Using platelets in haematology patients

Recent Studies

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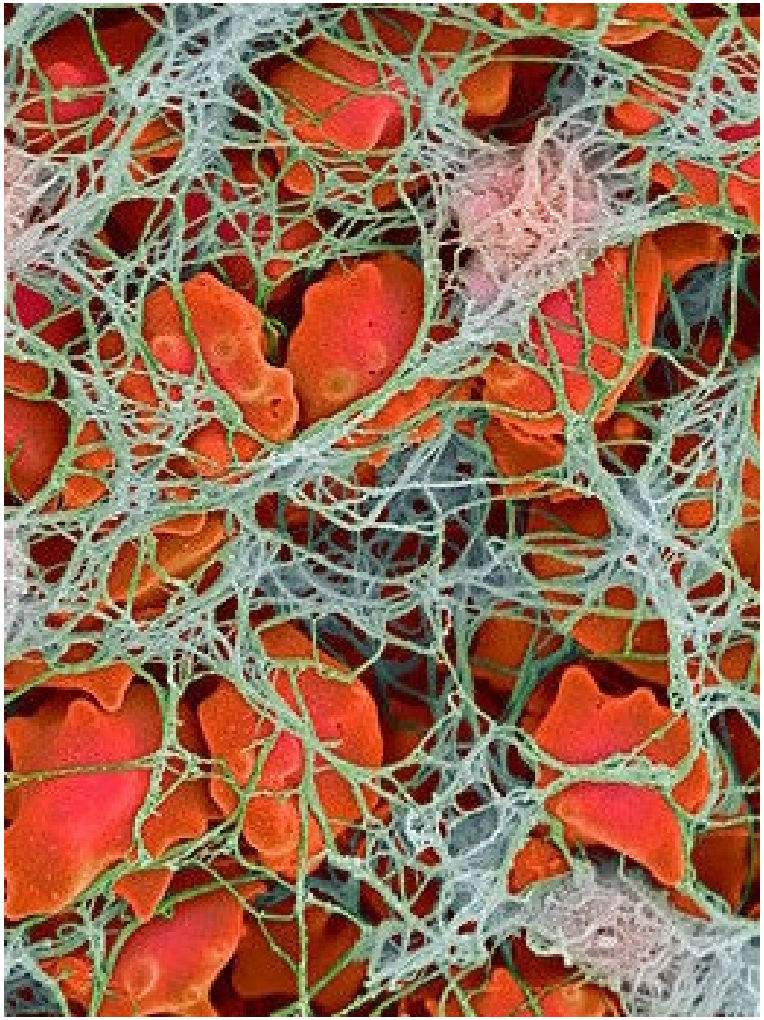
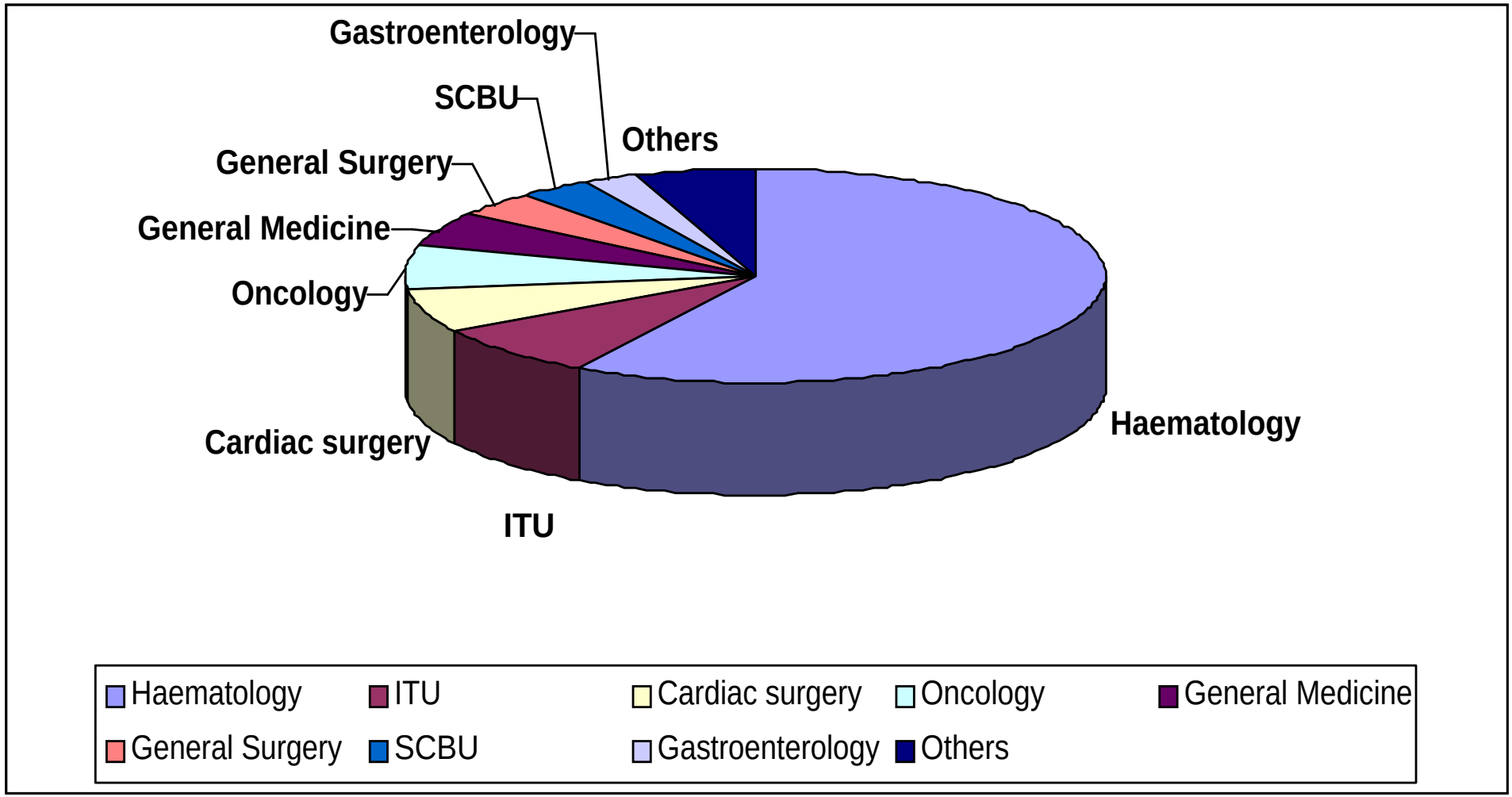
Prevention of bleeding

