Appendix A. Tables.

Supplementary Table S1. Quality assessment of the systematic review (Estcourt et al [21]) addressing prophylactic platelet transfusion, platelet dose and platelet transfusion triggers

Reviewers	NS, ST
A priori design?	Yes
Duplicate study selection?	Yes, Two independent review authors screened all citations, full text of potentially relevant trials assessed by two independent review authors and two review authors conducted data extraction
Comprehensive literature search?	Yes
Status of publication disclosed?	Yes
Included grey literature?	Yes
List of included/excluded studies provided?	Yes
Characteristics of studies provided?	Yes
Quality of studies assessed and documented?	Yes
Scientific quality used appropriately?	Yes
Appropriate method for combining studies?	Yes
Publication bias assessed?	No
Conflict of interest stated?	Yes, with declarations of interest (none declared) and sources of support at end of manuscript
Outcomes assessed?	Yes
Population included?	Yes

Supplementary Table S2. Outcomes of the systematic review

First author, year	Study design included	Number of studies/ Randomized patients/ Analyzed patients	Mortality·	Bleeding	Refractoriness	Utilization
Estcourt L, 2012 [21]	Transfusion triggers					
	RCTs N=2 compared 10 vs 20 x 10^9/L, N=1 compared 10 vs 30 x 10^9/L	3/520/499	Comparisons are for higher vs lower triggers: All cause mortality RR = 1.17; 95% CI, 0.85–1.60 Mortality from bleeding RR = 2.67, 95% CI, 0.11–64.91	Comparisons are for higher vs lower triggers: Patients with significant bleeding RR = 1.35; 95% CI, 0.95–1.90 Patients with WHO Grade 3 or 4 RR = 0.99; 95% CI, 0.52–1.88 Number of days with bleeding RR = 1.27; 95% CI, 1.10–1.46 Number of days with significant bleeding RR = 1.72; 95% CI, 1.33–2.22	RR = 0.66; 95% CI, 0.16–2.67	Comparisons are for higher vs lower triggers: Mean number of platelet transfusion RR = -2.09; 95% CI, -3.20– -0.99 Mean number of red cell transfusion RR = 0.66; 95% CI, -0.43–1.76
	Platelet dose					
	RCTs	6/1808/1714	All cause mortality: Low dose vs standard dose RR = 2.04; 95% CI, 0.70–5.93, High dose vs standard dose RR = 1.71; 95% CI, 0.51–5.81 Mortality from bleeding: Low dose vs standard dose RR = 0.0; 95% CI, 0.0–0.0, High dose vs standard dose RR = 1.47; 95% CI, 0.06–35.90	Number with bleeding events: Low dose vs standard events RR = 1.04; 95% CI, 0.95–1.13, High dose vs standard dose RR = 1.02; 95% CI, 0.93–1.11 WHO grade 3 or 4 bleeding: Low dose vs standard dose RR = 1.33; 95% CI, 0.91–1.92, High dose vs standard dose RR = 1.11; 95% CI, 0.73–1.68		

				Number of days with significant bleeding: Low dose vs standard dose RR = 1.16; 95% CI, 0.91–1.47, High dose vs standard dose RR = 1.13; 95% CI, 0.26–4.95		
	Prophylactic vs no prophylaxis					
	RCTs No prophylaxis vs < 20 x 10^9/L	3/99/97	Mortality RR = 0.97; 95% CI, 0.48–1.93 Mortality from bleeding RR = 1.08; 95% CI, 0.23–5.06	Number with bleeding events RR = 1.66; 95% CI, 0.90–3.04 Number of days with significant bleeding RR = 0.90; 95% CI, 0.62–1.32	RR = 0.33; 95% CI, 0.04–2.66	Mean number of platelet transfusion RR = -15.80; 95% CI, -19.20– -12.40 Mean number of red cell transfusion RR = 0.60; 95% CI, -0.14–1.34

Abbreviations: RCTs, randomized controlled trials; RR, relative risk; 95% CI, 95% confidence interval

Supplementary Table S3. Quality assessment for risk of bias of the randomized controlled trials addressing prophylactic vs no-prophylactic platelet transfusion

First author, year	Adequate sequence generation?	Adequate allocation concealment?	Blinding method described?	Adequate blinding?	Intention to treat analysis performed?	Outcome data complete?	Incomplete outcome data addressed?	Selective reporting of outcomes?	Adequate follow-up?	Proportion lost to follow-up accounted?
Wandt H, 2012 [29]	Yes	Yes	No	No	Yes	Yes	NR	No	Yes	No
Stanworth SJ, 2013 [30]	Yes	Yes	No	No	Yes	Yes	NR	No	Yes	No

