

# 44°

## CONVEGNO NAZIONALE di Studi di Medicina Trasfusionale

Rimini | Palacongressi, 3-5 maggio 2022



# Programmi di Patient Blood Management in pediatria



**Pierpaolo Berti**

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Il sottoscritto Pierpaolo Berti, in qualità di Relatore dichiara che nell'esercizio della Sua funzione e per l'evento in oggetto, **NON** è in alcun modo portatore 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 sue funzioni al fine di trarne vantaggio.



## Society for the advancement of blood management administrative and clinical standards for patient blood management programs. 4th edition (pediatric version)

Susan M. Goobie<sup>1</sup>  | Trudi Gallagher<sup>2</sup> | Irwin Gross<sup>3</sup> | Aryeh Shander<sup>4</sup>

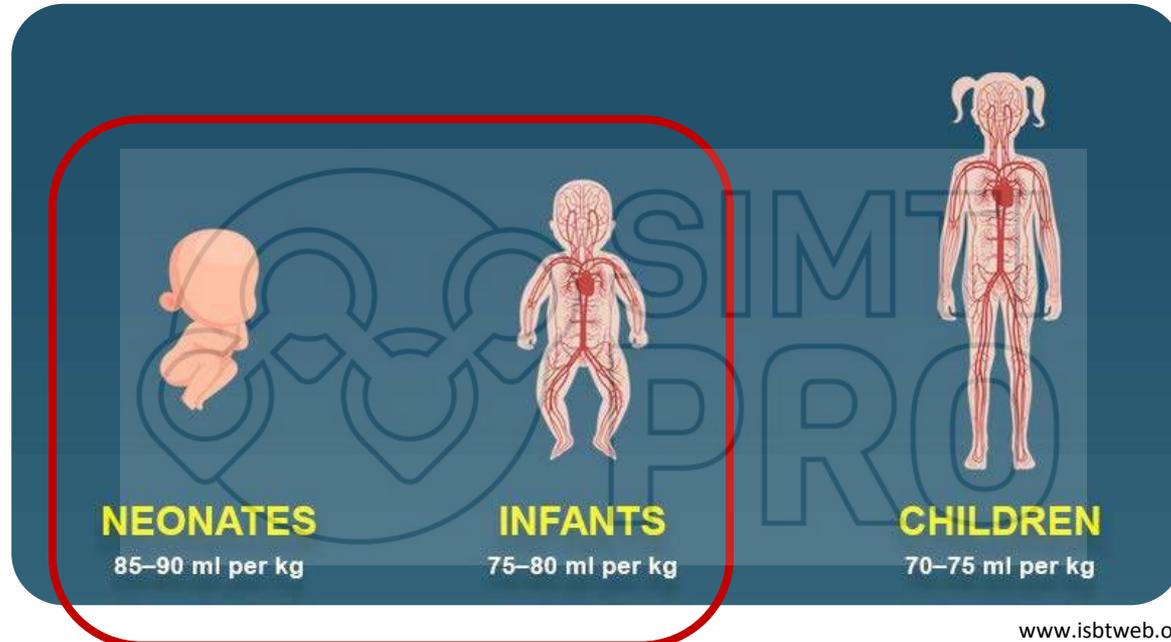
*Pediatric Anesthesia*. 2019;29:231–236.

*«Pediatric Patient Blood Management programs are currently **not commonly accepted as standard of care for pediatric patients**»*

*«This is partly due to the fact that, until recently, there was a paucity of robust evidence-based literature and expert consensus guidelines on pediatric PBM»*

# Pz pediatrico e tolleranza al sanguinamento

Il volume ematico e valore di Hb variano in base al peso ed all'età:



Minore tolleranza al sanguinamento (p.e. in un pz di 10 kg, una perdita di soli 160 ml può determinare grave ipotensione e conseguente ipoperfusione degli organi vitali)

## Analysis of pediatric adverse reactions to transfusions

*Sarah Vossoughi,<sup>1,2</sup> Gabriela Perez,<sup>3</sup> Barbee I. Whitaker,<sup>3</sup> Mark K. Fung,<sup>4</sup> and Brie Stotler<sup>1,2</sup>*

Analisi retrospettiva (2009-2015) relativa all'emovigilanza trasfusionale in 35 ospedali per adulti e 9 centri pediatrici.

