Platelets & Plasma components

How, why, when they are used and the impact of their use. What alternative options are there?

Dr Lise Estcourt

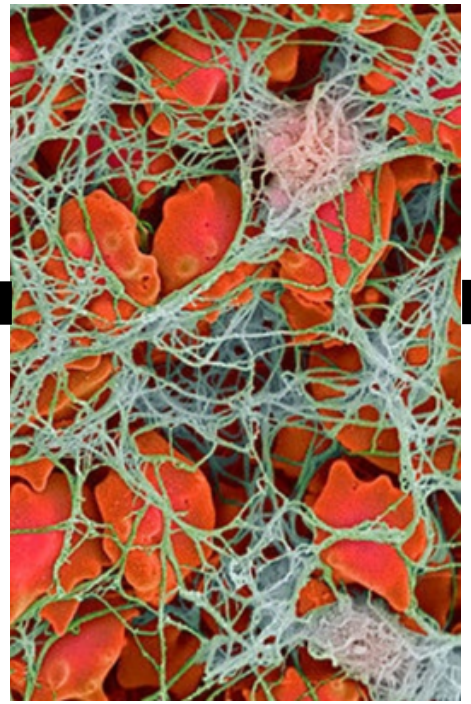
Conflicts of Interest

No conflicts of interest to declare

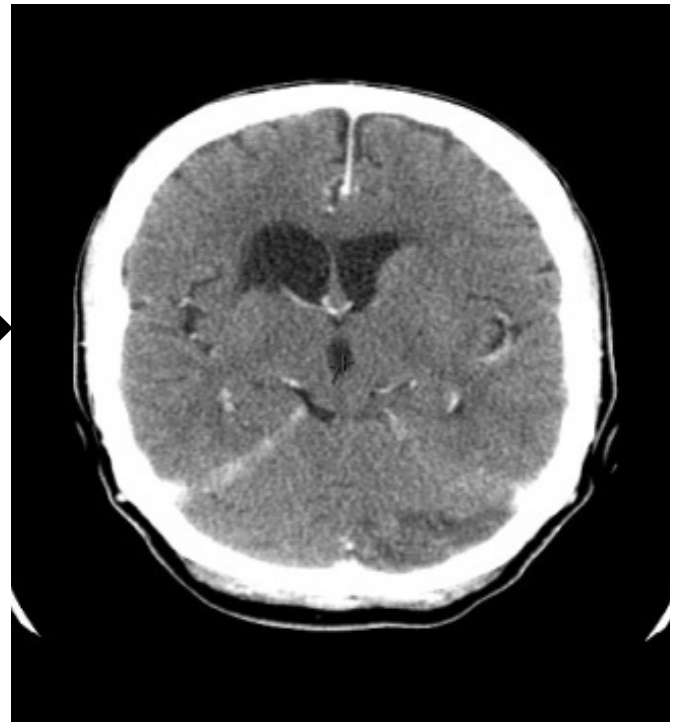
- Why do we use plasma and platelet components?
- Who uses them?
- What are the indications for their use?
- Are there any alternatives?

Why do we use platelet & plasma components?

STOP

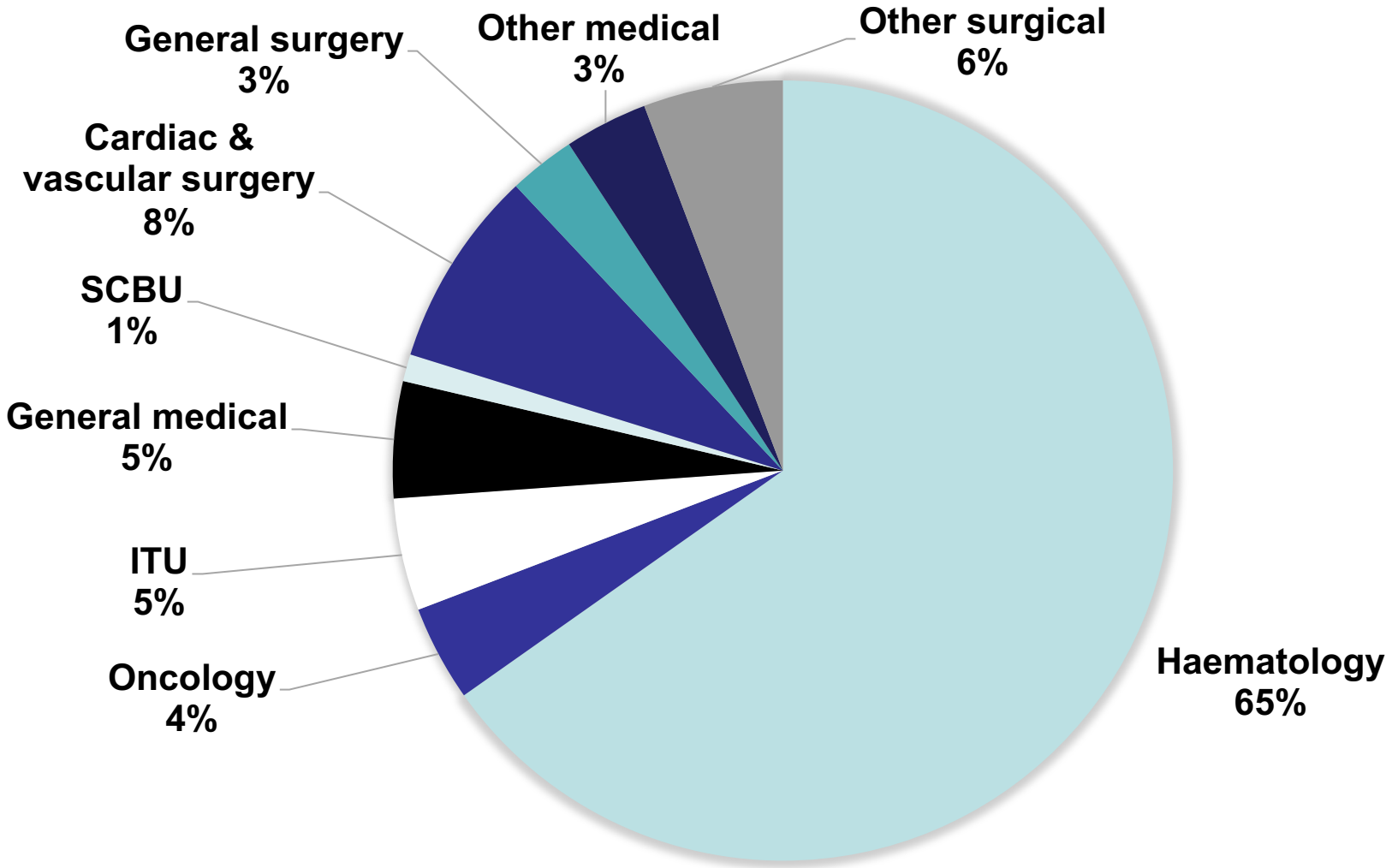


PREVENT



Who uses them?

Haematology patients use the majority of platelet transfusions



A survey of where and why platelets are used in hospitals in the South West region of England. Jones et al 2013. Transfusion Medicine 23(S2):P034

Platelet Transfusions in 2017 Audit

NHS Blood and Transplant

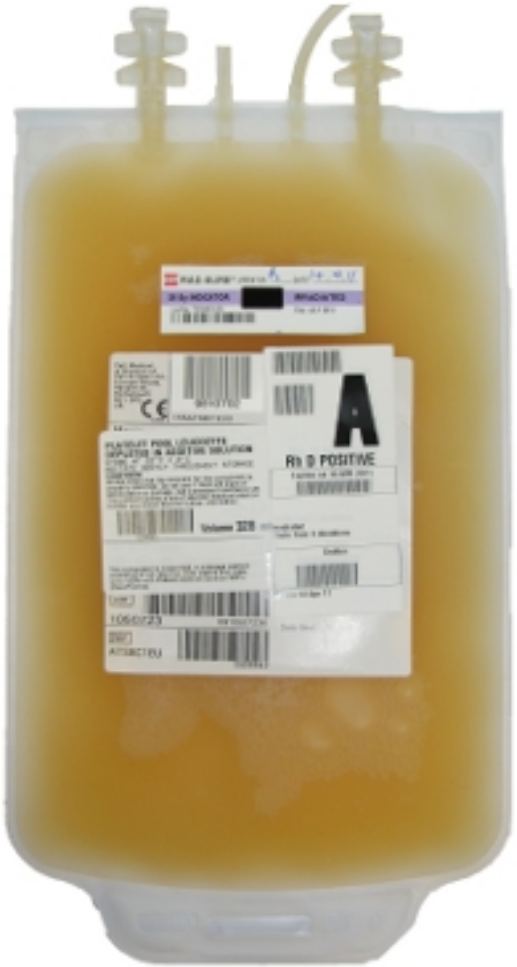
79% (1223/1553) were prophylactic and within this group

