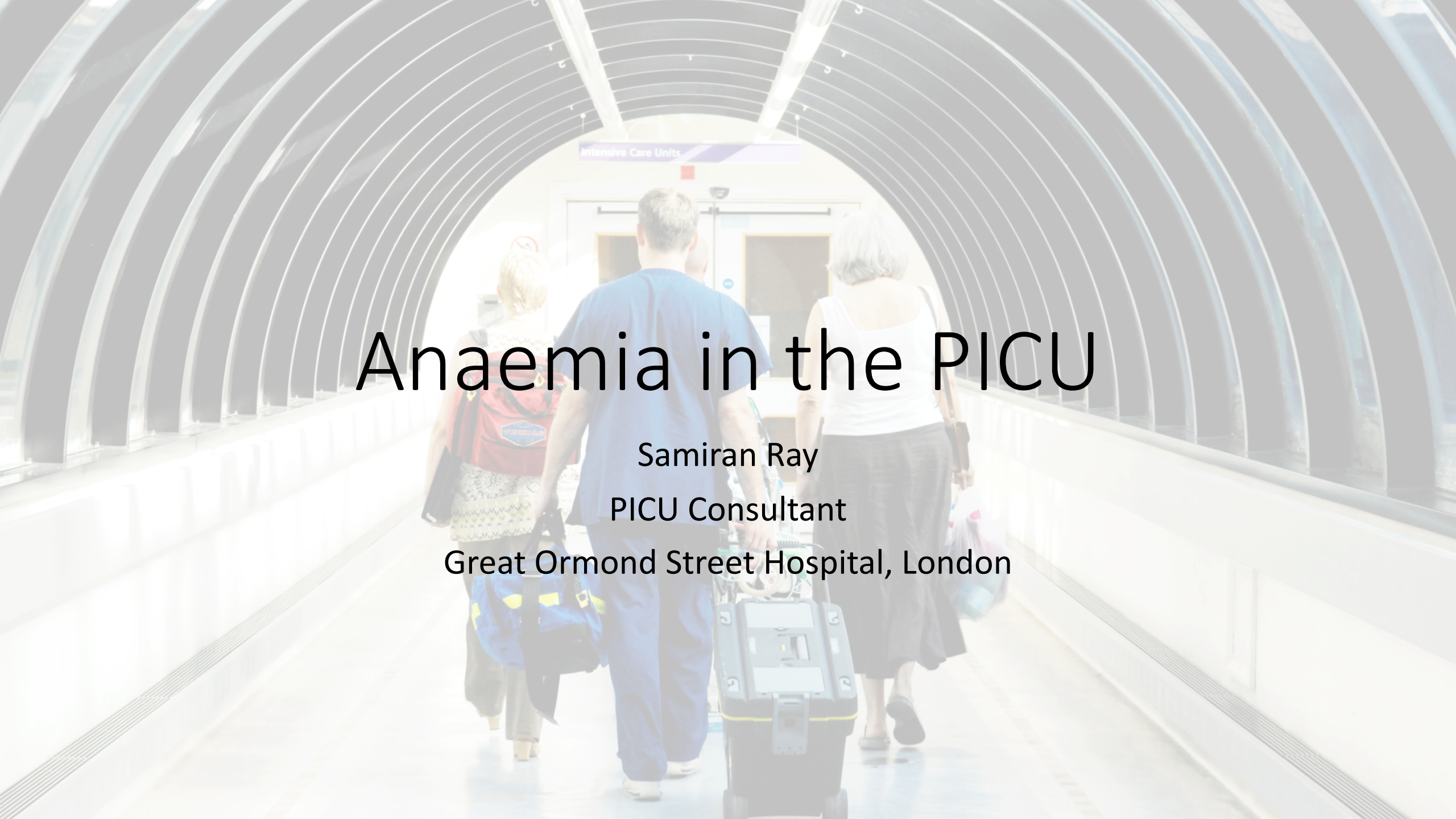


Anaemia in the PICU

Samiran Ray

PICU Consultant

Great Ormond Street Hospital, London

Paediatric Intensive Care in UK

29 NHS units in the UK and Ireland

Nearly 20000 admissions/year

60% emergency work

Half <1 year of age

Oxygen delivery

$$DO_2 = \{([Hb] \times SaO_2 \times 1.39) + (PaO_2 \times 0.0031)\} \times CO$$

where

DO_2 = oxygen delivery

[Hb] = haemoglobin concentration

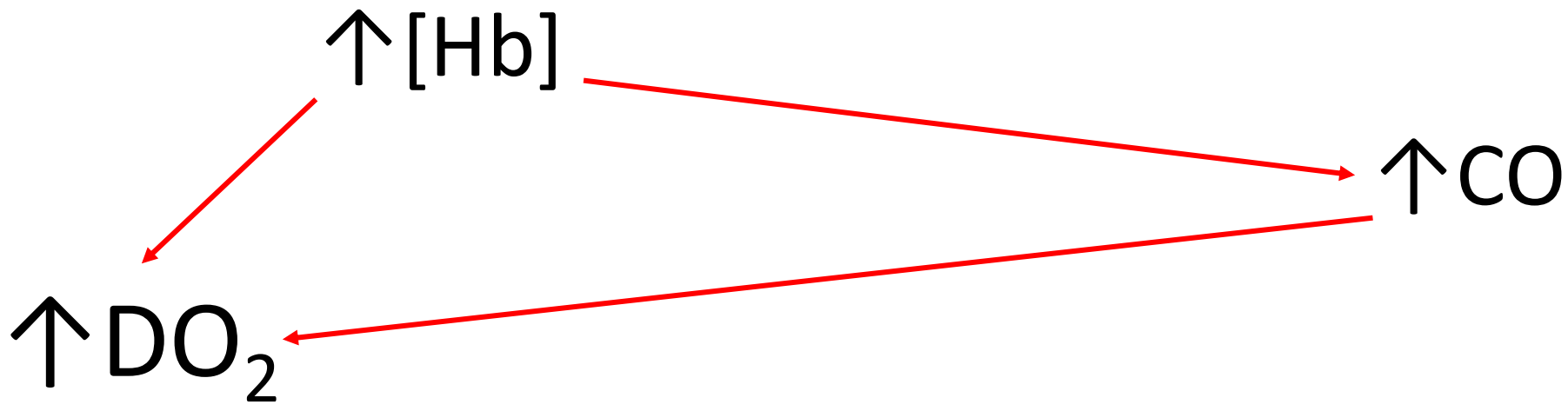
SaO_2 = arterial oxygen saturation of haemoglobin

PaO_2 = partial pressure of oxygen in blood

CO = cardiac output

Increasing Hb

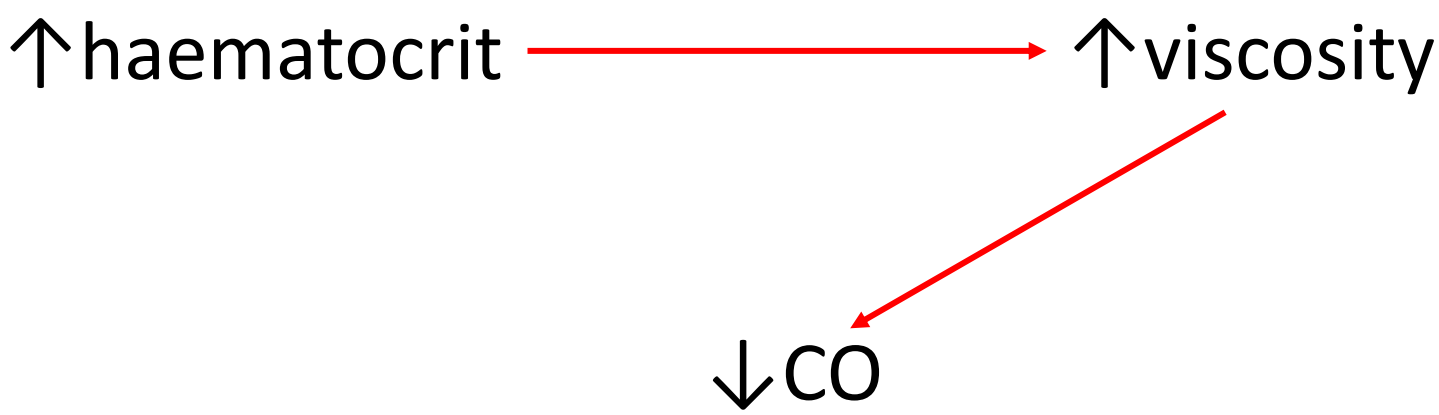
$$DO_2 = \{[Hb] \times SaO_2 \times 1.39 + (PaO_2 \times 0.0031)\} \times CO$$



