Platelet Transfusion Guidelines

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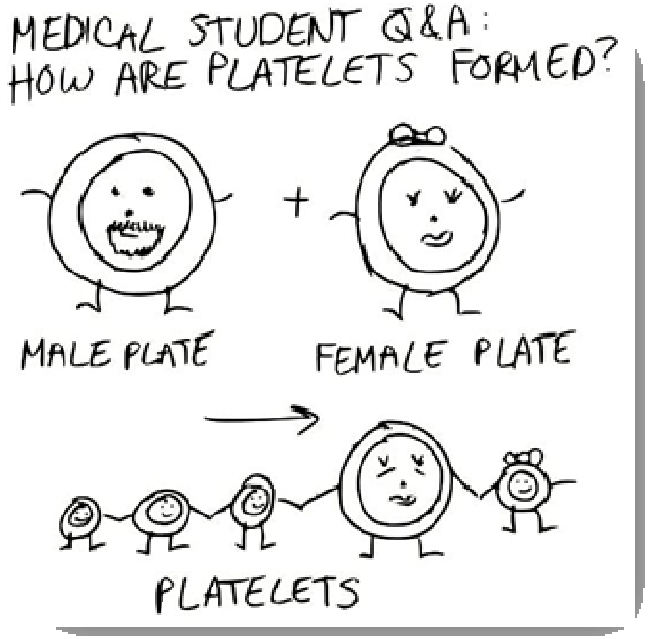
Today's topics

- Prophylaxis
  - Therapeutic versus prophylactic
  - Platelet threshold
  - Platelet dose
- Pre-procedure
- Therapeutic
  - Antiplatelet agents



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  - Bone marrow
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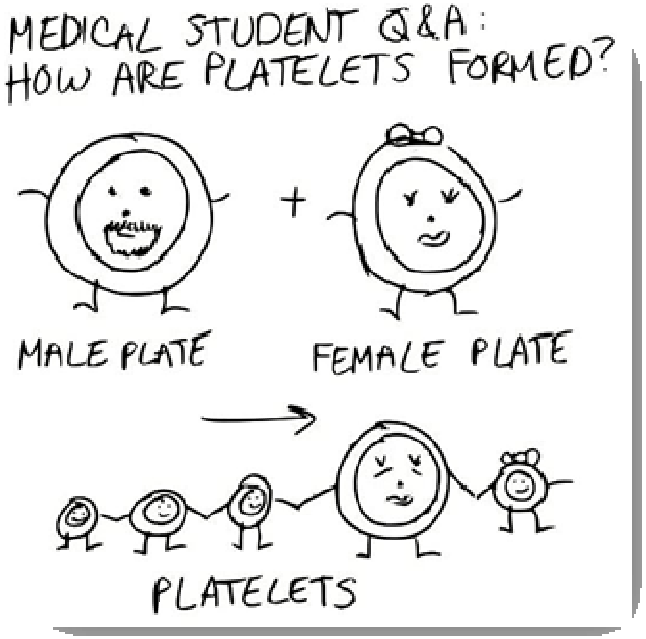
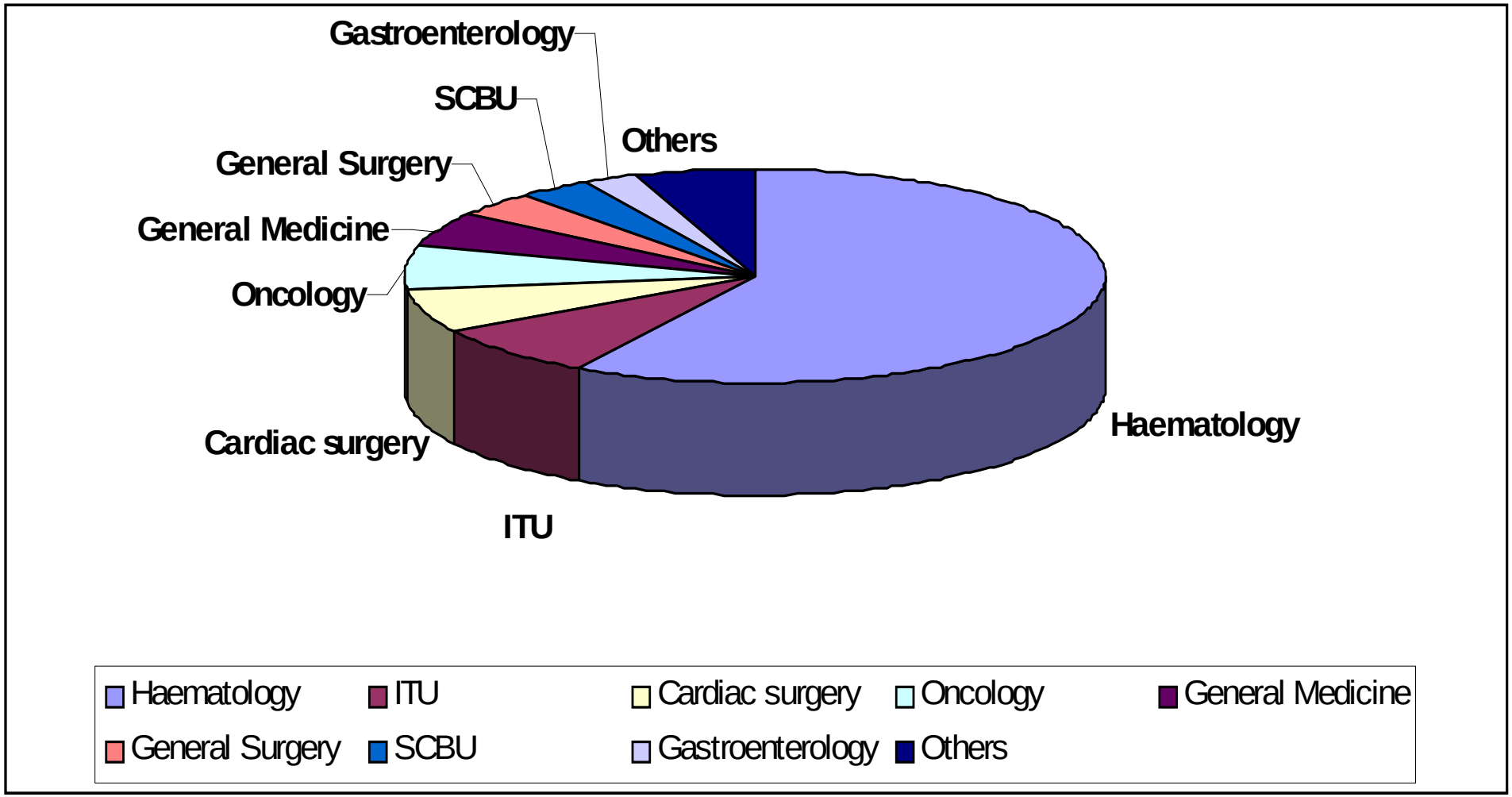


