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# Pathogen-Reduced Platelets for the Prevention of Bleeding

## Cochrane Systematic Review

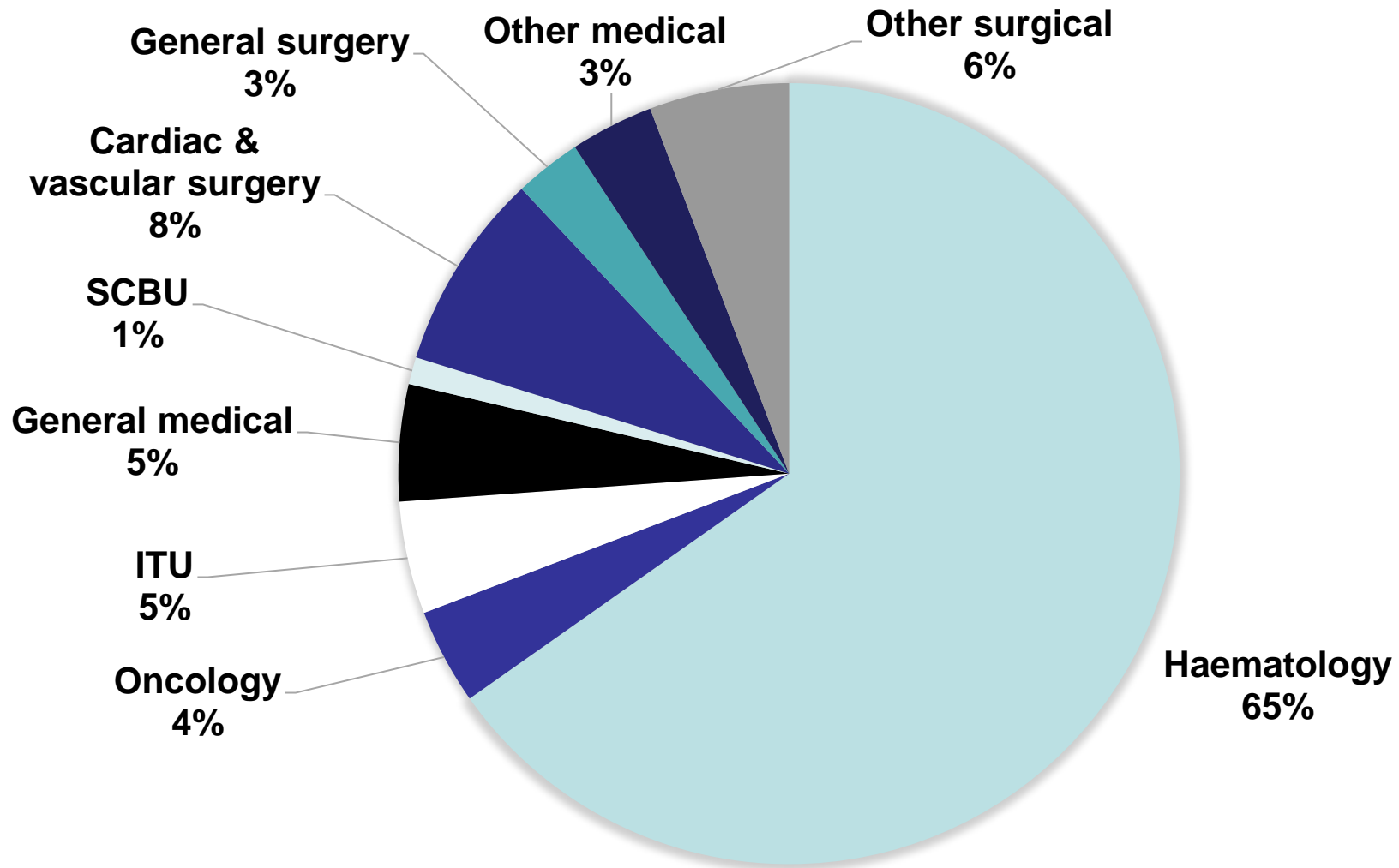
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NHSBT



# Summary of talk

- Pathogen-inactivation
  - Why it may be important for platelet transfusions
  - PRP methods assessed in RCTs
  - Findings from the review

# Haematology patients use the majority of platelet transfusions



# Transfusion transmitted infections in the UK from 1996 to 2017

Internal use

	Bacteria	HAV	HBV	HCV	HEV	HIV	HTLV1	Parvo	Malaria	vCJD	Total
<b>Transfusion transmitted infections for all types of blood component</b>											
<b>Overall incidents</b>	41	4	12	2	10	2	2	1	2	3	79
<b>Infected recipients</b>	44	4	14	2	13	4	2	1	2	4	90
<b>Overall deaths</b>	11	-	-	-	1	-	-	-	1	3	16
<b>Transfusion transmitted infection incidents for platelet transfusion</b>											
<b>Pooled platelets</b>	21	2	1	-	2	1	-	-	-	-	27
<b>Apheresis platelets</b>	16	1	1	-	1	-	-	-	-	-	19
<b>Total incidents</b>	37 (90%)	3 (75%)	2 (17%)	-	3 (30%)	1 (50%)	-	-	-	-	46 (58%)
<b>Total deaths</b>	9 (82%)	-	-	-	1 (100%)	-	-	-	-	-	

# Ideal PRP platelet component

- ↓ infectious agents below level required to cause infection
- Cost effective (reduction in risk or reduction in the need for other tests)
- Platelets as effective (or more so) than untreated platelets
- Additional benefits
  - ↓ Ta-GvHD
  - ↓ allergic reactions
  - No need for irradiation
  - No need for CMV negative components



# PRP methodologies for platelets

- **Intercept® (Cerus Corporation, Concord, CA, USA)**
  - UV light and amotosalen
  
- **Mirasol® (CaridianBCT, Lakewood, CO, USA)**
  - UV light and riboflavin (vitamin B2)
  
- **THERAFLEX (MacoPharma, Mouvaux, France)**
  - UV light alone

# PRP methodologies for platelets not perfect


- **Some bacteria relatively resistant**
    - *Pseudomonas aeruginosa*, *Bacillus cereus*, some strains of *K. pneumoniae*, *S. pneumoniae* and *S. agalactiae*
  - **Some viruses relatively resistant (non-enveloped viruses)**
    - Hepatitis A, Hepatitis E, parvovirus
  - **If high infectious load, component could still transmit infection**
- BUT**
- **May prevent the transmission of unexpected, or emerging infections**
    - SARS-CoV-2, Dengue virus, West Nile Virus, Chikungunya virus, Influenza A (H5N1), HIV variants, hepatitis B variants and Babesia spp



What is the  
evidence?