Increasing Hb

But

Cannot increase [Hb] indefinitely



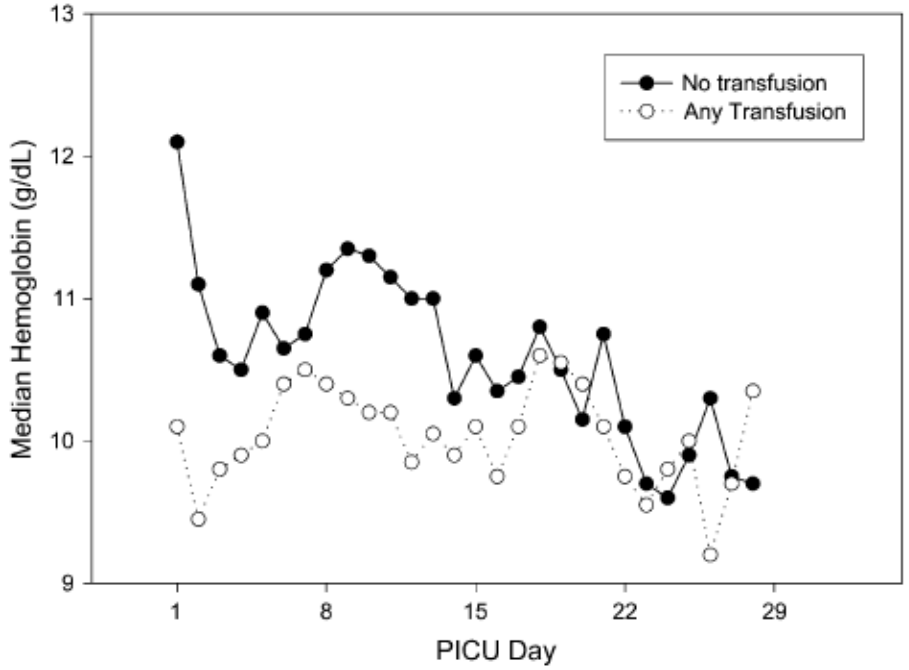
How common is anaemia?

- 32.9% of all patients anaemic on admission
- 18% develop anaemia after 48 hours of admission
- 48.6% given transfusion at any stage in PICU

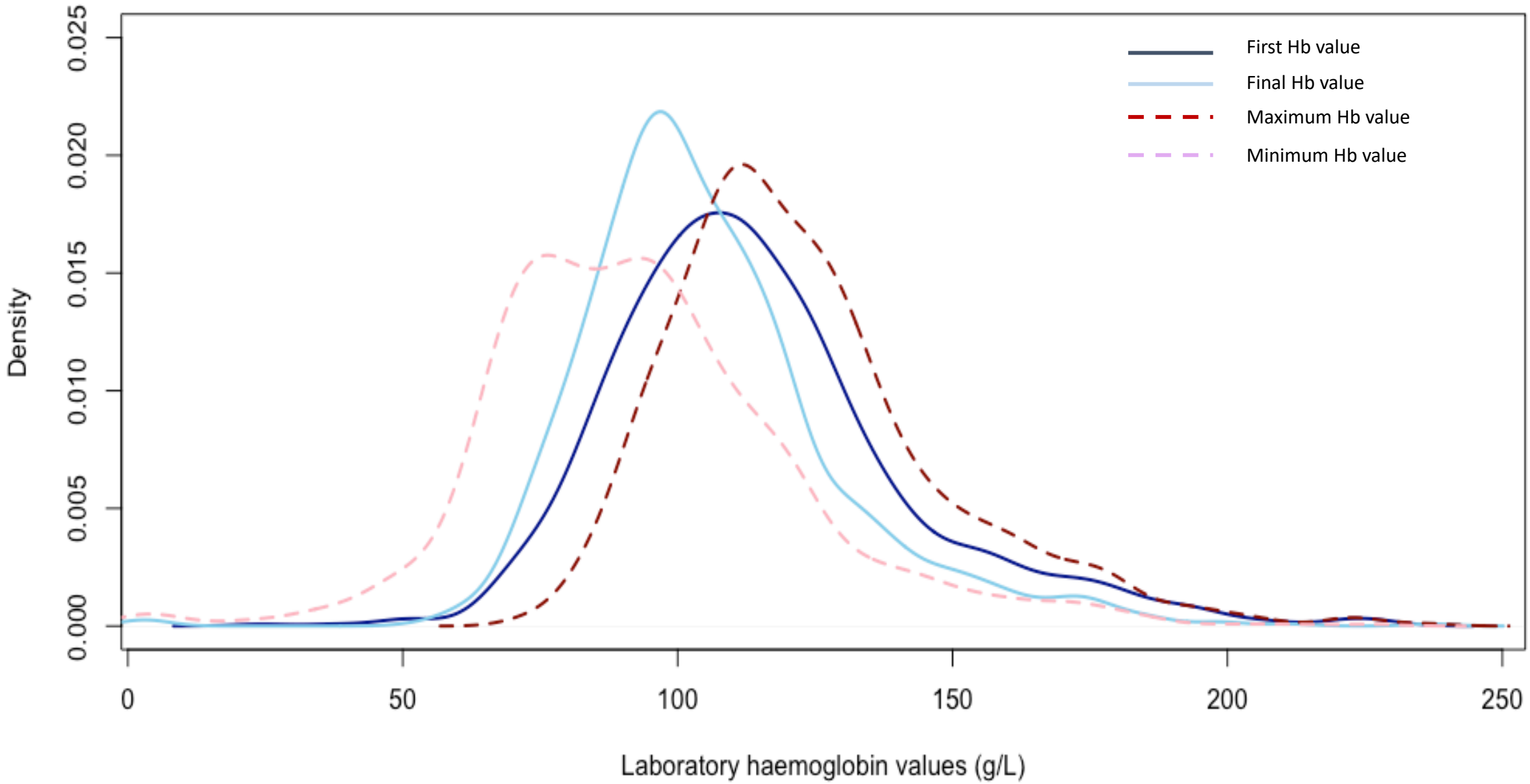
Anemia, Blood Loss, and Blood Transfusions in North American Children in the Intensive Care Unit

Scot T. Bateman[1], Jacques Lacroix[2], Katia Boven[3], Peter Forbes[4], Roger Barton[5], Neal J. Thomas[6], Brian Jacobs[7], Barry Markovitz[8], Brahm Goldstein[9], James H. Hanson[10], H. Agnes Li[3], and Adrienne G. Randolph[4], for the Pediatric Acute Lung Injury and Sepsis Investigators Network*

Am J Respir Crit Care Med Vol 178. pp 26–33, 2008



First, final, minimum and maximum laboratory haemoglobin levels from patients admitted to P/NICU at Great Ormond Street Hospital London in 2016



TRIPICU

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 19, 2007 VOL. 356 NO. 16

Transfusion Strategies for Patients in Pediatric Intensive Care Units

Jacques Lacroix, M.D., Paul C. Hébert, M.D., James S. Hutchison, M.D., Heather A. Hume, M.D., Marisa Tucci, M.D., Thierry Ducruet, M.Sc., France Gauvin, M.D., Jean-Paul Collet, M.D., Ph.D., Baruch J. Toledano, M.D., Pierre Robillard, M.D., Ari Joffe, M.D., Dominique Biarent, M.D., Kathleen Meert, M.D., and Mark J. Peters, M.D., for the TRIPICU Investigators,* the Canadian Critical Care Trials Group, and the Pediatric Acute Lung Injury and Sepsis Investigators Network

TRIPICU

- Non-inferiority trial
- Stable critically ill children admitted to PICU
- 320 randomised to be transfused at 70 g/L
- 317 randomised to be transfused at 95 g/L

- Primary outcome: new or progressive multi-organ dysfunction

TRIPICU

Variable	Restrictive-Strategy Group (N=320)	Liberal-Strategy Group (N=317)	P Value
Red-cell transfusion and hemoglobin concentration after randomization			
All patients			
No red-cell transfusion — no. of patients (%)	174 (54)	7 (2)	<0.001
No. of red-cell units per patient	0.9±2.6	1.7±2.2	<0.001
Lowest hemoglobin level in ICU — g/dl†	8.7±0.4	10.8±0.5	<0.001
Patients undergoing red-cell transfusion			
Any transfusion — no. of patients (%)	146 (46)	310 (98)	<0.001
1 transfusion — no. of patients (%)	104 (32)	194 (61)	
2 transfusions — no. of patients (%)	18 (6)	82 (26)	
>2 transfusions — no. of patients (%)	24 (8)	34 (11)	
No. of red-cell units per transfused patient	1.9±3.4	1.7±2.1	0.24
Volume of red-cell units per transfused patient — ml/kg	23.6±52.5	20.0±19.3	<0.04
First red-cell transfusion			
Time from randomization to first transfusion — days	1.7	0.1	<0.001
Hemoglobin level — g/dl			
Before first transfusion	6.7±0.5	8.1±0.1	<0.001
After first transfusion	9.4±1.2	11.2±1.1	<0.001
All red-cell transfusions			
Total no. of transfusions‡	301	542	<0.001
Average length of storage — days	16.0±10.5	15.7±10.3	0.62
Adherence to threshold hemoglobin level — no. of patients (%)§	319 (100)	307 (97)	0.006