Haematology patients use the majority of platelet transfusions



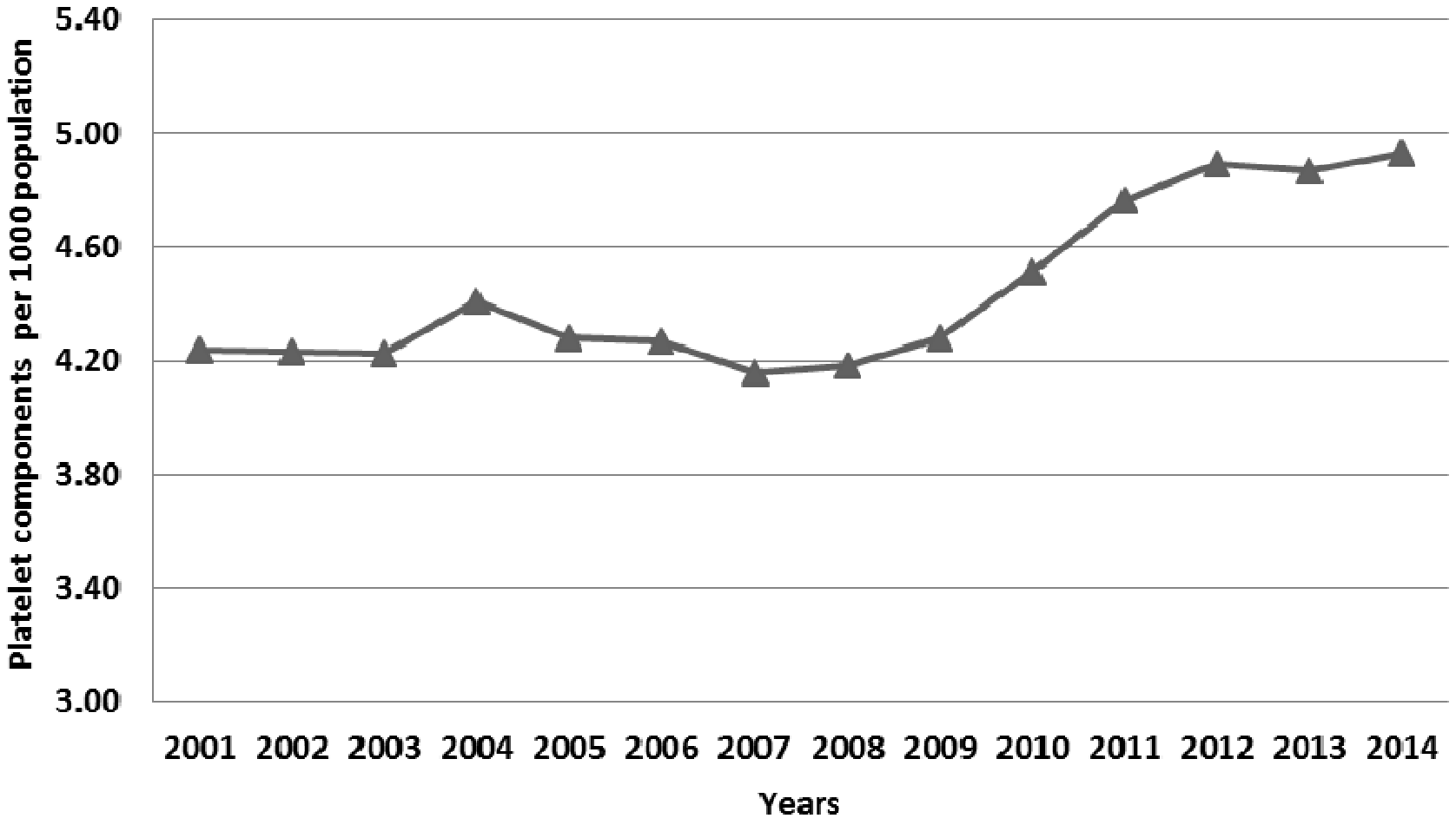
Data from NW England & Wales Audit of platelet use and wastage. Pendry & Davies 2011. Blood and Transplant Matters.