9% (138/1553) were prior to a procedure

9% (145/1553) were therapeutic

3% (47/1553) reason for transfusion was unknown

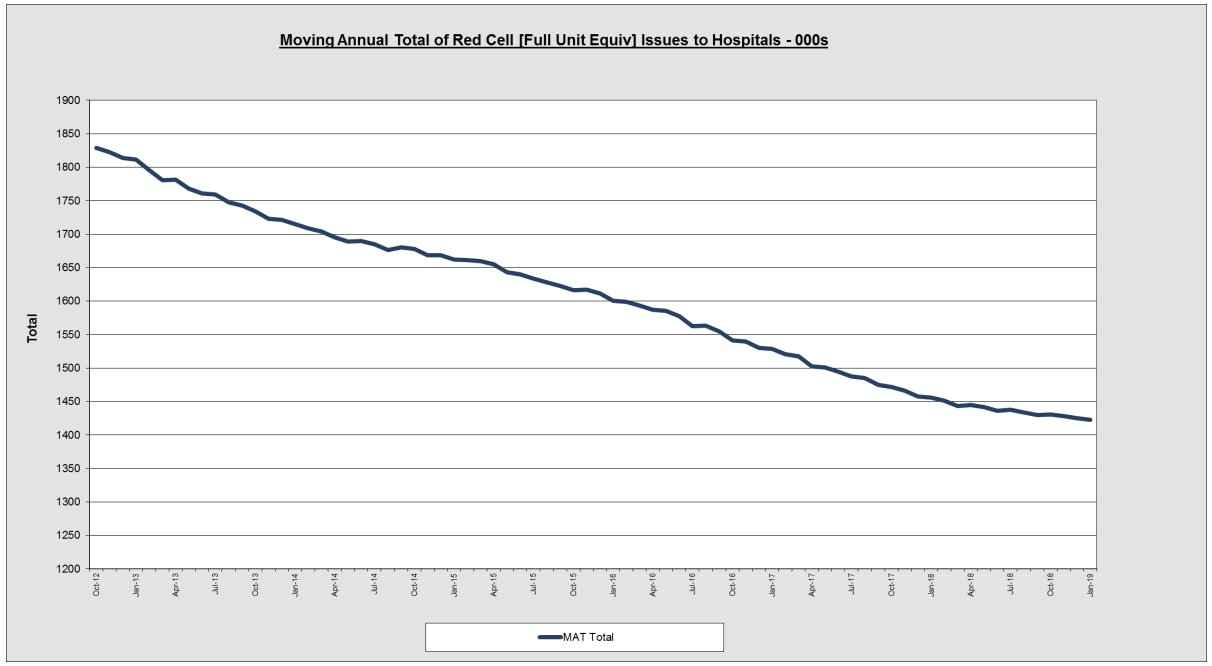
88% given to prevent bleeding



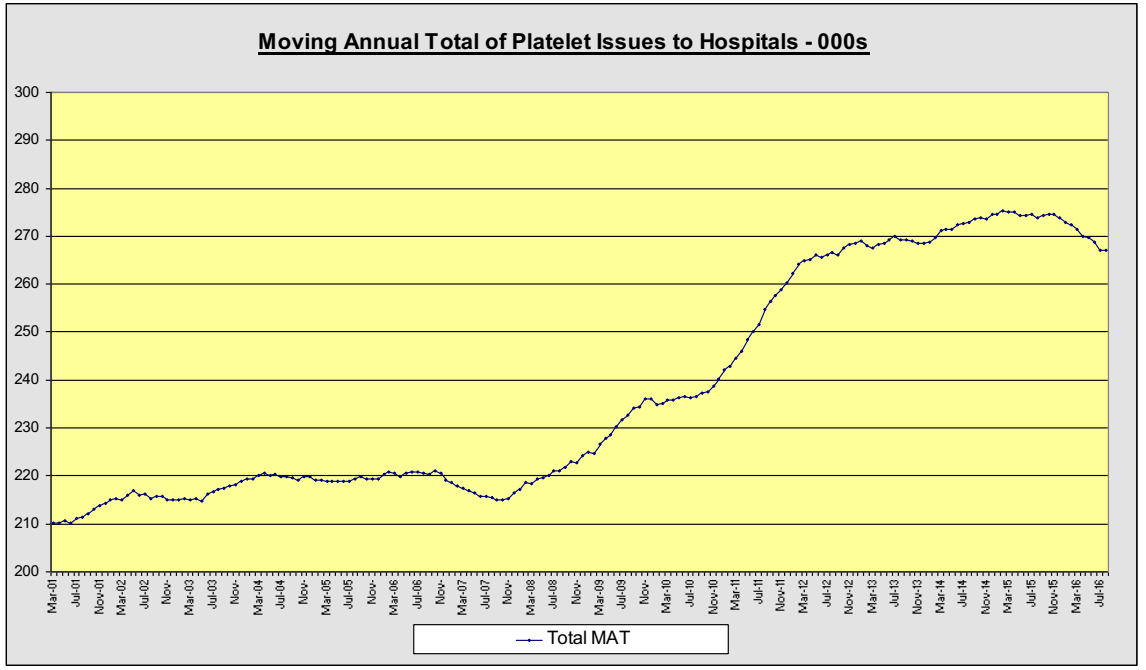
NHS Blood and Transplant

Red cell demand has decreased but not platelets

Red cells

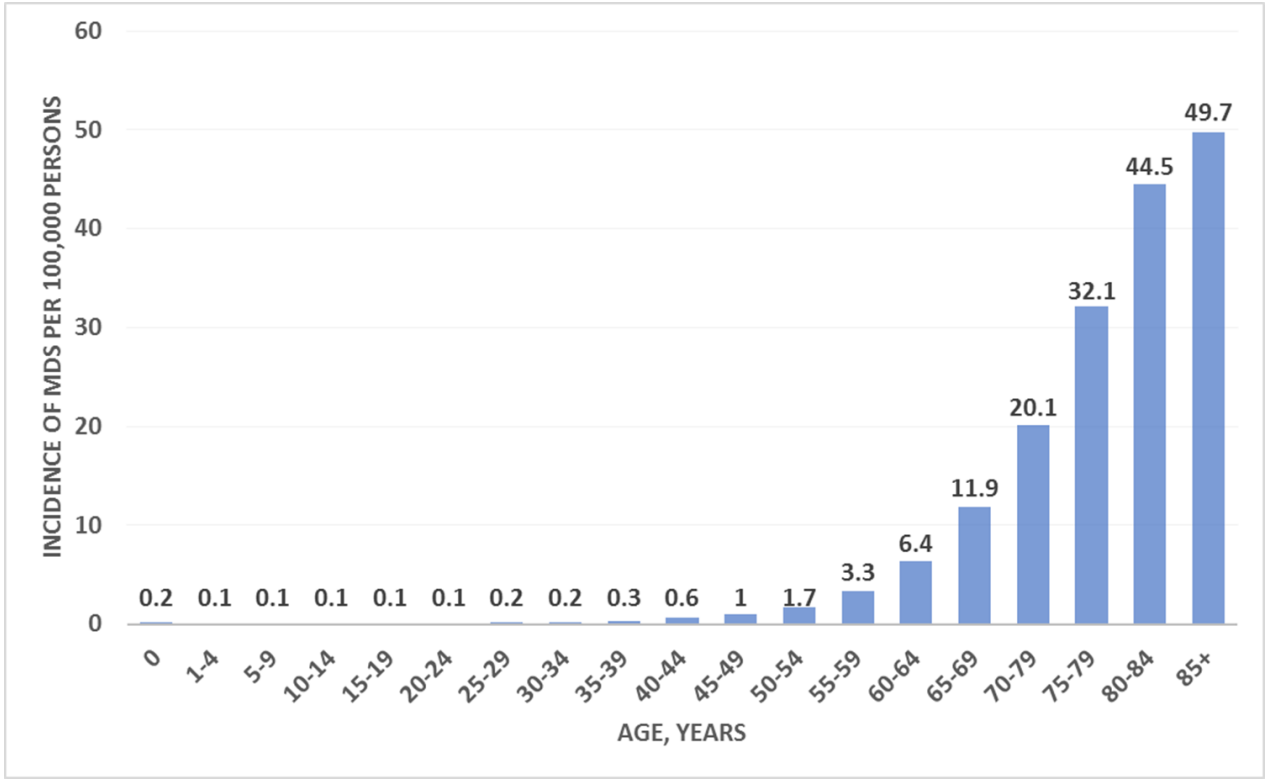


Platelets



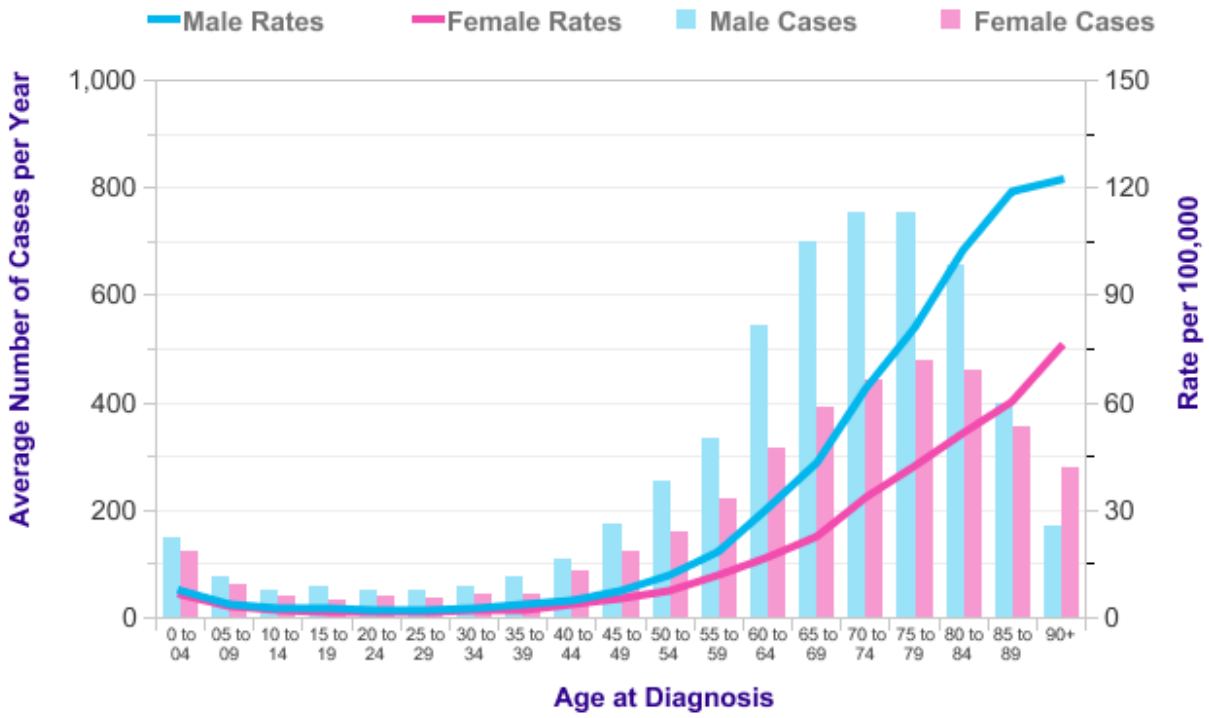
Conditions that may require platelet transfusion support increase with age

MDS



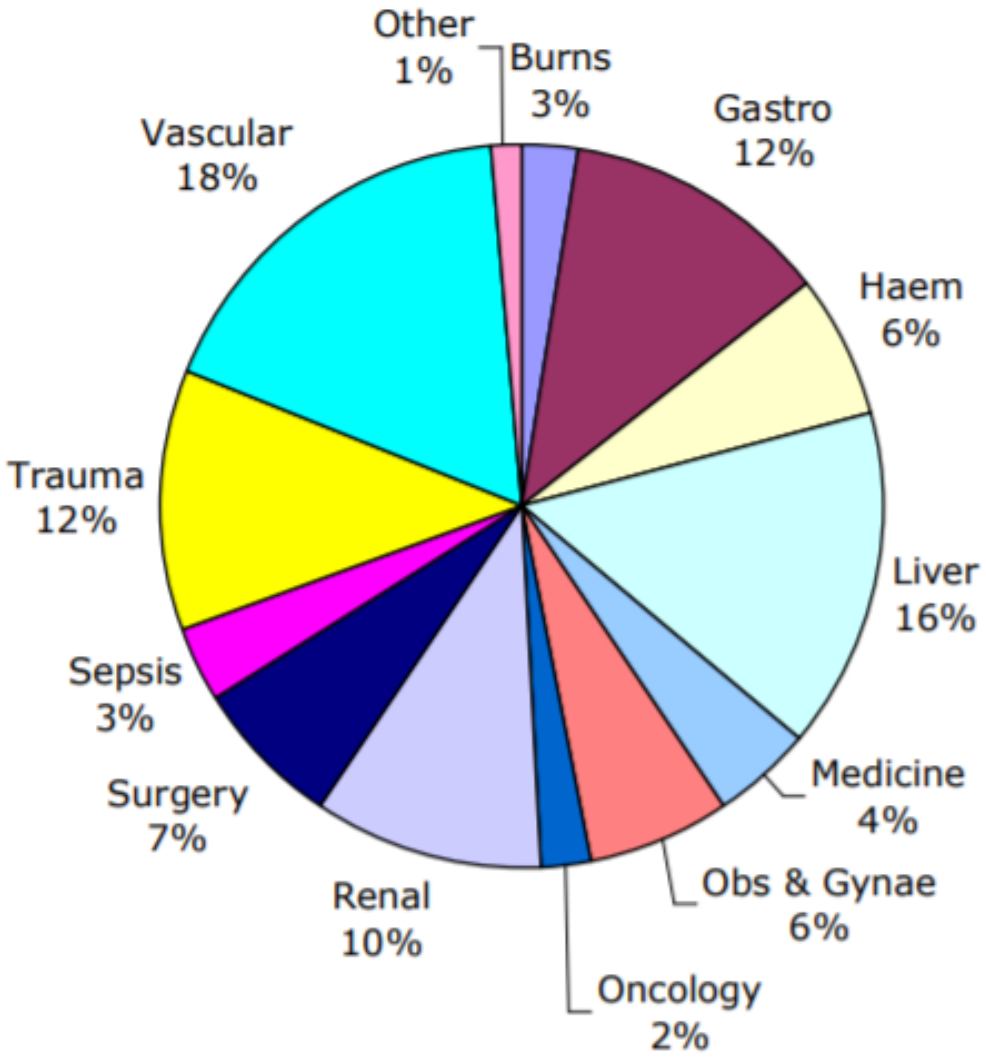
Ma et al, 2012 Am J Med;125(7 Suppl):S2–S5

Leukaemia

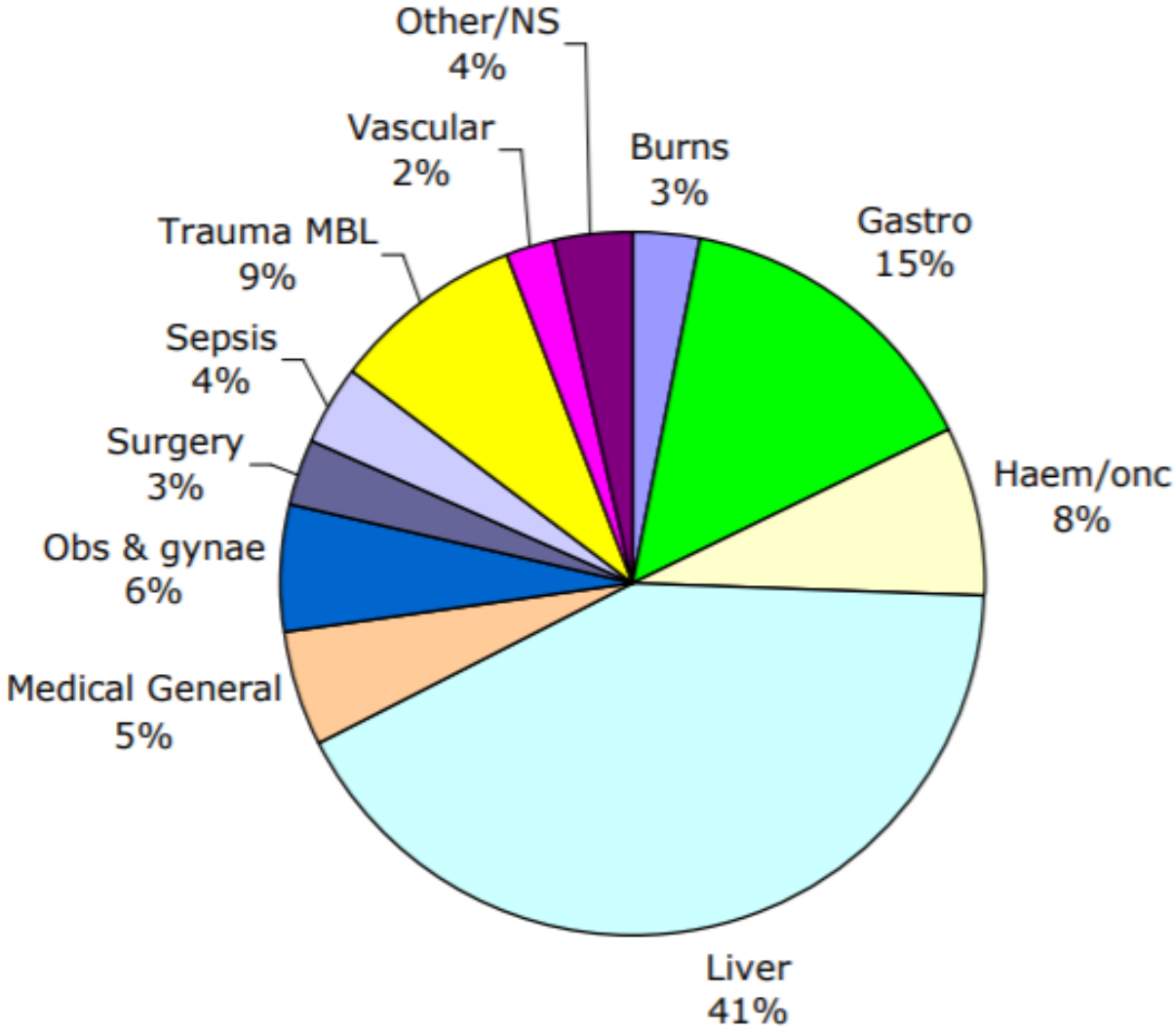


www.cruk.org/cancerstats

Fresh Frozen Plasma



Cryoprecipitate



East of England RTC Audit 2016 by units of FFP and cryoprecipitate

Majority used for massive transfusion and liver disease

Fresh Frozen Plasma

43% massive transfusion

21% liver disease

4% Acute DIC

1% clotting factor deficiencies

Cryoprecipitate

35% hypofibrinoginaemia due to massive transfusion

26% liver disease

14% Acute DIC

5% Bleeding associated with thrombolytic therapy

Why do we ABO and Rh match platelets?