Pazienti adulti	2.420 reazioni/962.205 trasfusioni	0,25%
Pazienti pediatrici	1.402 reazioni/260.664 trasfusioni	0,54%

I pazienti pediatrici ( $\leq 18$  yrs) hanno un'incidenza doppia di reazioni trasfusionali (soprattutto allergiche, febbrili non emolitiche ed emolitiche) rispetto agli adulti.

## Relationship between transfusion volume and outcomes in children undergoing noncardiac surgery

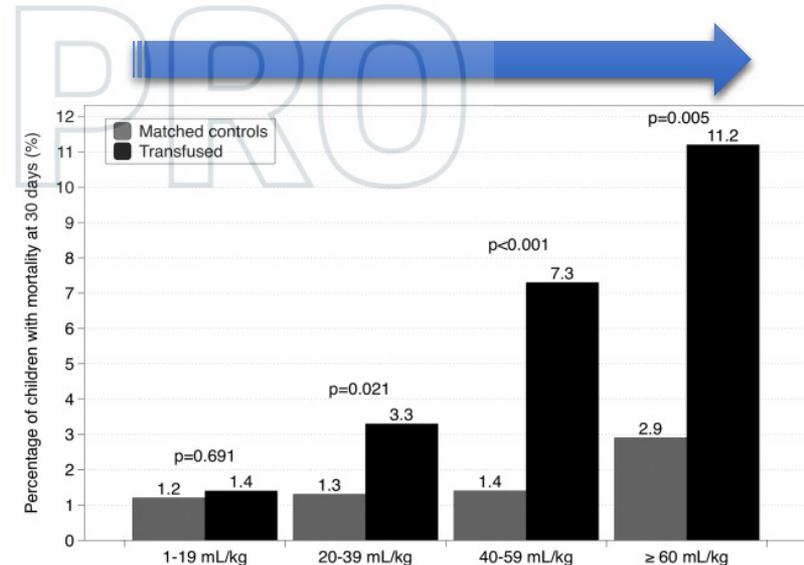
*Susan M. Goobie, James A. DiNardo, and David Faraoni*

Studio osservazionale retrospettivo su 6.897 pazienti pediatrici.

La trasfusione di RBC si associa ad un incremento della mortalità a 30 gg (2.8 vs 1.4%) e ad un' aumentata incidenza di complicanze maggiori.

### Complicanze maggiori:

- ✓ Infezione della ferita (6.5% vs 5.2%)
- ✓ Polmonari (31.3% vs 19.9%)
- ✓ Neurologiche (1.0% vs 0.3%)
- ✓ Cardiache (1.1% vs 0.4%)
- ✓ Settiche (2.7% vs 1.5%)
- ✓ Giorni di degenza (5 vs 3 gg)



# Pediatric Anesthesia

EDITORIAL

Goobie, Pediatric Anesthesia (2015)

## A blood transfusion can save a child's life or threaten it

*«On one hand, a blood transfusion may be clinically necessary for life and maintaining vital organ perfusion.»*

*However, alternatives to blood product transfusion in our pediatric patients may be the safest choice to avoid transfusion-related adverse events»*



# Perioperative bleeding management in pediatric patients

Curr Opin Anesthesiol 2016, 29:352–358

Susan M. Goobie<sup>a</sup> and Thorsten Haas<sup>b</sup>

Preoperative	Intraoperative	Postoperative
Early diagnosis and treatment of anemia	Careful blood pressure and fluid management (avoid hemodilution)	Treat and tolerate anemia
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	Antifibrinolytics	
	Consider recombinant coagulation products	
	Cell salvage	

Modified from Curr Opin Anesthesiol 2016, 29:352-358

# Anemia preoperatoria ed andamento clinico

In letteratura è dimostrata la presenza di correlazione tra anemia preoperatoria e mortalità nel paziente adulto<sup>1,2</sup>.

<sup>1</sup> Musallam KM, Lancet (2011); <sup>2</sup> Baron DM, Br J Anaesth (2014)

In ambito pediatrico i due studi principali sono i seguenti:

JAMA Pediatrics | Original Investigation

## Association of Preoperative Anemia With Postoperative Mortality in Neonates

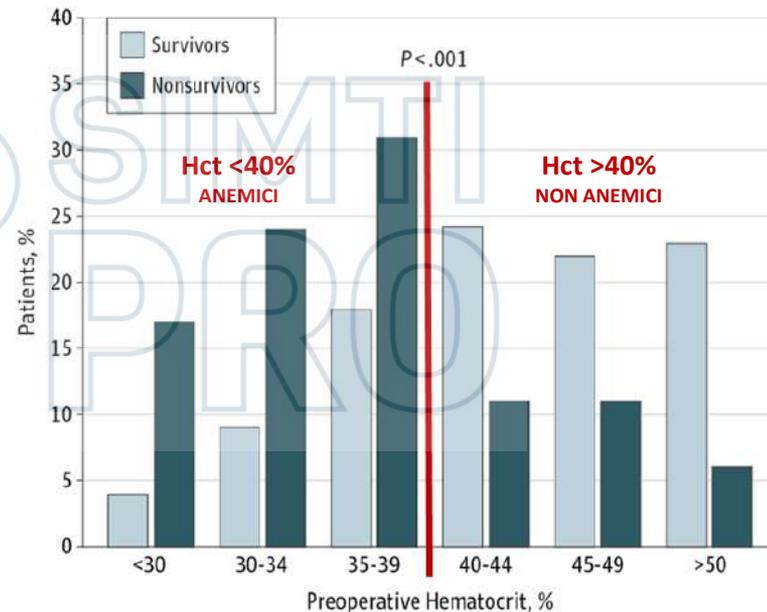
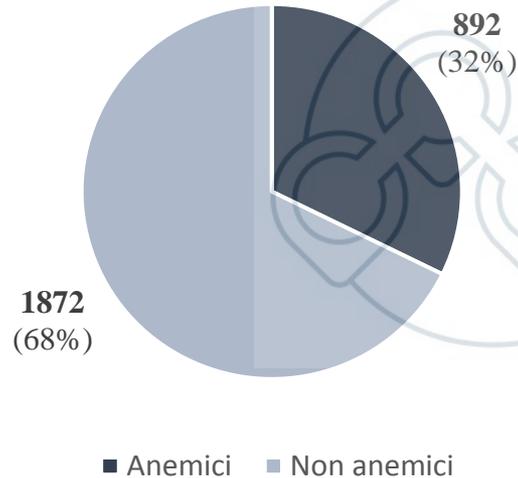
Susan M. Goobie, MD, FRCPC; David Faraoni, MD, PhD; David Zurakowski, PhD; James A. DiNardo, MD

## Relationship Between Preoperative Anemia and In-Hospital Mortality in Children Undergoing Noncardiac Surgery

David Faraoni, MD, PhD, FCCP; James A. DiNardo, MD, FAAP; and Susan M. Goobie, MD, FRCPC

# Association of Preoperative Anemia With Postoperative Mortality in Neonates

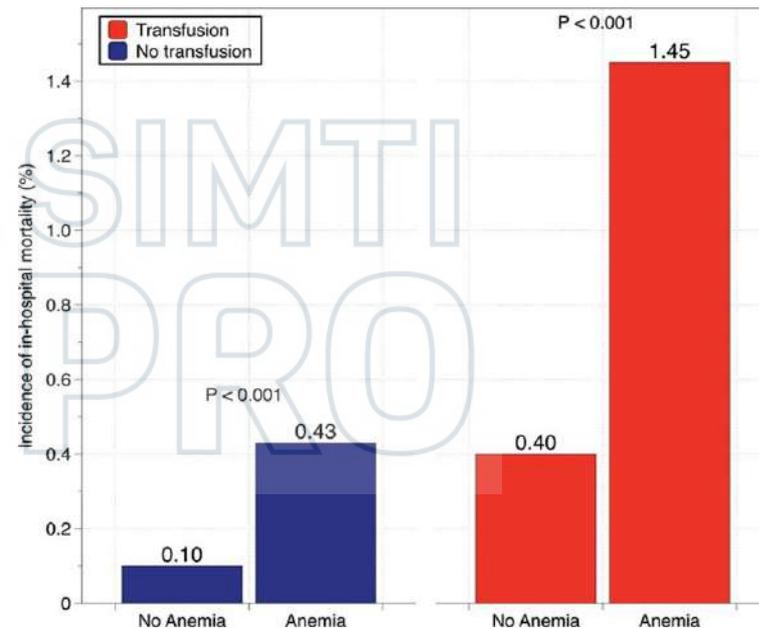
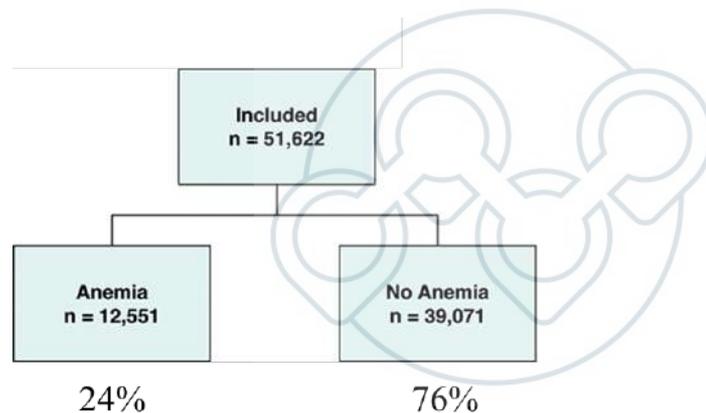
Susan M. Goobie, MD, FRCPC; David Faraoni, MD, PhD; David Zurakowski, PhD; James A. DiNardo, MD