Majority of platelet transfusions are prophylactic

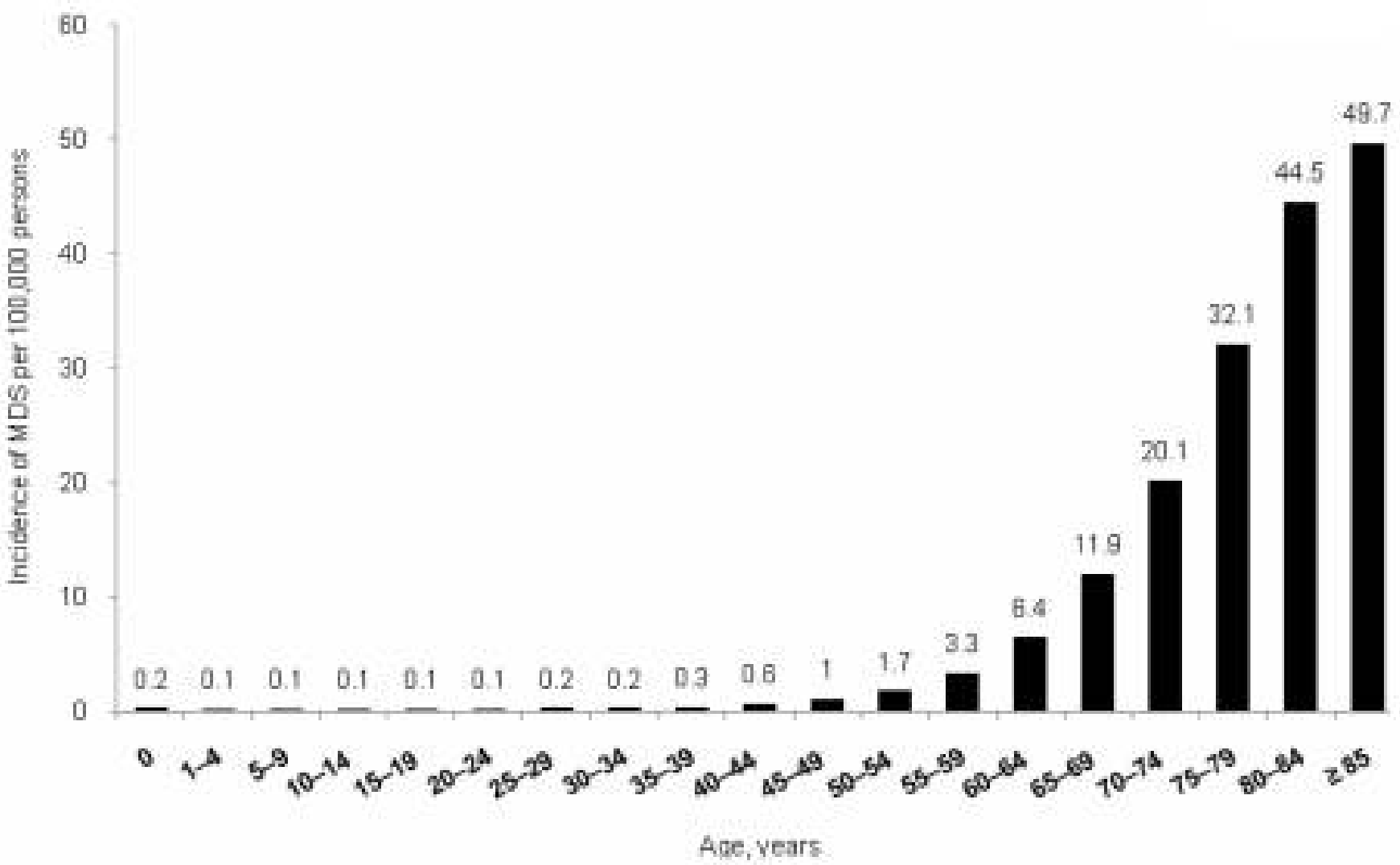
Reason for Transfusion	Audited episodes in each category	Appropriate	Indeterminate	Outside guidelines
Prophylactic	77%	55%	8%	37%
Pre - procedure	9%	61%	20%	19%
Therapeutic	10%	87%	7%	6%
Unclear	4%	0%	100%	0%

NCABT Audit in Haematology Patients 2016

Platelet component demand

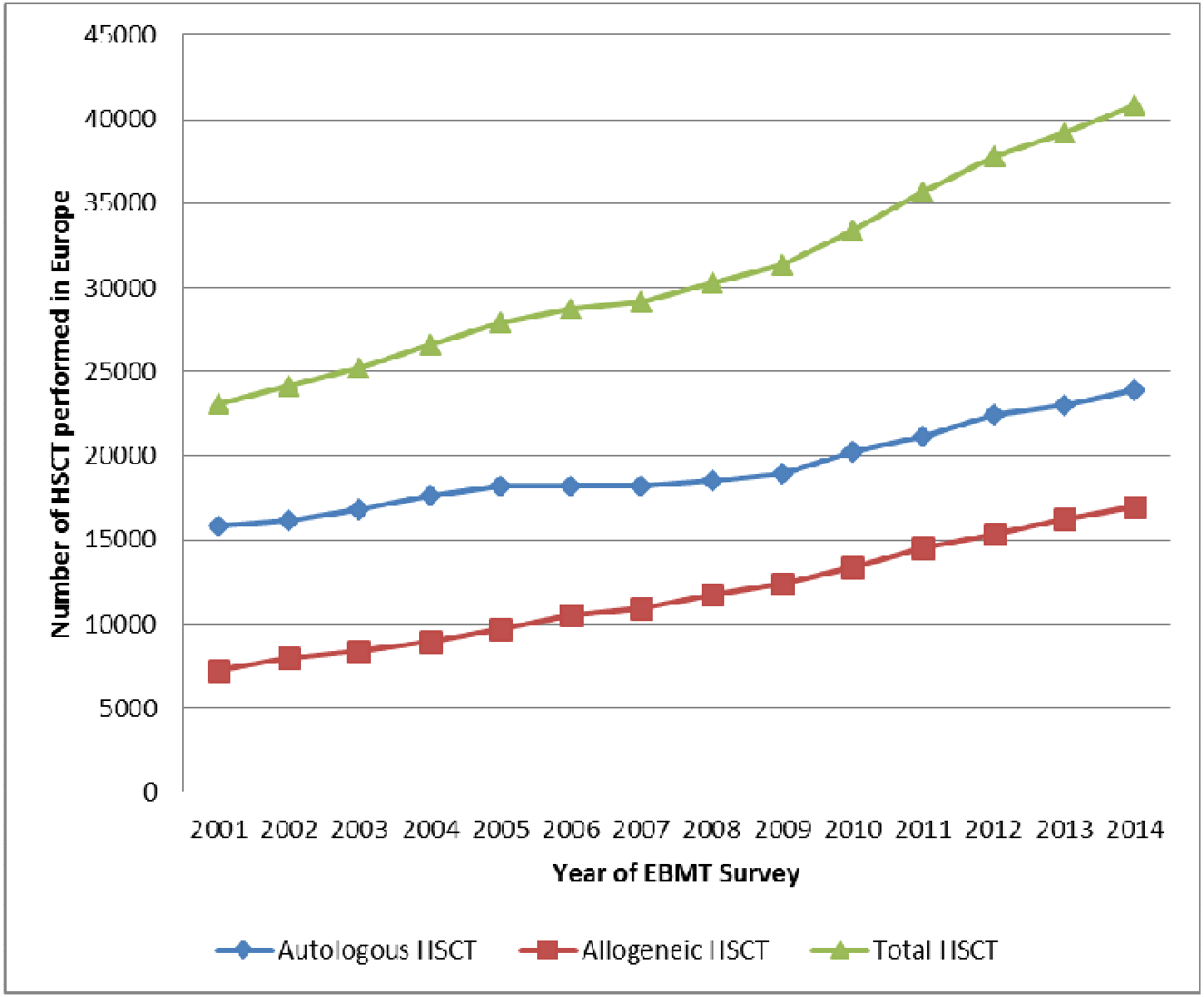


Incidence of MDS



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

HSCT Europe 2001 to 2014



Avoid unnecessary usage

- Risks to the patient
  - Safest transfusion is the one not given because it is not needed
- Costs to the health service