- 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
- Platelet transfusions are given to prevent and treat bleeding



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

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	69%	60%	6%	34%
Pre - procedure	15%	64%	13%	23%
Therapeutic	13%	84%	12%	5%
Unclear	3%	0%	100%	0%

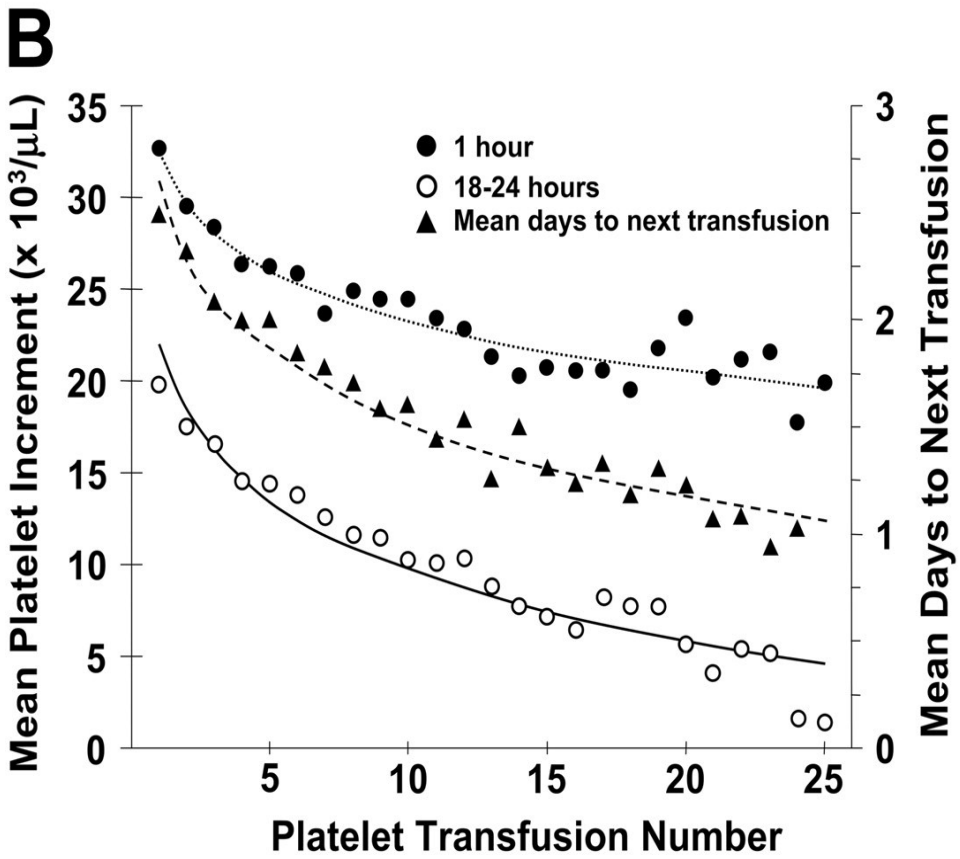
Platelet Transfusions in Haematology Patients: Are we using them appropriately? Estcourt *et al* 2012. Vox Sanguinis