L'anemia preoperatoria è associata ad una maggiore mortalità nei neonati (7.5% vs 1.4%).

# Relationship Between Preoperative Anemia and In-Hospital Mortality in Children Undergoing Noncardiac Surgery

David Faraoni, MD, PhD, FCCP, James A. DiNardo, MD, FAAP, and Susan M. Goobie, MD, FRCPC



L'anemia si associa ad una maggiore mortalità sia nei pazienti pediatrici (1-18 yrs) non trasfusi che in quelli trasfusi (OR 2.16, P<0.01).

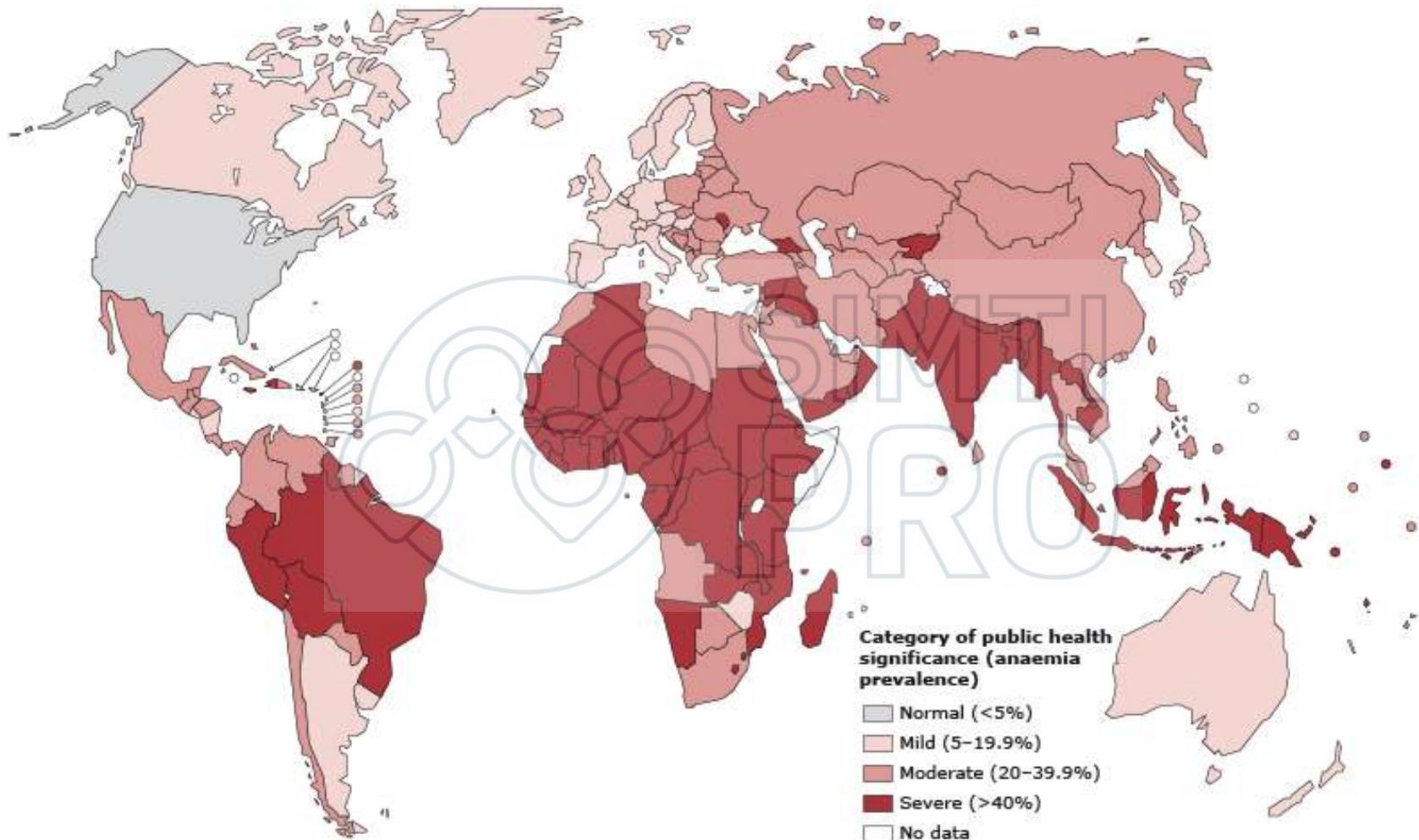
# Relationship Between Preoperative Anemia and In-Hospital Mortality in Children Undergoing Noncardiac Surgery

