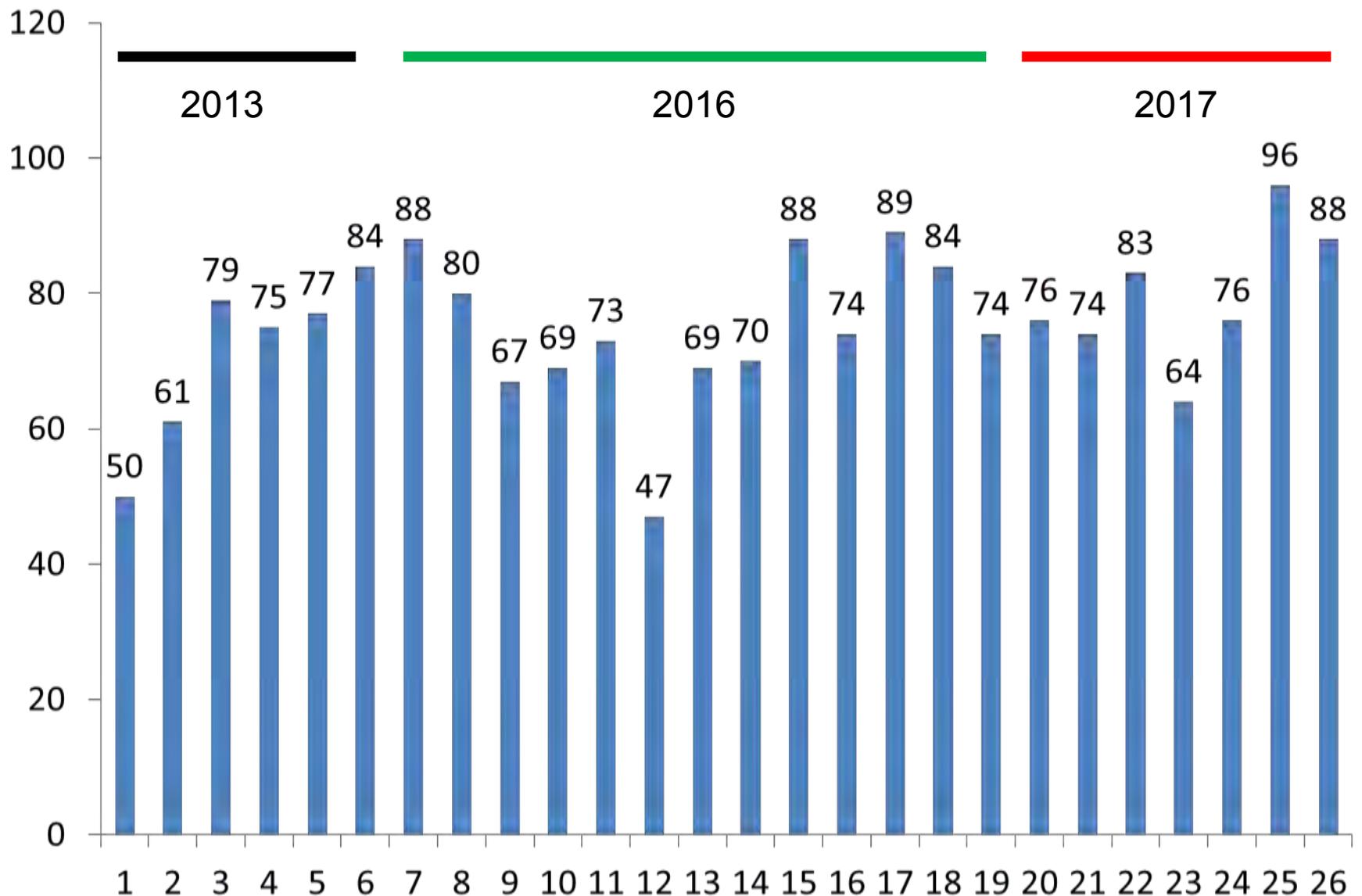


OTQIP Indicators

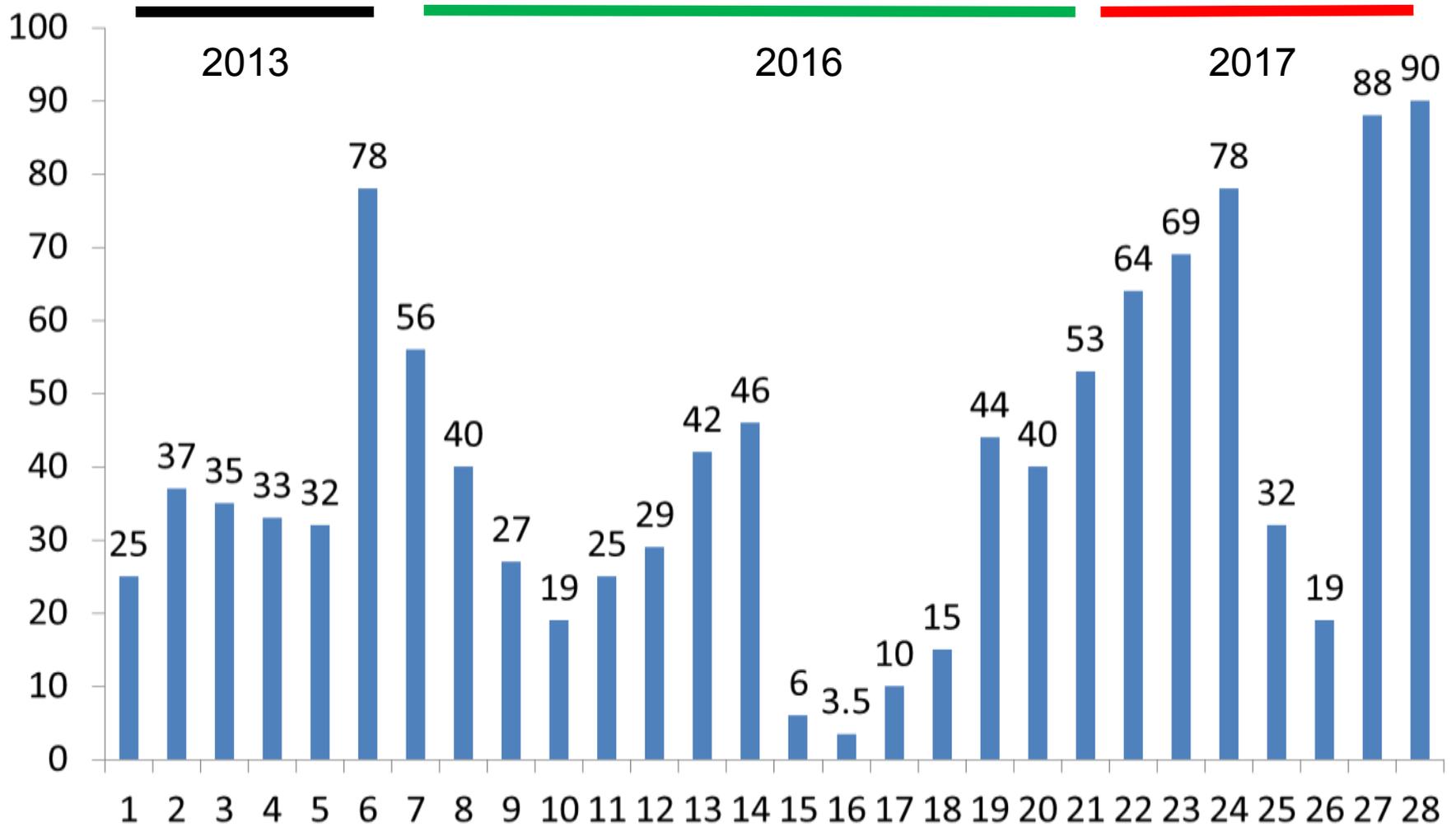
1. % RBC transfusions with a pre-transfusion Hb < 80 g/L
 - eventual goal 80%
 - justification: matching best performance
2. % RBC transfusions which are single unit
 - prescribe 1 unit at a time and reassess the patient (preferably including Hb) before second unit
 - eventual goal 80%
 - justification: matching best performance