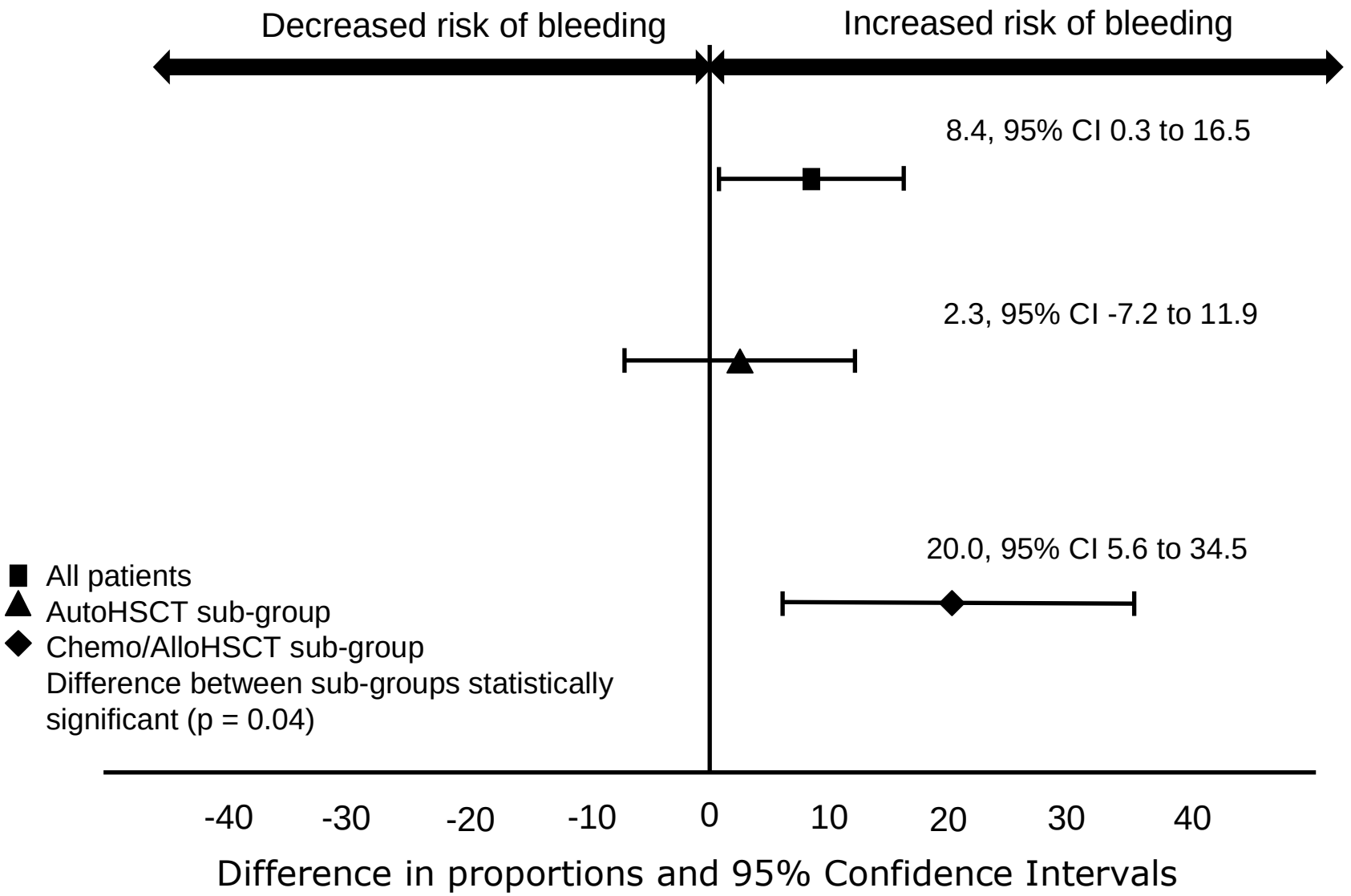
- Preservation of national blood supply

Prophylactic Platelet transfusions

	German Study (Wandt 2012)		TOPPS (Stanworth 2013)	
	Prophylaxis	No Prophylaxis	Prophylaxis	No Prophylaxis
Number of Patients	194	197	298	300
Autologous SCT	98 (29%)	103 (34%)	210 (70%)	210 (70%)
Clinically significant bleeding	19%	42%	43% (128/298)	50% (151/300)
Severe or life-threatening bleeding	2% (7/343 Rx cycles)	6% (21/301 Rx cycles)	0.3% (1/298)	2% (6/300)