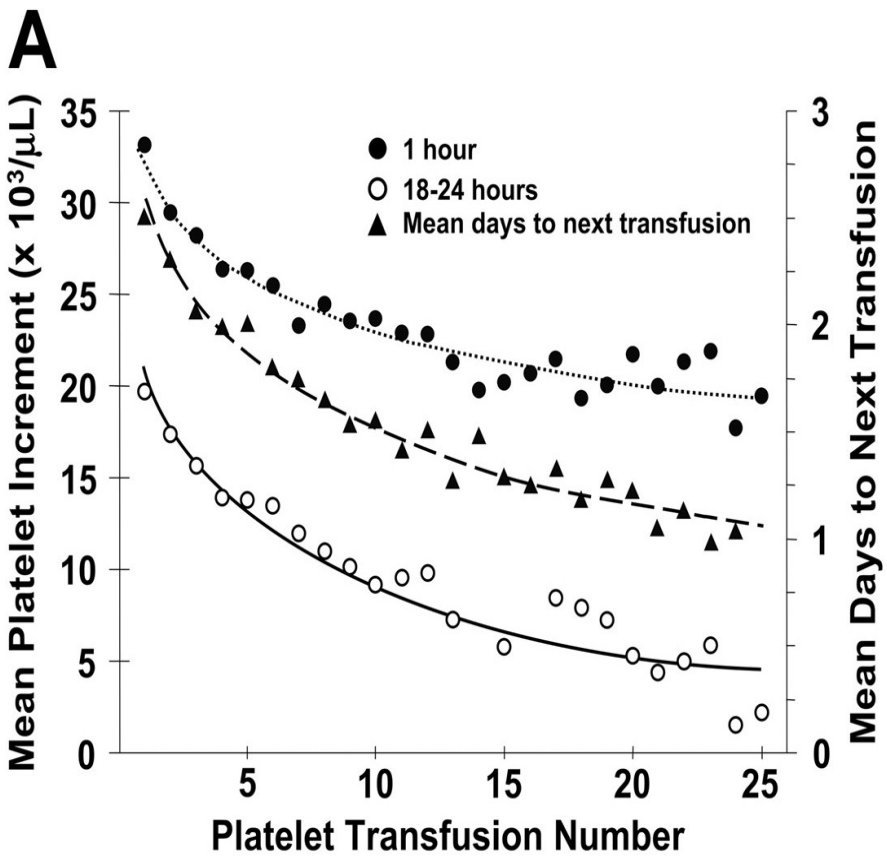
Avoid unnecessary usage

- 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

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

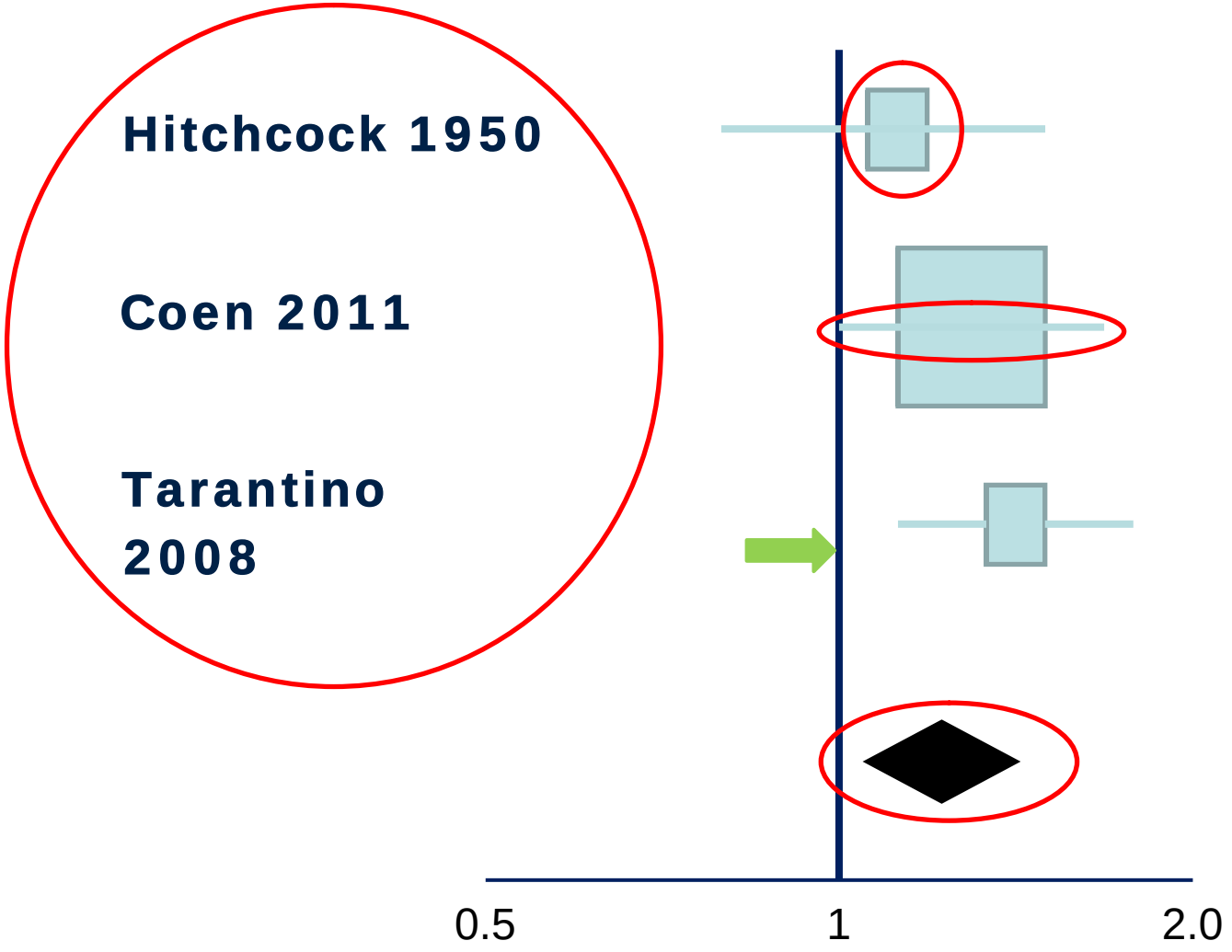
Current Issues in Prophylactic Platelet Transfusion Studies

- Platelet dose
- Platelet threshold
- Therapeutic versus prophylactic

If the number of platelets in prophylactic transfusions is doubled. By how much is the chance of bleeding reduced?