Ontario hospitals: % pre-Tx Hb < 80

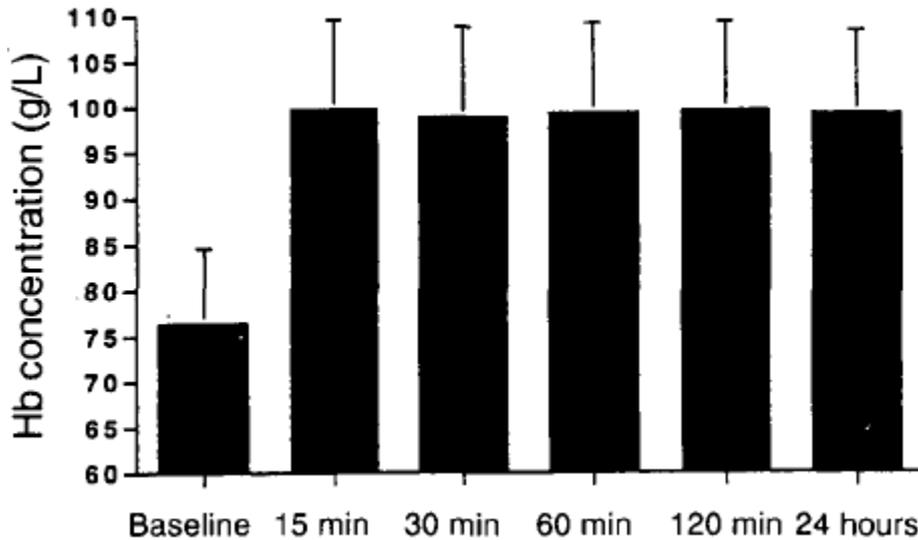


Ontario hospitals: % Single Unit



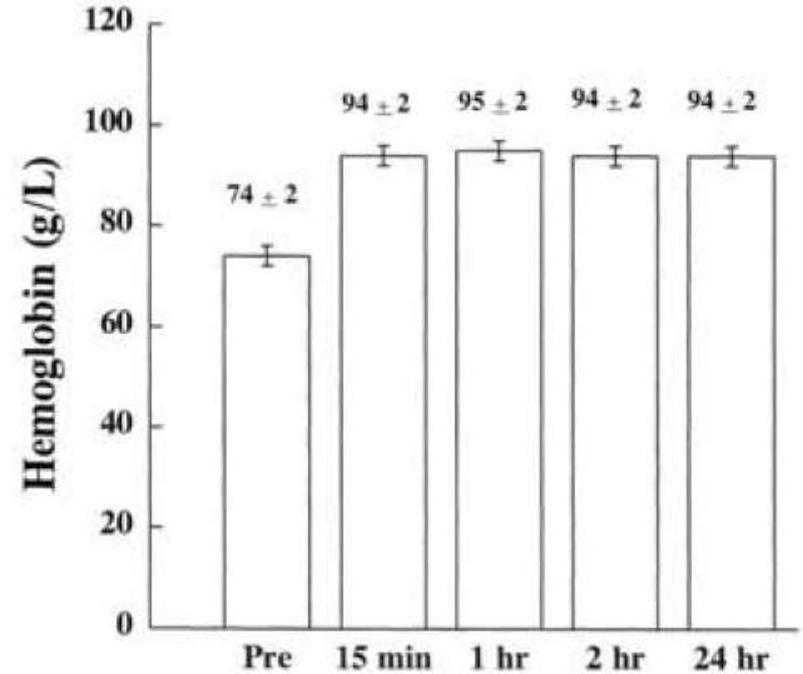
How soon can the post-transfusion CBC be drawn?

15 minutes



Acute anemia, normovolemic GI patients

Elizade. Transfusion 1997;37:573



General medicine ward, not bleeding

Wiesen. Ann Int Med 1994;121(4):278



4. Don't routinely transfuse platelets for patients with chemotherapy-induced thrombocytopenia if the platelet count is greater than $10 \times 10^9/L$ in the absence of bleeding.