David Faraoni, MD, PhD, FCCP, James A. DiNardo, MD, FAAP, and Susan M. Goobie, MD, FRCPC

*«Our study confirms the urgent need for the development of patient blood management programs in children undergoing noncardiac surgery.»*

*...to identify children with preoperative anemia... to optimize hemoglobin level before surgery...»*

## Anemia as a public health problem in preschool-aged children, by country



Modified from UpToDate

## Risk factors for iron deficiency anemia in infants and young children

Period	Risk factors
Perinatal	Maternal iron deficiency
	Prematurity
	Administration of erythropoietin for anemia of prematurity
	Perinatal hemorrhagic events (eg, twin-twin transfusion or fetal-maternal hemorrhage)
Infancy	Dietary risk factors: <ul style="list-style-type: none"> <li>▪ Lack of iron supplements for breastfed infants*</li> <li>▪ Use of low-iron infant formula</li> <li>▪ Feeding of unmodified (non-formula) cow's milk, goat's milk, or soy milk<sup>¶</sup></li> <li>▪ Insufficient iron-rich complementary foods<sup>Δ</sup></li> </ul>
	Other risk factors: <ul style="list-style-type: none"> <li>▪ Disorders with GI blood loss (eg, milk protein-induced proctocolitis)</li> <li>▪ Malabsorptive disease</li> </ul>
1 to <12 years	Dietary risk factors: <ul style="list-style-type: none"> <li>▪ Excessive intake of cow's milk<sup>◇</sup></li> <li>▪ Insufficient iron in foods<sup>§</sup></li> </ul>
	Other risk factors: <ul style="list-style-type: none"> <li>▪ Disorders with GI blood loss (eg, inflammatory bowel disease, or chronic gastritis)</li> <li>▪ Malabsorptive disease (eg, celiac disease, or chronic intestinal infections)</li> <li>▪ Obesity</li> </ul>

GI: gastrointestinal.

\* For all breastfed infants, iron supplements should be introduced by two weeks for premature infants, and by four months for term infants, and should be continued until sufficient iron is supplied by complementary foods.

¶ Unmodified cow's milk (non-formula cow's milk) increases intestinal blood loss in infants as compared with formula feeding or breast feeding.

Δ Iron-rich complementary foods include infant cereals and pureed meats, and should be introduced by six months. Refer to UpToDate content on prevention of iron deficiency in infants and young children.

◇ In children one to five years old, cow's milk should be limited to no more than 20 oz (600 mL) daily.

§ Preschool-aged children should have at least 3 servings/day of iron-rich foods (eg, fortified breakfast cereal or meats).

Modified from UpToDate

# Terapia (formulazioni orali ed EV)

- **ferrous sulfate**, 3 mg/kg<sup>#</sup> elemental iron, administered once daily. For optimal absorption, the iron should be given in the morning or between meals and with water or juice.

# Powers JM, JAMA (2017)

Drug	FDA (US)	AIFA
<b>Iron sucrose</b> (ferro saccarato)	≥2 years of age*	Not recommended
<b>Ferric gluconate</b> (gluconato ferrico)	≥6 years of age*	≥6 years of age*
<b>Ferric carboxymaltose</b> (ferro carbossimaltoso)	≥1 year of age <sup>#</sup>	≥14 years of age

\* approved in Chronic Kidney Disease (CKD)

# limited experience in children

# Predeposito per autotrasfusione (PAD)

- PAD indicata in chirurgie dove sono stimate perdite  $\geq 20\%$  del volume ematico circolante;
- Storicamente molto utilizzati (periodo diffusione HIV, HCV), ultimamente in forte riduzione.
- L'intervento chirurgico deve essere sincronizzato con il PAD per evitare di eliminare le unità prelevate;
- Notevole efficacia nel prevenire la trasfusione allogenica (63-94%);
- Problema delle unità non trasfuse (31%), degli eventi avversi alla donazione e della riduzione della Hb preoperatoria;
- Favorevole associazione con EPO.