- Risk of red cell alloimmunisation
  - Residual red blood cells (rRBC)

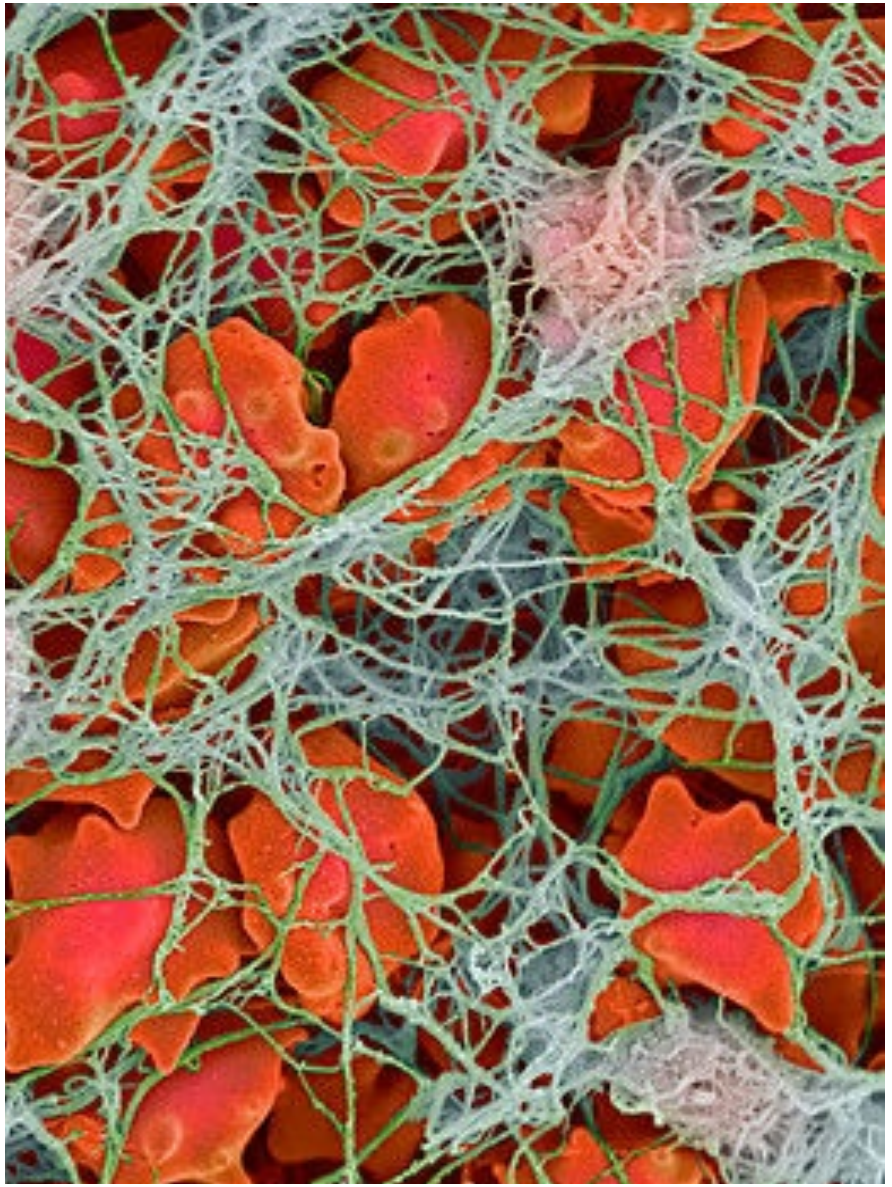
- Risk of haemolytic transfusion reaction
  - E.g. Anti A antibodies in plasma transfused into patient with blood group A

- Increased destruction of transfused platelets
  - E.g. Blood group A platelets transfused into patient with Anti A antibodies

What are the indications for use?

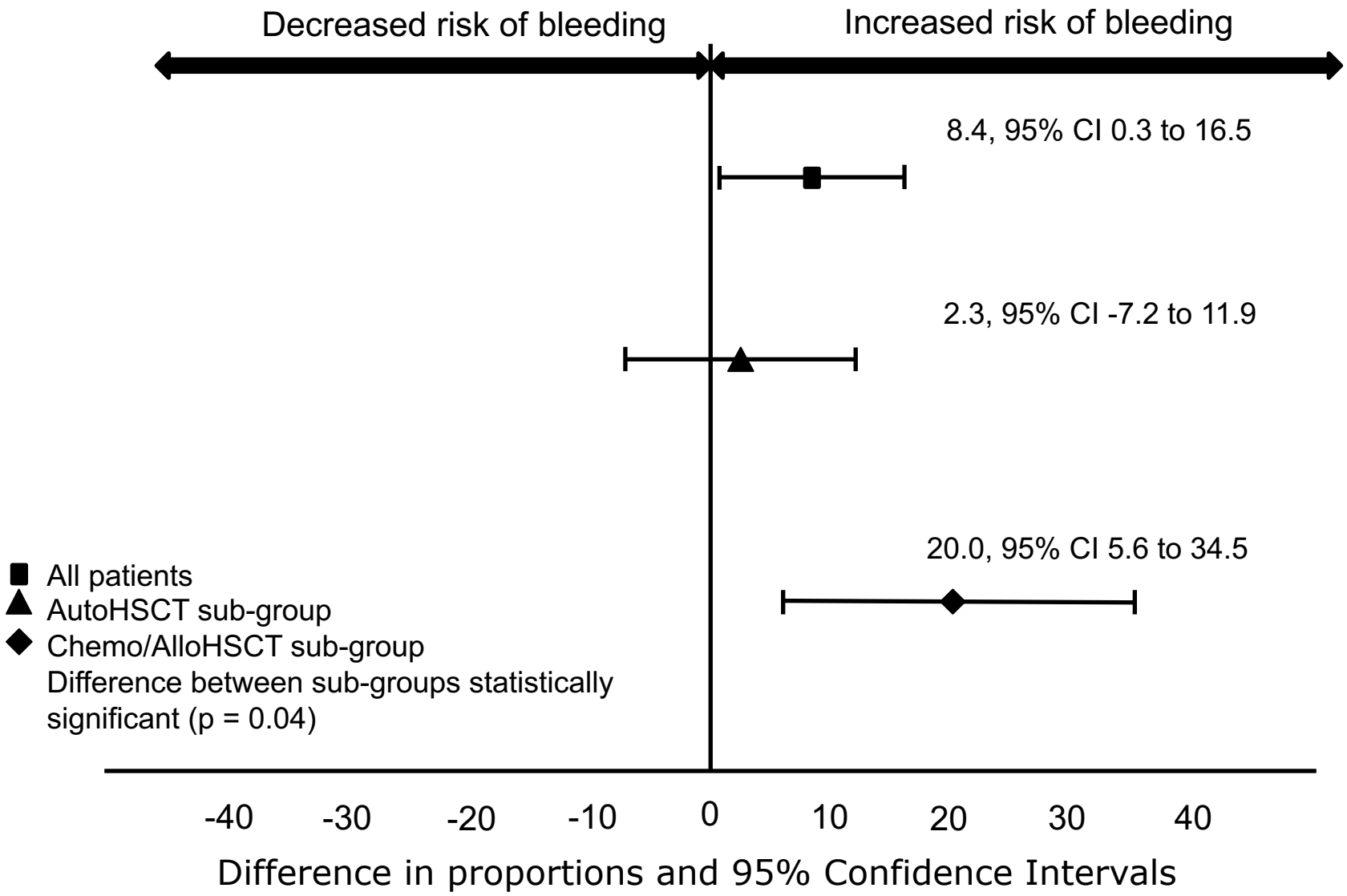
Prevention of bleeding (platelets)

- Bleeding remains an important complication in patients with haematological malignancies with low platelet counts
- Up to 70% will have clinically significant bleeding
- Up to 10% will have severe or life-threatening bleeding



Slichter et al, 2010 NEJM;362(7):600-13

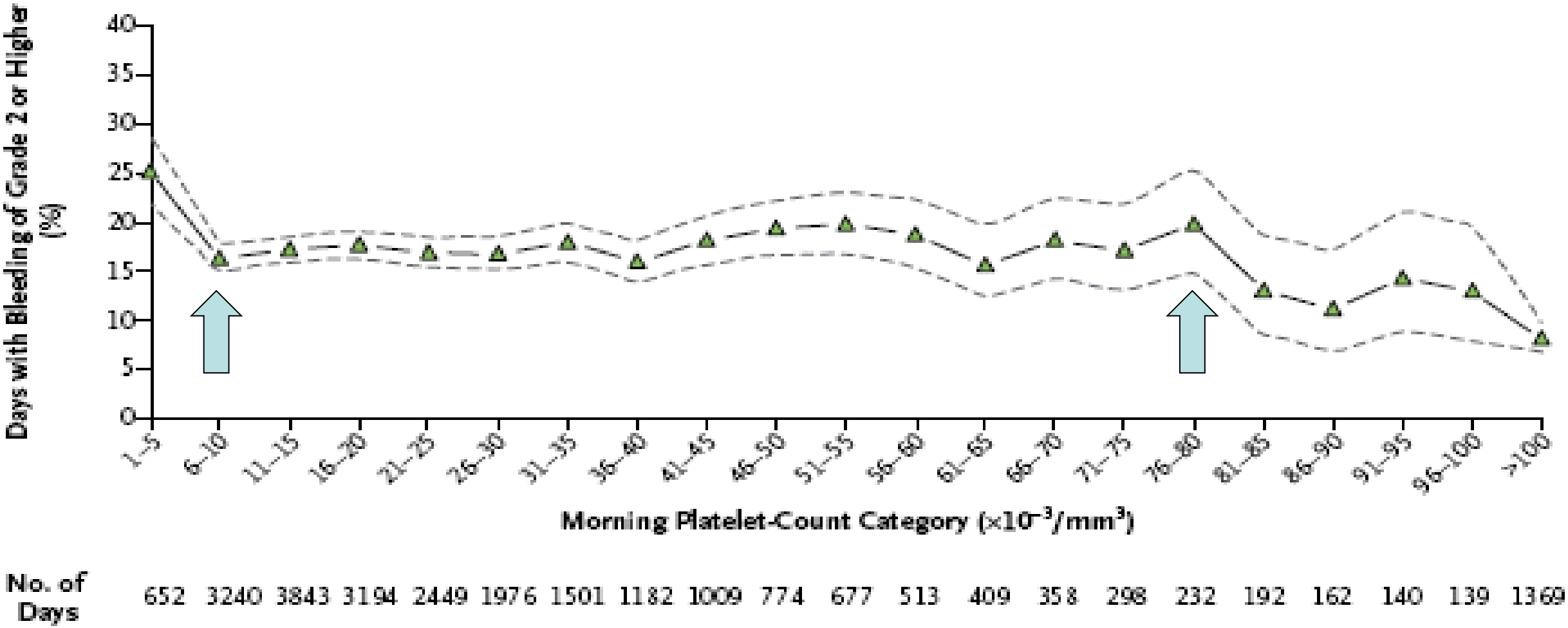
Variability in effectiveness of prophylactic platelet transfusions



	Number of patients needed to be treated with prophylactic platelet transfusions to prevent 1 patient from WHO grade 2 or above bleeding within a 30 day period	
	NNTB	**95% CI**
All patients	12	6 to 333
Autologous HSCT	43	Not estimable
Chemotherapy/ Allogeneic HSCT	5	3 to 18

Stanworth et al. A no-prophylaxis platelet transfusion strategy for hematologic malignancies. *NEJM 2013*

Morning platelet count is a poor predictor of bleeding risk



Dose of prophylactic platelet transfusions and prevention of hemorrhage. Slichter *et al. NEJM* 2010;362:600-613

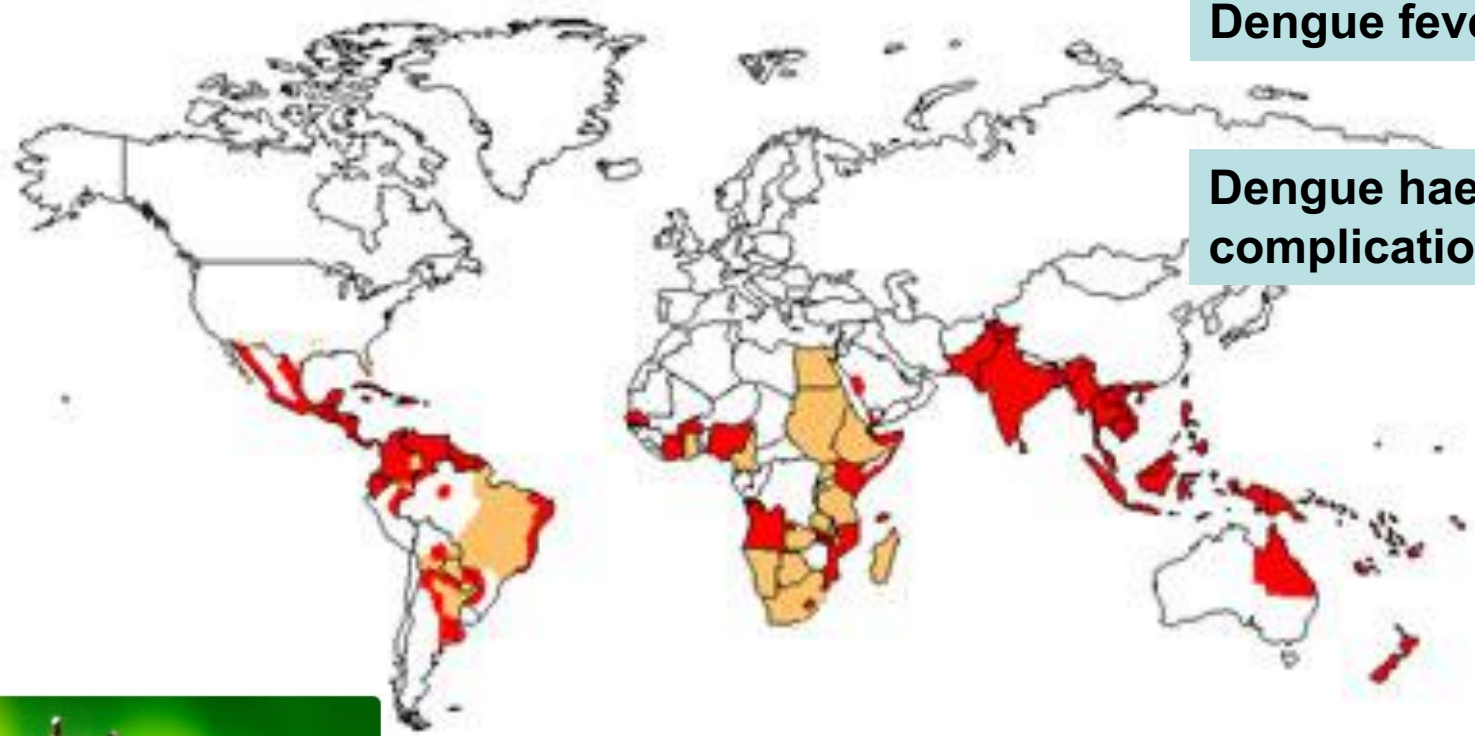
bjh guideline

Guidelines for the use of platelet transfusions

Give prophylactic platelet transfusions to patients with reversible bone marrow failure receiving intensive chemotherapy or undergoing allogeneic haematopoietic stem cell transplantation to maintain a platelet count at or above 10 x 10^9/l.