# Systematic review

- 16 completed RCTS (3429 Participants). 4 new RCTs.
  - All trials were in high-income countries
  - No trials compared different methodologies head-to-head
  - Search up to February 2023
  - 1 ongoing RCT – PEDITREC – planned to recruit 252 children, cardiac surgery NCT05293106
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# Intercept PRT (11 trials)

Study	Participants	Type of participant	Type of platelet	Platelet dose (Mean, SD)
De Francisci 2004	44 (22/22)	Adult liver transplant/ paediatric cardiac surgery	NR	NR
Lozano 2011 (TESSI)	211 (105/106)	Adult haemato- oncological disease	86% BC 14% Aph (Control In PAS)	Intermediate (Both arms 4.2; 0.67)
Simonsen 2006 Cross-over	20 PCT-std: 9 std-PCT: 11	Adult haemato- oncological disease	BC (Control In PAS)	Low/intermediate (PCT 2.8; 0.38) (C 3.0; 0.43)
Slichter 2006 Cross-over	32 PCT-std: NR std-PCT: NR	Adult haemato- oncological disease	Aph (Control In plasma)	High (PCT 7.6; 1.3) (C 7.4; 0.9)
Agliastro 2006	30 (19/11)	Paediatric haemato- oncological disease	PCT plts BC Std plts Aph (Control unknown)	Low/intermediate (Both arms 2.9; NR)
Garban 2018 (EFFIPAP)	790 (263/262)	Adult haemato- oncological disease	PCT: BC 48.5% PCT Aph 51.5% C: BC 46.4% C: Aph 53.6% Controls in PAS and plasma	Intermediate <b>(PCT 4.1; 0.4)</b> <b>(PAS 4.4; 0.5)</b> <b>(C 4.9; 0.6)</b>

# Intercept PRT (cont.)

Study	Participants	Type of participant	Type of platelet	Platelet dose (Mean, SD)
Janetzko 2005	43 (22/21)	Adult haemato-oncological disease	Aph (Control in plasma)	Intermediate (PCT 4.1; 1.2) (C 3.8; 0.4)
Kerkhoffs 2010	184 (85/99)	Adult haemato-oncological disease	BC (Controls In PAS and plasma)	Intermediate <b>(PCT 3.4; 0.8)</b> <b>(C 3.9; 1.0)</b>
McCullough 2004 (SPRINT)	645 (318/327)	Paediatric + adult haemato-oncological disease	Aph (Control in plasma)	Intermediate <b>(PCT 3.7; 0.51)</b> <b>(C 4.0; 0.67)</b>
Rebulla 2017 (IPTAS)	228 (113/115)	Adult haemato-oncological disease	1% Aph 99% BC (Control in PAS)	Low/intermediate (PCT 2.9; 0.3) (C 3.1; 0.4)
van Rhenen 2003 (euroSPRITE)	103 (52/51)	Paediatric + adult haemato-oncological disease	BC (Control in PAS or plasma)	Intermediate <b>(PCT 3.9; 1.0)</b> <b>(C 4.3; 1.2)</b>

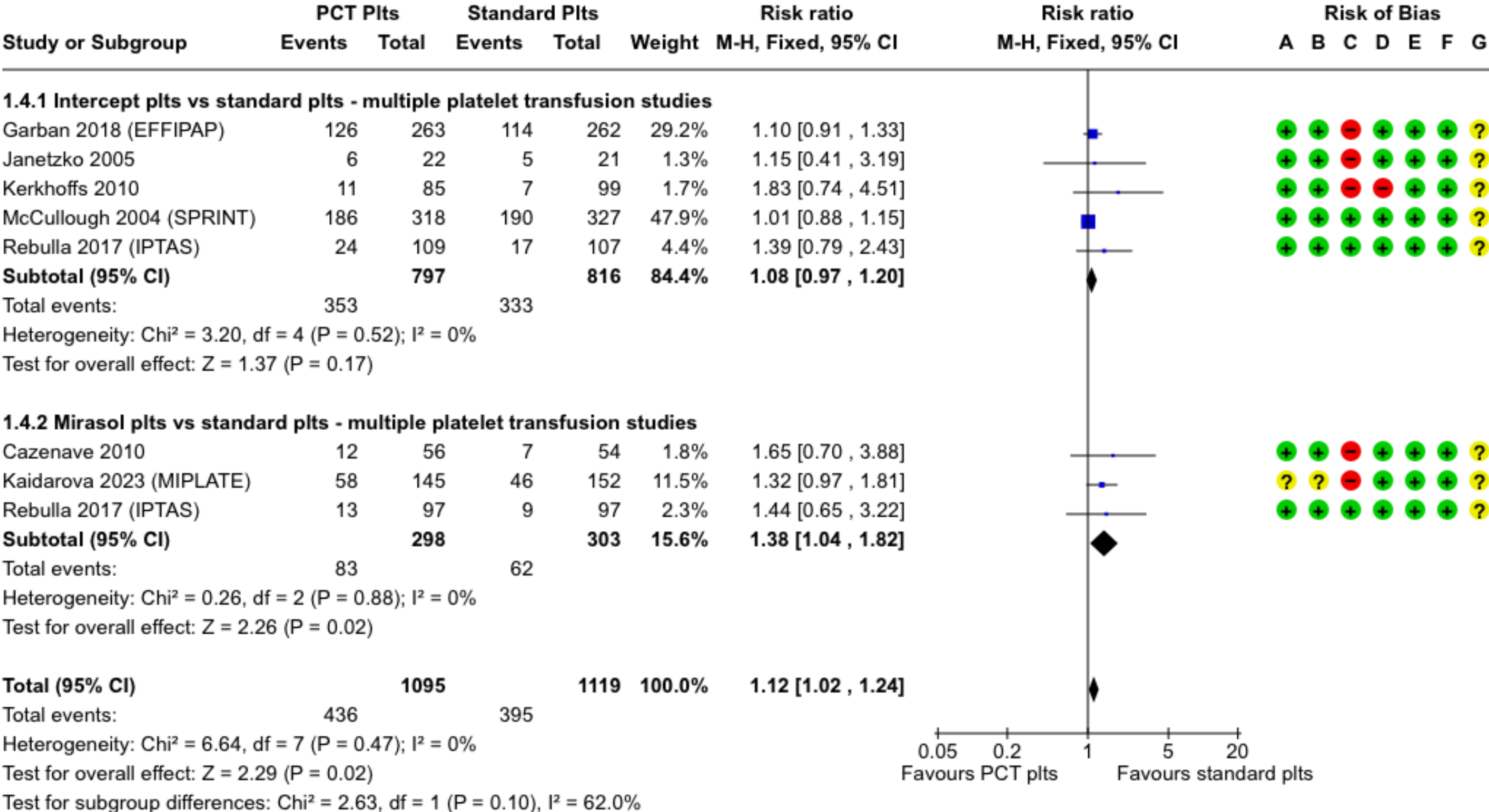
# Mirasol PRT (5 trials)