- 50%
- 25%
- 10%
- 0%

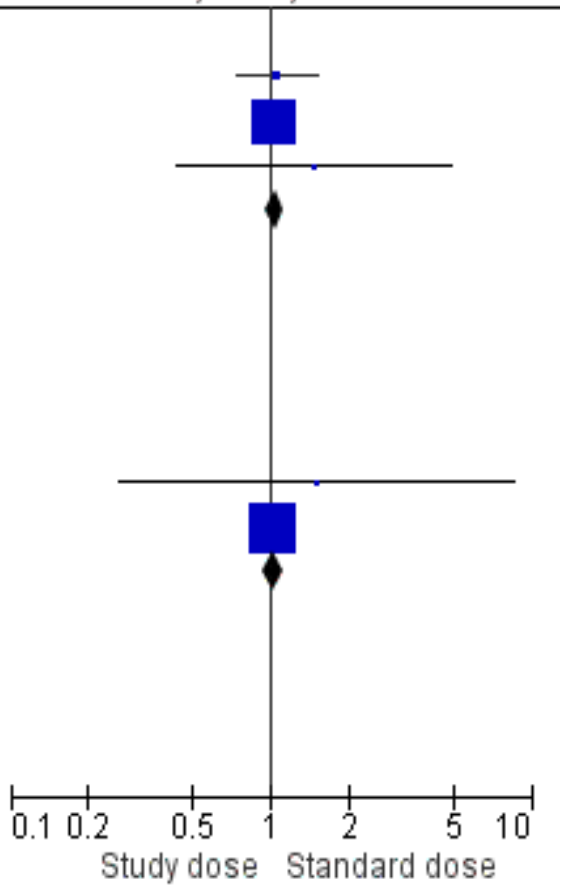
Forest Plot



Platelet Dose

Number of Patients with clinically significant bleeding

Study or Subgroup	Study dose Events	Total	Standard dose Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
3.2.1 Low dosage platelet transfusions versus standard dosage platelet transfusions						
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]
Subtotal (95% CI)		**531**		**539**	**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)						
3.2.2 High dosage platelet transfusions versus standard dosage platelet transfusions						
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]
Subtotal (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)						



Prophylactic platelet transfusion for prevention of bleeding in patients with haematological disorders after chemotherapy and stem cell transplantation Estcourt *et al* 2012. Cochrane Database of Systematic Reviews

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

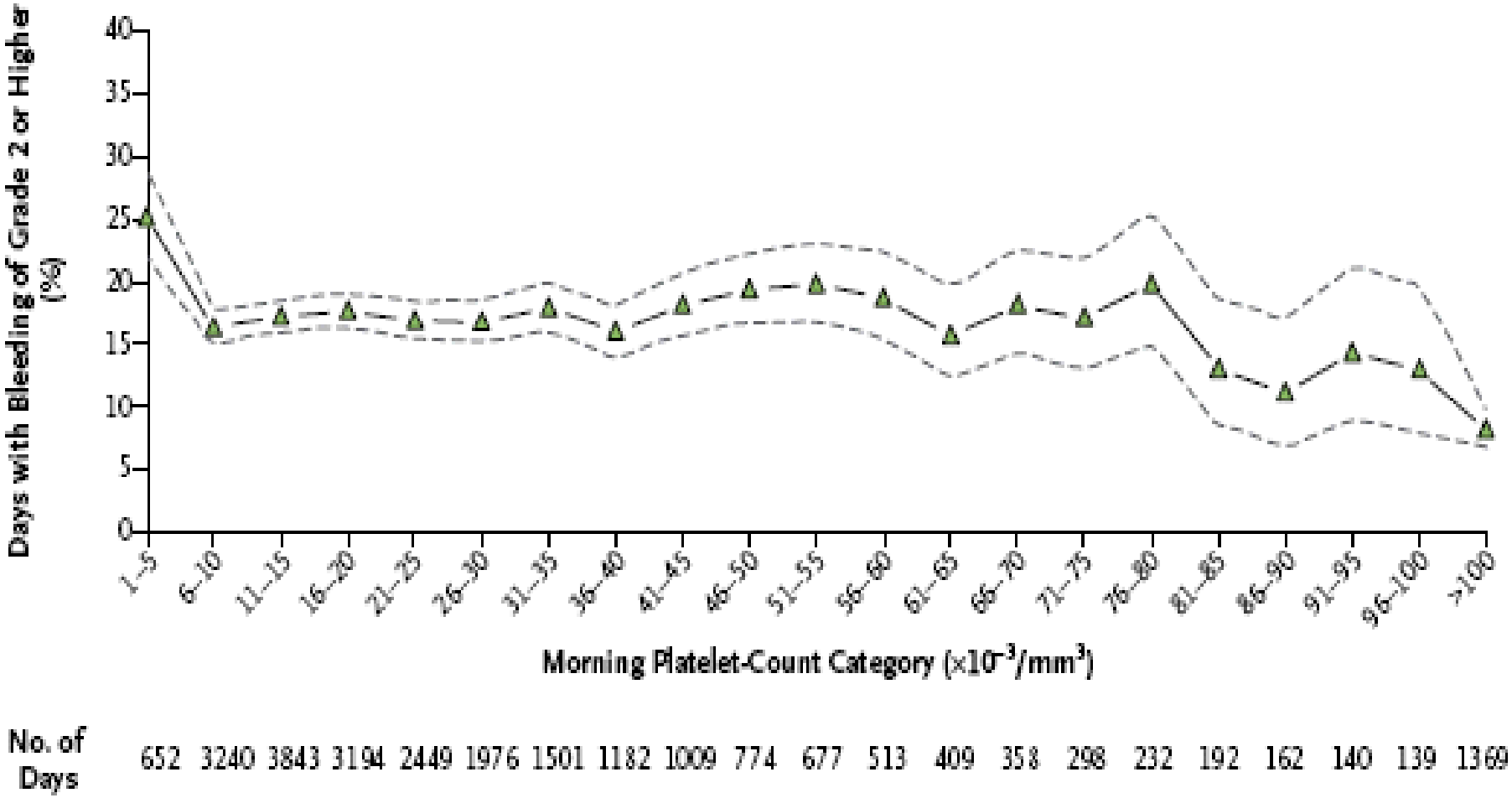
approximately 20 - 40 x 10^9/l[1]