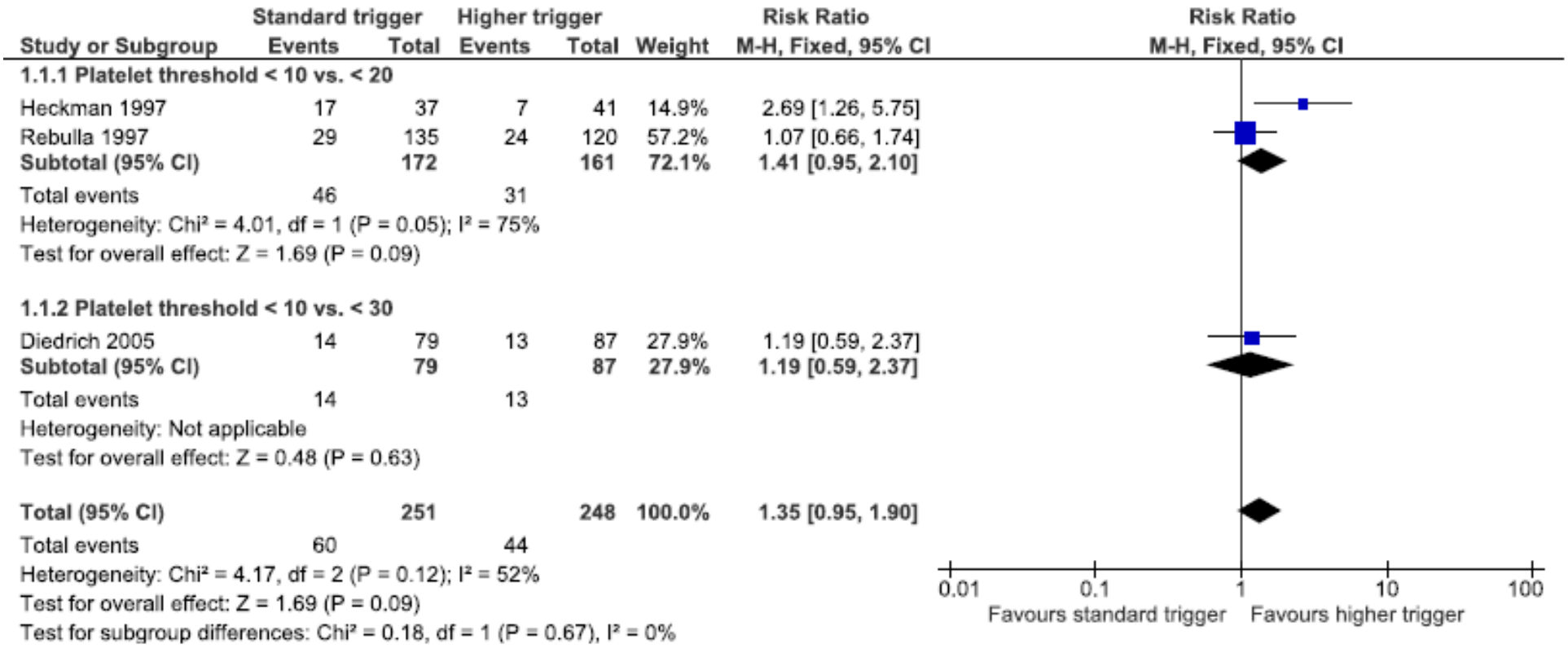
Wandt *et al.* Therapeutic platelet transfusion versus routine prophylactic transfusion in patients with haematological malignancies: an open-label, multicentre, randomised study. *Lancet 2012.*
Stanworth et al. A no-prophylaxis platelet transfusion strategy for hematologic malignancies. *NEJM 2013*

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*


Standard trigger
Higher trigger
Risk Ratio
Risk Ratio
Study or Subgroup
Events
Total
Events
Total
Weight
M-H, Fixed, 95% CI
M-H, Fixed, 95% CI
1.1.1 Platelet threshold < 10 vs. < 20
Heckman 1997 17 37 7 41 14.9% 2.69 [1.26, 5.75]
Rebulla 1997 29 135 24 120 57.2% 1.07 [0.66, 1.74]
Subtotal (95% CI) 172 161 72.1% 1.41 [0.95, 2.10]
Total events 46 31
Heterogeneity: Chi² = 4.01, df = 1 (P = 0.05); I² = 75%
Test for overall effect: Z = 1.69 (P = 0.09)
1.1.2 Platelet threshold < 10 vs. < 30
Diedrich 2005 14 79 13 87 27.9% 1.19 [0.59, 2.37]
Subtotal (95% CI) 79 87 27.9% 1.19 [0.59, 2.37]
Total events 14 13
Heterogeneity: Not applicable
Test for overall effect: Z = 0.48 (P = 0.63)
Total (95% CI) 251 248 100.0% 1.35 [0.95, 1.90]
Total events 60 44
Heterogeneity: Chi² = 4.17, df = 2 (P = 0.12); I² = 52%
Test for overall effect: Z = 1.69 (P = 0.09)
Test for subgroup differences: Chi² = 0.18, df = 1 (P = 0.67), I² = 0%
0.01
0.1
1
10
100
Favours standard trigger
Favours higher trigger

BCSH Recommendations

- Give prophylactic platelet transfusions to patients with reversible bone marrow failure receiving intensive chemotherapy or undergoing allogeneic HSCT
- Consider not giving prophylactic platelet transfusions to well patients who have had an autologous stem cell transplant
- Consider increasing the threshold for prophylactic platelet transfusion to between 10 and 20 $x10^9/L$ in patients judged to have additional risk factors for bleeding. Individual review is required.

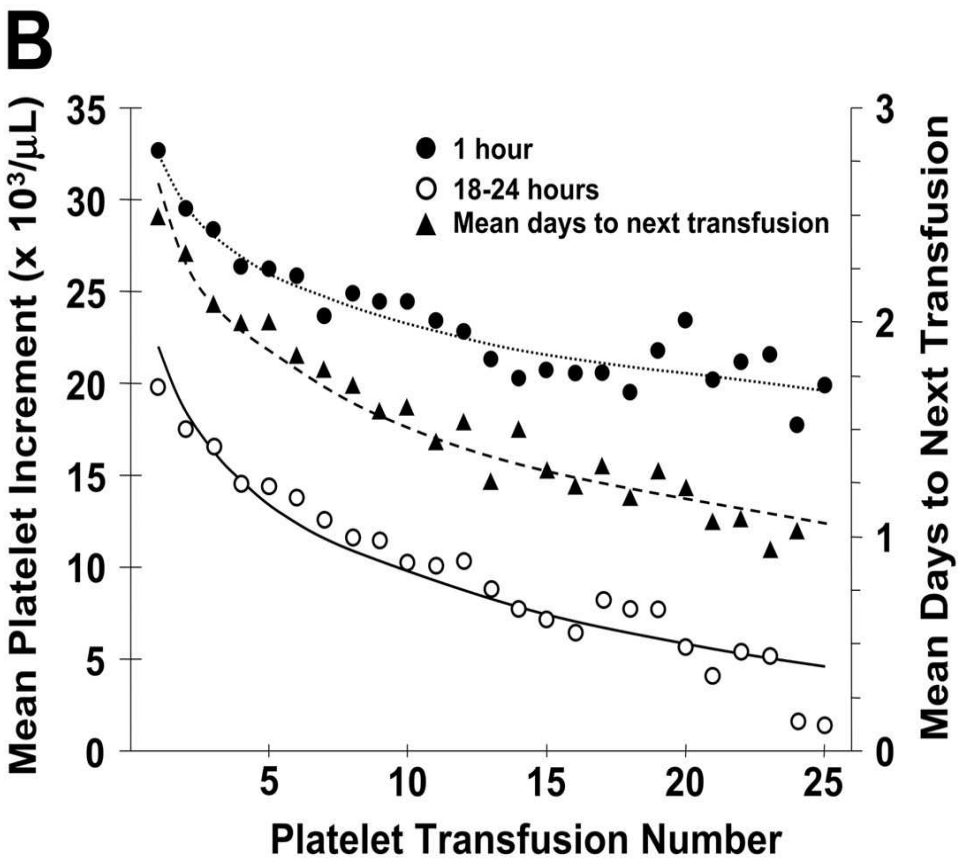
What about evidence for other patient groups?