Abbreviation: NR, not reported

Supplementary Table S4. Assessment of the risk of bias for the randomized controlled trials addressing prophylactic vs no-prophylactic platelet transfusion

Bias	Wandt H, 2012 [29]	Stanworth SJ, 2013 [30]
Random sequence generation	Low risk of bias, computer generated randomization sequence	Low risk of bias, centralized computer generated sequence
Allocation concealment	Low risk of bias, computer generated randomization sequence	Low risk of bias, centralized computer generated sequence
Blinding Assessor of platelet counts and bleeding	Low risk of bias, blinded outcome assessment	Low risk of bias, bleeding assessment made by 2 assessors blinded to treatment
Blinding Physician/Medical Staff	High risk of bias, unblinded to physicians/medical staff and patients	High risk of bias, Unblended
Incomplete outcome data	Unclear risk of bias, 7 patients not included in the final analysis, but the number missing bleeding data not described	Low risk of bias, complete bleeding data recorded [median 30 days (interquartile range, 29 to 30) no prophylaxis arm, median 30 days (interquartile range, 30 to 30) prophylaxis arm]
Selective reporting	Low risk of bias	Low risk of bias

Supplementary Table S5. Characteristics and outcomes of the randomized controlled trials for prophylactic vs no-prophylactic platelet transfusion

First author, year	Country	Center status	Population	Treatment	Sample size	Hemorrhage	Platelet utilization	Red cell utilization
Wandt H, 2012 [29]	Germany	Multi-center	AML (16–80 years); SCT (16–68 years)			WHO grade ≥ 2/3/4	Mean platelet transfusion/patient	Mean red cell transfusion/patient
				Prophylactic strategy (≤ 10 x 10^9/L)	197	19%/1%/1%	2.4 (95% CI, 2.2-2.7)	2.8 (95% CI, 2.6-3.1)
				Therapeutic strategy	199	42%/2%/5%, *P* = < 0.001/0.21/0.02	1.63 (95% CI, 1.4-1.8) 33.5% reduction (95% CI, 22.2-43.1) Primary outcome	3.14 (95% CI, 2.8-3.4)
Stanworth SJ, 2013 [30]	United Kingdom and Australia	Multi-center	Patients with hematological malignancy receiving chemotherapy or SCT	Prophylactic strategy (≤ 10 x $10^{9/L}$)	299	WHO grade ≥ 2 43%; WHO grade 3 or 4 <1%	3.0(SD3.2)	NR
				Therapeutic strategy	300 (70% SCT)	WHO Grade ≥ 2 50%, *P* = 0.06 not significant for non-inferiority (Primary outcome); WHO grade 3 or 4 2%, *P* = 0.13	1.7(SD2.6)	

Abbreviations: AML, acute myeloid leukemia; CI, confidence interval; NR, not reported; SD, standard deviation; SCT, stem cell transplant

Supplementary Table S6. GRADE evidence profile: prophylactic versus no-prophylactic platelet transfusion

Quality assessment						Number of patients		Quality	Importance
Number of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Prophylactic platelet transfusion	No-prophylactic platelet transfusion		
WHO grade ≥ 2 bleeding									
2	RCT	serious[1]	not serious	not serious	not serious	188/498 (37.8%)	212/498 (42.6%)	MODERATE	CRITICAL
Platelet utilization									
2	RCT	serious[1]	not serious	not serious	not serious	460/989 (46.5%)	373/989 (37.7%)	MODERATE	IMPORTANT
Red Cell utilization									
1	RCT	serious[1]	not serious	not serious	not serious	194/391 (49.6%)	197/391 (50.4%)	MODERATE	IMPORTANT

Abbreviations: GRADE, Grades of Recommendation, Assessment, Development and Evaluation; RCT, randomized controlled trial

[1] High risk of bias, unblinded

Supplementary Table S7. Quality assessment of the systematic review for ABO-identical platelet transfusion

First author, Year	Shehata N, 2009 [22]
A priori design?	Yes
Duplicate study selection?	Yes
Comprehensive literature search?	Yes
Status of publication disclosed?	Yes
Included grey literature?	No
List of included/excluded studies provided?	No
Characteristics of studies provided?	Yes
Quality of studies assessed and documented?	Yes
Scientific quality used appropriately?	Yes
Appropriate method for combining studies?	Yes
Publication bias assessed?	No
Conflict of interest stated?	Yes
Outcomes assessed?	Yes
Population included?	Yes

Supplementary Table S8. Outcomes of the systematic review of ABO-identical platelet transfusion