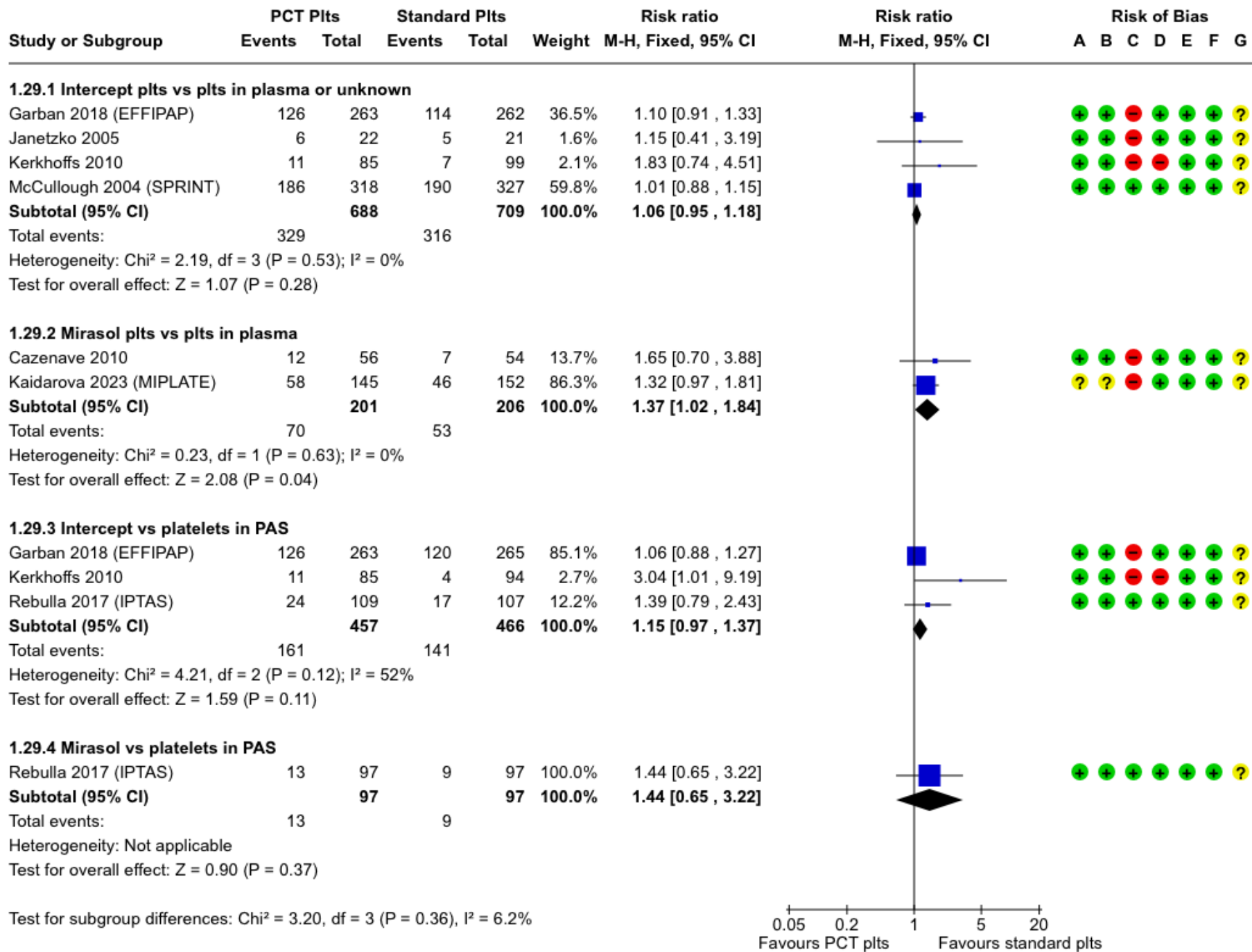
Study	Participants	Type of participant	Type of platelet	Platelet dose (Mean, SD)
Johansson (PRESS) Crossover	15 PCT-std: 8 std-PCT: 7	Adult haemato-oncological disease	BC (Control in PAS)	Low/intermediate (PCT 2.7; 0.4) (C 3.0; 0.2)
Cazenave 2010	110 (56/54)	Adult haemato-oncological disease	25% BC 75% Aph (Control in plasma)	Intermediate (PCT 5.2; 2.1) (C 5.2; 2.0)
Rebulla 2017 (IPTAS)	196 (99/97)	Adult haemato-oncological disease	49% Aph 51% BC (Control in PAS)	Low/intermediate (PCT 3.3; 0.7) (C 3.3; 0.6)
van der Meer 2018 (PREPAREs)	469 (244/225)	Adult haemato-oncological disease	BC (Control in plasma)	Low/intermediate (PCT 3.3; 0.6) (C 3.5; 0.8)
MIPLATE 2021	330 (164/166)	Paediatric + adult haemato-oncological disease	Aph (Control in plasma)	NR