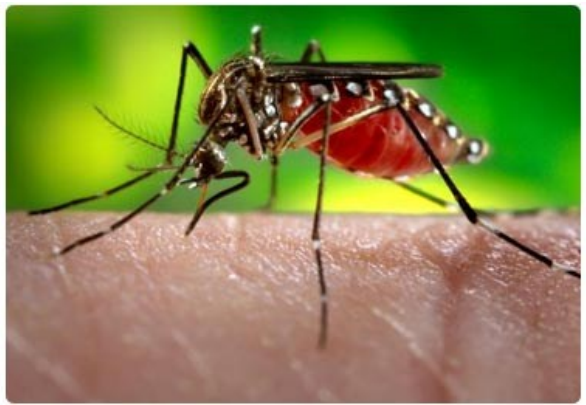
Consider not giving prophylactic platelet transfusions to well patients with no evidence of bleeding who have had an autologous stem cell transplant.

World Distribution of Dengue - 2005



Areas infested with *Aedes aegypti*

Areas with *Aedes aegypti* and dengue epidemic activity



Dengue fever affects 50 million people worldwide

Dengue haemorrhagic fever potentially fatal complication

Increased vascular permeability
Hypovolaemia
Thrombocytopenia

Dengue

Prophylactic platelet transfusion plus supportive care versus supportive care alone in adults with dengue and thrombocytopenia: a multicentre, open-label, randomised, superiority trial

David C Lye, Sophia Archuleta, Sharifah F Syed-Omar, Jenny G Low, Helen M Oh, Yuan Wei, Dale Fisher, Sasheela S L Ponnampalavanar, Limin Wijaya, Linda K Lee, Eng-Eong Ooi, Adeeba Kamarulzaman, Lucy C Lum, Paul A Tambyah, Yee-Sin Leo

- Open-label superiority RCT
  - Randomised adults with proven dengue & platelet count < 20 x 10^9/L
  - Platelet transfusion + supportive care vs. supportive care
- 5 hospitals (372 participants) Singapore & Malaysia
  - Recruited 2010 to 2014
- Assumed clinical bleeding would occur in 20% of participants

Prophylactic platelet transfusion plus supportive care versus supportive care alone in adults with dengue and thrombocytopenia: a multicentre, open-label, randomised, superiority trial. Lye, David C et al. The Lancet , Volume 389 , Issue 10079 , 1611 - 1618

Dengue

Prophylactic platelet transfusion plus supportive care versus supportive care alone in adults with dengue and thrombocytopenia: a multicentre, open-label, randomised, superiority trial

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- Hypothesis – platelet transfusion decreases clinical bleeding by 50%

- Clinical bleeding by day 7 or hospital discharge
  - 40 (21%) participants transfusion group
  - 48 (26%) participants in the control group
  - No difference in risk of bleeding (relative risk 0·81, 95% CI 0·56 to 1·17)
- Adverse events
  - 13 in the transfusion group, including 3 SAEs (anaphylaxis, TRALI, fluid overload)
  - 2 in the control group, including 1 SAE (hypotension)
  - Increased risk of adverse events (relative risk 6·26, 95% CI 1·43 to 27·34)

Prophylactic platelet transfusion plus supportive care versus supportive care alone in adults with dengue and thrombocytopenia: a multicentre, open-label, randomised, superiority trial. Lye, David C et al. The Lancet , Volume 389 , Issue 10079 , 1611 - 1618

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Randomized Trial of Platelet-Transfusion Thresholds in Neonates

Anna Curley, M.D., Simon J. Stanworth, F.R.C.P., D.Phil., Karen Willoughby, B.Sc., Susanna F. Fustolo-Gunnink, M.D., Vidheya Venkatesh, M.D., Cara Hudson, M.Sc.,

Planet-2

- Open-label superiority RCT
  - Randomised neonates < 34 weeks gestation, platelets < 50 x 10^9/L, no IVH
  - Platelet transfusion if platelets < 50 x 10^9/L vs. transfusion if platelets < 25 x 10^9/L

- 43 hospitals (660 participants) UK, Netherlands, Ireland
  - Recruited June 2011 to August 2017

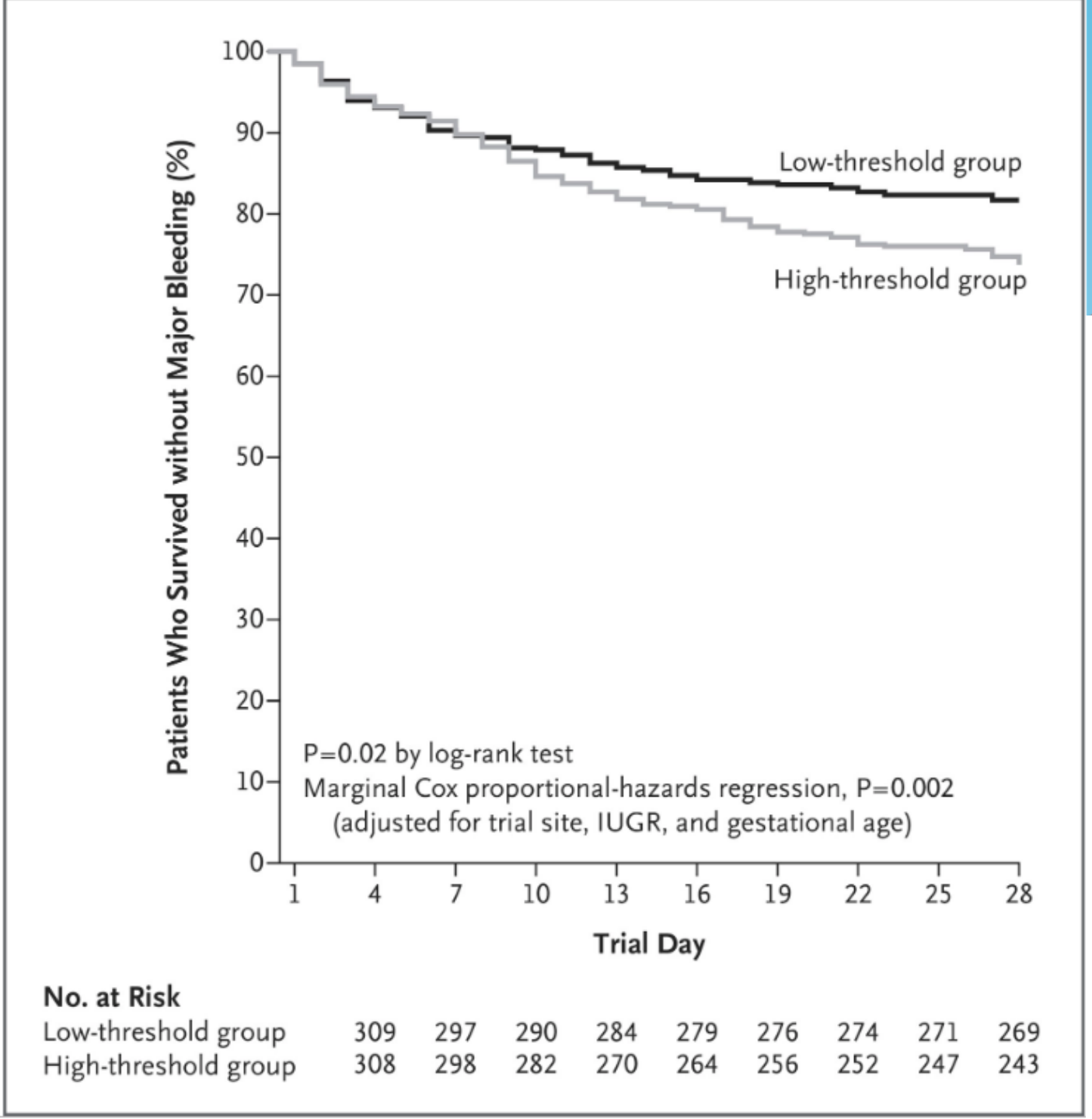
Curley, A., et al., *Randomized Trial of Platelet-Transfusion Thresholds in Neonates*. New England Journal of Medicine, 2018.

PlaNeT-Study 2 / MATISSE: A randomised trial of platelet transfusion thresholds

Research question:

Is prophylactic platelet transfusion in preterm babies at platelet count <50x10^9/L superior to <25x10^9/L for outcomes of mortality and major bleeding?

Assumed clinical bleeding or death would occur in 20% of participants in low threshold group (<25 x 109/L) (standard in UK)



Planet-2

Death or major bleeding at 28 days

61/329 (19%) low threshold
85/324 (26%) high threshold
Odds Ratio (OR) 1.57 (95% CI 1.06 to 2.32)

Death at 28 days

33/330 (10%) low threshold
48/326 (15%) high threshold
OR, 1.56 (95% CI 0.95 to 2.55)

≥1 episode major bleeding at 28 days

35/330 (11%) low threshold
45/328 (14%) high threshold
Hazard ratio 1.32 (95% CI 1.00 to 1.74)

Table 3 Suggested thresholds of platelet count for neonatal platelet transfusion

Platelet count ($\times 10^9$/l)	Indication for platelet transfusion
< 25	Neonates with no bleeding (including neonates with NAIT if no bleeding and no family history of ICH).
< 50	Neonates with bleeding, current coagulopathy, before surgery, or infants with NAIT if previously affected sibling with ICH
< 100	Neonates with major bleeding or requiring major surgery (e.g. neurosurgery)

ICH: intracranial haemorrhage

New, H., et al., *Guidelines on transfusion for foetuses, neonates, and older children*. British Journal of Haematology, 2016.

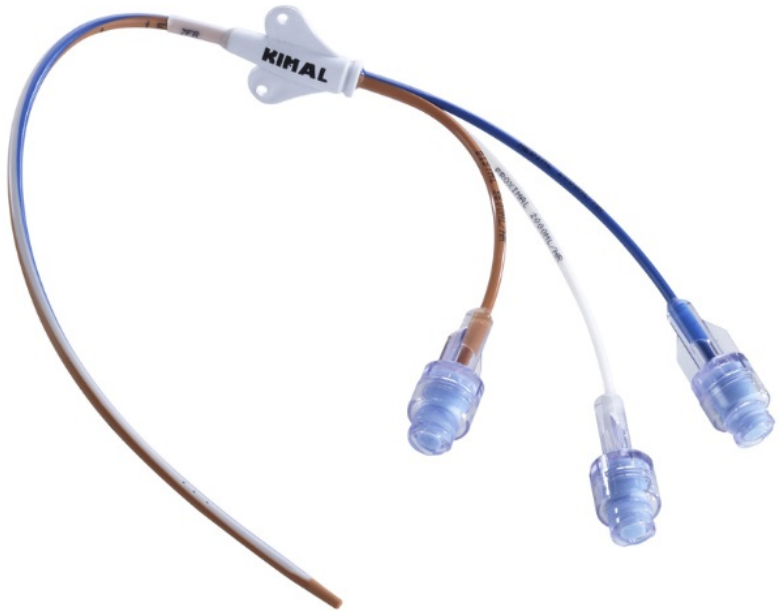
Prophylactic fresh frozen plasma and cryoprecipitate

If a patient is NOT bleeding and NOT about to have surgery or a procedure with a moderate or high risk of bleeding DO NOT give fresh frozen plasma or cryoprecipitate to correct abnormal coagulation