First author, year	Study design included	Number of studies/ Abstracts	Mortality/ Survival	Bleeding	Transfusion Reactions*	Refractoriness	Utilization	Platelet increment
Shehata N, 2009 [22]	RCT	3	N = 1: reported survival associated with ABO-identical vs non-identical, 25 months vs 13 months, *P* = 0.02 N = 2: survival NR	N = 1: bleeding in two of 26 patients requiring transfusion support N = 2: NR	N = 1: reported no transfusion reaction N = 2: NR	N = 2: refractoriness reduced by 39% and 61% with ABO-identical platelet transfusion N = 1: NR	N = 1: reduction in platelet transfusion with ABO-identical platelet transfusion N = 2: NR	N = 2: significant increase in CCI associated with ABO-identical platelet transfusion vs non-identical N = 1: not significantly different between ABO-identical vs ABO-incompatible
	Prospective study	5	N = 5: mortality NR	N = 5: NR	N = 1: detectable hemolytic transfusion reaction N = 1: no reaction to ABO grouping N = 3: NR	N = 5: NR	N = 5: NR	N = 1: difference not significant between ABO-identical and ABO non-identical transfusions N = 1: significant difference between ABO-identical and ABO-compatible transfusions N = 1: no significant difference between ABO-compatible and ABO-incompatible transfusions N = 1: lower platelet recovery with ABO-incompatible transfusions

								N = 1: lower CCI with ABO-mismatched transfusions
	Retrospective study	11	N = 1: no difference in mortality between LR ABO-identical vs non LR ABO-mismatched transfusion N = 1: no difference in mortality (survival) between ABO-identical vs ABO-unmatched transfusion N = 9: NR	N = 1: no difference in number of days with hemorrhage between LR ABO-identical vs non LR ABO non-identical transfusions N = 10: NR	N = 1: significant difference between ABO-identical vs ABO-compatible transfusions N = 1: no difference between ABO-identical vs ABO-compatible transfusions N = 1: fewer in LR ABO-identical vs non LR ABO non-identical transfusions N = 1: no difference between ABO-compatible vs ABO-incompatible N = 1: no difference between ABO-identical vs ABO-	N = 1: difference not significant N = 9: NR N = 1: not an endpoint	N = 1: fewer transfusions associated with LR ABO-identical vs non LR ABO-unmatched (74 vs 151, *P* = 0.003) N = 1: difference not significant between ABO-identical vs ABO-compatible (16.3 vs15.1) N = 1: difference not significant between ABO-identical vs ABO-unmatched (125 vs 137) N = 8: NR	N = 4: significantly higher with ABO-identical/compatible vs non ABO-identical transfusions N = 2: significant increase with ABO-compatible vs ABO-incompatible transfusions N = 1: increase with ABO-compatible vs ABO-incompatible, not significant N = 1: increase not demonstrated with ABO-identical vs ABO non-identical transfusions N = 3: NR

					unmatched vs LR ABO-identical vs washed LR ABO-identical N = 6: NR			

Abbreviations: CCI = corrected count increment; LR = leucoreduced; N = number of studies; NR = not reported; RCT = randomized controlled trial
*Leucoreduced products were not used.

Supplementary Table S9. Quality assessment of additional non randomized studies for ABO-identical platelet transfusion

First author, year	Source of sample appropriate?	Sampling method appropriate?	Sample size pre-determined?	Eligibility criteria clearly defined?	Control group acceptable?	Comparable characteristics?	Clear definitions of outcomes?	Blinded outcome assessment?	Quality control* measures instituted?	Proportion of missing data assessed?	Confound-ing factors analyzed?
Triulzi DJ, 2012 [50]	Yes	Yes	No	Yes	NA	NA	Yes	No	NA	0.1% for bleeding, 15% for 4-hour increment, 11% for 24-hour increment†	Only for bleeding outcomes
Marktel S, 2010 [49]	NS	NS	No	No	NA	NA	Yes	No	NA	No	No

Abbreviations: NA, not applicable; NS, not stated

* Quality control measures for the collection of data and laboratory tests: accuracy and repeatability of observers, calibration and random calibration and accuracy of instruments, checks for errors in data recording

† 4-h and 24-h increment missing data also included platelets of a mixed storage duration

Supplementary Table S10. Outcomes of additional non randomized studies for ABO-identical platelet transfusion