AABB Platelet Guideline 2014

Indication	Threshold PLT count	Quality of Evidence	Strength of Recommendation
Therapy-induced thrombocytopenia	≤ 10		
Elective central venous catheter	< 20		
Lumbar puncture	< 50		
Major surgery	< 50		
Cardiopulmonary bypass	For perioperative bleeding only		
Intracranial bleed and anti-platelet therapy	cannot recommend for or against		

AABB Platelet Guideline 2014

Indication	Threshold PLT count	Quality of Evidence	Strength of Recommendation
Therapy-induced thrombocytopenia	≤ 10	Moderate	Strong
Elective central venous catheter	< 20	Low	Weak
Lumbar puncture	< 50	Very low	Weak
Major surgery	< 50	Very low	Weak
Cardiopulmonary bypass	For perioperative bleeding only	Very low	Weak
Intracranial bleed and anti-platelet therapy	cannot recommend for or against	Very low	Uncertain

Prophylactic PLTs before Lumbar Puncture?

Organisation	Recommended PLT count
National Plan for the Management of Blood Shortages (Canada)	50 in Green Phase 20 in Amber Phase
AABB (U.S.)	50 Use clinical judgment for 20-50
British Committee for Standards in Haematology	40
C17 Guidelines (Children's Oncology Group, Canada)	20
Cardiovascular and Interventional Radiology Society of Europe	50
American Society of Clinical Oncology	Discusses evidence for 20 More research needed

References for Previous Slide

1. Kaufman. Ann Int Med 2015;162(3):205
2. Estcourt. BJH 2017;176:365
3. New. BJH 2016;175:784
4. www.C17.ca
5. Patel. J Vasc Interv Radiol 2012;23:727
6. Schiffer. J Clin Oncol 2001. 19(5);1519



Recommended PLT Transfusion Thresholds

Dose is 1 pool of 4 single-donor platelets or 1 apheresis unit

Clinical Setting	PLT	Recommendation
Non-immune thrombocytopenia	<10	1 dose
Procedures not associated with significant blood loss	<20	1 dose
Therapeutic anticoagulation that cannot be stopped	<30	1 dose, consult thrombosis expert
<ul style="list-style-type: none">• Epidural anesthesia, LP• major surgery (EBL >500 mL)• Significant bleeding	<50	1 dose immediately before procedure and check platelet count before starting procedure
<ul style="list-style-type: none">• Head trauma, neuraxial surgery• Life threatening hemorrhage	<100	1 dose and check platelet count
Platelet dysfunction (e.g. anti-platelet drugs, post CPB) with significant hemorrhage	any	1 dose
Immune thrombocytopenia (ITP)	any	Transfuse for life-threatening bleeding only, consult hematologist



Plasma

- Dose is 15 mL/kg
 - = **3-5 units for an adult** (250 mL/unit)
- Each dose increases coagulation factor levels by 20%

