

# Pathogen-Reduced Platelets for the Prevention of Bleeding

Cochrane Systematic Review

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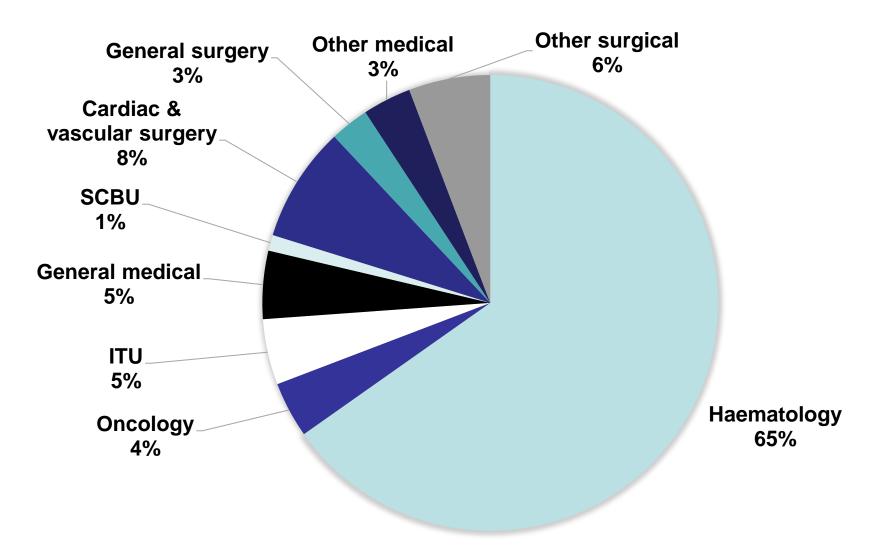
# Summary of talk



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

Internal use

# Haematology patients use the majority of platelet transfusions



Transfus	Transfusion transmitted infections in the UK from 1996 to 2017													
	Bacteria	HAV	HBV	HCV	HEV	HIV	HTLV1	Parvo	Malaria	vCJD	Total			
Transfusion tra	ansmitted infe	ections for	all types	of blood	d componen	t								
Overall incidents	41	4	12	2	10	2	2	1	2	3	79			
Infected recipients	44	4	14	2	13	4	2	1	2	4	90			
Overall deaths	11	-	-	-	1	-	-	-	1	3	16			
Transfusion tra	ansmitted infe	ection inci	dents for	platelet	transfusion									
Pooled platelets	21	2	1	-	2	1	-	-	+	-	27			
Apheresis platelets	16	1	1	-	1	-	-	-	-	-	19			
Total	37	3	2	-	3	1	-	-	-	-	46			

(30%)

(100%)

(50%)

(58%)

(17%)

(75%)

(90%)

9

(82%)

incidents

**Total deaths** 

### Ideal PRP platelet component

- \$\square\$ 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



# 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

Intercept F	PRT (11 ·	trials)
Study	Participants	Type of par

44

211

20

32

30

790

(263/262)

(19/11)

(22/22)

(105/106)

PCT-std: 9

std-PCT: 11

PCT-std: NR

std-PCT: NR

De Francisci 2004

Lozano 2011 (TESSI)

Simonsen 2006

Cross-over

Slichter 2006

Agliastro 2006

Garban 2018 (EFFIPAP)

Cross-over

	/	
Туре	of participant	

Adult liver transplant/

Adult haemato-

Adult haemato-

Adult haemato-

oncological disease

oncological disease

oncological disease

Paediatric haemato-

oncological disease

Adult haemato-

oncological disease

paediatric cardiac surgery

Type of platelet

NR

BC

Aph

86% BC

14% Aph

(Control In PAS)

(Control In PAS)

(Control In plasma)

(Control unknown)

PCT: BC 48.5% PCT Aph

C: BC 46.4% C: Aph 53.6%

Controls in PAS and plasma

PCT plts BC

Std plts Aph

51.5%

Platelet dose

Intermediate

(Both arms 4.2; 0.67)

Low/intermediate

(PCT 2.8; 0.38)

(PCT 7.6; 1.3)

Low/intermediate

(Both arms 2.9; NR)

(C7.4; 0.9)

Intermediate

(PCT 4.1; 0.4)

(PAS 4.4; 0.5)

(C 4.9; 0.6)

(C 3.0; 0.43)

High

(Mean, SD)

NR

Internal use

(Control in plasma)

1% Aph

99% BC

BC

(Control in PAS)

(Control in PAS or plasma

Intermediate

(C 4.0; 0.67)

(PCT 2.9; 0.3)

**Intermediate** 

(PCT 3.9; 1.0)

(C 4.3; 1.2)

(C 3.1; 0.4)

(PCT 3.7; 0.51)