First author, year	Country	Center Status	Population	Treatment	Sample Size	Hemorrhage	Platelet increment	Duration of Follow up
Triulzi DJ, 2012 [50]	United States	Multi-center	HT (median age 48.6 years)	ABO-identical ABO major mismatch ABO minor mismatch	467 198 75 (patients)	36% 24% 24% Time to WHO grade ≥ 2 bleeding ABO-identical vs minor mismatch HR = 0.85; 95% CI, 0.52–1.40 ABO-identical vs major mismatch HR = 0.78; 95% CI, 0.56–1.09	4-hour increment ~25,000/µl N = 2451 platelet transfusion ~23,000/µl N = 1111 platelet transfusion *P* = 0.0001 vs ABO-identical ~24,000/µl N = 431 platelet transfusion *P* = 0.40 vs ABO-identical ABO major mismatch associated with 2635/µl lower 24-hour increment vs ABO-identical platelet transfusions (*P* < 0.0001)	30 days after the first platelet transfusion, after a 10-day period without a platelet transfusion, at hospital discharge, at death, or at withdrawal
Marktel S, 2010 [49]	Italy	Single-center	β thalassemia undergoing HSCT (pediatric)	IR, LR, SDP HLA-matched vs non HLA-matched RDP	50	Not analyzed by ABO group	Increment median (range) ABO-compatible	NS

							41,000/µl (0–230,000/µl) vs ABO-incompatible 24,500/µl (0–170,000/µl), CCI > 4.5 n transfusion (%) ABO-compatible 43/59 (73%) vs ABO-incompatible 14/25 (56%), (*P* = 0.20)	

Abbreviations: CCI, corrected count increment; CI, confidence interval; HR, hazard ratio; HSCT, hematopoietic stem cell transplantation; IR, irradiated; LR, leucoreduced; NS, not stated; RDP, random-donor platelets; SDP, single-donor platelets

Supplementary Table S11. GRADE evidence profile: ABO-identical versus ABO non-identical platelet transfusion

Quality assessment						Number of patients		Effects	Quality	Importance
Number of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	ABO-identical	ABO non-identical			
Mortality (Survival rate)										
1	RCT	serious[1,2]	not serious	not serious	serious[3]	19 (in 25 months)	21 (in 13 months)	--	LOW	CRITICAL
Mortality (Survival rate)										
2	Observational study	serious[4,5]	serious[6,7]	not serious	serious[3]	10/29[8]	4/ 25[8]	--	VERY LOW	CRITICAL
Bleeding										
1	RCT	very serious[1,9,10]	serious[6]	not serious	serious[3]	--	--	--	VERY LOW	CRITICAL
WHO grade $\geq$ 2 bleeding										
1	Observational study	serious[4,11]	not serious	not serious	serious[12]	168/740	65/740	Time to WHO grade $\geq$ 2 bleeding ABO-identical vs minor mismatch HR = 0.85; 95% CI, 0.52–1.40, ABO-identical vs major mismatch HR = 0.78; 95% CI, 0.56–1.09	VERY LOW	CRITICAL
Refractoriness										
2	RCT	very serious[1,2,9,10]	serious[6]	not serious	serious[3]	8/32	25/34	--	VERY LOW	IMPORTANT
Platelet increment[13]										
3	RCT	serious[1,2]	not serious	not serious	serious[3]	32/66[14]	34/66[14]	--	LOW	IMPORTANT
Platelet increment[13]										
18	Observational study	serious[4,11]	serious[6]	serious[6]	serious[3]	588/932[15]	344/932[15]	--	LOW	IMPORTANT

Platelet utilization										
1	RCT	serious[1,16]	serious[16]	not serious	serious[3]	19/40	21/40	--	LOW	IMPORTANT
Platelet utilization										
3	Observational study	serious[6,17]	very serious[6, 17]	very serious[6,17]	serious[3]	--	--	--	VERY LOW	IMPORTANT

Abbreviations: GRADE, Grades of Recommendation, Assessment, Development and Evaluation; RCT, randomized controlled trial

[1] Not blinded

[2] Incomplete outcome assessment due to loss of follow-up

[3] Small sample size; not adequately powered

[4] Sample size not pre-determined

[5] Eligibility criteria not defined

[6] Heterogeneous populations of acute leukemia patients and transplant recipients

[7] Heterogeneous outcomes since measurement of survival rate as outcome not clearly defined in the two studies

[8] Patients surviving at last follow up and death during induction therapy (eg, mean survival months); in the other study survival rate after three years classified as no difference

[9] Groups not comparable with more females in ABO-identical platelet transfusion group

[10] Allocation not concealed

[11] Outcome measurement not blinded

[12] Number of censored observations reduced statistical power for ABO variable for statistical analysis

[13] Refers to higher value in ABO-identical vs ABO non-identical platelet transfusion group

[14] From the 2 RCTs that have indicated sample sizes of ABO-identical group versus ABO non-identical group