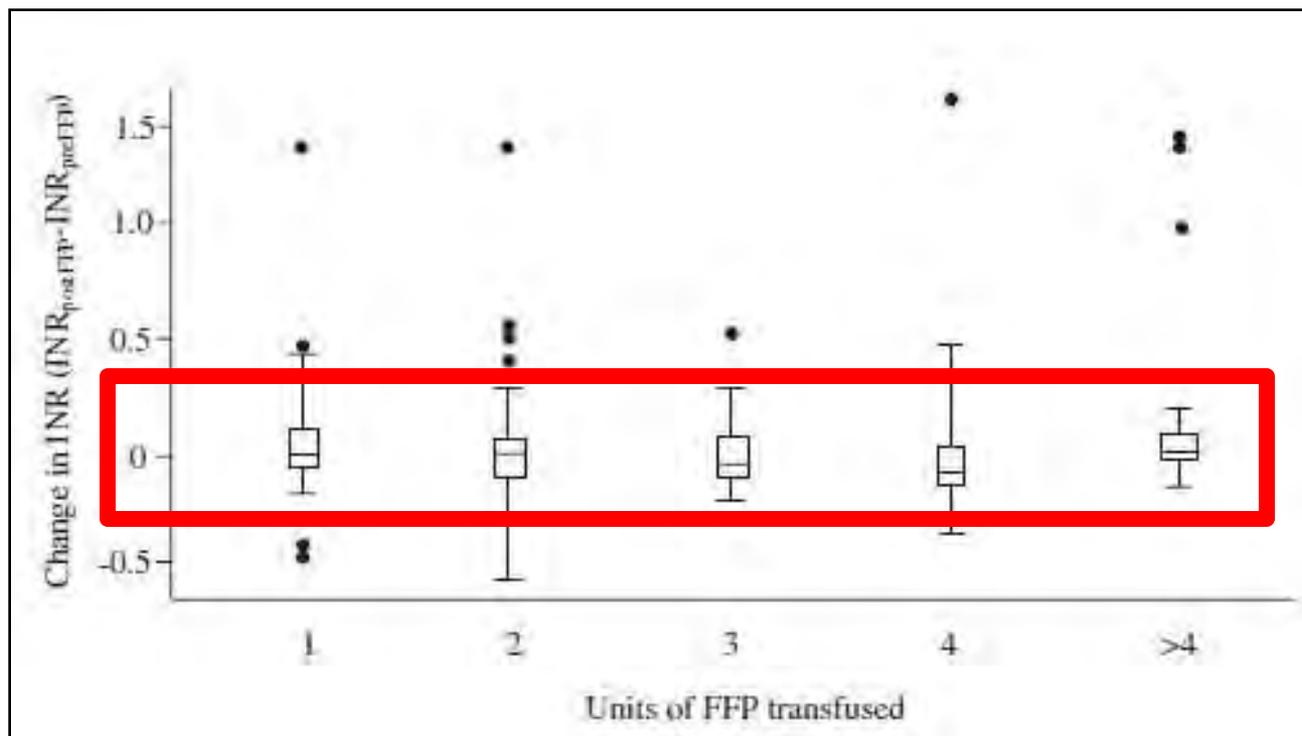


3. Don't transfuse plasma to correct a mildly elevated (<1.8) INR or aPTT before a procedure.
 - a mildly elevated INR is not predictive of bleeding risk
 - transfusion of plasma has not been demonstrated to significantly change the INR value when the INR was only mildly elevated (<1.8)



Effect of FFP with Mild Elevation of INR

(121 patients with INR 1.1 to 1.9)