TRIPICU

Variable	Restrictive-Strategy Group	Liberal-Strategy Group	Absolute Risk Reduction, Odds Ratio, or Difference in Means (95% CI)	P Value
Primary outcome				
New or progressive MODS — no./total no. (%)†	38/320 (12)	39/317 (12)	0.4 (–4.6 to 5.5)	NI‡
Age†				
≤28 days	1/11 (9)	0	–9.1 (–26.1 to 7.9)	1.00
29–364 days	14/143 (10)	20/142 (14)	4.3 (–3.2 to 11.8)	0.28
>364 days	23/166 (14)	19/167 (11)	–2.5 (–9.6 to 4.7)	0.51
Country§				
Belgium	3/66 (5)	4/66 (6)	0.74 (0.16 to 3.43)	0.70
Canada	32/205 (16)	28/203 (14)	1.16 (0.67 to 2.00)	0.60
United Kingdom	2/26 (8)	5/23 (22)	0.30 (0.05 to 1.73)	0.17
United States	1/23 (4)	2/25 (8)	0.52 (0.04 to 6.18)	0.61
Severity of illness (PRISM score)†¶				
0 (lowest quartile)	3/64 (5)	4/64 (6)	1.5 (–6.3 to 9.4)	1.00
1–4 (second quartile)	13/128 (10)	11/111 (10)	–0.3 (–7.9 to 7.4)	0.94
5–7 (third quartile)	6/54 (11)	6/67 (9)	–2.2 (–13.0 to 8.7)	0.69
≥8 (highest quartile)	16/74 (22)	18/75 (24)	2.4 (–11.1 to 15.9)	0.73
Suspended protocol — no./total no. (%)	18/39 (46)	13/20 (65)	18.9 (–7.3 to 45.0)	0.17

Disease specific thresholds

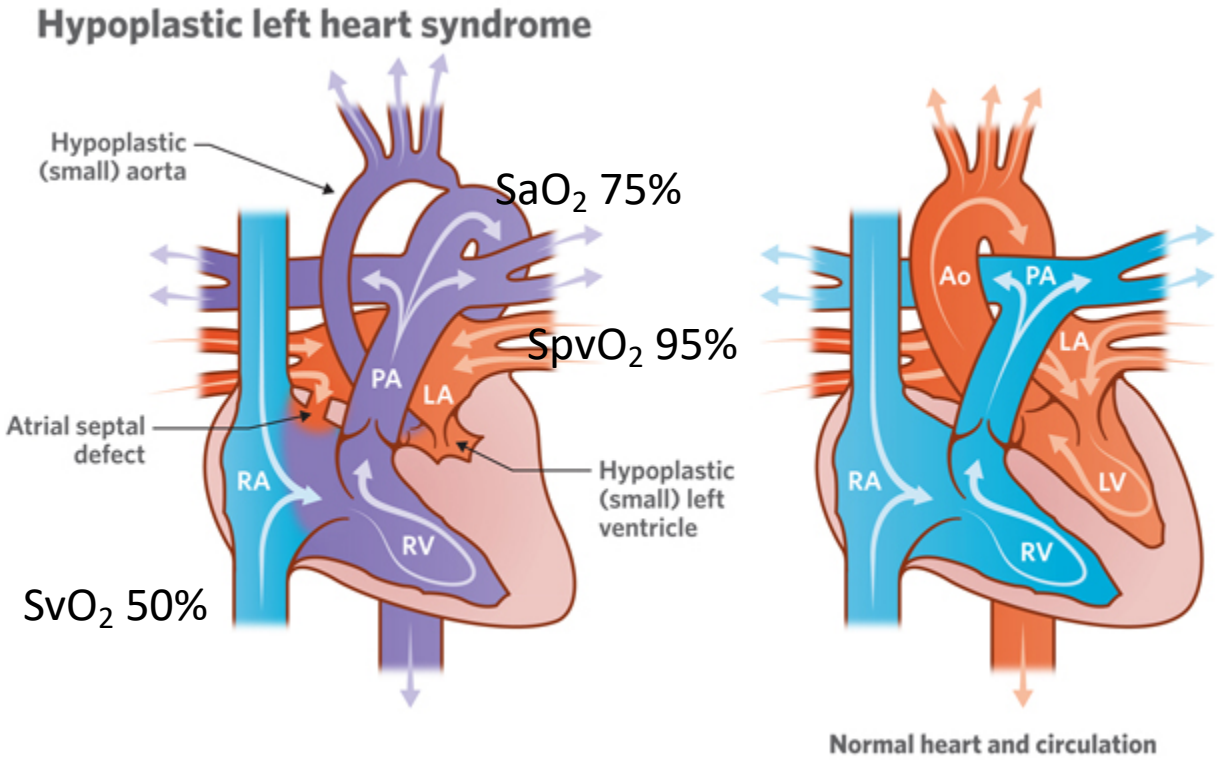
Cyanotic heart disease

- SpO_2 75%
- therefore need for higher [Hb] to preserve DO2
- Hb > 12 g/L?

Sickle cell disease

Pulmonary hypertension

- 10 g/L?



TRACT

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transfusion Volume for Children with Severe Anemia in Africa

K. Maitland, P. Olupot-Olupot, S. Kiguli, G. Chagaluka, F. Alaroker, R.O. Opoka, A. Mpoya, C. Engoru, J. Nteziyaremye, M. Mallewa, N. Kennedy, M. Nakuya, C. Namayanja, J. Kayaga, S. Uyoga, D. Kyeyune Byabazaire, B. M'baya, B. Wabwire, G. Frost, I. Bates, J.A. Evans, T.N. Williams, P. Saramago Goncalves, E.C. George, D.M. Gibb, and A.S. Walker, for the TRACT Group*

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 1, 2019 VOL. 381 NO. 5

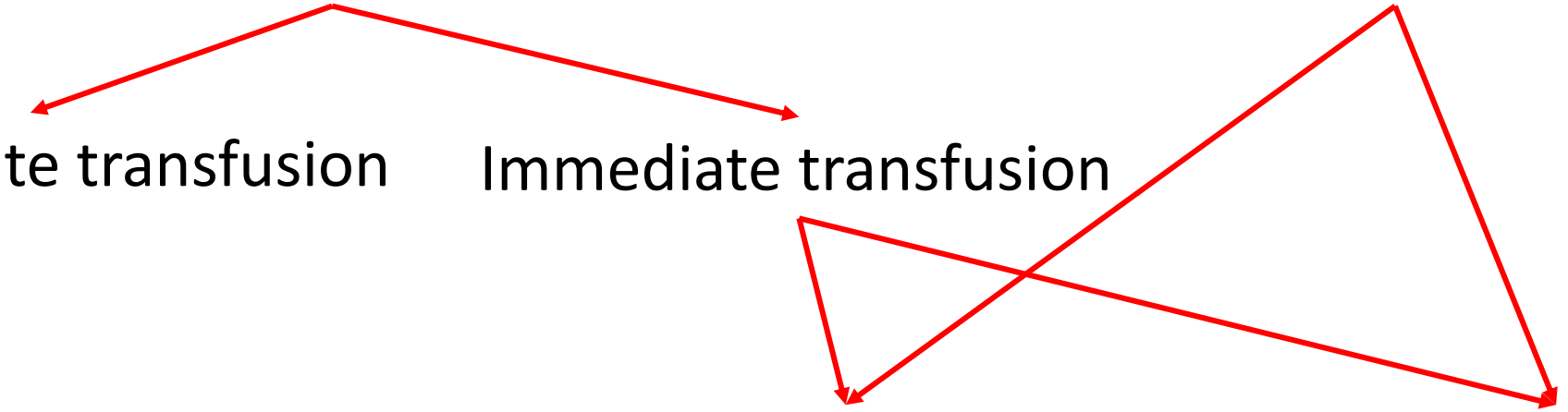
Immediate Transfusion in African Children with Uncomplicated Severe Anemia

K. Maitland, S. Kiguli, P. Olupot-Olupot, C. Engoru, M. Mallewa, P. Saramago Goncalves, R.O. Opoka, A. Mpoya, F. Alaroker, J. Nteziyaremye, G. Chagaluka, N. Kennedy, E. Nabawanuka, M. Nakuya, C. Namayanja, S. Uyoga, D. Kyeyune Byabazaire, B. M'baya, B. Wabwire, G. Frost, I. Bates, J.A. Evans, T.N. Williams, E.C. George, D.M. Gibb, and A.S. Walker, for the TRACT Group*