Lauder G.R. Transfus. Med. 2007; Tasaki T. Transfusion 2007; Lavoie J. Paediatr Anaesth. 2011

# Perioperative bleeding management in pediatric patients

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	Antifibrinolytics	
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# Restrictive vs liberal RBC-transfusion strategy

The NEW ENGLAND  
JOURNAL of MEDICINE

## Transfusion Strategies for Patients in Pediatric Intensive Care Units

APRIL 19, 2007

VOL. 356 NO. 16

Children with single-ventricle physiology do not benefit from higher hemoglobin levels post cavopulmonary connection: Results of a prospective, randomized, controlled trial of a restrictive versus liberal red-cell transfusion strategy\*

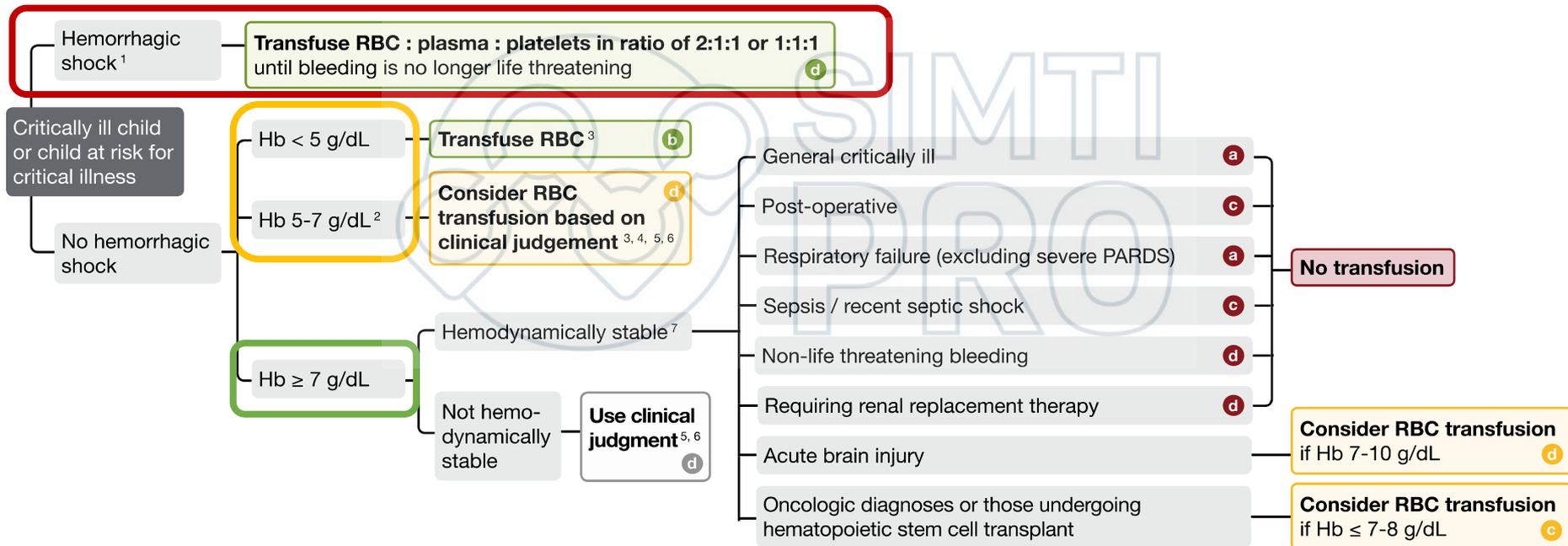
Pediatr Crit Care Med 2011 Vol. 12, No. 1



Entrambi questi non-inferiority RCT hanno dimostrato che una strategia trasfusionale restrittiva non peggiora l'outcome del pz in PICU, lo espone ad un minor numero di trasfusioni e potenziali eventi avversi alle stesse.

# Consensus Recommendations for RBC Transfusion Practice in Critically Ill Children From the Pediatric Critical Care Transfusion and Anemia Expertise Initiative

Valentine et al. *Pediatr Crit Care Med* 2018



# Pediatric Massive Transfusion

## *A Systematic Review*

*Pediatric Emergency Care* • Volume 34, Number 8, August 2018

Massive transfusion in children has been defined:

- replacement by transfusion of 50% of total blood volume in 3 hours
- transfusion of 100% of total blood volume in 24 hours.