# Theraflex PRT (1 trial)

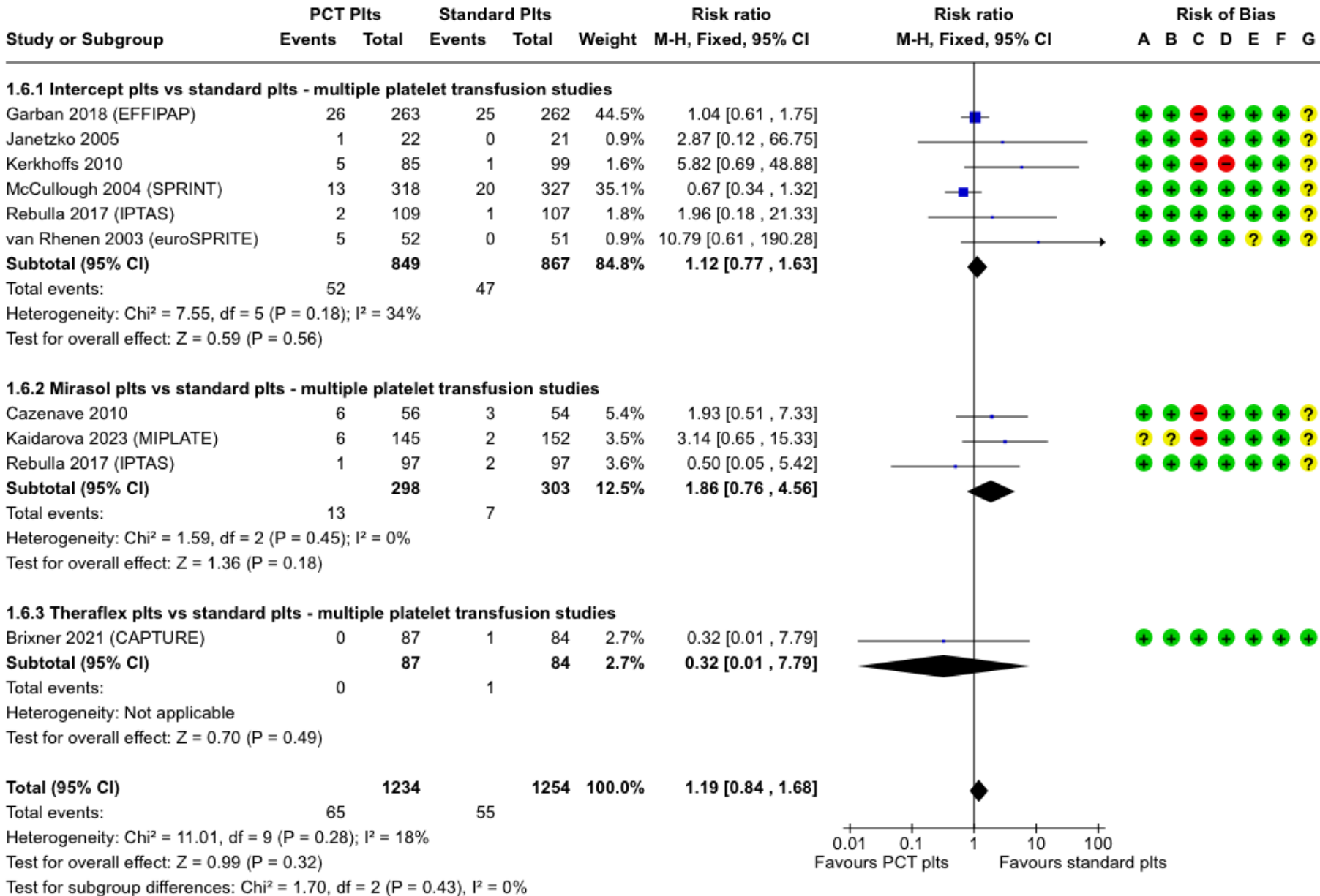
Study	Participants	Type of participant	Type of platelet	Platelet dose (Mean, SD)
Brixner 2021 (CAPTURE)	175 (89/86)	Adult haemato-oncological disease	68% BC 32% Aph (Control in PAS)	Low/intermediate (PCT 3.26, 0.37) (C 3.30, 0.37)