TRACT

Children with Hb between 40-60 g/L and asymptomatic

Children with Hb<40 g/L or (<60 gl/L and symptomatic)



No immediate transfusion

Immediate transfusion

30 ml/kg whole blood (15 ml/kg PRBC)

20 ml/kg whole blood (10 ml/kg PRBC)

Primary outcome 28 day mortality

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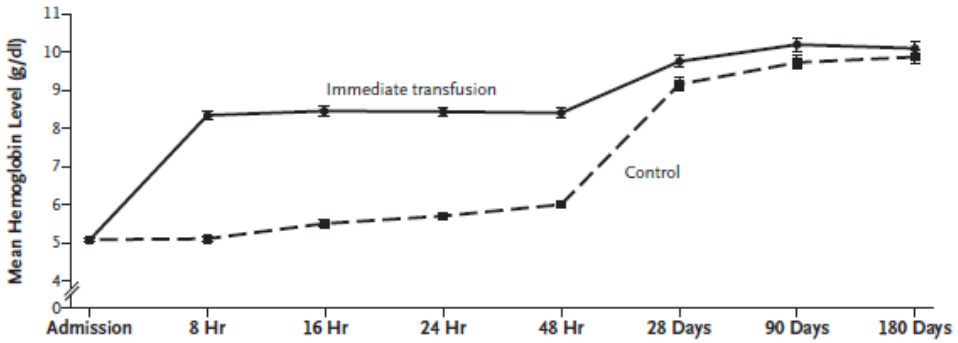
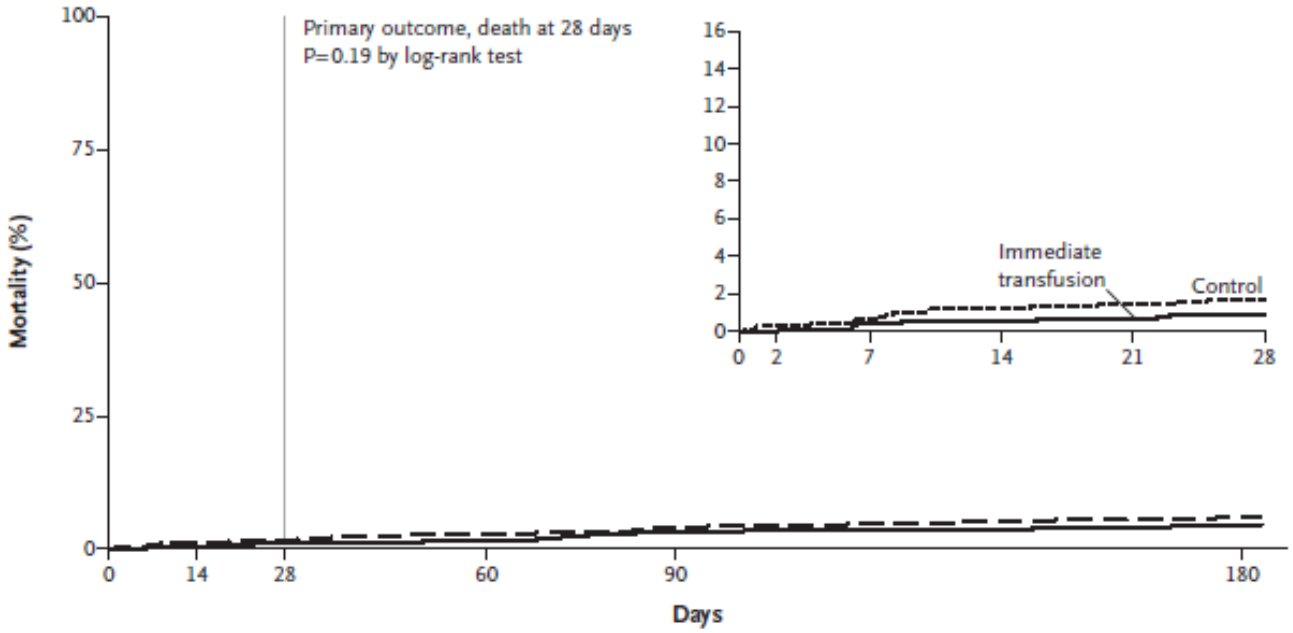


Initial increase in Hb
But did not persist to 28 or 180 days

Hazard ratio at 28 days 0.54 (0.22-1.36)
p-value 0.19



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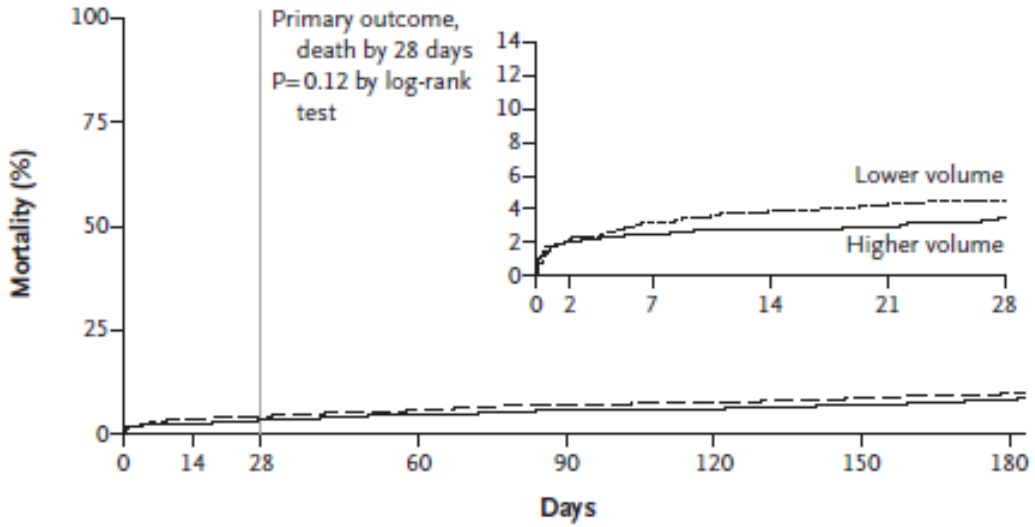
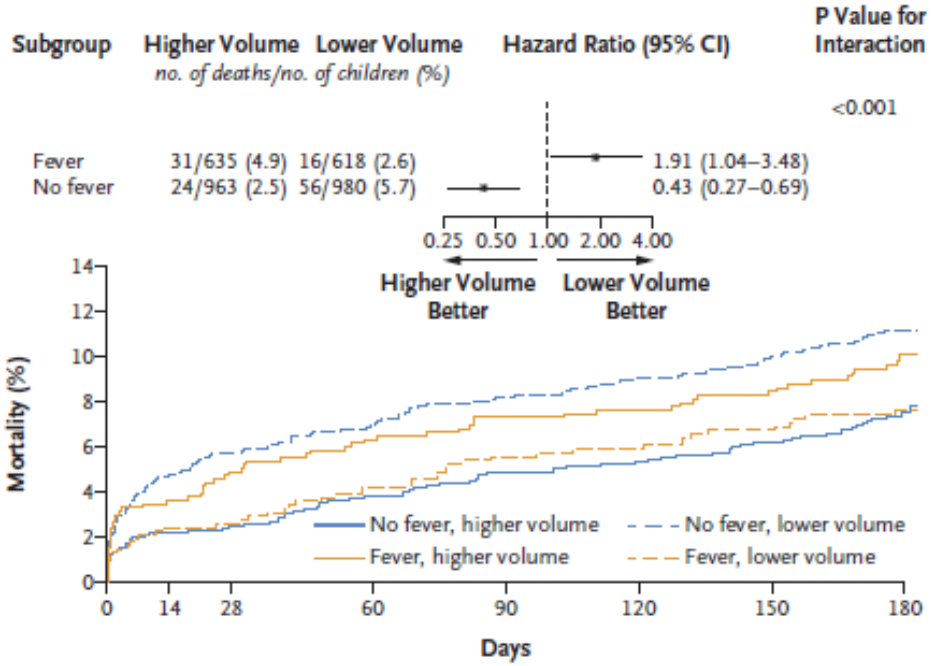
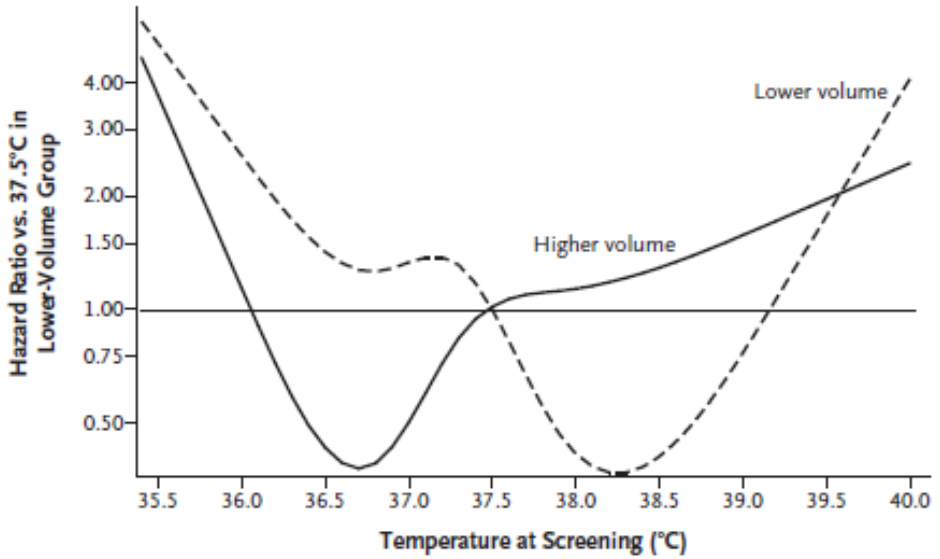