Low/intermediate

# Intercept PRT (cont.)

(SPRINT)

Rebulla 2017 (IPTAS)

van Rhenen 2003

(euroSPRITE)

(318/327)

(113/115)

228

103

(52/51)

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 (PCT 3.4; 0.8) (C 3.9; 1.0)

Paediatric + adult haemato-McCullough 2004 645 Aph

oncological

oncological

disease

Adult haemato-

oncological disease

Paediatric + adult haemato-

disease

# Mirasol PRT (5 trials)

(56/54)

(99/97)

196

469

330

(244/225)

(164/166)

Rebulla 2017 (IPTAS)

van der Meer 2018

(PREPAReS)

MIPLATE 2021

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	Adult haemato-	25% BC	Intermediate

oncological disease

oncological disease

Adult haemato-

Adult haemato-

oncological disease

oncological disease

Paediatric + adult haemato-

75% Aph

49% Aph

51% BC

BC

Aph

(Control in plasma)

(Control in PAS)

(Control in plasma)

(Control in plasma)

(PCT 5.2; 2.1)

(PCT 3.3; 0.7)

(PCT 3.3; 0.6)

(C 3.5; 0.8)

NR

(C 3.3; 0.6)

Low/intermediate

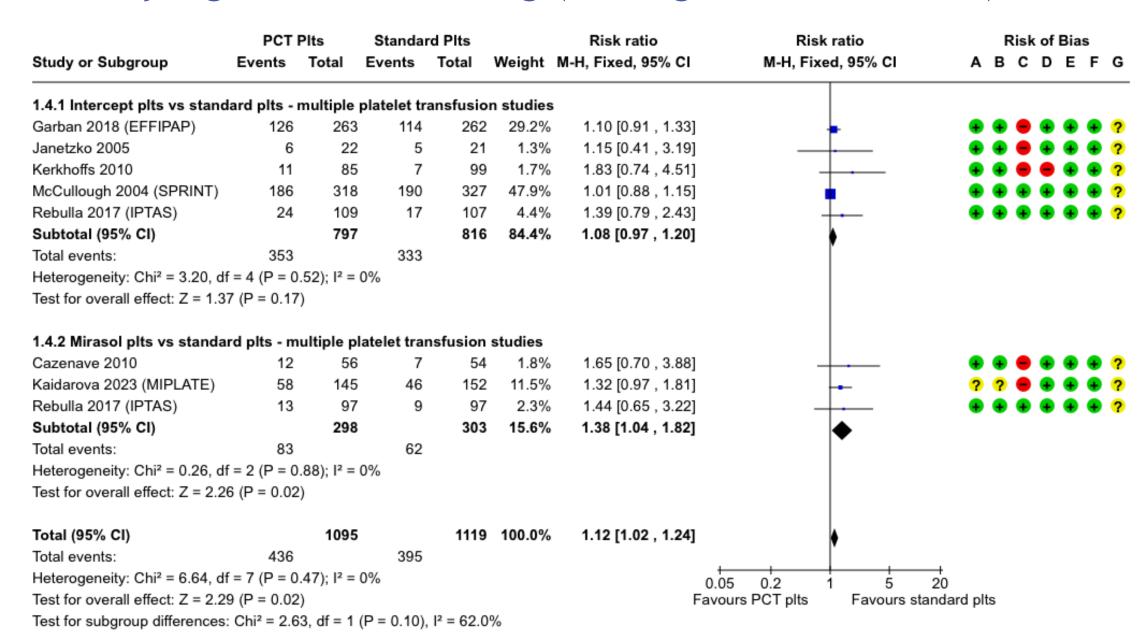
Low/intermediate

(C 5.2; 2.0)