# Clinically significant bleeding (WHO grade 2 or above)



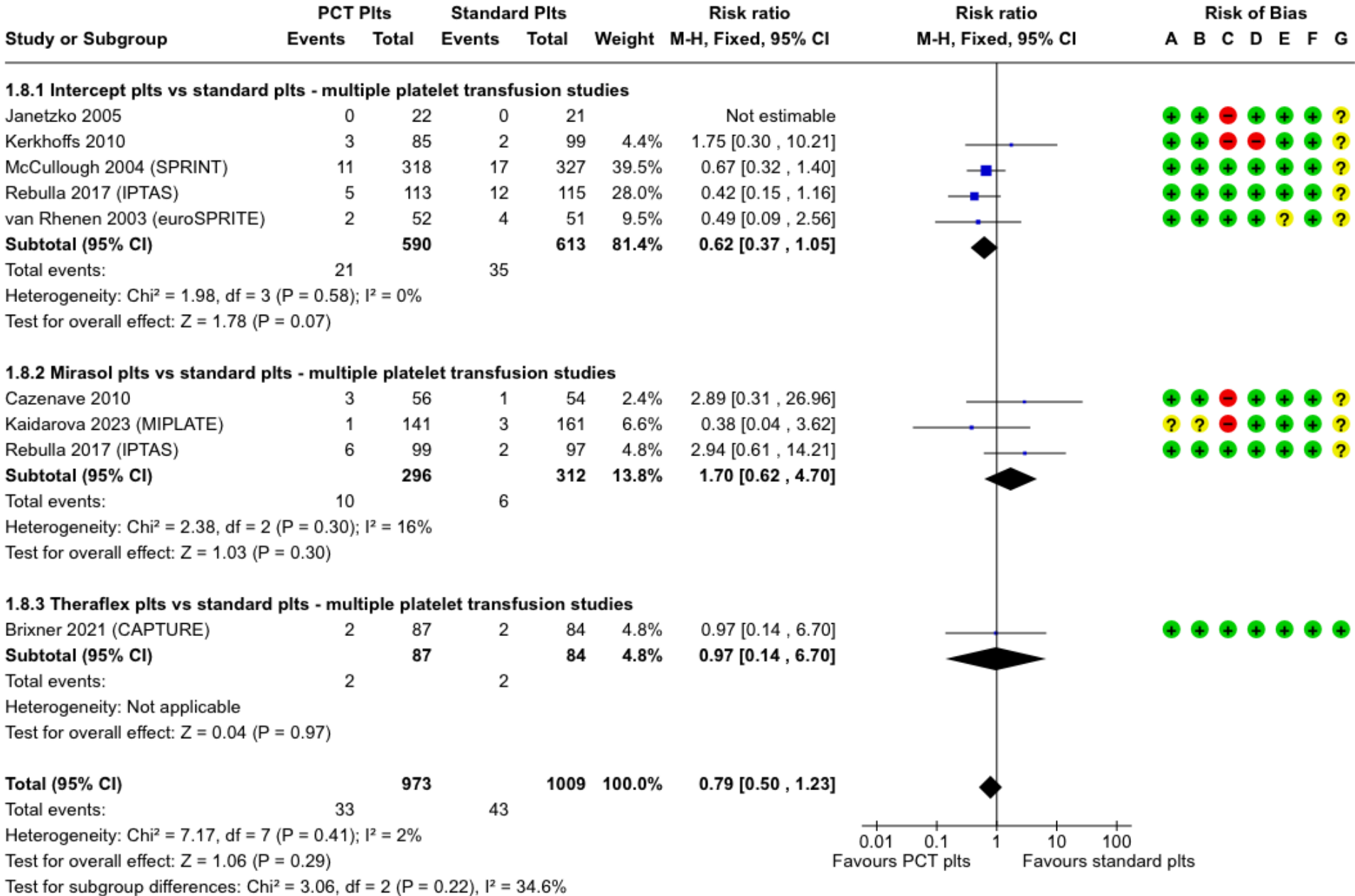


# Clinically severe bleeding (WHO grade 3 or above)