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[3]

Morning platelet count is a poor predictor of bleeding risk

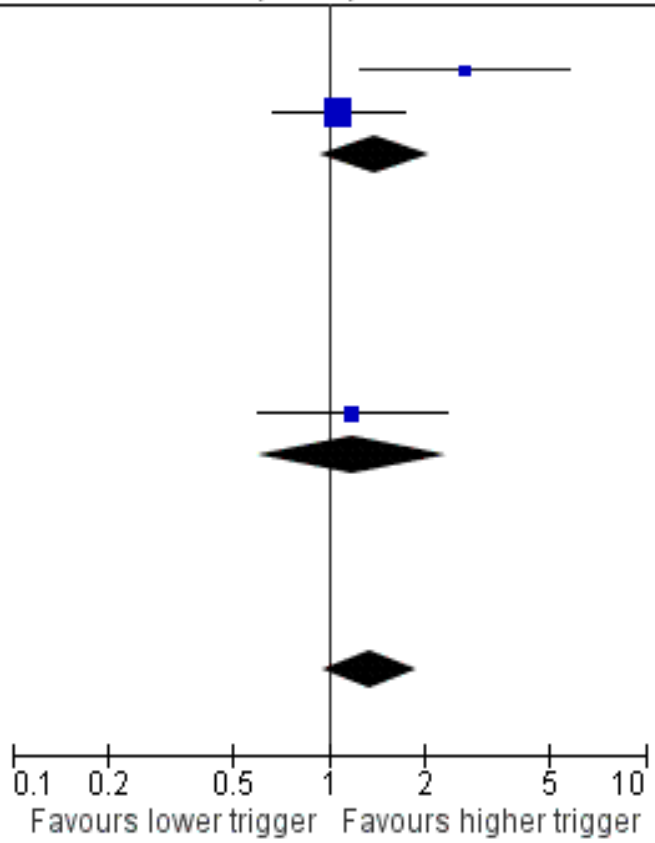


Dose of prophylactic platelet transfusions and prevention of hemorrhage. Slichter *et al. NEJM* 2010;362:600-613

Platelet Threshold

Number of Patients with clinically significant bleeding

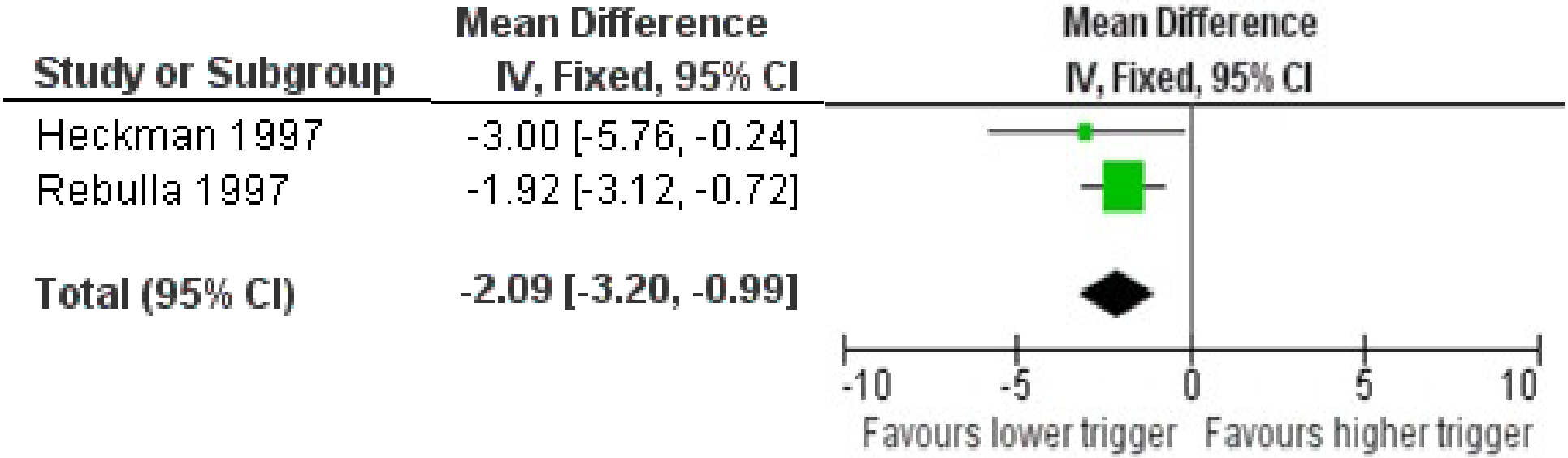
Study or Subgroup	Lower trigger Events	Total	Higher trigger Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
2.2.1 Platelet threshold < 10 vs. < 20						
Heckman 1997	17	37	7	41	14.9%	2.69 [1.26, 5.75]
Rebulla 1997	29	135	24	120	57.2%	1.07 [0.66, 1.74]
Subtotal (95% CI)		**172**		**161**	**72.1%**	**1.41 [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)						
2.2.2 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)						