- No evidence of benefit
- Risk of harm

NICE National Institute for Health and Care Excellence

Low risk procedures



No platelet transfusions, FFP, or cryoprecipitate required

Low platelet count prior to surgery at moderate or high risk of bleeding

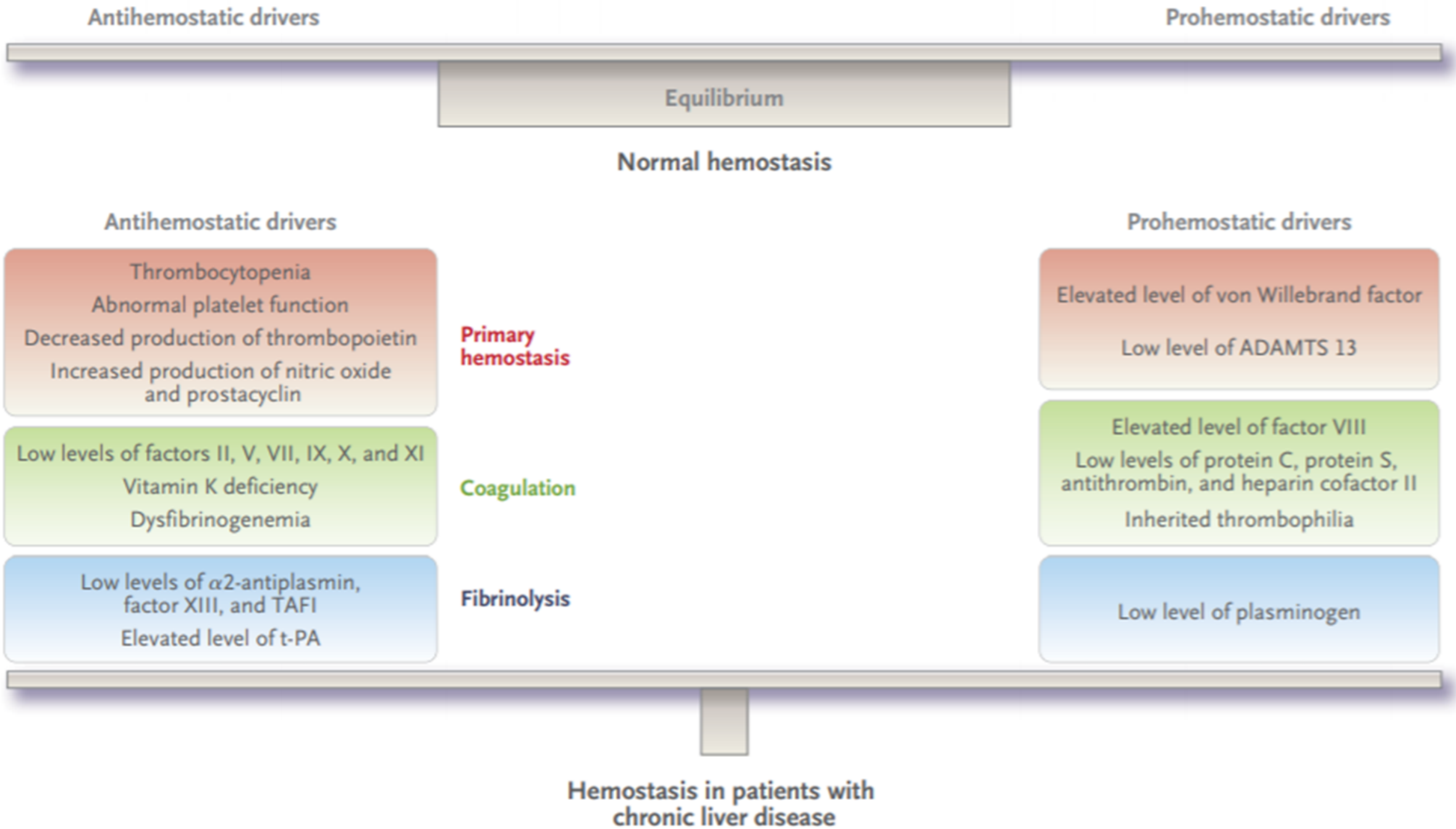
- Consider if procedure can be performed in a different way
- Aim for platelet count above 50 x 10^9/L
- Platelet count > 100 x 10^9/L if any bleeding would be catastrophic

NICE National Institute for Health and Care Excellence

Abnormal coagulation prior to surgery at moderate or high risk of bleeding

- Consider if procedure can be performed in a different way
- Tranexamic acid if expected to have at least 500ml blood loss
- FFP if PT or aPTT ratio > 1.5 (> 2.0 if liver disease)
- Cryoprecipitate if fibrinogen < 1g/L

NICE National Institute for Health and Care Excellence


Antihemostatic drivers
Prohemostatic drivers
Equilibrium
Normal hemostasis
Antihemostatic drivers
Prohemostatic drivers
Thrombocytopenia
Abnormal platelet function
Decreased production of thrombopoietin
Increased production of nitric oxide and prostacyclin
Primary hemostasis
Elevated level of von Willebrand factor
Low level of ADAMTS 13
Low levels of factors II, V, VII, IX, X, and XI
Vitamin K deficiency
Dysfibrinogenemia
Coagulation
Elevated level of factor VIII
Low levels of protein C, protein S, antithrombin, and heparin cofactor II
Inherited thrombophilia
Low levels of α2-antiplasmin, factor XIII, and TAFI
Elevated level of t-PA
Fibrinolysis
Low level of plasminogen
Hemostasis in patients with chronic liver disease

Guidelines for the use of platelet transfusions

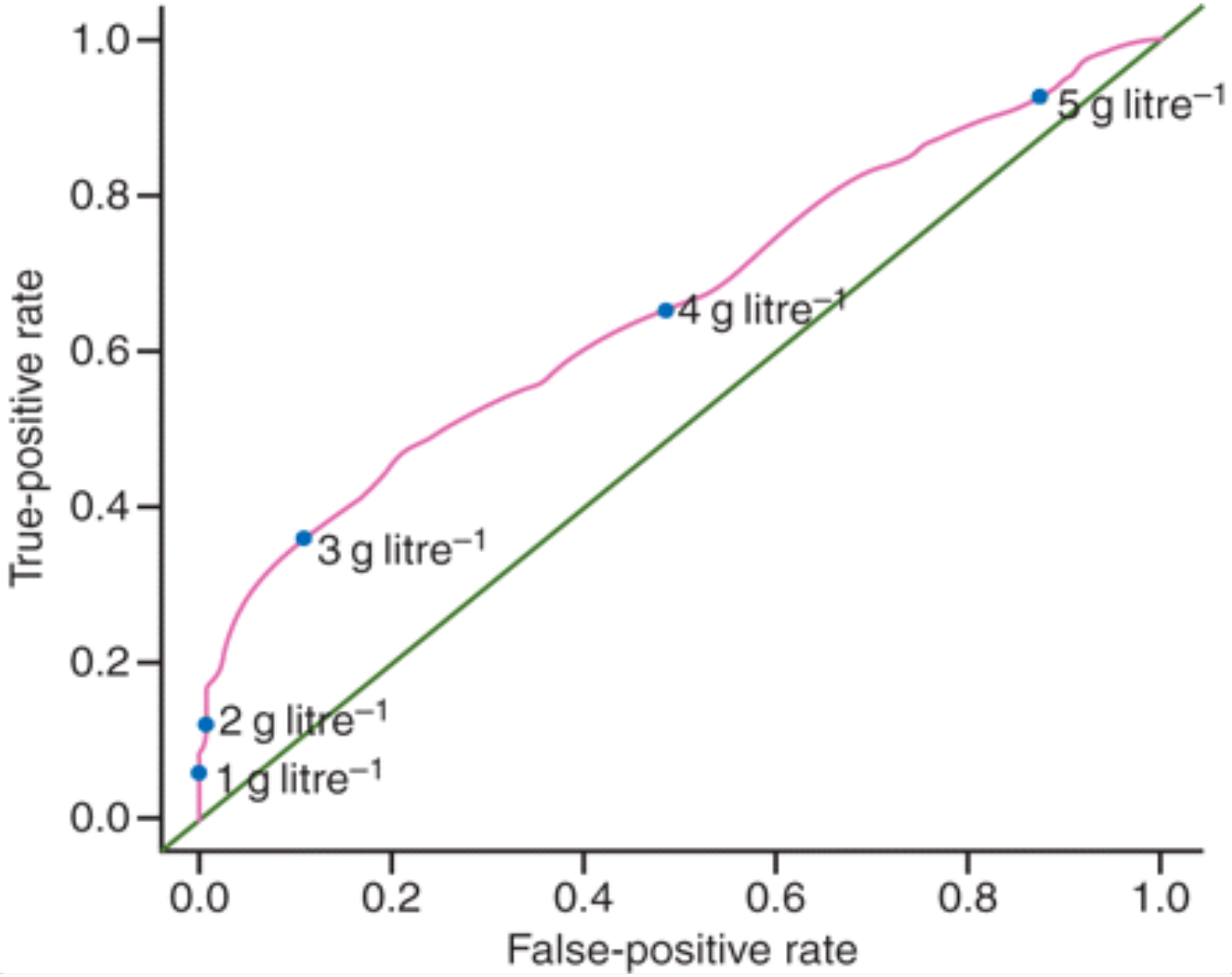
- WHO grade 2 bleeding – transfuse if platelet count < 30 x 10^9/L
- Major bleeding – transfuse if platelet count < 50 x 10^9/L
- Bleeding at a critical site – transfuse if platelet count < 100 x 10^9/L

Abnormal coagulation and bleeding

- FFP if PT or aPTT ratio > 1.5 (> 2.0 if liver disease)
- Cryoprecipitate if fibrinogen < 1.5 g/L (<2.0g/L in pregnancy)

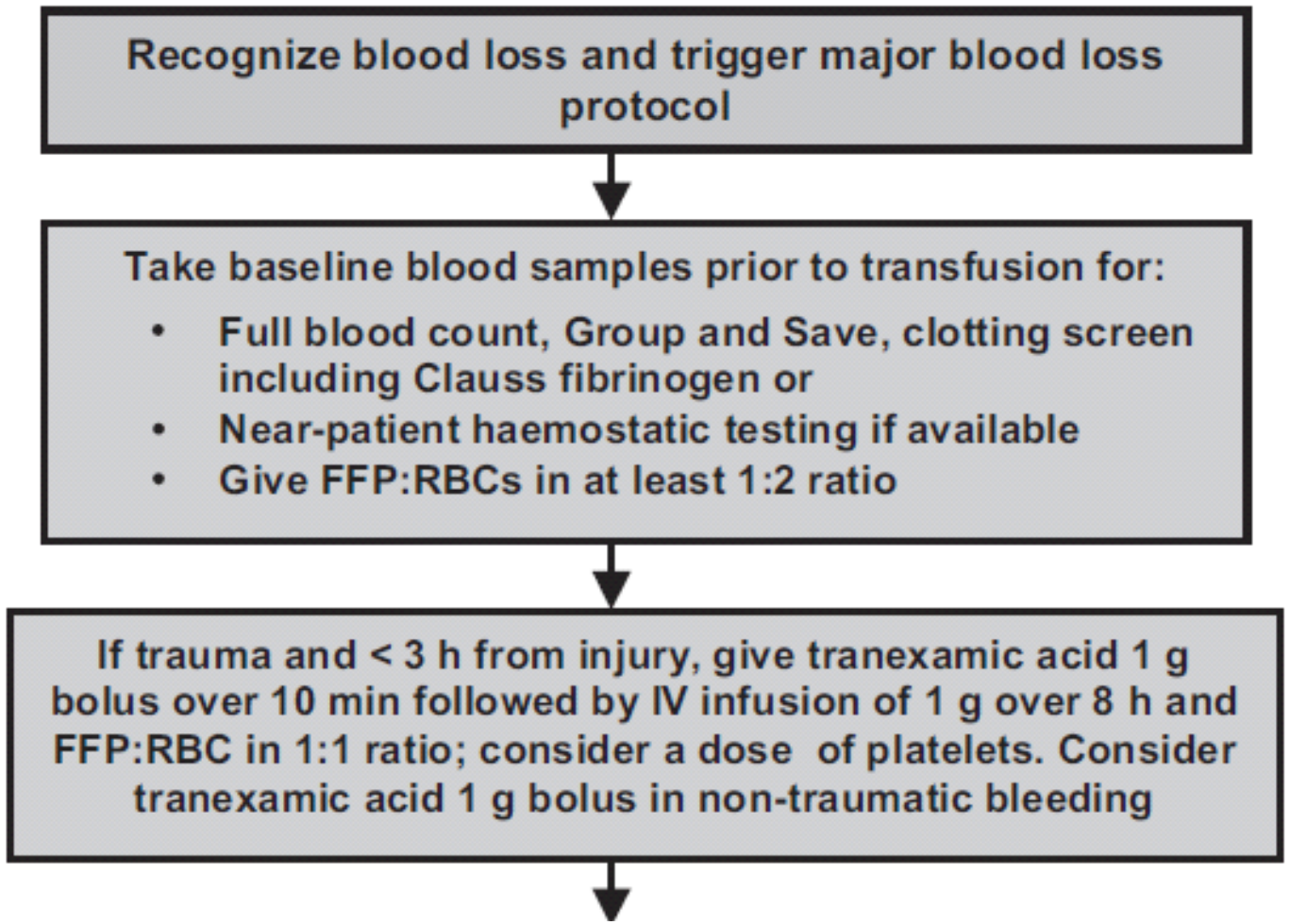
NICE National Institute for Health and Care Excellence