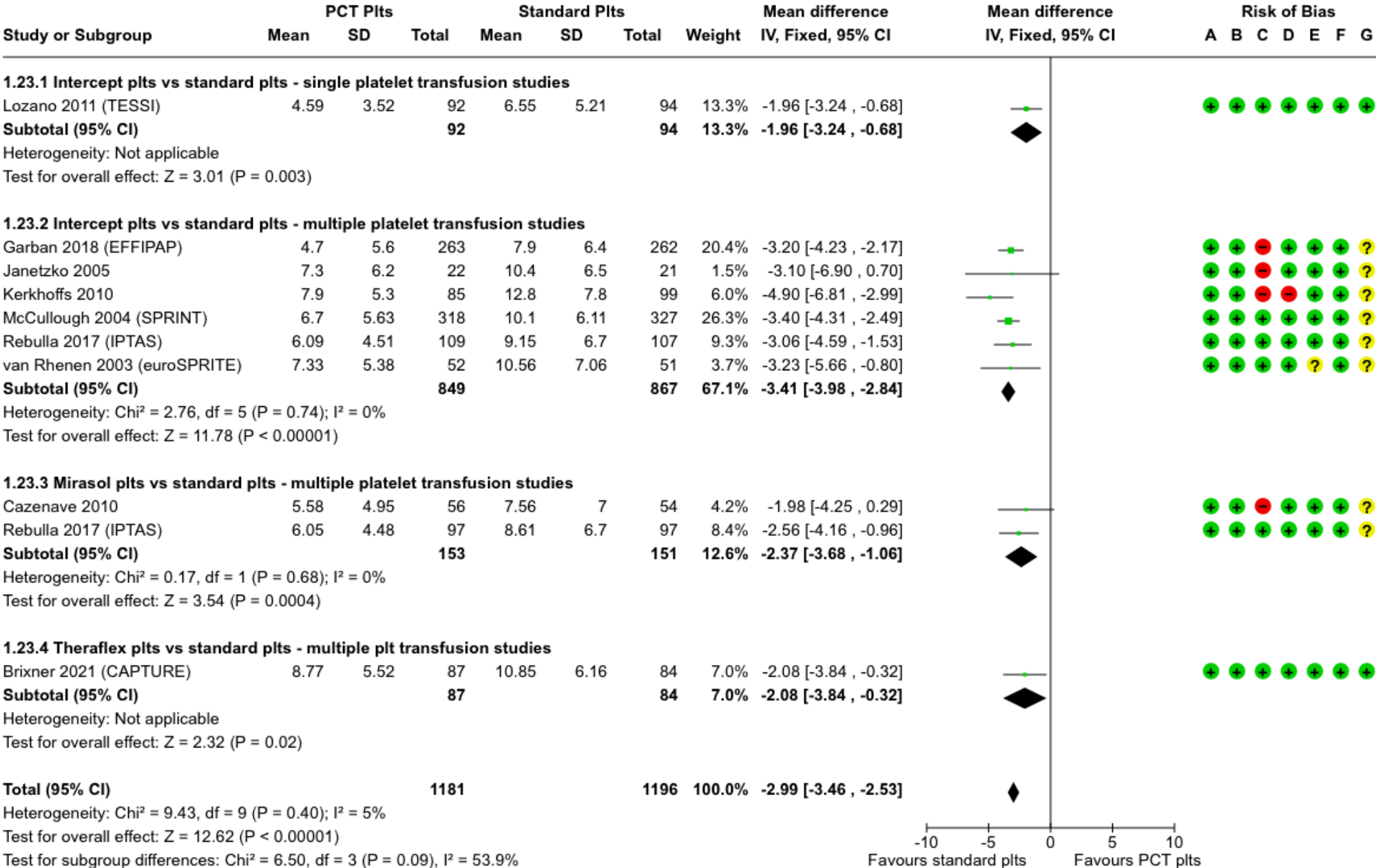


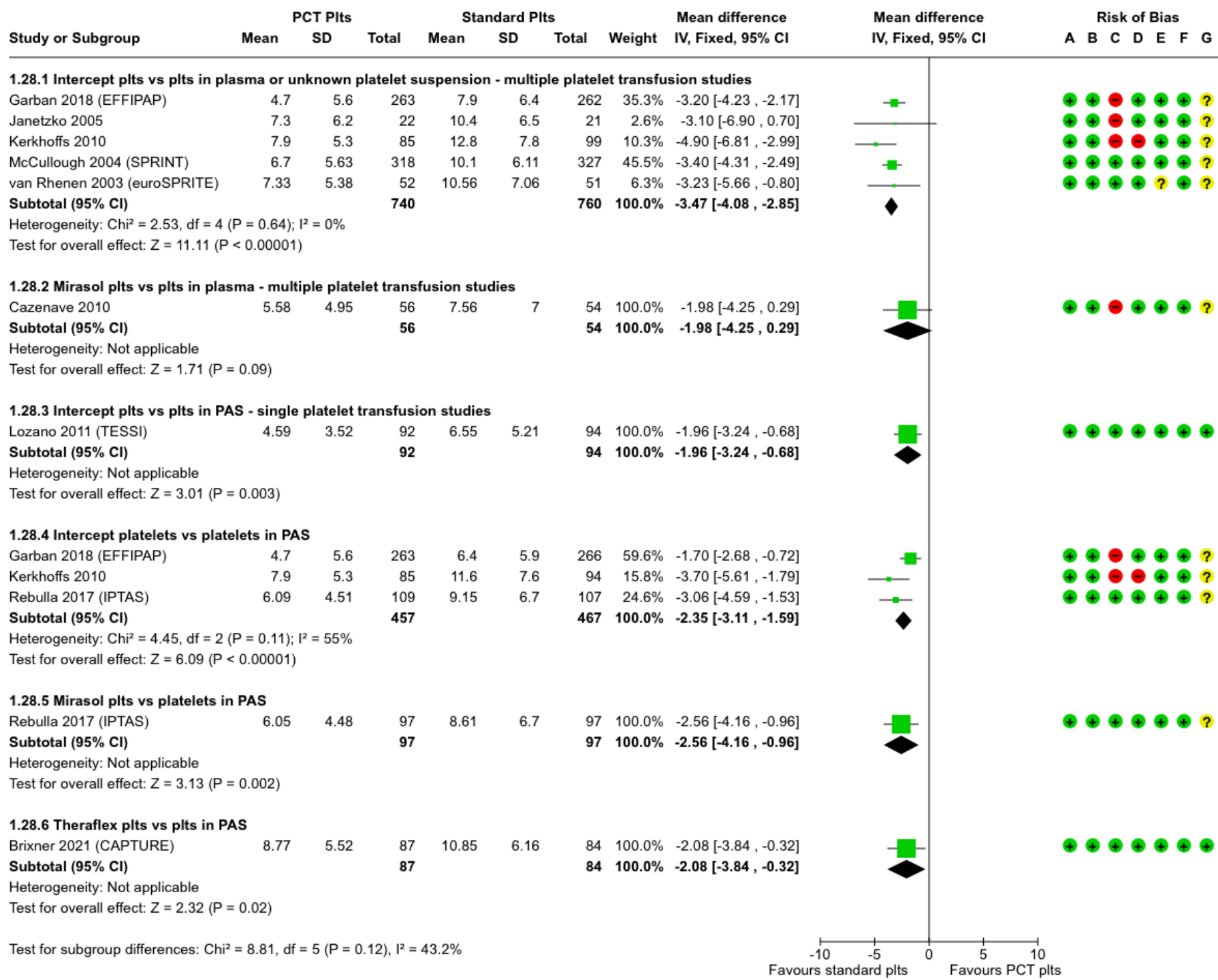


# All-cause mortality

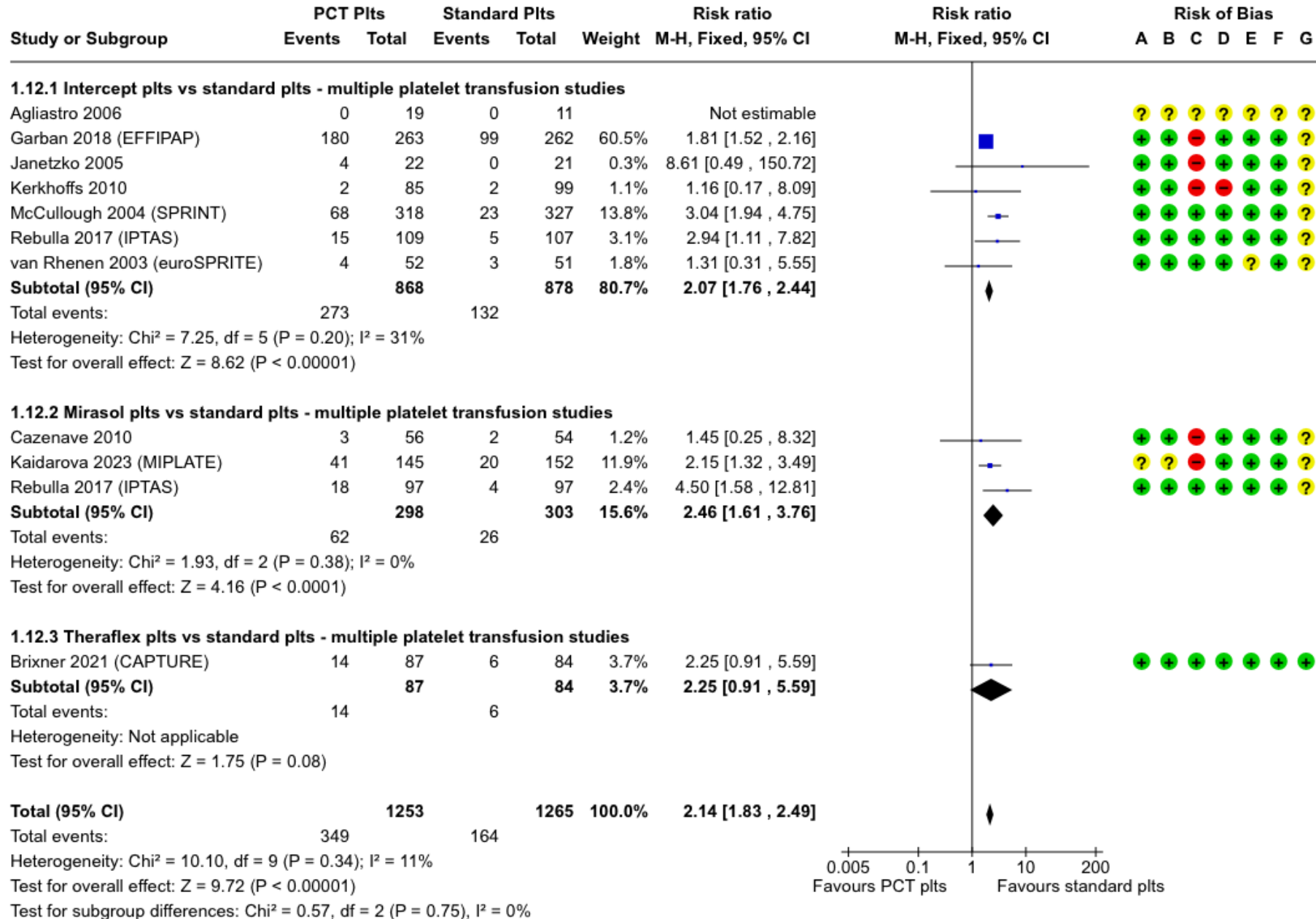


# 24 hour corrected count