# 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)

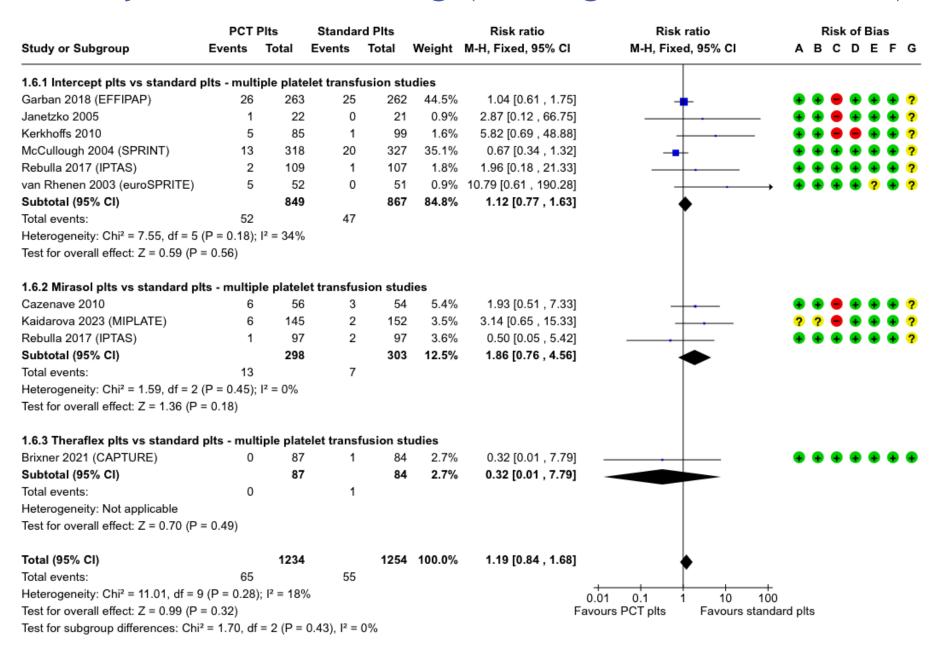
#### Clinically significant bleeding (WHO grade 2 or above)



	40					

	PCT	Plts	Standa	rd Plts		Risk ratio	Risk ratio	Risk of Bias
tudy or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI	ABCDEFG
.29.1 Intercept pits vs pits	in plasma	or unkn	own					
arban 2018 (EFFIPAP)	126	263	114	262	36.5%	1.10 [0.91 , 1.33]	-	● ● ● ● ● ?
anetzko 2005	6	22	5	21	1.6%	1.15 [0.41 , 3.19]		● ● ● ● ● ?
erkhoffs 2010	11	85	7	99	2.1%	1.83 [0.74 , 4.51]		● ● ● ● ● ?
cCullough 2004 (SPRINT)	186	318	190	327	59.8%	1.01 [0.88 , 1.15]	•	$\bullet$ $\bullet$ $\bullet$ $\bullet$ $\bullet$ $\bullet$ ?
ubtotal (95% CI)		688		709	100.0%	1.06 [0.95 , 1.18]	<b>T</b>	
otal events:	329		316				ſ	
eterogeneity: Chi <sup>2</sup> = 2.19, d	If = 3 (P = 0.	.53); I <sup>2</sup> =	0%					
est for overall effect: Z = 1.0	7 (P = 0.28	)						
.29.2 Mirasol plts vs plts i	n plasma							
azenave 2010	. 12	56	7	54	13.7%	1.65 [0.70 , 3.88]	<b></b>	● ● ● ● ● ?
aidarova 2023 (MIPLATE)	58	145					-	? ? • • • ?
ubtotal (95% CI)		201		206	100.0%	1.37 [1.02 , 1.84]	•	
otal events:	70		53				•	
eterogeneity: Chi² = 0.23, d	If = 1 (P = 0	.63); I <sup>2</sup> =	0%					
est for overall effect: Z = 2.0	08 (P = 0.04	)						
.29.3 Intercept vs platelets	s in PAS							
arban 2018 (EFFIPAP)	126	263	120	265	85.1%	1.06 [0.88 , 1.27]	•	● ● ● ● ● ?
erkhoffs 2010	11	85	4	94	2.7%	3.04 [1.01, 9.19]	Τ	● ● ● ● ● ?
ebulla 2017 (IPTAS)	24	109	17	107	12.2%	1.39 [0.79, 2.43]	<b></b>	$\bullet$ $\bullet$ $\bullet$ $\bullet$ $\bullet$ $\bullet$ ?
ubtotal (95% CI)		457	•	466	100.0%	1.15 [0.97 , 1.37]	•	
otal events:	161		141				ľ	
eterogeneity: Chi <sup>2</sup> = 4.21, d	f = 2 (P = 0)	.12); I <sup>2</sup> =	52%					
est for overall effect: Z = 1.5	59 (P = 0.11)	)						
.29.4 Mirasol vs platelets	in PAS							
ebulla 2017 (IPTAS)	13	97	9	97	100.0%	1.44 [0.65 , 3.22]	_	$\bullet$ $\bullet$ $\bullet$ $\bullet$ $\bullet$ $\bullet$ ?
ubtotal (95% CI)		97	•	97	100.0%	1.44 [0.65 , 3.22]	<u> </u>	
otal events:	13		9			- · · •		
eterogeneity: Not applicable	е							
est for overall effect: Z = 0.9		)						
oot for outgroup difference	. Chi2 = 2.2	0 df = 2	/D = 0.26\	12 = 6 20	,	+		<del>-</del>
est for subgroup differences	s: Cni* = 3.2	υ, ατ = 3	(P = 0.36)	, 1 = 6.29	ro .	0.0		20 ndard pits
est for overall effect: Z = 1.5  29.4 Mirasol vs platelets  bebulla 2017 (IPTAS)  ubtotal (95% CI)  otal events:  eterogeneity: Not applicable	in PAS 13 13 e 90 (P = 0.37)	97 <b>97</b>	9	97	100.0%	1.44 [0.65 , 3.22]	5 0.2 1 5 Favours sta	