Prophylactic platelet transfusion for prevention of bleeding in patients with haematological disorders after chemotherapy and stem cell transplantation Estcourt *et al* 2012. Cochrane Database of Systematic Reviews

Platelet Threshold

Mean number of platelet transfusions per patient



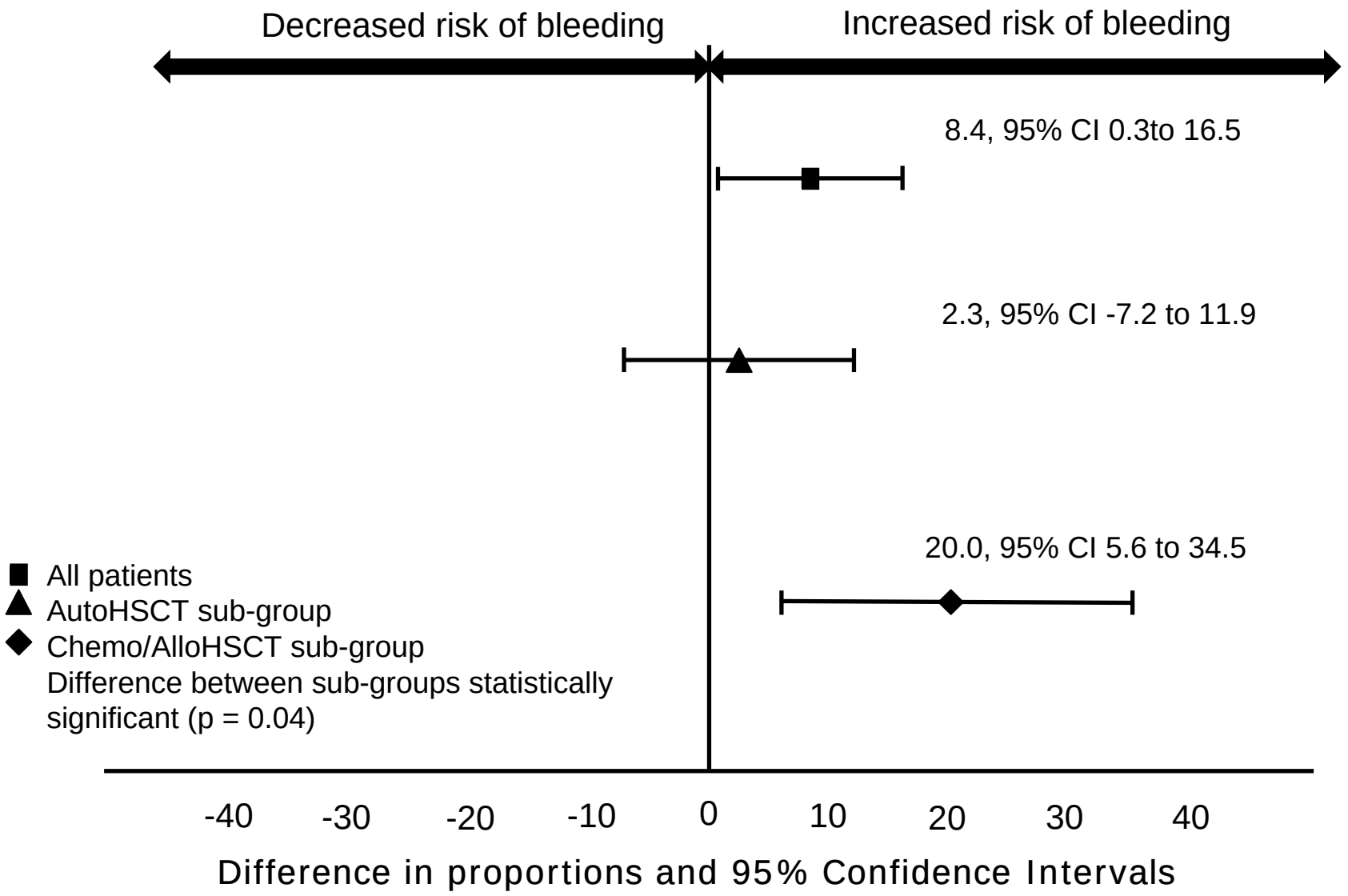
Heterogeneity: Chi² = 0.49, df = 1 (P = 0.48); I² = 0%
Test for overall effect: Z = 3.72 (P = 0.0002)

Prophylactic platelet transfusion for prevention of bleeding in patients with haematological disorders after chemotherapy and stem cell transplantation Estcourt *et al* 2012. Cochrane Database of Systematic Reviews