The optimal volume trigger for initiating a massive transfusion protocol in children is unknown but some experts use the following weight-based approach:

<5 kg (neonate)	55 mL/kg
5 to 25 kg (infant)	50 mL/kg
25 to 50 kg (child)	45 mL/kg
>50 kg (adolescent)	40 mL/kg or 6 units PRBC

## Perioperative Blood Management in the Pediatric Patient

Dr. Jared Spilka<sup>1†</sup>, Dr. Susan M. Goobie<sup>2</sup>

Preferably blood product administration should be goal directed and guided by PoC-T (TEG or ROTEM), if available.

RBC transfusion should be balanced with “yellow” blood product transfusion:



# Management of Dilutional Coagulopathy during Pediatric Major Surgery

Transfus Med Hemother 2012;39:114–119

Thorsten Haas<sup>a</sup> Jacqueline Mauch<sup>a</sup> Markus Weiss<sup>a</sup> Markus Schmugge<sup>b</sup>

Careful fluid management is mandatory to avoid hemodilution

Replacing blood loss with intravenous fluids which do not contain adequate clotting factors (i.e. crystalloids, colloids and packed red blood cells)



## Dilutional coagulopathy

It seems to be mainly based on complex disturbances of clot firmness including **acquired fibrinogen** as well as **factor XIII deficiencies**, while clotting time and platelet counts remained fairly stable.

**Transfusion-associated hyperkalemia in pediatric population: Prevalence, risk factors, survival, infusion rate, and RBC unit features**

TAHCA has been recognized as a complication of massive RBC transfusion in children.

During storage, potassium in the extracellular fluid of RBC units stored in additive solutions increases linearly over time.

Avoid transfusing older RBC units in infants <10 kg or <1 year of age requiring massive transfusions to prevent hyperkalemic cardiac arrest.



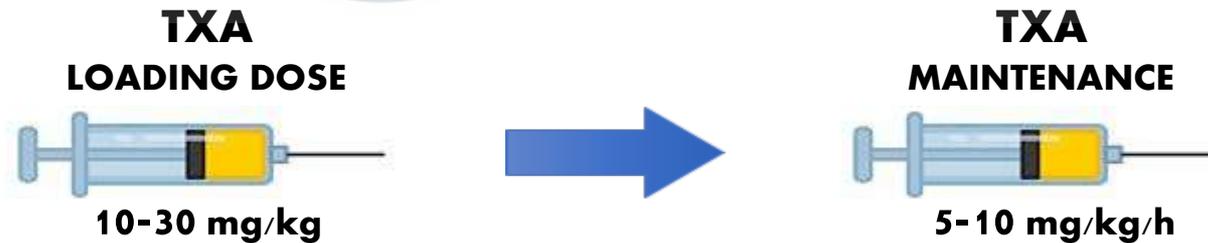
**≤7 days**

# Tranexamic acid and perioperative bleeding in children

what do we still need to know?

Goobie, Susan M.<sup>a</sup>; Faraoni, David<sup>b</sup>

- Prophylactic or therapeutic TXA administration is an effective strategy to reduce bleeding, decrease allogeneic blood product transfusion, and improve pediatric patients' outcomes.



# Indications and Outcomes of Cell Saver in Adolescent Scoliosis Correction Surgery

*A Systematic Review*

Nicholas Stone, BScH,\* Vandit Sardana, MSc, MD,† and Paul Missiuna, MD, FRCSC†

- Analisi, attraverso la valutazione di 7 studi, del ruolo del recupero intraoperatorio nel prevenire la trasfusione allogenica.

349 pz  
Cell Saver

244 pz  
non-Cell Saver

- I pazienti sottoposti a recupero intraoperatorio, rispetto al gruppo di controllo, hanno ricevuto un minor numero di trasfusioni (-32.6% fase intraoperatoria; -45.9% nella fase post-operatoria e, complessivamente, -47.3% nel periodo peri-operatorio).

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	Antifibrinolytics	
	Consider recombinant coagulation products	
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Modified from Curr Opin Anesthesiol 2016, 29:352-358

# Identifying factors to minimize phlebotomy-induced blood loss in the

**SPECIAL INTEREST ARTICLE**

WILEY **Pediatric Anesthesia**

Stacey Society for the advancement of blood management administrative and clinical standards for patient blood management programs. 4th edition (pediatric version)

Studio os  
volumi e

Susan M. Goobie<sup>1</sup> | Trudi Gallagher<sup>2</sup> | Irwin Gross<sup>3</sup> | Aryeh Shander<sup>4</sup>

iatrogena, in particolare per pz <10 kg.