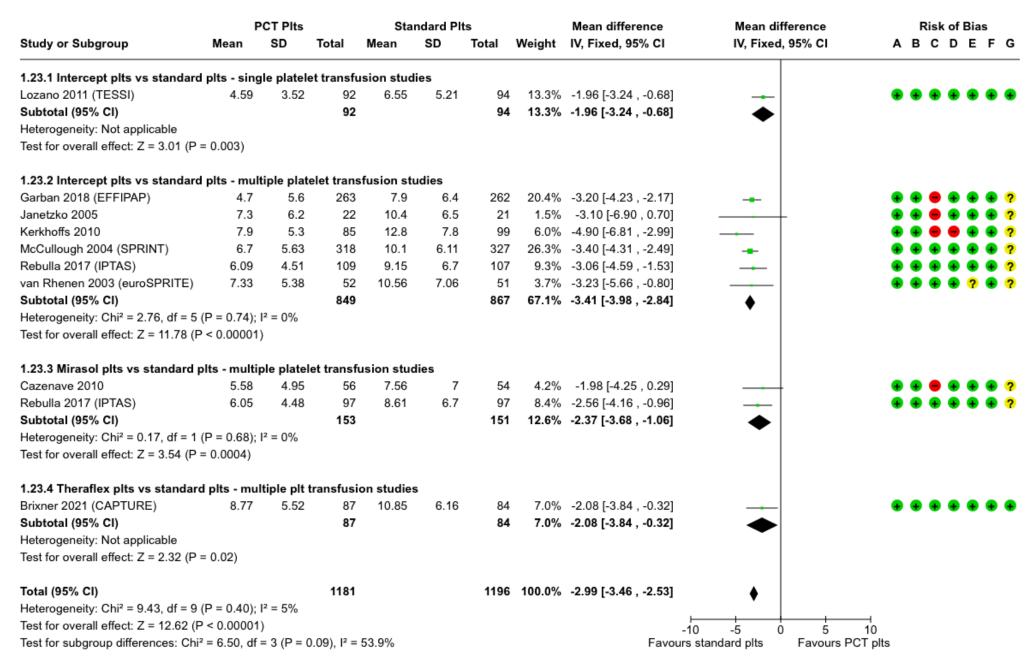
#### Clinically severe bleeding (WHO grade 3 or above)