increment

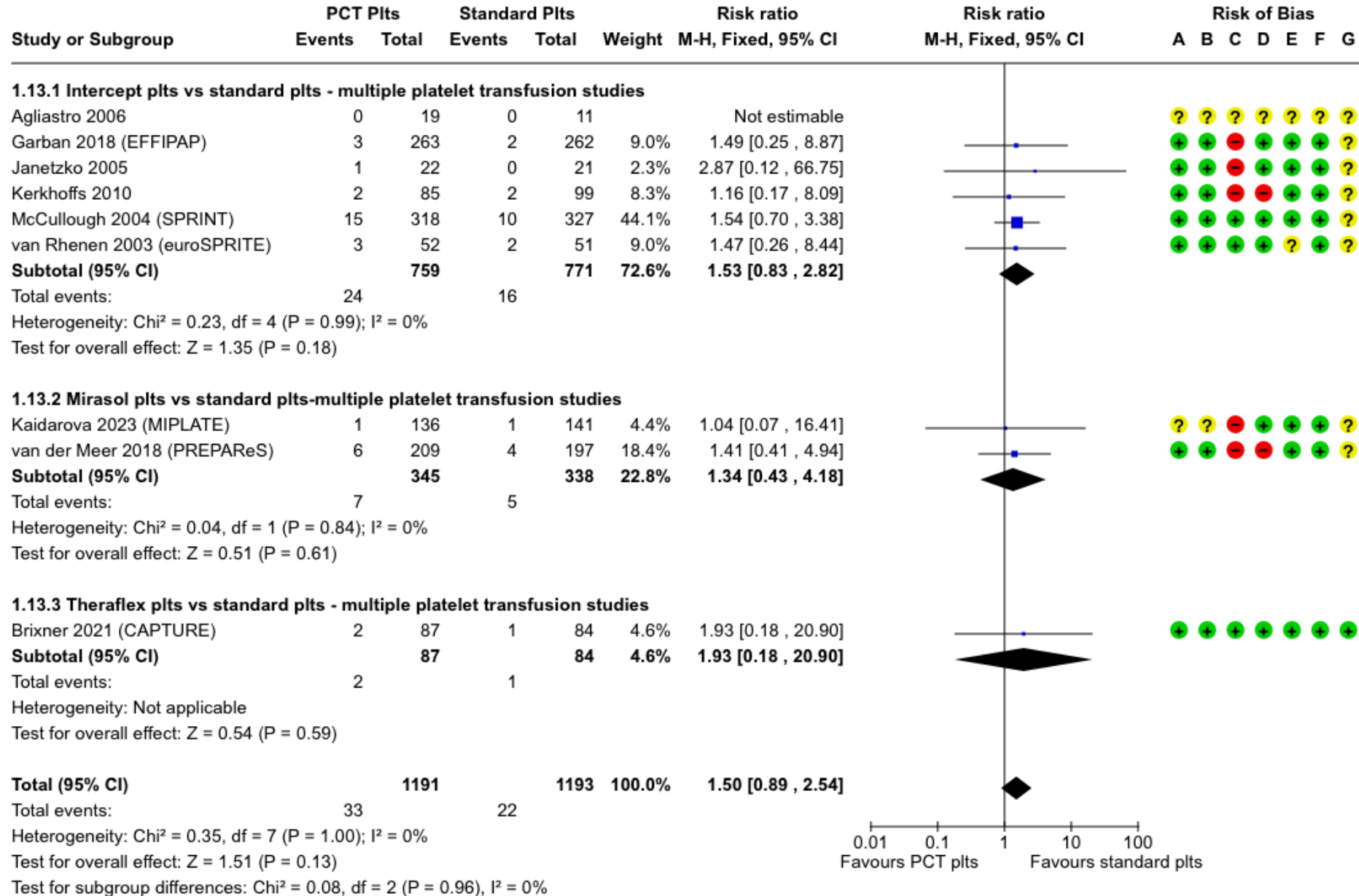




# Platelet refractoriness



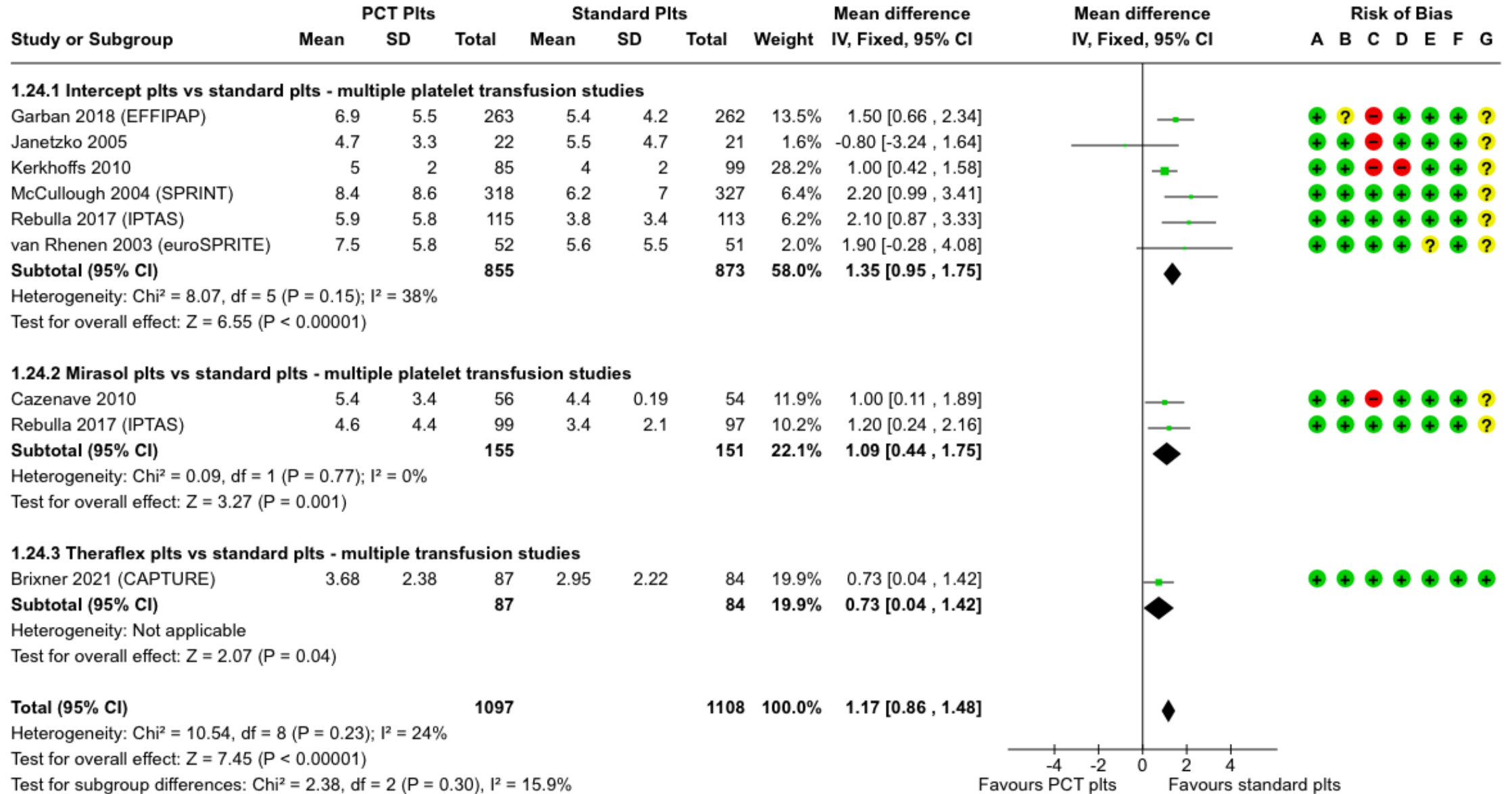
# Platelet refractoriness and alloimmunisation