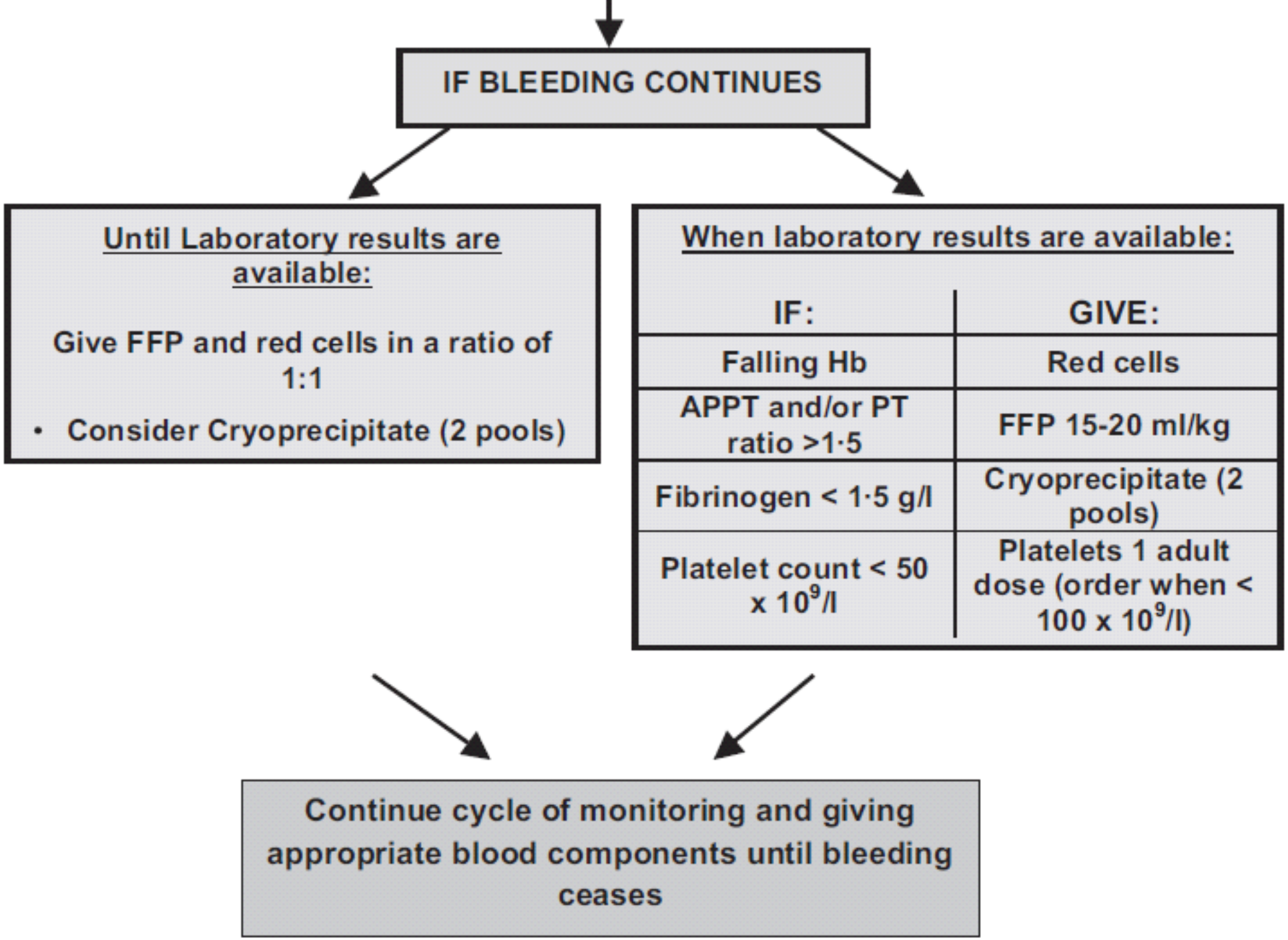
Specificity of a fibrinogen level <2 g/L for prediction of severe PPH was 99.3% [95% confidence interval (CI)=(98.4–1.00)]



BJA: British Journal of Anaesthesia, Volume 108, Issue 6, June 2012, Pages 984–989, https://doi.org/10.1093/bja/aes096

A practical guideline for the haematological management of major haemorrhage



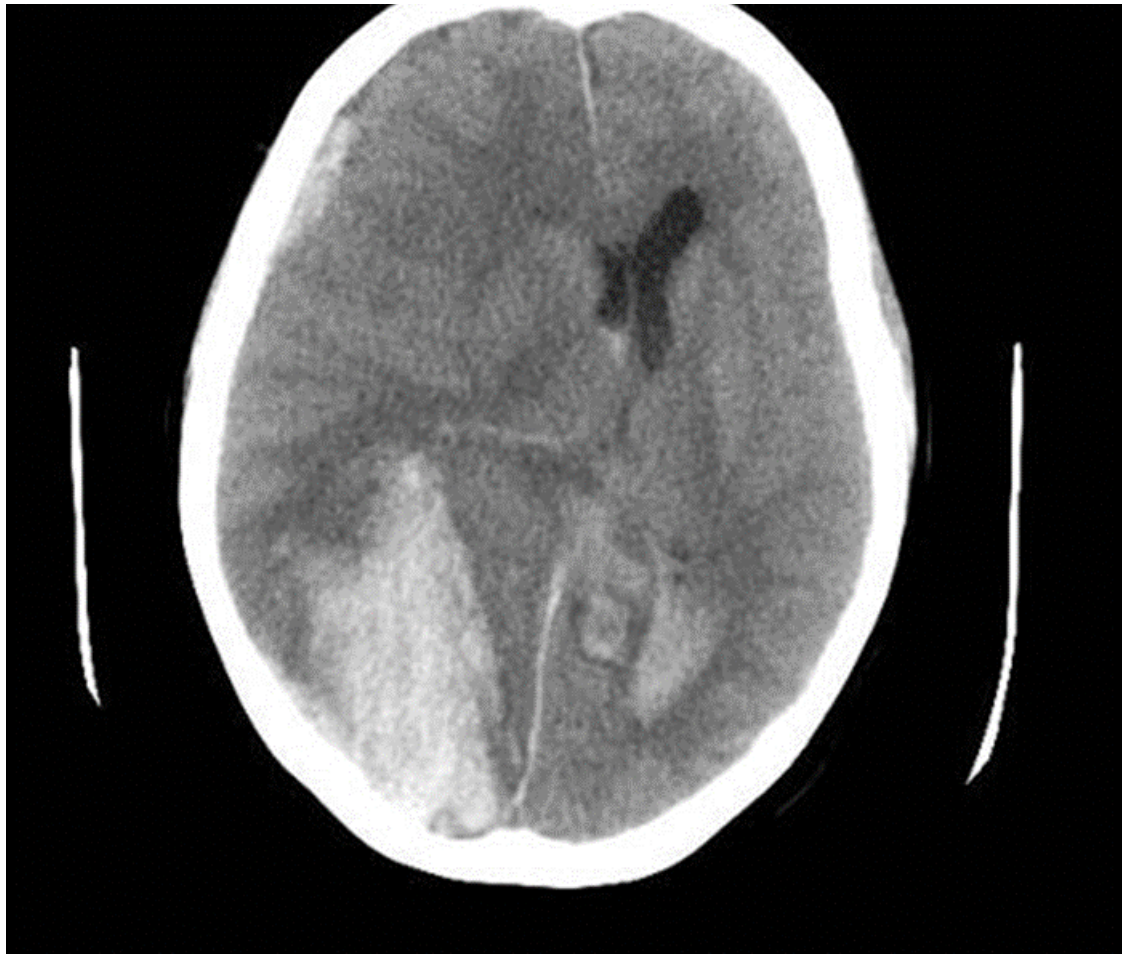

IF BLEEDING CONTINUES
Until Laboratory results are available:
Give FFP and red cells in a ratio of 1:1
• Consider Cryoprecipitate (2 pools)
When laboratory results are available:
IF:
GIVE:
Falling Hb
Red cells
APPT and/or PT ratio >1·5
FFP 15-20 ml/kg
Fibrinogen < 1·5 g/l
Cryoprecipitate (2 pools)
Platelet count < 50 x 10⁹/l
Platelets 1 adult dose (order when < 100 x 10⁹/l)
Continue cycle of monitoring and giving appropriate blood components until bleeding ceases

PATCH trial

- Open-label superiority RCT
- Randomised adults, non-traumatic supratentorial ICH GCS 8 – 15, on antiplatelet agents
- Randomized to standard care with platelet transfusion or standard care within 90 minutes of allocation
- 60 Hospitals (190 participants)- Netherlands, UK, and France
-

Platelet transfusion versus standard care after acute stroke due to spontaneous cerebral haemorrhage associated with antiplatelet therapy (PATCH): a randomised, open-label, phase 3 trial

M Irem Baharoglu, Charlotte Cordonnier*, Rustam Al-Shahi Salman*, Koen de Gans, Maria M Koopman, Anneke Brand, Charles B Majoie, Ludo F Beenen, Henk A Marquering, Marinus Vermeulen, Paul J Nederkoorn, Rob J de Haan, Yvo B Roos, for the PATCH Investigators†*



Platelet transfusion versus standard care after acute stroke due to spontaneous cerebral haemorrhage associated with antiplatelet therapy (PATCH): a randomised, open-label, phase 3 trial. Baharoglu *et al. Lancet* 2016;online

PATCH trial

- Hypothesis
- Platelet transfusion decreases odds of death or dependence at 3 months
- Unadjusted OR

OR 1·84, 95% CI 1·10–3·08

- Adjusted OR

2·05, 95% CI 1·18 to 3·56

(type of antiplatelet & severity of ICH)

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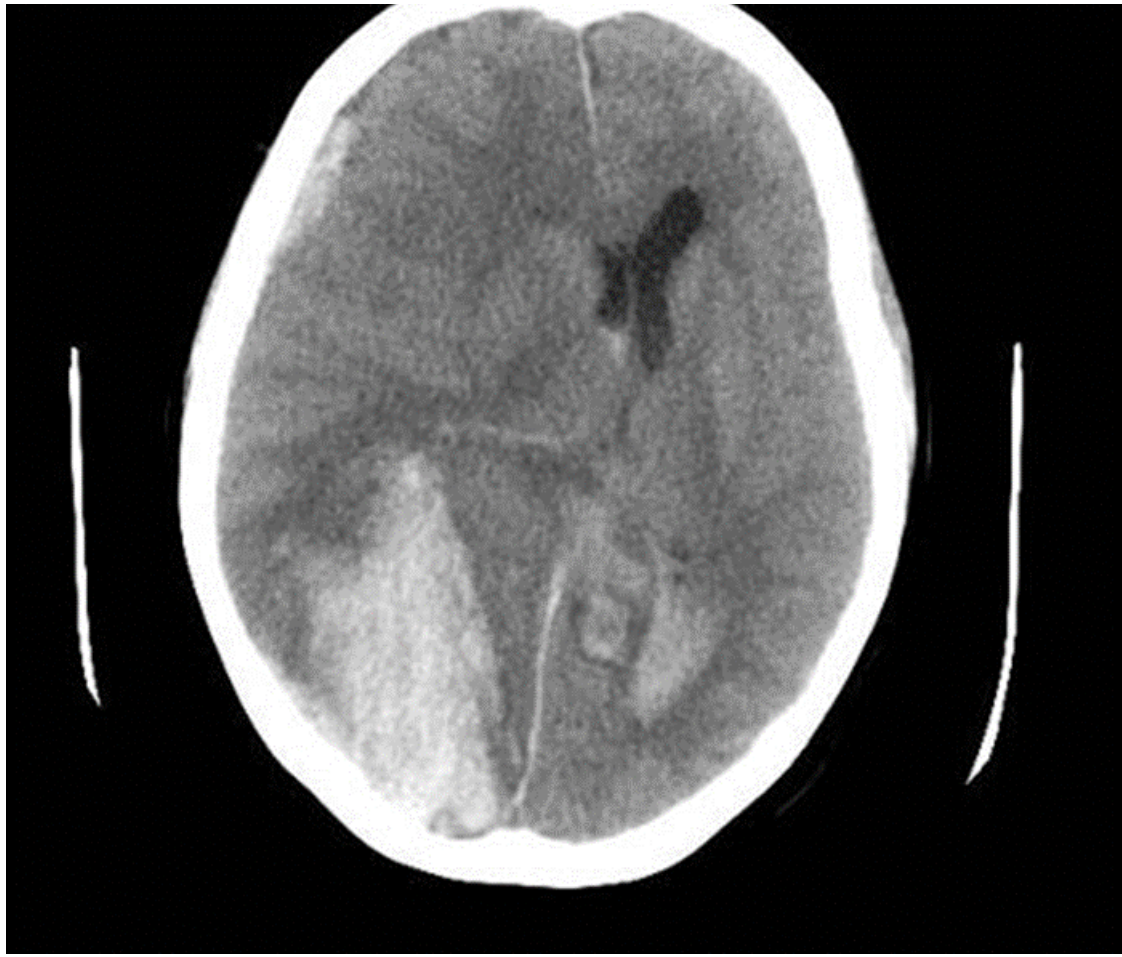