### All-cause mortality

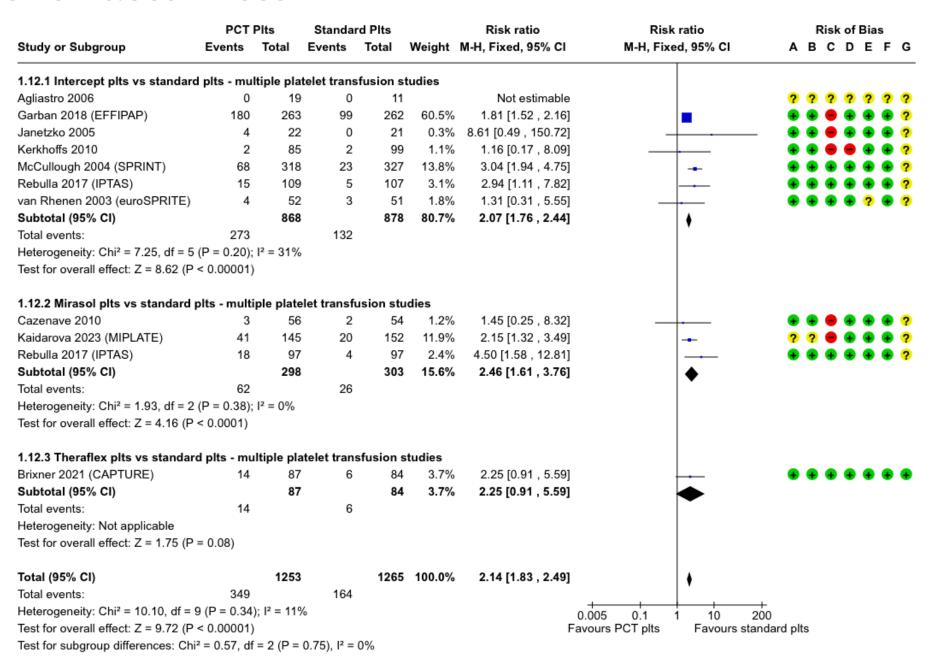
	PCT	Plts	Standa	rd Plts		Risk ratio	Risk ra	atio		Ris	sk of	Bias		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed	95% CI	A	в с	D	E	F	G
1.8.1 Intercept plts vs standard	plts - mult	iple plate	elet transf	usion stu	udies									
Janetzko 2005	0	22	0	21		Not estimable			• •	•	•	• (	• (	?
Kerkhoffs 2010	3	85	2	99	4.4%	1.75 [0.30 , 10.21]			• •	₽ €	•	• (	• (	?
McCullough 2004 (SPRINT)	11	318	17	327	39.5%	0.67 [0.32, 1.40]	-		•	<b>D</b> (	•	• (	• (	?
Rebulla 2017 (IPTAS)	5	113	12	115	28.0%	0.42 [0.15, 1.16]	_		•	<b>.</b>	•	• (	• (	?
van Rhenen 2003 (euroSPRITE)	2	52	4	51	9.5%	0.49 [0.09, 2.56]		_	•	<b>D</b> (	•	? (	• (	?
Subtotal (95% CI)		590		613	81.4%	0.62 [0.37 , 1.05]	•							
Total events:	21		35				•							
Heterogeneity: Chi <sup>2</sup> = 1.98, df = 3	(P = 0.58);	$I^2 = 0\%$												
Test for overall effect: Z = 1.78 (P	= 0.07)													
1.8.2 Mirasol plts vs standard p	lts - multip	ole platel	et transfu	sion stud	lies									
Cazenave 2010	3	56	1	54	2.4%	2.89 [0.31, 26.96]			• •	₽ €	•	• (	• (	?
Kaidarova 2023 (MIPLATE)	1	141	3	161	6.6%	0.38 [0.04, 3.62]		_	?	? •	•	• (	•	?
Rebulla 2017 (IPTAS)	6	99	2	97	4.8%	2.94 [0.61 , 14.21]			•	Ð	•	• (	•	?
Subtotal (95% CI)		296		312	13.8%	1.70 [0.62 , 4.70]								
Total events:	10		6											
Heterogeneity: Chi <sup>2</sup> = 2.38, df = 2	(P = 0.30);	I <sup>2</sup> = 16%												
Test for overall effect: Z = 1.03 (P	= 0.30)													
1.8.3 Theraflex plts vs standard	pits - mul	tiple plat	elet trans	fusion st	udies									
Brixner 2021 (CAPTURE)	. 2					0.97 [0.14, 6.70]			•	<b>D G</b>	•	• (	•	Ð
Subtotal (95% CI)		87		84	4.8%									
Total events:	2		2											
Heterogeneity: Not applicable														
Test for overall effect: Z = 0.04 (P	= 0.97)													
	,													
Total (95% CI)		973		1009	100.0%	0.79 [0.50 , 1.23]	•							
Total events:	33		43				1							
Heterogeneity: $Chi^2 = 7.17$ , $df = 7$	(P = 0.41);	$I^2 = 2\%$					0.01 0.1 1	10 10	00					
Test for overall effect: Z = 1.06 (P	= 0.29)					Fa	avours PCT plts	Favours sta	ndard plts					
Test for subgroup differences: Chi	$^{2}$ = 3.06, df	= 2 (P =	$0.22$ ), $I^2 =$	34.6%										