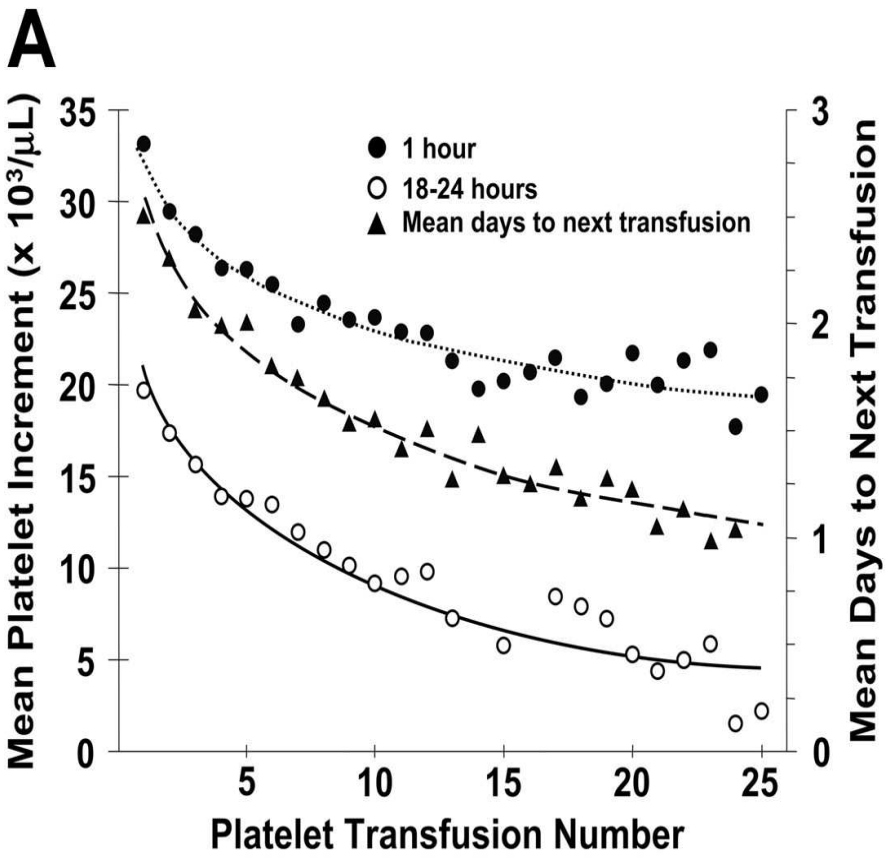
- One RCT in progress in patients with long term bone marrow failure.

- One RCT in 87 patients with dengue haemorrhagic fever.
  - Prophylactic plt Tx not prevent bleeding
  - 3 anaphylactic reactions

Assir *et al*, 2013. Platelet transfusion in dengue fever: A randomized controlled trial. International Journal of Infectious Diseases

Relationship between number of platelet transfusions, platelet increments and days to next transfusion





- ● 1-hr increment
- ○ 18-24 hr increment
- ▲ Days to next transfusion

Slichter S J et al. Blood 2005;105:4106-4114

BCSH Recommendations

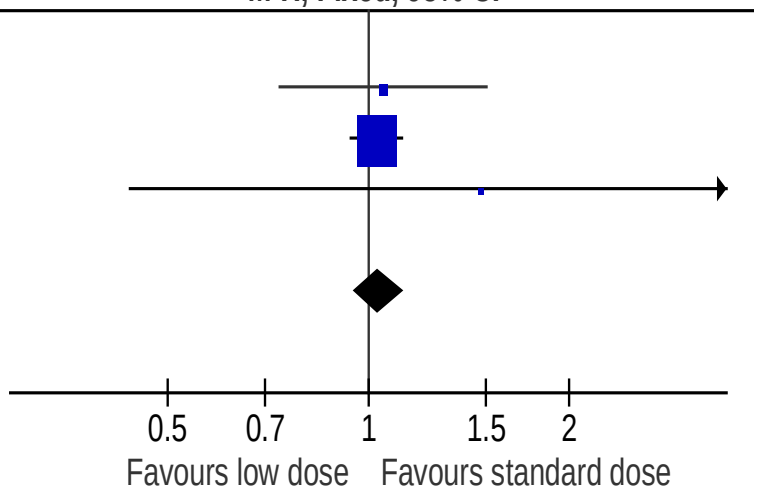
- Use a ‘no prophylactic platelet transfusion’ strategy for asymptomatic patients with chronic bone marrow failure (including those taking low dose oral chemotherapy or azacitidine)
- Give prophylactic platelet transfusions to patients with chronic bone marrow failure receiving intensive treatment
- Use the platelet count thresholds for reversible bone marrow failure as a general guide for other patient groups

Platelet dose

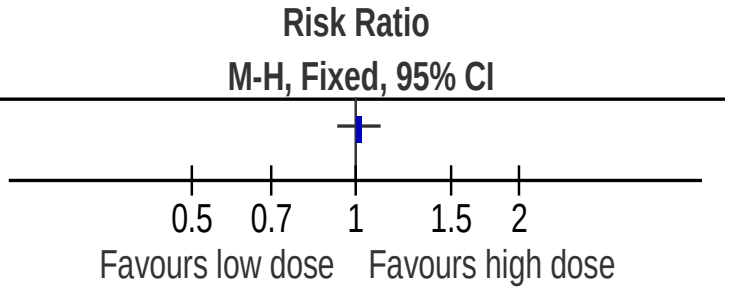
Study or Subgroup	Low dose Events	Total	Standard dose Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Akay 2015	0	48	0	52		Not estimable
Heddle 2009	30	58	30	61	9.0%	1.05 [0.74, 1.50]
Slichter 2010	296	417	292	423	89.7%	1.03 [0.94, 1.12]
Tinmouth 2004	6	56	4	55	1.2%	1.47 [0.44, 4.94]
Total (95% CI)		**579**		**591**	**100.0%**	**1.04 [0.95, 1.13]**
Total events	332		326			