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PATCH trial

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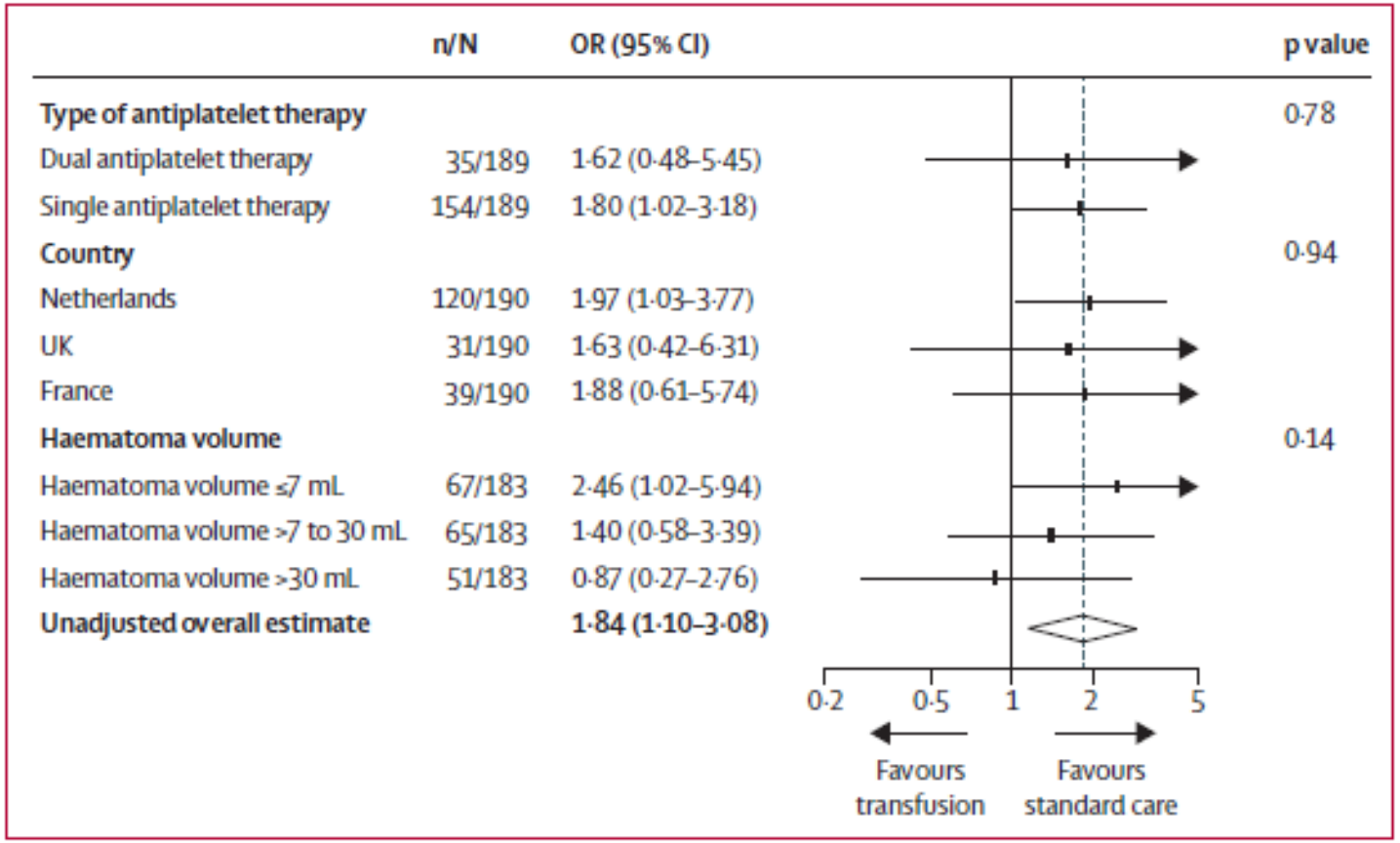

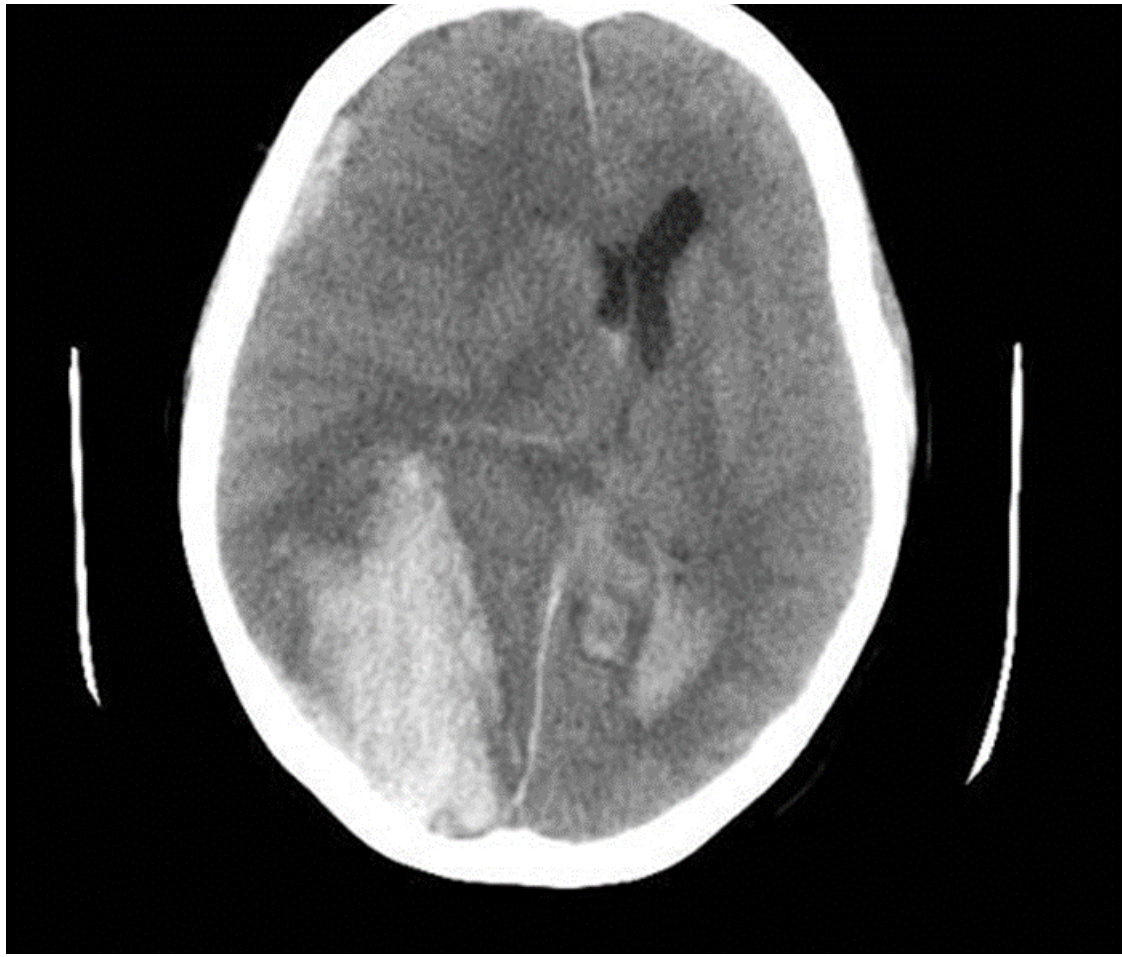

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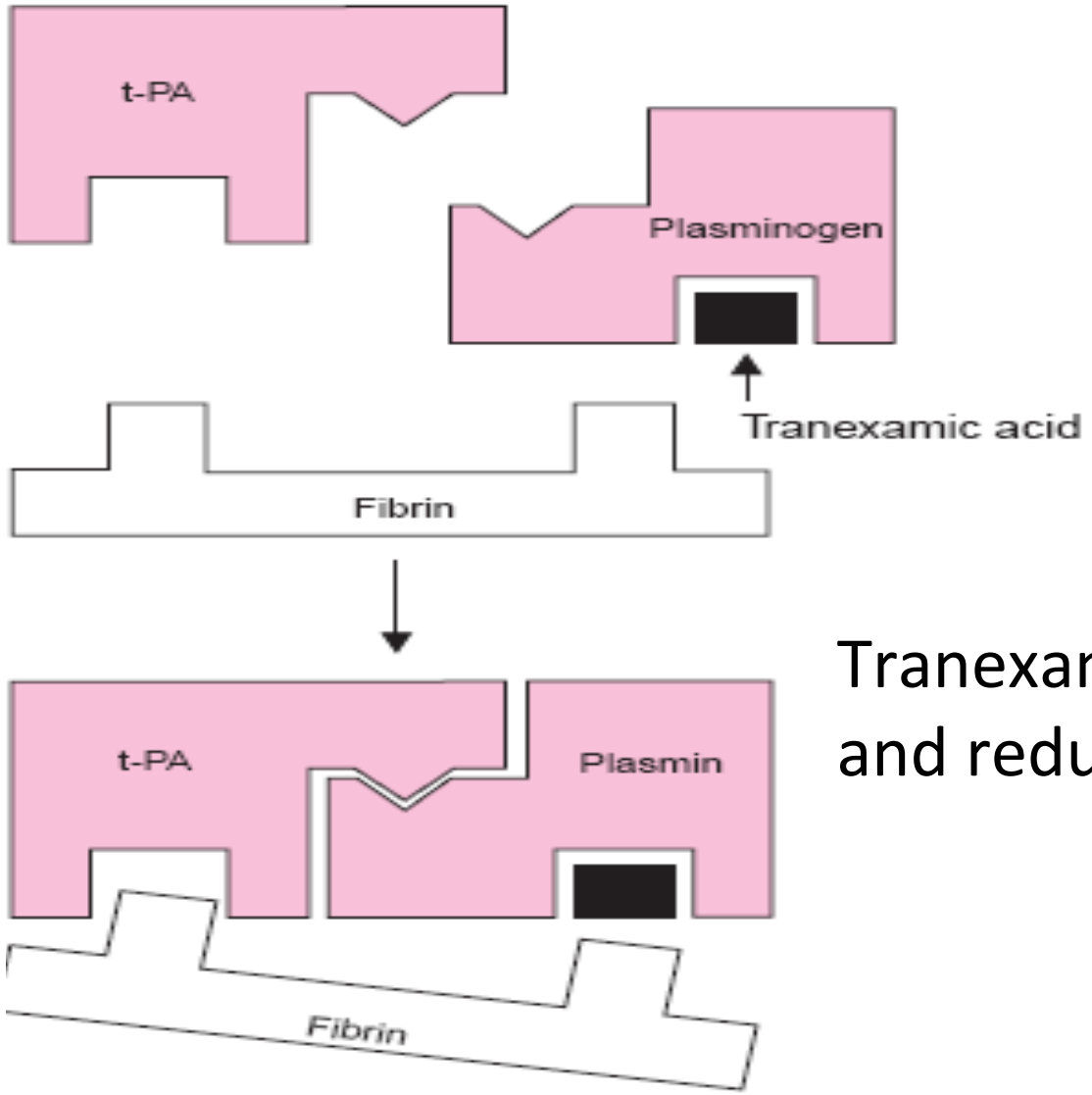
Secondary Outcomes

NHS Blood and Transplant

	Platelet Transfusion (97)	Standard (93)	Odds Ratio (95% CI)
Alive at 3 months (survival)	66 (68%)	72 (77%)	0·62 (0·33–1·19)
mRS score 4–6 at 3 months	70 (72%)	52 (56%)	2·04 (1·12–3·74)
Median ICH growth at 24 h (ml)	2·01 (0·32–9·34)	1·16 (0·03–4·42)	-
Serious Adverse Events	40 (42%)	28 (29%)	1·74 (0·96–3·17)

Platelet transfusion versus standard care after acute stroke due to spontaneous cerebral haemorrhage associated with antiplatelet therapy (PATCH): a randomised, open-label, phase 3 trial. Baharoglu *et al. Lancet* 2016;online

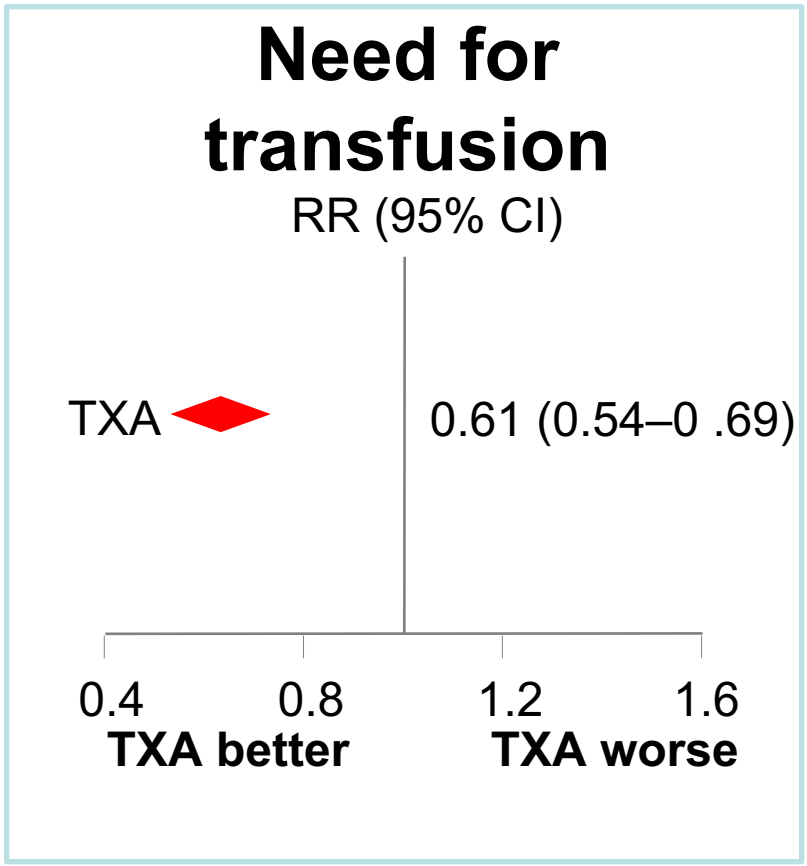
Tranexamic acid reduces fibrinolysis



Tranexamic acid inhibits plasmin and reduces clot breakdown.