#### 24 hour corrected count increment



	ı	PCT Plts		Sta	ndard Pli	s		Mean differen	ice	Mean difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95%	CI	IV, Fixed, 95% CI	ABCDEFG
1.28.1 Intercept plts vs plts in pl	asma or u	nknown j	platelet s	uspensior	ı - multip	le platele	et transfu	ısion studies			
Garban 2018 (EFFIPAP)	4.7	5.6	263	7.9	6.4	262		-3.20 [-4.23 , -	2.17]	-	<b>• • • • • • ?</b>
Janetzko 2005	7.3	6.2	22	10.4	6.5	21	2.6%	-3.10 [-6.90,	0.70]		• • • • • · · ·
Kerkhoffs 2010	7.9	5.3	85	12.8	7.8	99	10.3%	-4.90 [-6.81 , -	2.99]		• • • • • ?
McCullough 2004 (SPRINT)	6.7	5.63	318	10.1	6.11	327	45.5%	-3.40 [-4.31 , -	2.49]	-	$\bullet$ $\bullet$ $\bullet$ $\bullet$ $\bullet$ ?
van Rhenen 2003 (euroSPRITE)	7.33	5.38	52	10.56	7.06	51	6.3%	-3.23 [-5.66 , -	0.80]		• • • ? • ?
Subtotal (95% CI)			740			760	100.0%	-3.47 [-4.08 , -2	2.85]	<b>♦</b>	
Heterogeneity: Chi <sup>2</sup> = 2.53, df = 4	(P = 0.64);	$I^2 = 0\%$								.	
Test for overall effect: Z = 11.11 (P	< 0.00001	)									
1.28.2 Mirasol plts vs plts in plas	sma - mult	tiple plate	elet trans	fusion stu	dies						
Cazenave 2010	5.58	4.95	56	7.56	7	54	100.0%	-1.98 [-4.25,	0.29]	_	<b>• • • • • • ?</b>
Subtotal (95% CI)			56			54	100.0%	-1.98 [-4.25 ,	0.29]	•	
Heterogeneity: Not applicable										•	
Test for overall effect: Z = 1.71 (P =	= 0.09)										
1.28.3 Intercept plts vs plts in PA	AS - single	platelet	transfusi	on studies	5						
Lozano 2011 (TESSI)	4.59	3.52	92	6.55	5.21	94	100.0%	-1.96 [-3.24 , -	0.68]	-	$\bullet \bullet \bullet \bullet \bullet \bullet$
Subtotal (95% CI)			92			94		-1.96 [-3.24 , -	_	<u>.</u>	
Heterogeneity: Not applicable								-	-	•	
Test for overall effect: Z = 3.01 (P =	= 0.003)										
1.28.4 Intercept platelets vs plate	elets in PA	\s									
Garban 2018 (EFFIPAP)	4.7	5.6	263	6.4	5.9	266	59.6%	-1.70 [-2.68 , -	0.72]	-	<b>• • • • • • ?</b>
Kerkhoffs 2010	7.9	5.3	85	11.6	7.6	94		-3.70 [-5.61 , -		<b>—</b>	<b>• • • • • • ?</b>
Rebulla 2017 (IPTAS)	6.09	4.51	109	9.15	6.7	107	24.6%	-3.06 [-4.59 , -	1.53]		$\bullet$ $\bullet$ $\bullet$ $\bullet$ $\bullet$ ?
Subtotal (95% CI)			457			467	100.0%	-2.35 [-3.11 , -	1.59]	•	
Heterogeneity: Chi <sup>2</sup> = 4.45, df = 2	(P = 0.11);	I <sup>2</sup> = 55%								•	
Test for overall effect: Z = 6.09 (P	< 0.00001)										
1.28.5 Mirasol plts vs platelets in	n PAS										
Rebulla 2017 (IPTAS)	6.05	4.48	97	8.61	6.7	97	100.0%	-2.56 [-4.16 , -	0.96]	-	$\bullet$ $\bullet$ $\bullet$ $\bullet$ $\bullet$ ?
Subtotal (95% CI)			97			97		-2.56 [-4.16 , -		•	
Heterogeneity: Not applicable										•	
Test for overall effect: Z = 3.13 (P =	= 0.002)										
1.28.6 Theraflex plts vs plts in P	AS										
Brixner 2021 (CAPTURE)	8.77	5.52	87	10.85	6.16	84	100.0%	-2.08 [-3.84 , -	0.321		
Subtotal (95% CI)			87					-2.08 [-3.84 , -		_	
Heterogeneity: Not applicable								•	-	•	
Test for overall effect: Z = 2.32 (P =	= 0.02)										
Test for subgroup differences: Chi <sup>2</sup>	e = 8.81, df	= 5 (P = 0	).12), I <sup>2</sup> =	43.2%					1		10
									Favours	standard plts Favours	PCT pits