Heterogeneity: Chi² = 0.36, df = 2 (P = 0.84); I² = 0%

Test for overall effect: Z = 0.79 (P = 0.43)



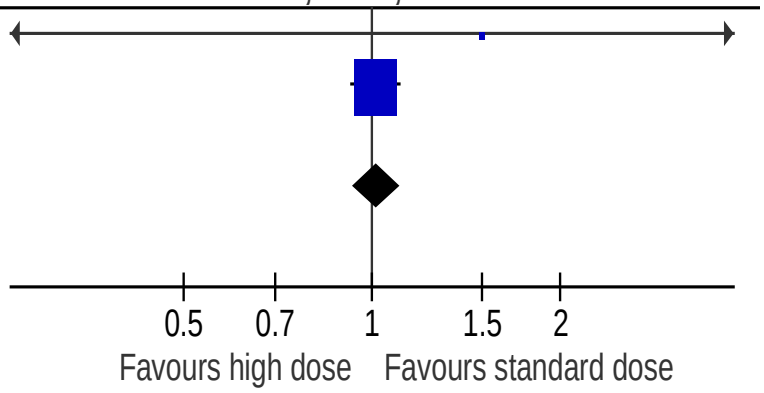
Study or Subgroup	Low dose Events	Total	High dose Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Slichter 2010	296	417	302	432		1.02 [0.93, 1.11]



Study or Subgroup	High dose Events	Total	Standard dose Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Sensebe 2004	3	48	2	48	0.7%	1.50 [0.26, 8.58]
Slichter 2010	302	432	292	423	99.3%	1.01 [0.93, 1.11]
Total (95% CI)		**480**		**471**	**100.0%**	**1.02 [0.93, 1.11]**
Total events	305		294			

Heterogeneity: Chi² = 0.20, df = 1 (P = 0.66); I² = 0%

Test for overall effect: Z = 0.35 (P = 0.73)



Platelet usage

	Number of Platelet Transfusions/patient Median	Number of Platelet Components/patient Median
Low dose	5 (IQR 3 to 9)	3.9 (IQR 2.0 to 7.5)
Intermediate dose	3 (IQR 2 to 6)	4.7 (IQR 2.9 to 9.5)
High dose	3 (IQR 2 to 6)	8.2 (IQR 4.4 to 15.6)

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

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Platelets

Don't use two...

...when one will do

For prophylactic use in a 70kg adult, one adult therapeutic dose (ATD) typically gives an immediate rise in platelet count of

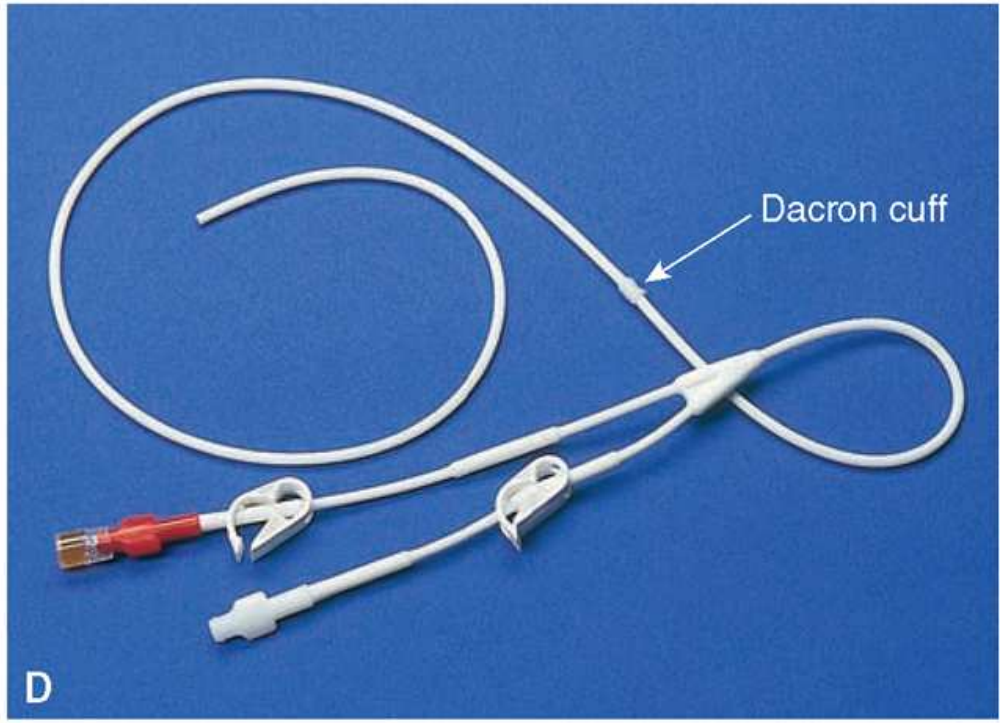
approximately 20 - 40 x 10^9/l [1]

Do not administer double dose platelets for prophylactic transfusions as this practice does not decrease the risk of bleeding [2]

Request and administer one unit/ATD, then reassess your patient.