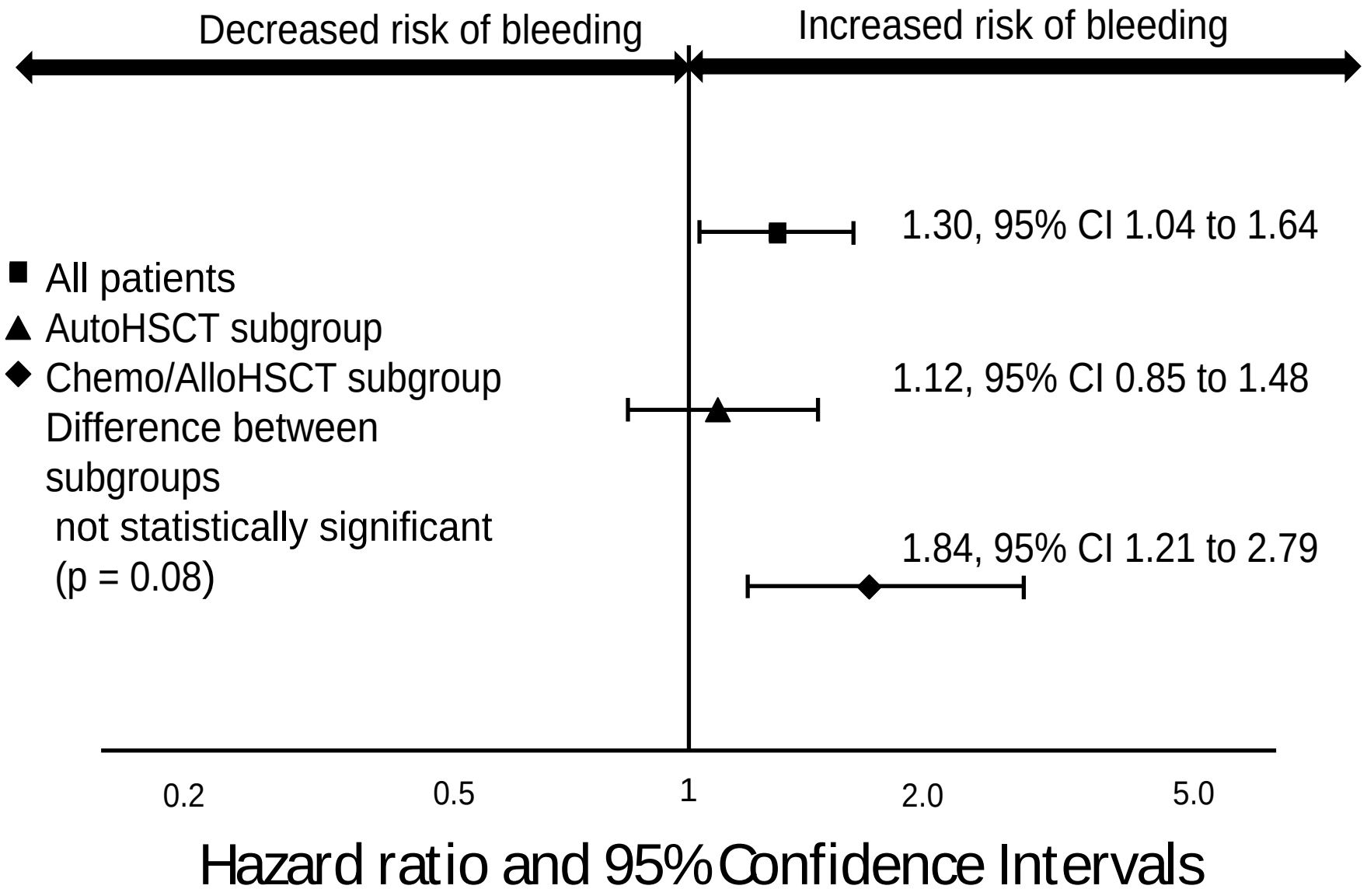
	German Study (Wandt 2012)		TOPPS (Stanworth 2013)	
	Prophylaxis	No Prophylaxis	Prophylaxis	No Prophylaxis
Number of Patients	194	197	298	300
Autologous SCT	98 (29%)	103 (34%)	210 (70%)	210 (70%)
Clinically significant bleeding	19%	42%	43% (128/298)	50% (151/300)
Severe or life-threatening bleeding	2%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



Time to first WHO Grade 2-4



	German Study (Wandt 2012)		TOPPS (Stanworth 2013)	
	Prophylaxis	No Prophylaxis	Prophylaxis	No Prophylaxis
Number of Patients	194	197	298	300
Platelet transfusions/ patient	2.44 (2.22 to 2.67)	1.63 (1.42 to 1.83)	3.0 ± 3.2	1.7 ± 2.6
Proportion of patients receiving platelet transfusions	NR	NR	89% (266/298)	59% (176/300)

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*

What about long term bone marrow failure?

- One study in progress, one previous non-randomised study (25 patients)
- Avoid platelet transfusions when patient well, not bleeding, no history of severe bleeding
- Management should be individualised

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

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 adverese events 2011. Br J Haematol 2013;161:22-3.

Number of procedures Total (Platelets < 50)	Number of haemorrhages Total (Platelets < 50)	Number of major haemorrhages
259 (122)	0 (0)	0 (0)
3,170 (344)	3 (0)	0 (0)
604 (173)	8 (5)	0 (0)
431 (39)	8 (1)	0 (0)
108 (67)	5 (4)	0 (0)
80 (22)	2 (0)	0 (0)

Foster PF, et al. Central venous catheterization in patients with coagulopathy. Arch Surg 1992;127:273-5.

Haas B, et al. Large-bore Tunneled Central Venous Catheter Insertion in Patients with Coagulopathy. J Vasc Interv Radiol 2010;21:212-7.