Hazard ratio at 28 days 0.76 (0.54-1.08)
p-value = 0.12

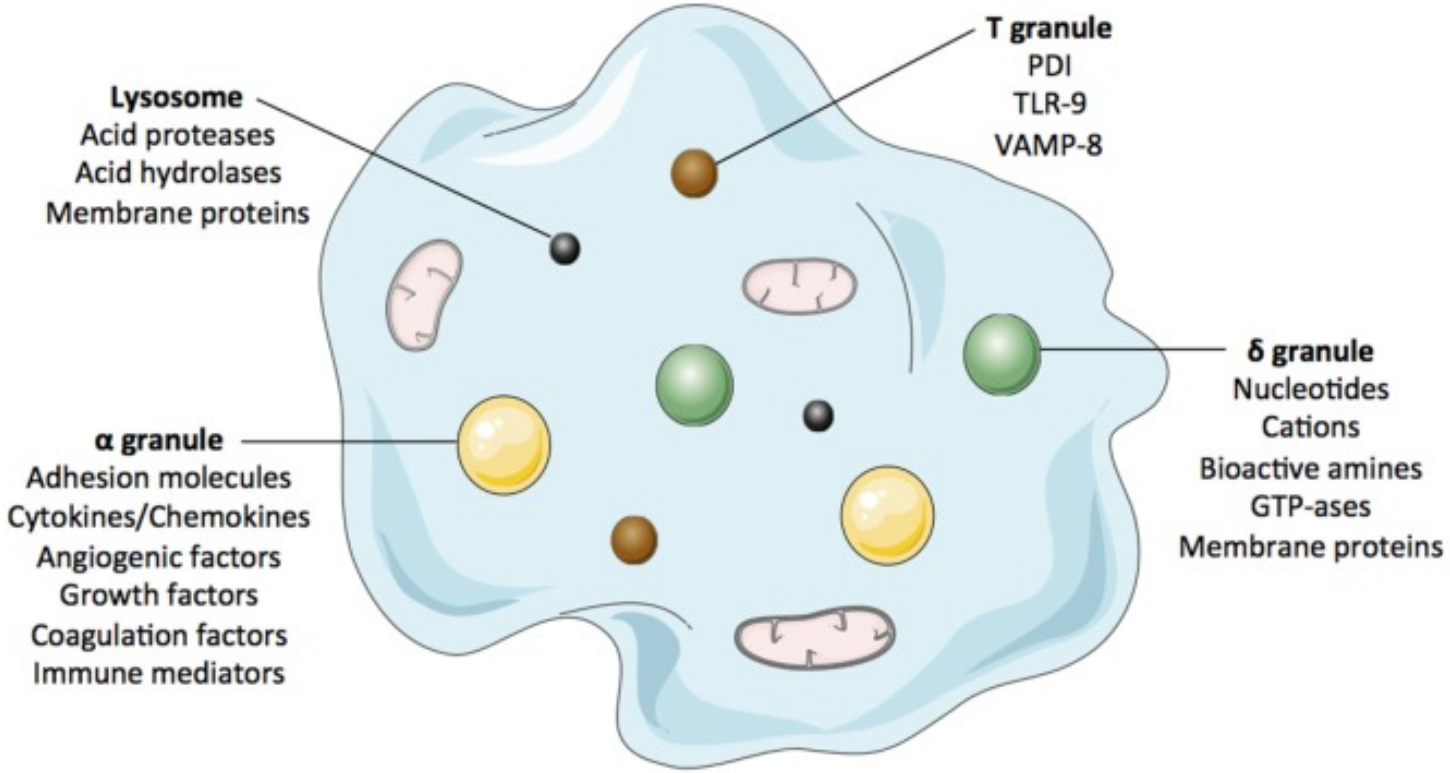




Mechanisms against transfusion

Inflammatory effect

- Products of cell lysis
- DAMPs
- Interactions with endothelium



Mechanisms against transfusion

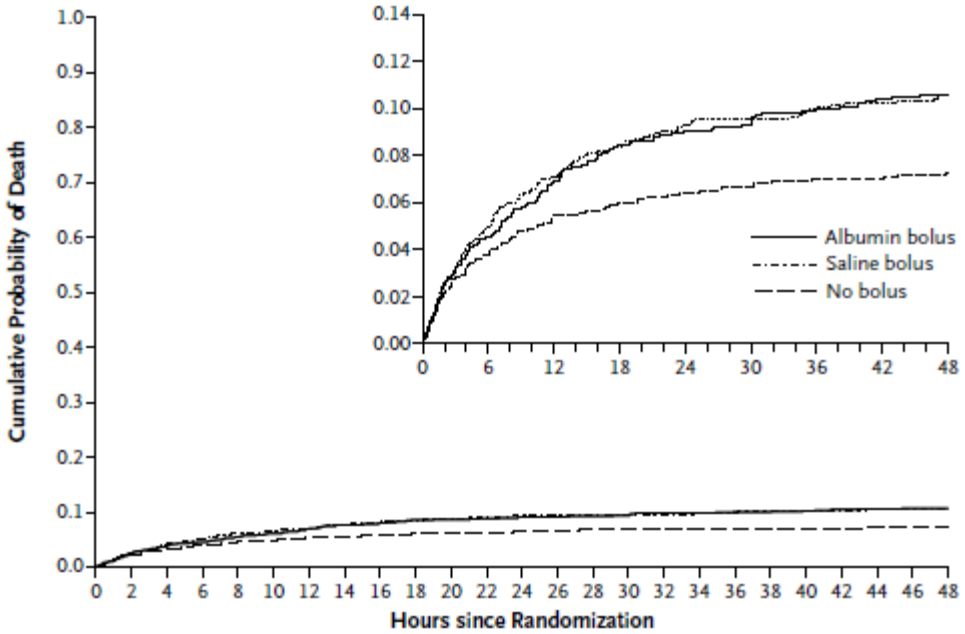
Volume effect

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 30, 2011 VOL. 364 NO. 26

Mortality after Fluid Bolus in African Children with Severe Infection

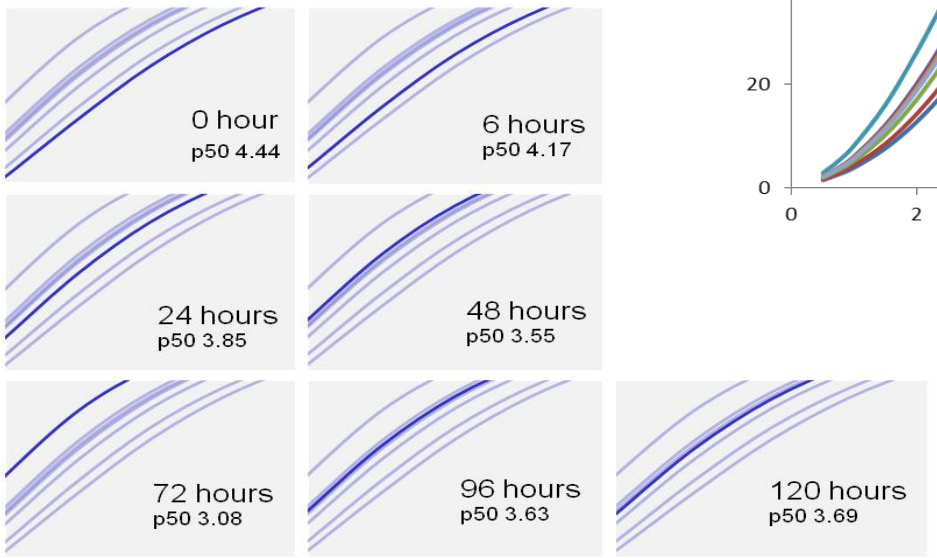
land, M.B., B.S., Ph.D., Sarah Kiguli, M.B., Ch.B., M.Med., Robert O. Opoka, M.B., Ch.B., M.Med., ngoru, M.B., Ch.B., M.Med., Peter Olupot-Olupot, M.B., Ch.B., Samuel O. Akech, M.B., Ch.B., Nyeko, M.B., Ch.B., M.Med., George Mtove, M.D., Hugh Reyburn, M.B., B.S., Trudie Lang, Ph.D., tte Brent, M.B., B.S., Jennifer A. Evans, M.B., B.S., James K. Tibenderana, M.B., Ch.B., Ph.D., M.B., B.S., M.D., Elizabeth C. Russell, M.Sc., Michael Levin, F.Med.Sci., Ph.D., Abdel G. Babiker, Ph.D., and Diana M. Gibb, M.B., Ch.B., M.D., for the FEAST Trial Group*