*Pediatric Anesthesia*. 2019;29:231–236.

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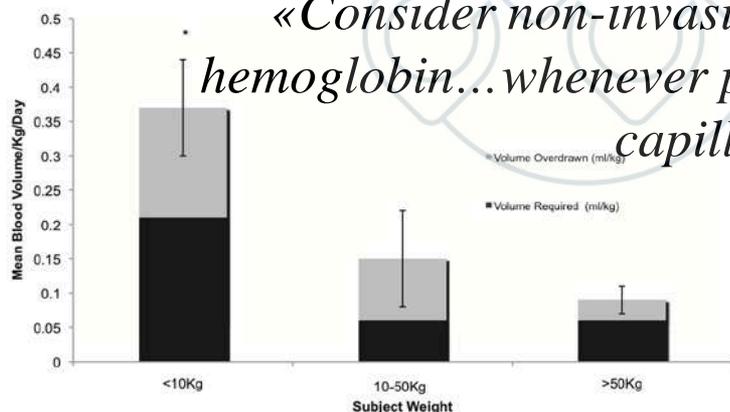


Figure 1. Comparison of the mean volume of blood drawn and overdrawn per kilogram per day by patient weight. Patients <10 kg had significantly greater volumes of blood drawn per kilogram per day compared to patients 10–50 kg and patients >50 kg, \* $p < .001$ . Error bars represent 95% confidence interval.

*«Consider non-invasive techniques for monitoring of hemoglobin... whenever possible (e.g. blood gas analysis or capillary sampling)»*

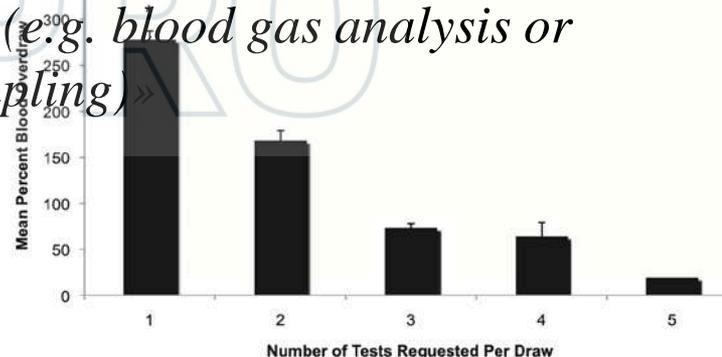


Figure 3. Comparison of the mean percent volume overdrawn by the number of laboratory blood tests requested per draw. Blood draws sent for one laboratory test had significantly greater mean percent blood volume overdraw when compared to mean percent blood volume overdraw for blood draws sent for 2, 3 and 4 tests, \* $p < .001$ . Error bars represent 95% confidence interval.

# An international consensus statement on the management of postoperative anaemia after major surgical procedures

Anaesthesia 2019, 73, 1418-1431

*«Despite numerous guidelines on the management of anaemia in surgical patients, there is no pragmatic guidance for the diagnosis and management of anaemia and iron deficiency in the postoperative period»*

# **An international consensus statement on the management of postoperative anaemia after major surgical procedures**

Anaesthesia 2019, 73, 1418-1431

- L'anemia post-operatoria interessa un'ampia percentuale di pazienti sottoposti a chirurgia maggiore e si associa ad un peggior andamento clinico (aumentata morbilità e mortalità).
- La riduzione del valore di Hb in fase post-operatoria (nadir 3-4 gg post-intervento) è spesso associato a deficit marziale, più difficile da evidenziare per via della risposta infiammatoria post-chirurgica.

# An international consensus statement on the management of postoperative anaemia after major surgical procedures

Anaesthesia 2019, 73, 1418-1431

- Non è definito un timing ideale per iniziare un trattamento, ma in tutti i casi di deficit marziale e/o riduzione del valore di Hb, esso andrebbe iniziato precocemente.
- Anche se l'infiammazione post-operatoria può stimolare la sintesi ed il rilascio di *epcidina*, il NICE<sup>#</sup> suggerisce di utilizzare la terapia marziale per OS e di riservare la EV solo in caso di mancata risposta o intolleranza alla stessa.

#NICE: National Institute for Health and Care Excellence (UK)

## Un ringraziamento particolare a:

Tutto il Personale

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# Grazie a tutti per l'attenzione!