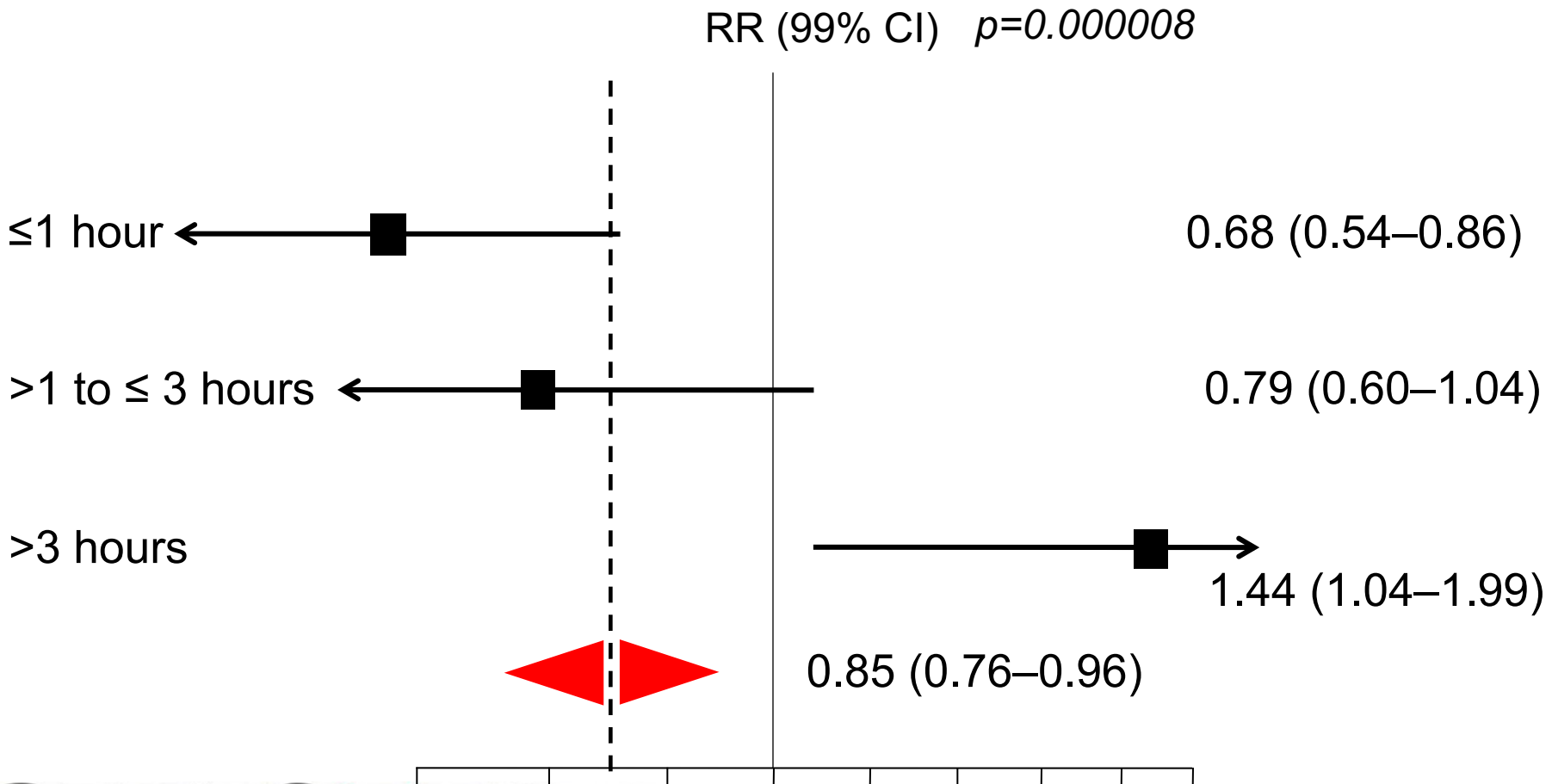
Tranexamic acid reduces surgical bleeding

In surgical patients tranexamic acid (TXA) reduces the need for blood transfusion by about one third.



Systematic review
129 trials

For bleeding deaths – early treatment is better

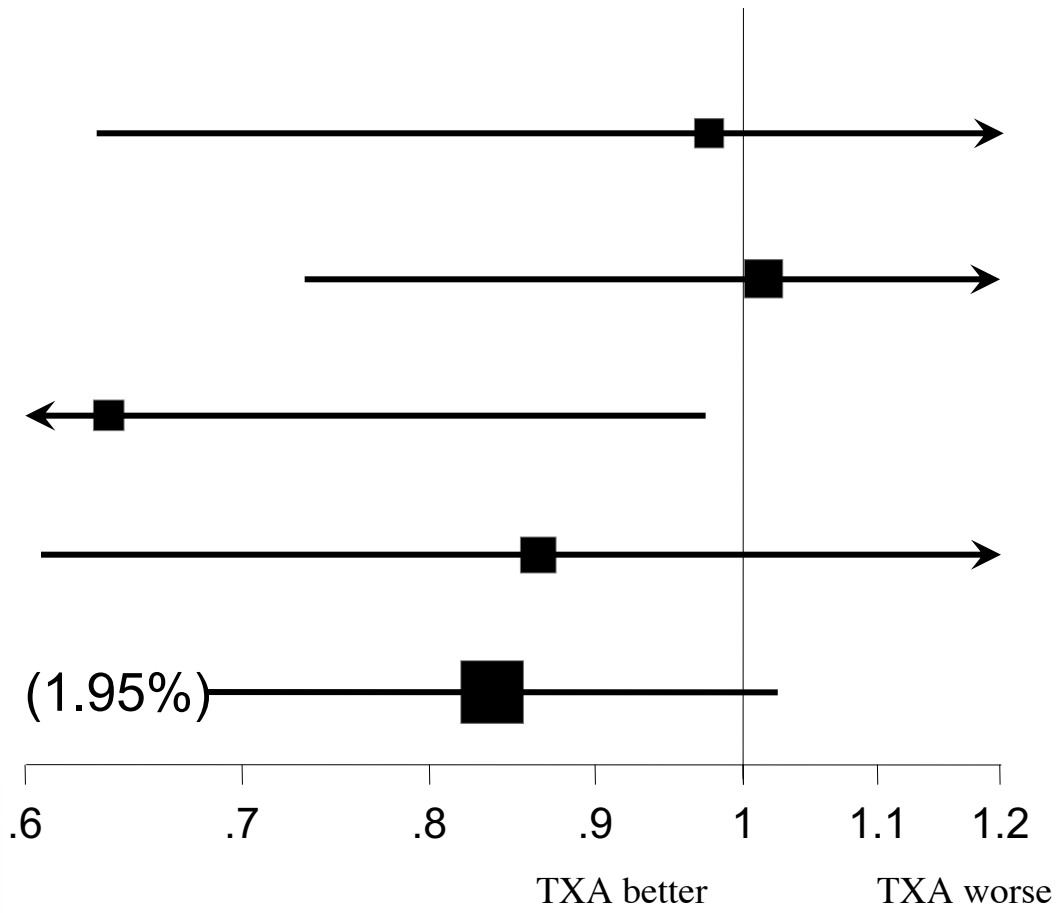


CRASH-2

Clinical Randomisation of an Antifibrinolytic in Significant Haemorrhage

There was no increase in thrombosis

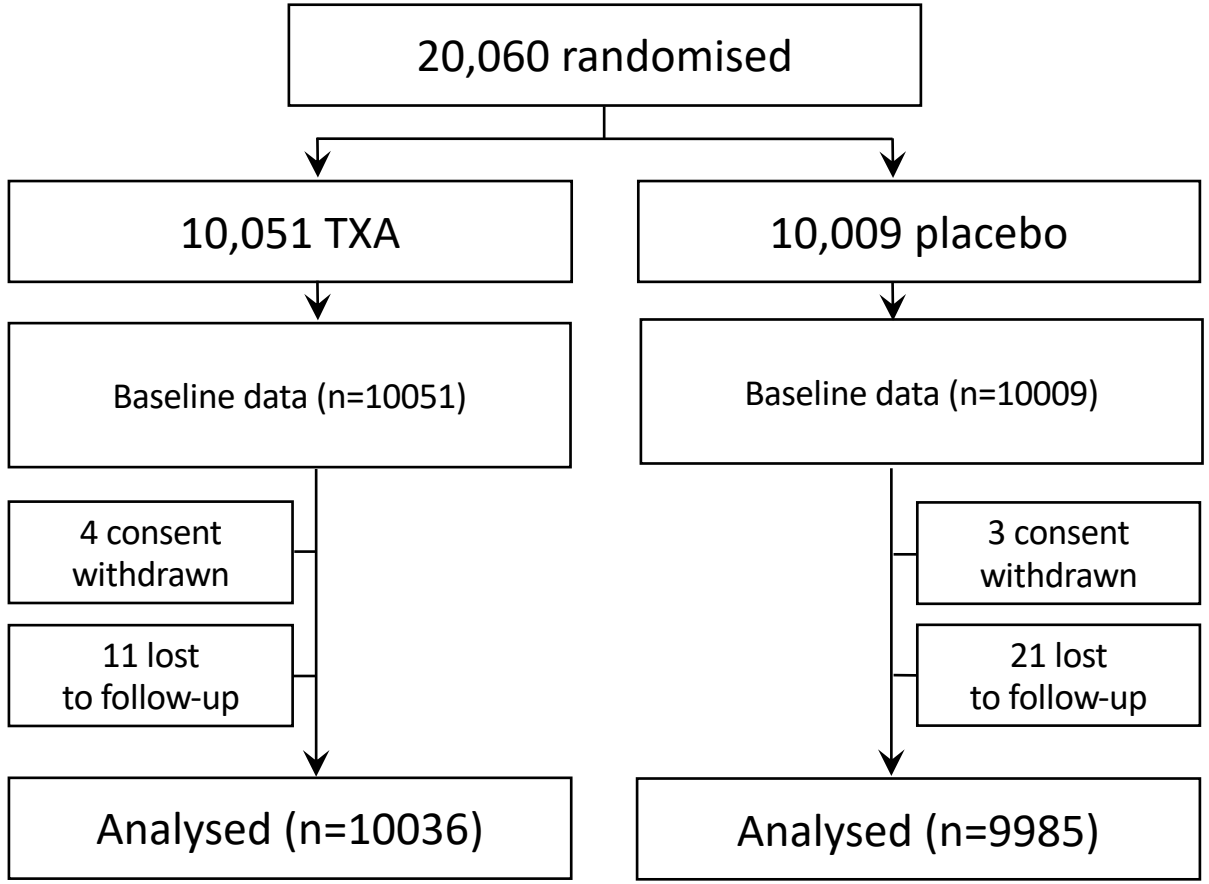
	TXA allocated (10,060)	Placebo allocated (10,067)
DVT	40 (0.40%)	41 (0.41%)
PE	72 (0.69%)	71 (0.70%)
MI	35 (0.35%)	55 (0.52%)
Stroke	57 (0.56%)	66 (0.65%)
Any	168 (1.63%)	201 (1.95%)



CRASH-2
Clinical Randomisation of an Antifibrinolytic in Significant Haemorrhage

woman

World Maternal Antifibrinolytic Trial



21 countries, 193 hospitals

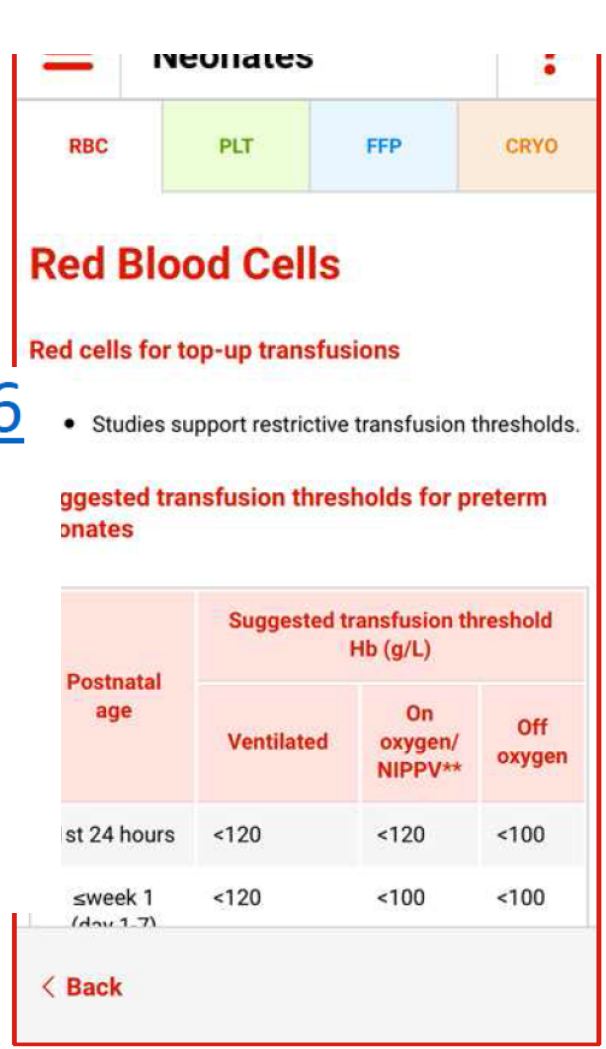
CLINICAL TRIALS UNIT

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

Cause of death	**TXA** N=10036 n (%)	**Placebo** N=9985 n (%)	**Risk ratio (95% CI)**	**P value**
Bleeding	155 (1.5)	191 (1.9)	0.81 (0.65–1.00)	0.045
Pulmonary embolism	10 (0.1)	11 (0.1)	0.90 (0.38–2.13)	0.82
Organ failure	25 (0.3)	18 (0.2)	1.38 (0.75–2.53)	0.29
Sepsis	15 (0.2)	8 (0.1)	1.87 (0.79–4.40)	0.15
Eclampsia	2 (0.02)	8 (0.1)	0.25 (0.05–1.17)	0.06
Other	20 (0.2)	20 (0.2)	0.99 (0.54–1.85)	0.99
All causes	227 (2.3)	256 (2.6)	0.88 (0.74–1.05)	0.16

NHS
Blood and Transplant

Blood Components App



Visit: https://goo.gl/whCRF6

Scan:

Summary

- Why do we use plasma and platelet components?
- Who uses them?
- What are the indications for their use?
- Are there any alternatives?

NHS Blood and Transplant

Acknowledgements

- Rebecca Cardigan
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