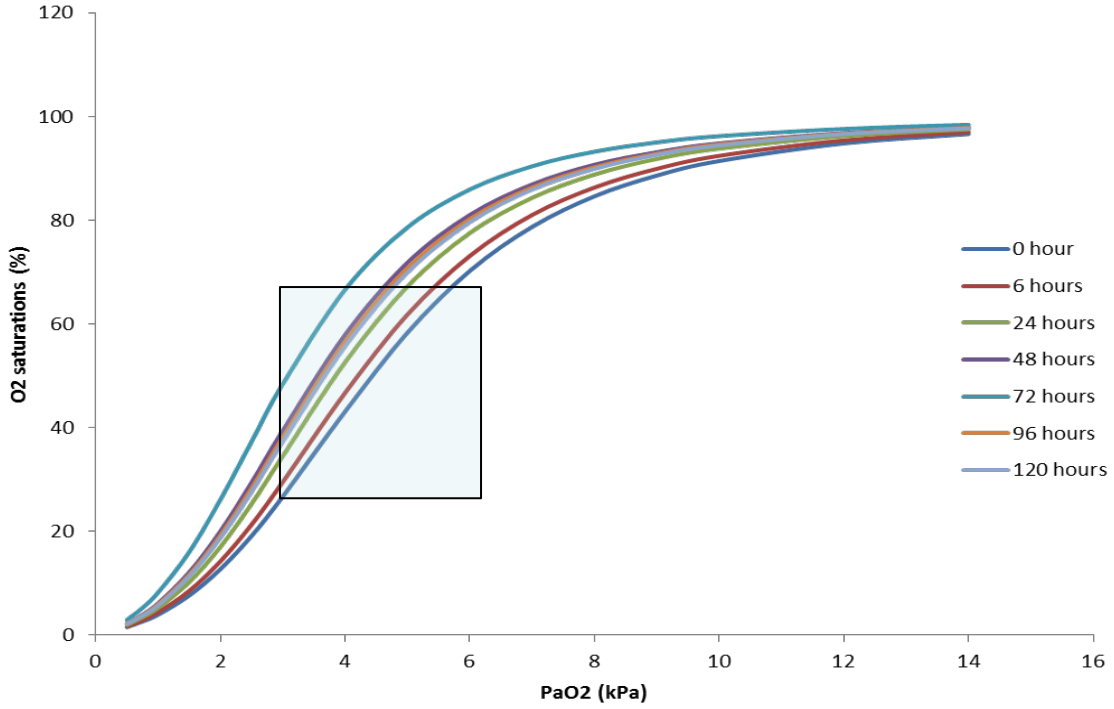


Mechanisms against transfusion

Decrease in oxygen affinity

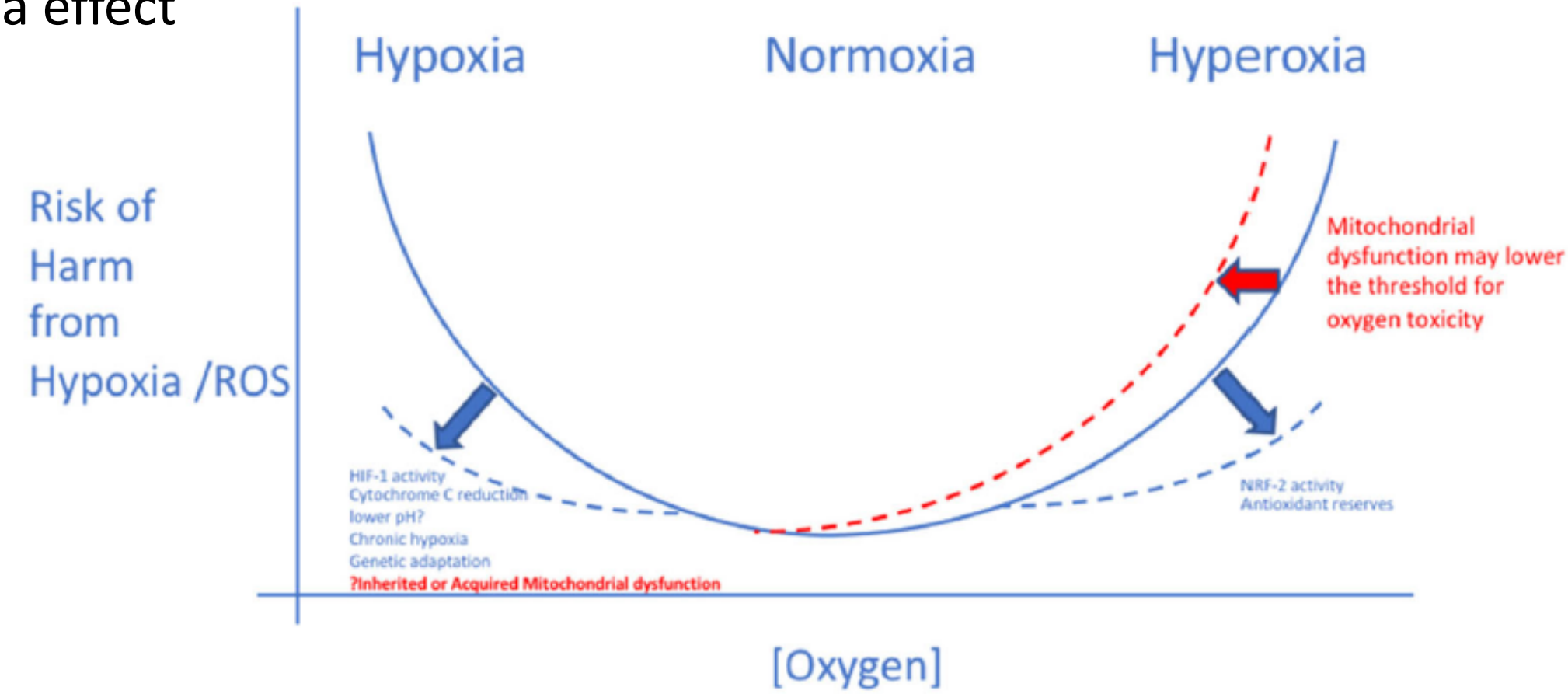
- Reduced 2,3 DPG in stored blood





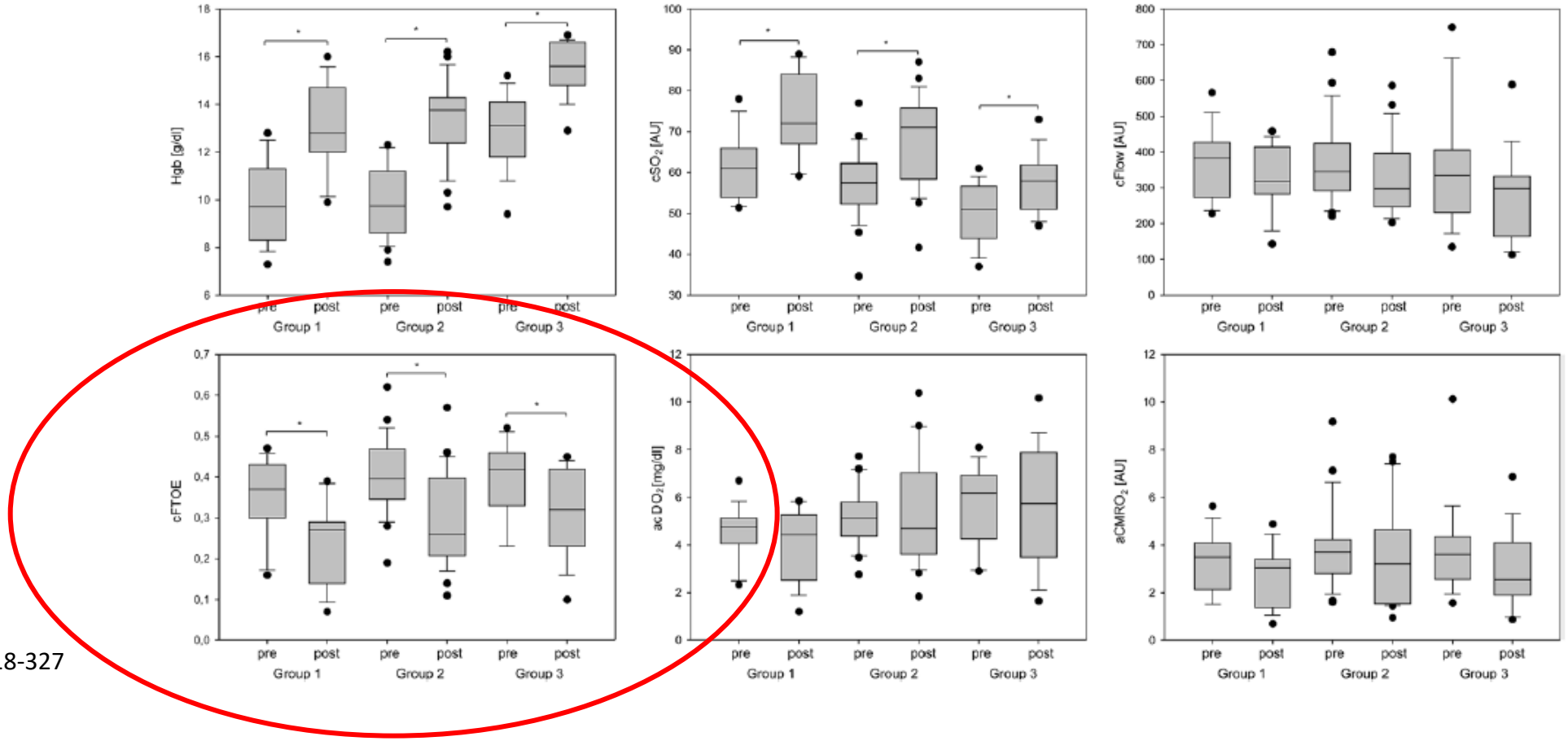