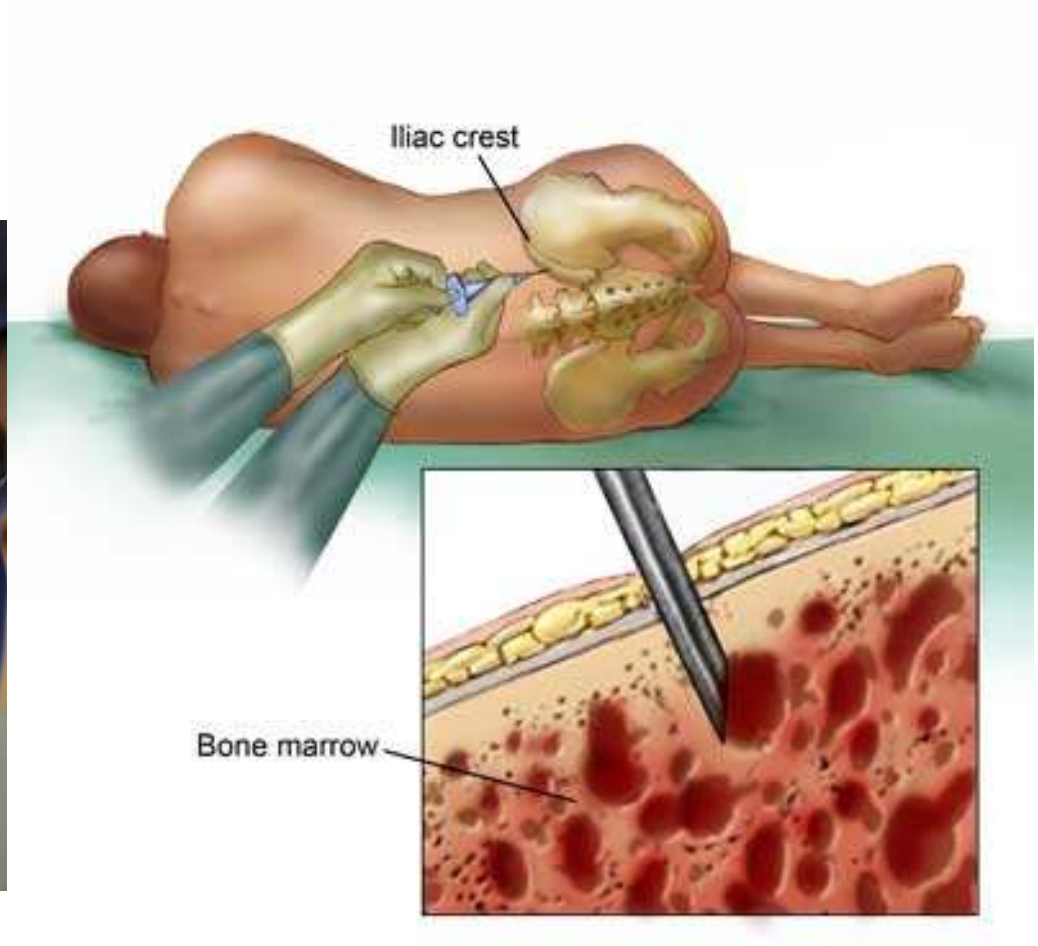
A platelet increment can be obtained 10 minutes after completion of the transfusion [2]

Pre-procedure



Central lines

	Number of procedures (Platelets < 50)	Number of haemorrhages (Platelets < 50)	Number of major haemorrhages
Foster 2010	122	0	0
Haas 2010	344	0	0
Zeidler 2011	173	5	0
Napolitano 2013	39	1	0
Tomoyose 2013	67	4	0
Hong Pheng Loh 2007	22	0	0
Total	**767**	**10 (Approx 1 in 77)**	**0**



Bone Marrows

Year	Number of bone marrows performed	Number of haemorrhages	Number of haemorrhages (plts < 50)	Risk of haemorrhage
2002	13,506	10	3	1 in 1,351
2003	19,259	11	2	1 in 1,751
2004	20,323	9	0	1 in 2,258
2006	15,388	8	1	1 in 1,924
2013	9,295	9	6	1 in 1,033
Total		**47**	**12**	

Bain BJ. Bone marrow biopsy morbidity and mortality: 2002 data. Clin Lab Haem 2004;26:315-8.
Bain BJ. Bone marrow biopsy morbidity: review of 2003. J Clin Pathol 2005;58:406-8.
Bain BJ. Morbidity associated with bone marrow aspiration and trephine biopsy - a review of UK data for 2004. Haematologica 2006;91:1293-4.
Devalia V. Annual British Society for Haematology confidential survey of bone marrow examination associated adverse events 2011. Br J Haematol 2013;161:22-3.

BCSH guideline recommendations

- Insertion of venous central lines can be performed by experienced staff using ultrasound guidance techniques when the platelet count is > $20x10^9/L$

- Platelet transfusions should not be given routinely prior to bone marrow aspirate or trephine biopsy

Therapeutic

Anti-platelet agents

- PATCH study
  - Randomised people with spontaneous ICH to platelet transfusion or no platelet transfusion
  - 60 hospitals (190 participants) Netherlands, UK, and France
  - Hypothesis – platelet transfusion decreases odds of death or dependence
  - odds of death or dependence at 3 months
    - 2·05, 95% CI 1·18 to 3·56
  - Serious adverse event
    - 40 (42%) who received platelet transfusion
    - 28 (29%) who received standard care

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

BCSH guideline recommendations

- Use general haemostatic measures to treat bleeding in patients during treatment with anti-platelet agents. If necessary, consider drug cessation and reversal of the effect of co-prescribed anticoagulants.
- Use TXA to counteract the effect of anti-platelet agents when a risk/benefit assessment would support this

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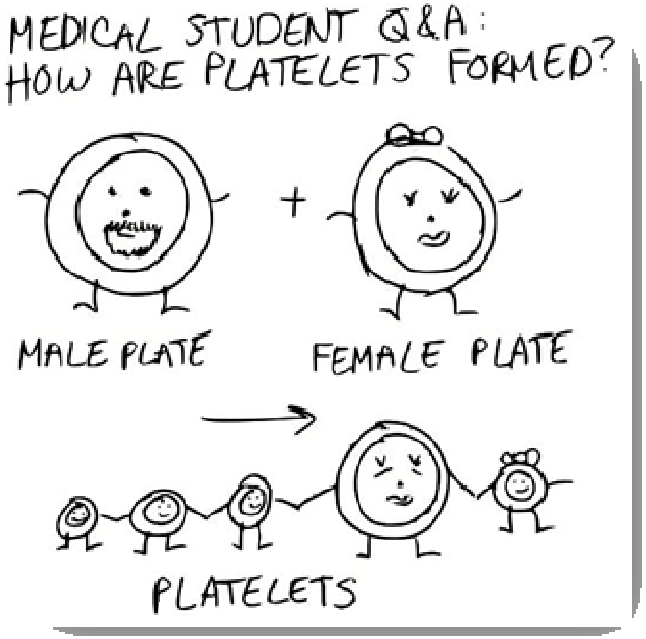

Any questions