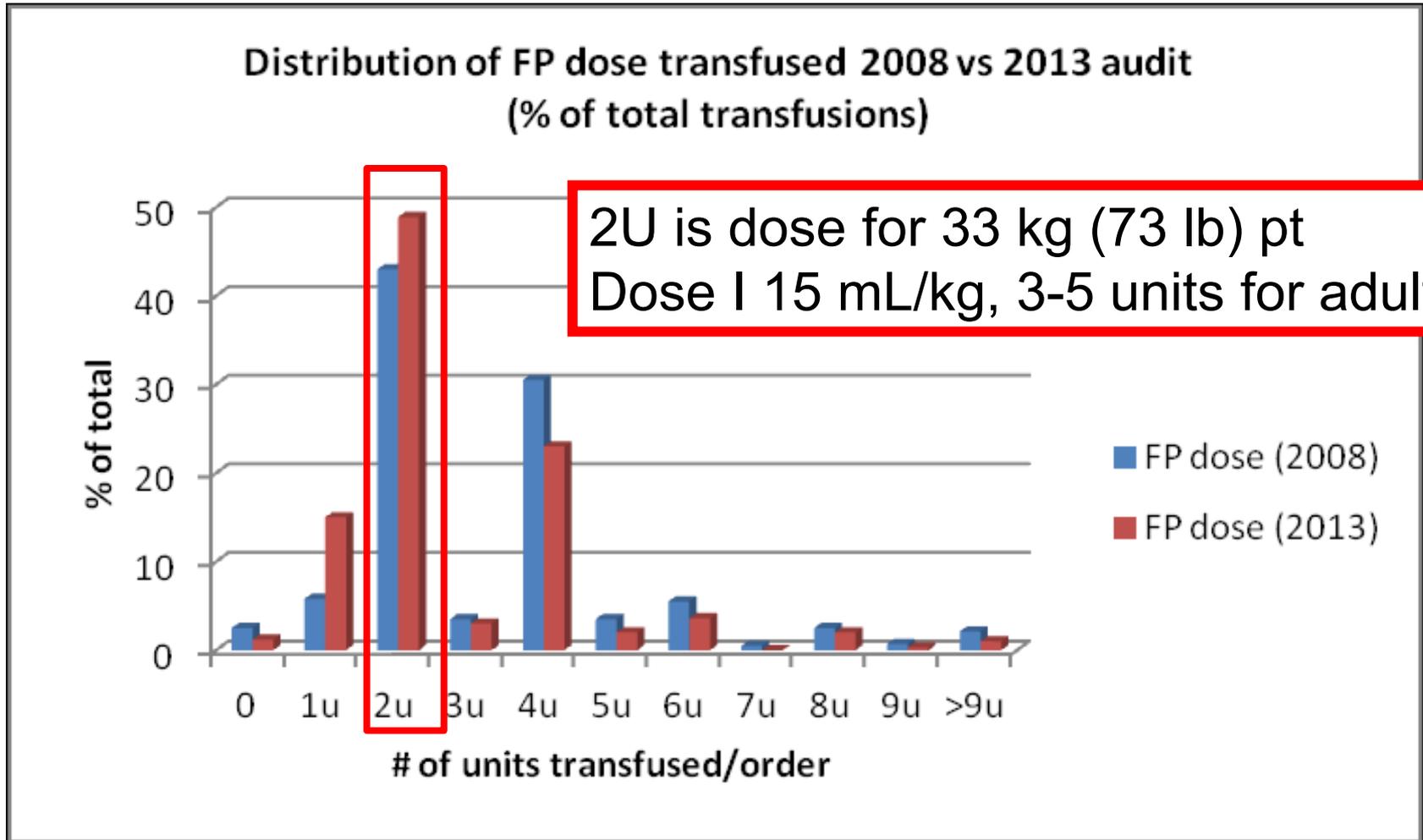


Failed to correct the INR in 99% of patients



Diagnosis/Indication	INR	Recommendation and dose
<ul style="list-style-type: none"> Significant bleeding Liver disease AND planned invasive procedure associated with blood loss 	greater than 1.7	Plasma 15 mL/kg (3-5 units) Note: Plasma transfusion is not required before minor procedures (IV, arterial line, PICC, thoracentesis, paracentesis, bone marrow procedure).
<ul style="list-style-type: none"> Microvascular bleeding Massive transfusion 	greater than 1.5-2.0 or unknown and cannot wait for INR result	Plasma 15 mL/kg (3-5 units) For massive transfusion: 2U plasma for every 4U red cells
Warfarin reversal/Vitamin K deficiency AND <ul style="list-style-type: none"> Emergency surgery (in < 6 hrs) Significant bleeding 	greater than 1.5	DO NOT USE PLASMA unless PCC unavailable or contraindicated (e.g. history of heparin-induced thrombocytopenia). Administer 10 mg IV Vit K with the PCC or plasma.

Dosing Plasma: Less May Not Be Better Here!



Why Restrictive Transfusion?

Evidence supports the safety of restrictive practice

Blood supply is limited (volunteer donors)

Risk of adverse events is often dose dependent

- Costs:
- blood products
 - transfusing them
 - adverse events



Risks of Transfusion(non-viral)

RISK OF EVENT	EVENT
1 in 100	Transfusion-associated circulatory overload (TACO)
1 in 10,000	Transfusion related acute lung injury (TRALI)
1 in 40,000	ABO-incompatible transfusion per RBC transfusion
1 in 40,000	Serious allergic reaction per unit of component
1 in 200,000	Death from bacterial sepsis per pool of platelets

Most common causes of death from transfusion:
TACO, TRALI, wrong ABO, anaphylaxis, sepsis



8 Rights of Transfusion

- Patient (hemolysis)
- Product (PCC vs plasma)
- Dose (volume overload)
- Route (hemolysis)
- Time (volume overload)
- Documentation (consent, vital signs)
- Reason (within guidelines)
- Response (adverse reactions, lab results)



Transfusion Associated Circulatory Overload

- Pulmonary edema in at-risk patients
 - older (>70 yrs), renal insufficiency
 - LV dysfunction, heart failure
 - severe anemia but normal blood volume
- Volumes of blood components:
 - RBC 300 mL, platelets 350 mL, FP 250 mL/unit (adult dose 3-5 units)
- Slower infusion rate, over 3-3½ hrs
- Pre-transfusion furosemide, monitor vital signs