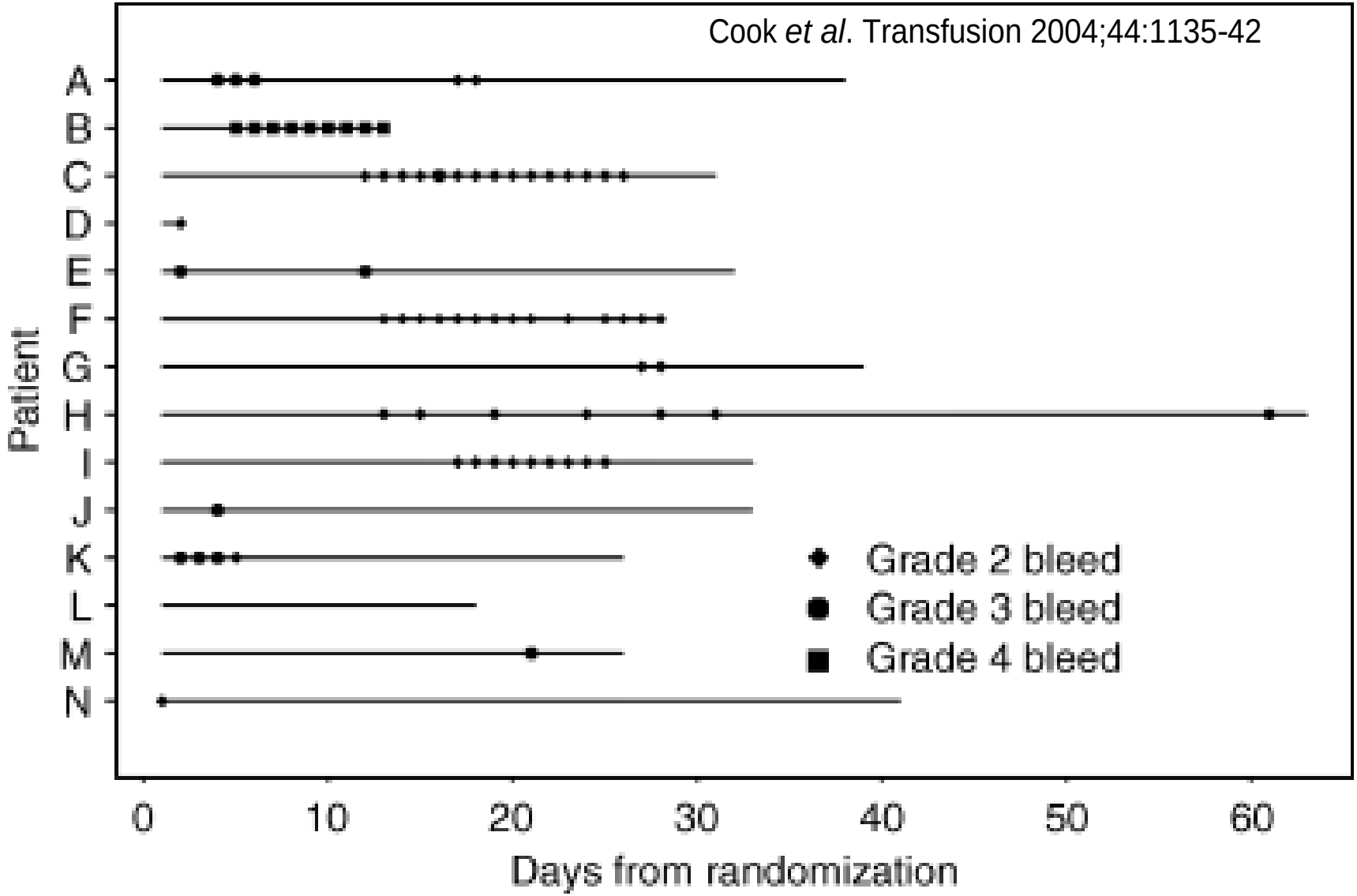
Zeidler K, et al. Optimal preprocedural platelet transfusion threshold for central venous catheter insertions in patients with thrombocytopenia. Transfusion 2011;51:2269-76.

Napolitano M, et al. Ultrasonography-guided central venous catheterisation in haematological patients with severe thrombocytopenia. Blood Transfus 2013:1-5.

Tomoyose T, et al. Real-time ultrasound-guided central venous catheterization reduces the need for prophylactic platelet transfusion in thrombocytopenic patients with hematological malignancy. Transfusion and Apheresis Science 2013;49:367-9.

Hong Pheng Loh A, et al. Port-A-Cath insertions in acute leukemia: does thrombocytopenia affect morbidity? Journal of Pediatric Surgery 2007;42:1180-4.

Variability in frequency and severity of bleeding between patients



Risk Factors for Bleeding

- Sepsis/inflammation
- Recent significant bleeding (last 5 days)
- Anticoagulation
- ???

Treatment of Bleeding

- Poor evidence base, no RCTs
- Clinically significant, but not major bleeding – give platelet Tx and reassess
- Major bleeding, keep platelet count above 50

Summary

- Prophylactic platelet transfusions
  - Don’t use two units when one will do
- Pre-procedure
  - Avoid routinely using platelet transfusions prior to bone marrow aspirates and trephines
- Think before prescribing a platelet transfusion
  - Does my patient need it?
  - Have they agreed to have a transfusion?

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