Mechanisms against transfusion

Hyperoxia effect



Hb thresholds?

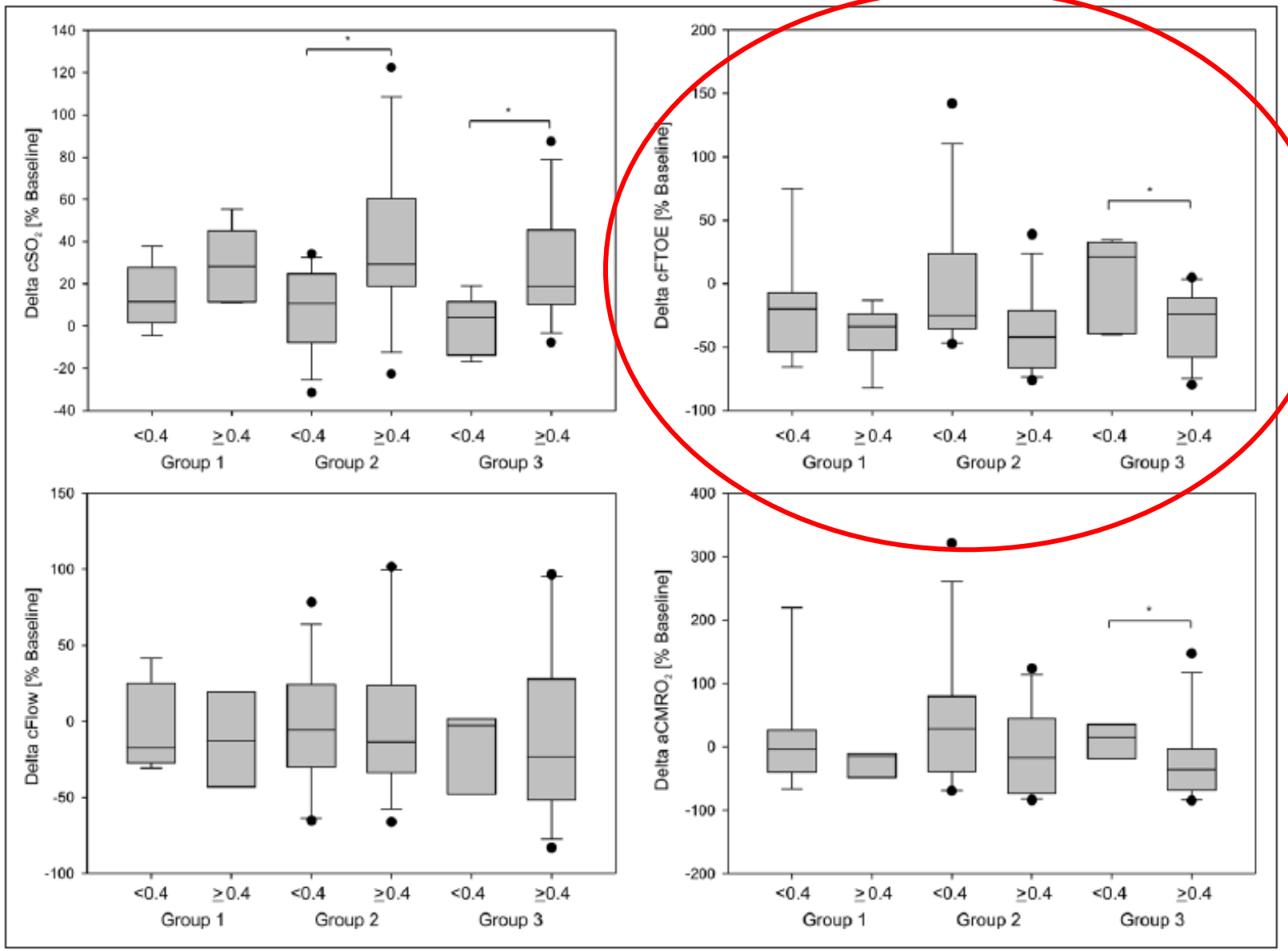
May not be the best number to guide transfusion…



Neunhoffer et al
Ped Crit Care Med; 19(4):318-327

Hb thresholds?