Blood Supply: CBS Inventory Report Feb 14, 2018



Daily Red Cell and Platelet Inventory Status

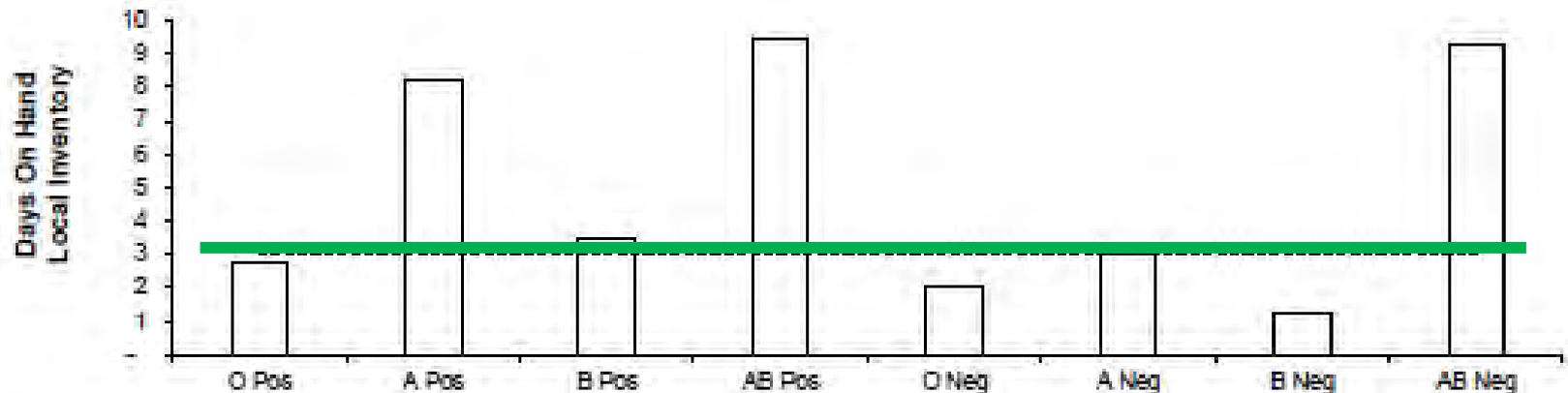
CBS Site: Brampton

Current Date: 2018-02-14

Time : 03:00 Hrs EST

If you require this report in an accessible format, please contact your local Hospital Liaison Specialist

RED BLOOD CELL INVENTORY



Costs of Transfusion

- CBS acquisition cost RBC **\$423**
 - total cost to transfuse it about **\$670** (Alberta 2014)
- US acquisition cost **\$211** (2015), \$221 (2013)
- One US review **\$760** USD per RBC transfused (2008)



Callum. Bloody Easy 4 2016.

Lagerquist. ISBT Science Series 2017;12(3):375

Ellingson. Transfusion 2017;57:1588



Costs of Transfusion Reactions

- Conservative estimate of cost of investigation of a febrile non-hemolytic transfusion reaction **\$160** (Toronto 2013-2015)
- Every transfusion carried an embedded cost of **\$2.16** for the cost of reactions (Netherlands 2016)
 - CBS issued 735,000 red cells in 2017/2018, so maybe \$1.6M in reaction costs for red cells only



Cohen. Transfusion 2017;57:1674

Janssen. Vox Sanguinis 2018;113:143

www.transfusionontario.org



Summary

- Restrictive transfusion practices address the issues of evidence-based practice, patient safety, preservation of the blood supply, and costs
- The Ontario Transfusion Quality Improvement Plan quality indicators are: % transfusions with pre-transfusion Hb less than 80 g/L, and % single unit transfusions



Summary

- The Hb threshold for stable adult inpatients, including ICU patients, is 70 g/L
- The platelet threshold for prophylactic platelet transfusion in therapy-induced thrombocytopenia is $10 \times 10^9/L$
- Plasma transfusion in the non-bleeding patient is unlikely to be effective if the INR is 1.7 or less



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Thank you. Questions?



Please consider
donating blood or
bone marrow
www.blood.ca