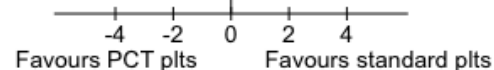
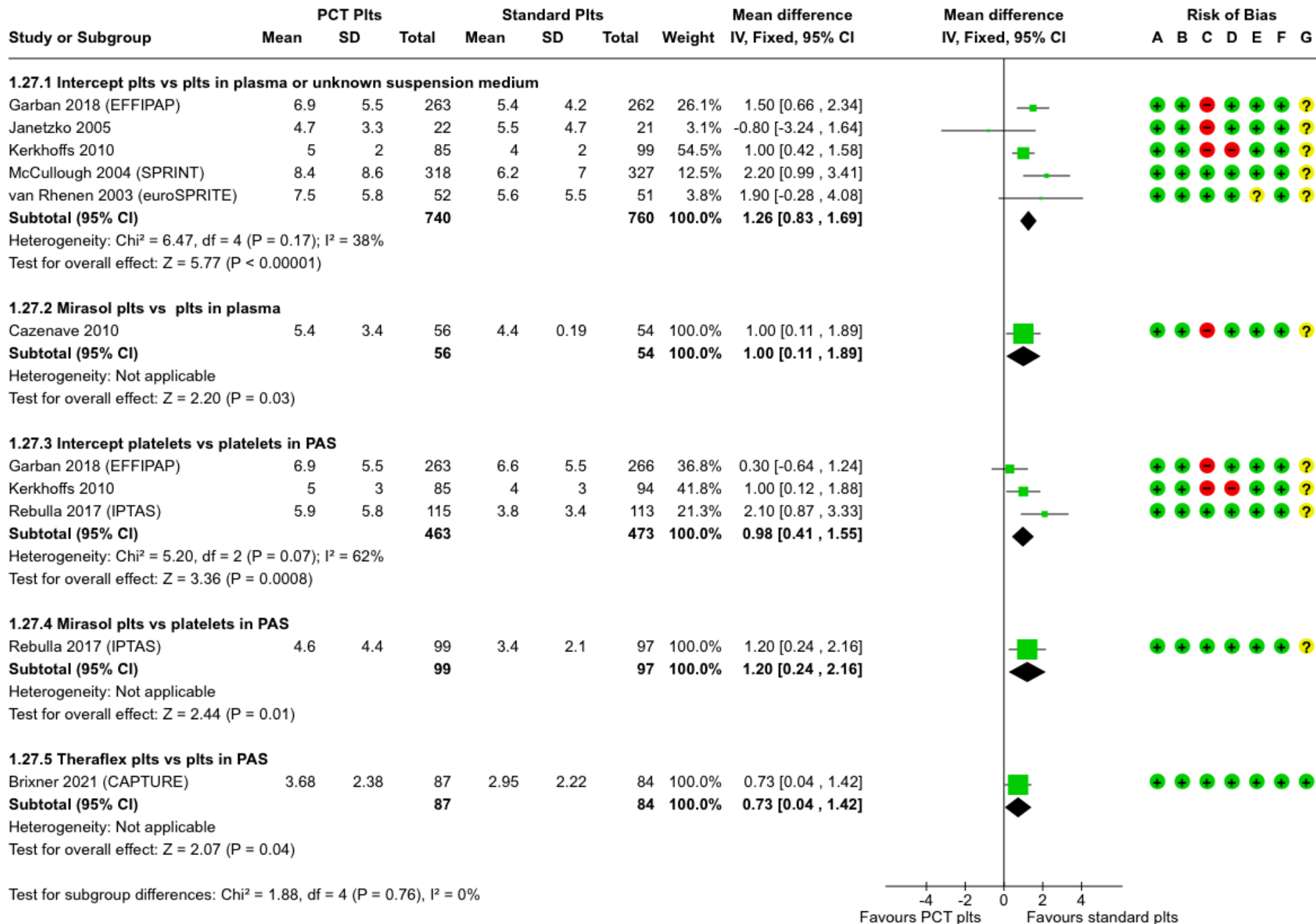


# Majority of platelet transfusions are prophylactic

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%

# Platelet transfusions required







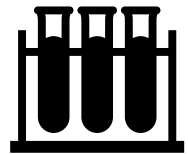
# So what do we know?



Nearly all the evidence is in adults with haematological malignancies in high-income countries



It may increase the risk of clinically significant bleeding (WHO 2 or above). It may or may not increase the risk of severe bleeding (WHO 3 or above)



It probably decreases the platelet count increment and corrected count increment, and therefore the risk of meeting trial definitions of platelet refractoriness. It probably does not affect the risk of alloimmunisation



It probably increases the number of platelet transfusions patients with haematological malignancies require to support them through their treatment

## Acknowledgements

Susan Brunskill

Lorna Cain

Carolyn Doree

Louise Geneen

Claire Iannizzi

Catherine Kimber

Reem Malouf

Yasan Migady

Ina Monsef

Vanessa Piechotta

Nicole Skoetz



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