May not be the best number to guide transfusion…



Neunhoffer et al
Ped Crit Care Med; 19(4):318-327

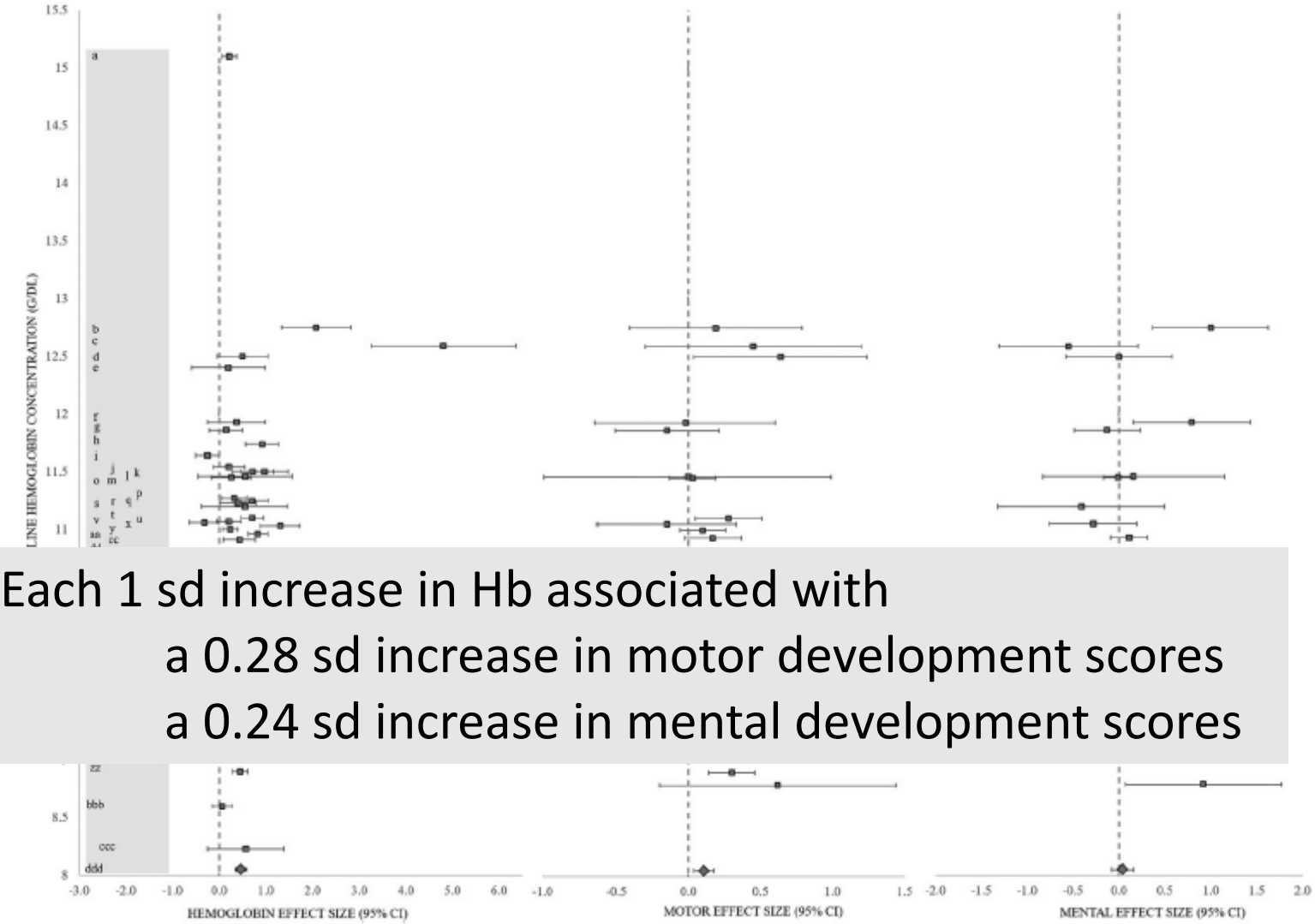
Long term effects

ANN
Specia
REVIE

Eff
dev
me

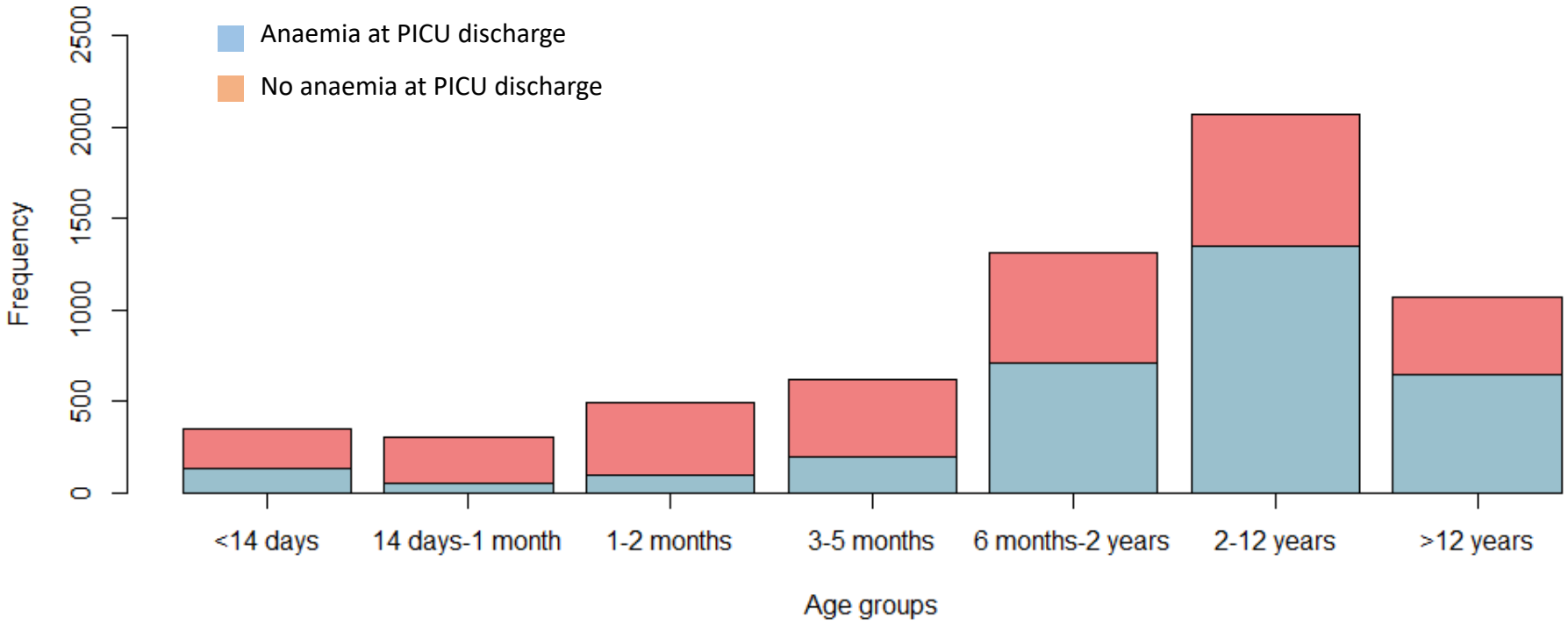
Leila
Sara

[1]Depa
Unive
Atlant
Clinic
Globa
Unive



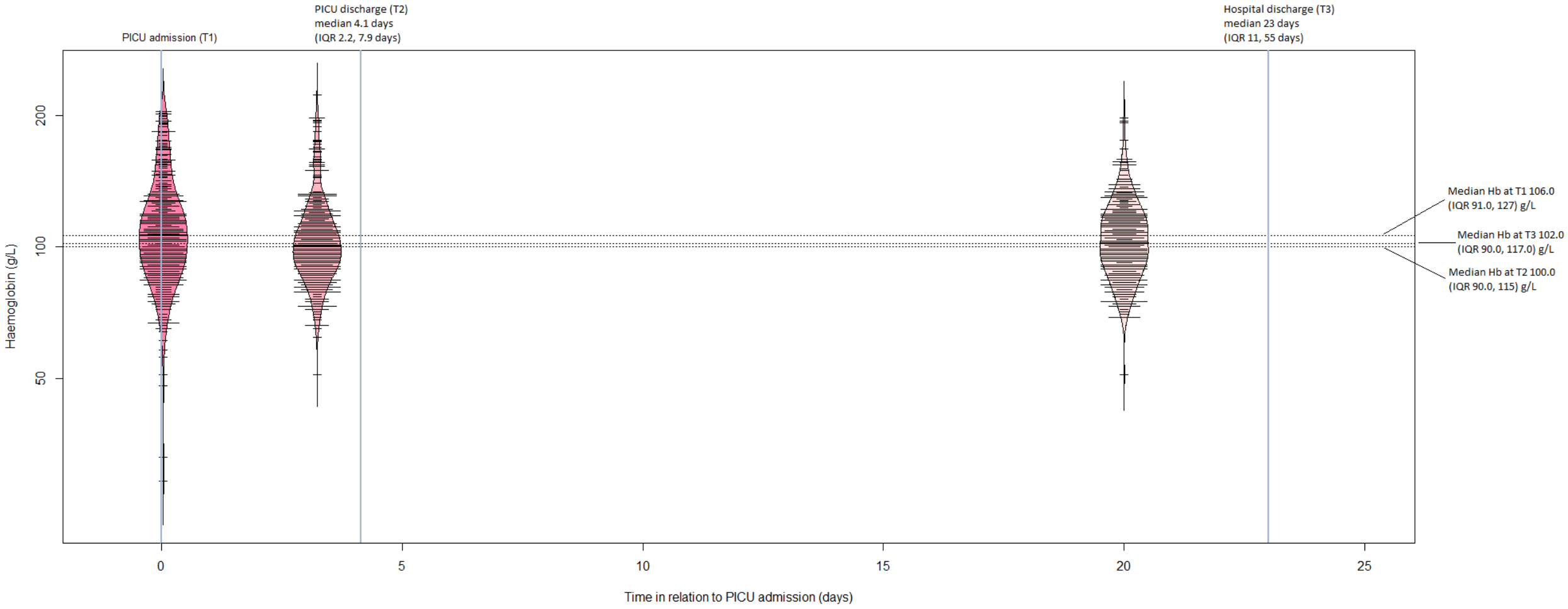
Each 1 sd increase in Hb associated with
a 0.28 sd increase in motor development scores
a 0.24 sd increase in mental development scores

Anaemia at PICU discharge



Bar plot showing distribution of anaemia at PICU according to age
3185/6210 (51.3%) with anaemia at discharge
Prevalence of anaemia greater in children > 6 months

Anaemia at hospital discharge



Long term treatments

Iron

- deficiency common problem
- side effects
- poor compliance with supplements

Folic acid

- deficiency rarer?

Erythropoeitin

- Use in renal patients in particular

Future research questions

Too many!!!

- ICU wide strategy – including unstable and cardiac patients
- Effects of transfusion on delivery/affinity
- Type of blood – rejuvenation?
- Personalisation? Physiology based thresholds?
- Post-ICU anaemia and treatment

Summary

- Restrictive transfusion strategy safe in PICU for most patients
- Need to develop strategy for unstable/cardiac patients
- Hb may not be best target
- Need to tackle anameia post ICU


Questions