#### Platelet refractoriness



#### Platelet refractoriness and alloimmunisation

	PCT	Plts	Standa	d Plts		Risk ratio	Risk ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI	ABCDEFG
1.13.1 Intercept pits vs standard	d plts - mu	ltiple pla	telet trans	fusion st	udies			
Agliastro 2006	0	19	0	11		Not estimable		? ? ? ? ? ? ?
Garban 2018 (EFFIPAP)	3	263	2	262	9.0%	1.49 [0.25, 8.87]		● ● ● ● ● ?
Janetzko 2005	1	22	0	21	2.3%	2.87 [0.12, 66.75]		. • • • • • • ?
Kerkhoffs 2010	2	85	2	99	8.3%	1.16 [0.17, 8.09]		● ● ● ● ● ?
McCullough 2004 (SPRINT)	15	318	10	327	44.1%	1.54 [0.70, 3.38]		$\bullet$ $\bullet$ $\bullet$ $\bullet$ $\bullet$ $\bullet$ ?
van Rhenen 2003 (euroSPRITE)	3	52	2	51	9.0%	1.47 [0.26 , 8.44]		• • • • ? • ?
Subtotal (95% CI)		759		771	72.6%		•	
Total events:	24		16				_	
Heterogeneity: Chi <sup>2</sup> = 0.23, df = 4	(P = 0.99);	$I^2 = 0\%$						
Test for overall effect: Z = 1.35 (P								
1.13.2 Mirasol plts vs standard	plts-multip	le platele	et transfus	ion stud	ies			
Kaidarova 2023 (MIPLATE)	1	136		141		1.04 [0.07 , 16.41]		? ? \varTheta 🗣 🗣 🗣
van der Meer 2018 (PREPAReS)	6	209	4	197	18.4%			
Subtotal (95% CI)		345		338	22.8%			
Total events:	7		5					
Heterogeneity: Chi <sup>2</sup> = 0.04, df = 1	(P = 0.84);	$I^2 = 0\%$						
Test for overall effect: Z = 0.51 (P								
1.13.3 Theraflex plts vs standard	d plts - mu	ltiple pla	telet trans	fusion s	tudies			
Brixner 2021 (CAPTURE)	2	87		84		1.93 [0.18 , 20.90]		
Subtotal (95% CI)		87	,	84	4.6%			
Total events:	2		1					
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.54 (P	= 0.59)							
,	,							
Total (95% CI)		1191		1193	100.0%	1.50 [0.89 , 2.54]	•	
Total events:	33		22			•	•	
Heterogeneity: Chi <sup>2</sup> = 0.35, df = 7	(P = 1.00);	I <sup>2</sup> = 0%				(	0.01 0.1 1 10	→ 100
Test for overall effect: Z = 1.51 (P							vours PCT plts Favours sta	
Test for subgroup differences: Chi		= 2 (P =	0.96), I <sup>2</sup> =	0%			•	-

# 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

	PCT Pits			Standard Plts		Mean difference		Mean difference	Risk o	Risk of Bias		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95%	CI	IV, Fixed, 95% CI	ABCI	DEF
1.24.1 Intercept plts vs standard	l pits - mul	tiple plat	elet trans	sfusion st	udies							
Garban 2018 (EFFIPAP)	6.9	5.5	263	5.4	4.2	262	13.5%	1.50 [0.66 , 2	2.34]		?	(
Janetzko 2005	4.7	3.3	22	5.5	4.7	21	1.6%	-0.80 [-3.24 , 1	.64]		● ● ●	• • •
Kerkhoffs 2010	5	2	85	4	2	99	28.2%	1.00 [0.42 , 1	.58]	-	● ● ●	• • (
McCullough 2004 (SPRINT)	8.4	8.6	318	6.2	7	327	6.4%	2.20 [0.99, 3	3.41]		$\bullet \bullet \bullet \bullet$	
Rebulla 2017 (IPTAS)	5.9	5.8	115	3.8	3.4	113	6.2%	2.10 [0.87, 3	3.33]		$\bullet \bullet \bullet \bullet$	
van Rhenen 2003 (euroSPRITE)	7.5	5.8	52	5.6	5.5	51	2.0%	1.90 [-0.28 , 4	.08]		$\bullet \bullet \bullet \bullet$	? \varTheta 🤅
Subtotal (95% CI)			855			873	58.0%	1.35 [0.95 , 1	.75]	•		
Heterogeneity: Chi <sup>2</sup> = 8.07, df = 5	(P = 0.15);	I <sup>2</sup> = 38%								•		
Test for overall effect: Z = 6.55 (P	< 0.00001)											
1.24.2 Mirasol plts vs standard բ	plts - multi	ple platel	let transf	usion stud	dies							
Cazenave 2010	5.4	3.4	56	4.4	0.19	54	11.9%	1.00 [0.11 , 1	.89]		● ● ●	
Rebulla 2017 (IPTAS)	4.6	4.4	99	3.4	2.1	97	10.2%	1.20 [0.24, 2	2.16]		$\bullet \bullet \bullet \bullet$	
Subtotal (95% CI)			155			151	22.1%	1.09 [0.44 , 1	.75]	•		
Heterogeneity: Chi <sup>2</sup> = 0.09, df = 1	(P = 0.77);	$I^2 = 0\%$								•		
Test for overall effect: Z = 3.27 (P	= 0.001)											
1.24.3 Theraflex plts vs standard	d plts - mu	ltiple trar	nsfusion	studies								
Brixner 2021 (CAPTURE)	3.68	2.38	87	2.95	2.22	84	19.9%	0.73 [0.04, 1	.42]	-	$\bullet \bullet \bullet \bullet$	
Subtotal (95% CI)			87			84	19.9%	0.73 [0.04, 1	.42]	•		
Heterogeneity: Not applicable										•		
Test for overall effect: Z = 2.07 (P	= 0.04)											
Total (95% CI)			1097			1108	100.0%	1.17 [0.86 , 1	.48]	•		
Heterogeneity: Chi <sup>2</sup> = 10.54, df = 8	8 (P = 0.23)	; I <sup>2</sup> = 24%	0						_	•		
Test for overall effect: Z = 7.45 (P	< 0.00001)								_	-4 -2 0 2 4	_	
Test for subgroup differences: Chi			0.30), I <sup>2</sup> =	15.9%					Favoi	urs PCT plts Favours sta	andard plts	

	F	PCT PIts		Standard Plts				Mean difference	Mean difference	Risk of Bias	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI	ABCDEFG	
1.27.1 Intercept plts vs plts in pl	lasma or u	nknown :	suspensi	on mediu	m						
Garban 2018 (EFFIPAP)	6.9	5.5	263	5.4	4.2	262	26.1%	1.50 [0.66, 2.34]		● ● ● ● ● ?	
Janetzko 2005	4.7	3.3	22	5.5	4.7	21	3.1%	-0.80 [-3.24 , 1.64]		<b>• • • • • • ?</b>	
Kerkhoffs 2010	5	2	85	4	2	99	54.5%	1.00 [0.42 , 1.58]	-	● ● ● ● ● ?	
McCullough 2004 (SPRINT)	8.4	8.6	318	6.2	7	327	12.5%	2.20 [0.99, 3.41]		$\bullet$ $\bullet$ $\bullet$ $\bullet$ $\bullet$ $\bullet$ ?	
van Rhenen 2003 (euroSPRITE)	7.5	5.8	52	5.6	5.5	51	3.8%	1.90 [-0.28 , 4.08]	<del>                                     </del>	⊕ ⊕ • • • • • • • • • • • • • • • •	
Subtotal (95% CI)			740			760	100.0%	1.26 [0.83 , 1.69]	•		
Heterogeneity: Chi <sup>2</sup> = 6.47, df = 4	(P = 0.17);	$I^2 = 38\%$							•		
Test for overall effect: Z = 5.77 (P	< 0.00001)										
1.27.2 Mirasol plts vs plts in pla	asma										
Cazenave 2010	5.4	3.4	56	4.4	0.19	54	100.0%	1.00 [0.11 , 1.89]	- <mark></mark> -	<b>. . . . . . . . .</b>	
Subtotal (95% CI)			56			54	100.0%	1.00 [0.11 , 1.89]	•		
Heterogeneity: Not applicable											
Test for overall effect: Z = 2.20 (P	= 0.03)										
1.27.3 Intercept platelets vs plat	elets in PA	s									
Garban 2018 (EFFIPAP)	6.9	5.5	263	6.6	5.5	266	36.8%	0.30 [-0.64 , 1.24]	<b>-</b>	<b>. . . . . . . . .</b>	
Kerkhoffs 2010	5	3	85	4	3	94	41.8%	1.00 [0.12 , 1.88]	-	<b>• • • • • • ?</b>	
Rebulla 2017 (IPTAS)	5.9	5.8	115	3.8	3.4	113	21.3%	2.10 [0.87 , 3.33]		$\bullet$ $\bullet$ $\bullet$ $\bullet$ $\bullet$ $\bullet$ ?	
Subtotal (95% CI)			463			473	100.0%	0.98 [0.41 , 1.55]	•		
Heterogeneity: $Chi^2 = 5.20$ , $df = 2$	(P = 0.07);	$I^2 = 62\%$									
Test for overall effect: Z = 3.36 (P	= 0.0008)										
1.27.4 Mirasol plts vs platelets i	n PAS										
Rebulla 2017 (IPTAS)	4.6	4.4	99	3.4	2.1	97	100.0%	1.20 [0.24 , 2.16]	- <del>  -</del>	$\bullet$ $\bullet$ $\bullet$ $\bullet$ $\bullet$ ?	
Subtotal (95% CI)			99			97	100.0%	1.20 [0.24 , 2.16]	•		
Heterogeneity: Not applicable											
Test for overall effect: Z = 2.44 (P	= 0.01)										
1.27.5 Theraflex plts vs plts in P	AS										
Brixner 2021 (CAPTURE)	3.68	2.38	87	2.95	2.22	84	100.0%	0.73 [0.04 , 1.42]		$\bullet \bullet \bullet \bullet \bullet \bullet \bullet$	
Subtotal (95% CI)			87			84	100.0%	0.73 [0.04 , 1.42]	•		
Heterogeneity: Not applicable											
Test for overall effect: Z = 2.07 (P	= 0.04)										
Test for subgroup differences: Chi	<sup>2</sup> = 1.88, df	= 4 (P = 0	0.76), I <sup>2</sup> =	0%					-4 -2 0 2 4	-	
								Fav	ours PCT plts Favours star	ndard plts	

#### 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

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Trusted evidence. Informed decisions. Better health.