[15] From 4 Observational studies that have indicated sample sizes of ABO-identical group versus ABO non-identical group

[16] ABO-identical platelets not always provided, reduced platelet dose or closest ABO-matched as alternatives; transfusions given at different stages of their clinical course eg, first treatment course, readmission, or subsequent relapse

[17] Platelet products used as comparator different: leucoreduced vs non-leucoreduced in one study, others not indicated; one study used ABO-identical vs ABO-compatible, one study used ABO-identical vs -unmatched platelets

Supplementary Table S12. Quality of non randomized studies for the need of Rh prophylaxis with RhD-positive platelet transfusion

First author, year	Source of sample appropriate?	Sampling method appropriate?	Sample size pre-determined?	Eligibility criteria clearly defined?	Control group acceptable?	Comparable characteristics?	Clear definitions of outcomes?	Blinded outcome assessment?	Quality control† measures instituted?	Proportion of missing data assessed?	Confound-ing factors analyzed?
Prospective											
Cid J, 2003 [60]	Yes	Yes	No	Yes	NA	NA	No	No	NS	NS	No
Retrospective											
Bartley AN, 2009 [61]	Yes	Yes	No	Yes	NA	NA	No	No	NS	NS	No
Molnar R, 2002 [62]	Yes	Yes	No	Yes	NA	NA	No	No	NS	NS	No
Atoyebi W, 2000 [63]	Yes	Yes	No	Yes	NA	NA	No	No	NS	NS	No
McLeod BC, 1990 [64]	Yes	Yes	No	Yes	NA	NA	No	No	NS	NS	No
Lichtiger B, 1983 [65]	Yes	Yes	No	Yes	NA	NA	No	No	NS	NS	No
Goldfinger D, 1971 [66]	NS	NS	NS	No	NA	NA	No	No	NS	NS	No

Abbreviations: NA, not applicable; NS, not stated

† Quality control measures for the collection of data and laboratory tests: accuracy and repeatability of observers, calibration and random calibration and accuracy of instruments, checks for errors in data recording

Supplementary Table S13. Characteristics and outcomes of non randomized studies for the need of Rh prophylaxis with RhD-positive platelet transfusion

First author, year	Country	Center status	Population	Treatment	Sample size	Mortality	Hemorrhage	Allo-immunization	Platelet utilization	Platelet count increment	Duration of follow up
Prospective											
Cid J, 2003 [60]	Spain	Single-center	Adult HT	BC- RDP, RhD+ No RhIg	32	NS	NS	0	NS	NS	Median 8, 16 weeks
Retrospective											
Bartley AN, 2009 [61]	United States	Single-center	Hematological disorders and malignancy	most LR SDP, RhD+	31	NS	NS	0	NS	NS	NS
Molnar R, 2002 [62]	United States	Single-center	Pediatric HT, osteopetrosis (n = 1),	SDP, LR, RhD+ no RhIg	35 non transplant D-, 7 transplant D- → D+ or D+ → D-	NS	NS	0	NS	NS	Follow up serology: mean, 87 days (range 14–1559) and 67 days (range 13–328) for transplant
Atoyebi W, 2000 [63]	United Kingdom	Single-center	Adult and pediatric HT	RDP/SDP, RhD+, no RhIg	24	NS	NS	0	NS	NS	NS
McLeod BC, 1990 [64]	United States	Single-center	Adult and pediatric autologous BMT	RDP/SDP, RhD+, no RhIG	16	NS	NS	N = 3 (19%) (n = 2 were previously pregnant)	NS	NS	Mean interval to the last antibody negative screen, 129–382 days
Lichtiger B, 1983 [65]	United States	Single-center	Adult and pediatric HT	RDP/SDP RhD+	30	NS	NS	0	NS	NS	Mean 14.6 weeks
Goldfinger D, 1971 [66]	United States	Single-center	Adult and pediatric HT (ITP, n = 1; WAS, n = 3)	RDP	102	NS	NS	8 (8%)	NS	NS	2–325 weeks

Abbreviations: BC, Buffy Coat method; BMT, bone marrow transplantation; HT, hypoproliferative thrombocytopenia; ITP, immune thrombocytopenia; LR, leucoreduced; NS, not stated; RDP, pooled random-donor platelets; RhIg, Rh immunoglobulin; SDP, single-donor platelet transfusion; WAS, Wiskott-Aldrich Syndrome

Supplementary Table S14. GRADE evidence profile: need of Rh prophylaxis with RhD-positive platelet transfusion

Quality assessment						Number of patients		Quality	Importance
Number of studies	**Design**	**Limitations**	**Inconsistency**	**Indirectness**	**Imprecision**	**Rh-compatible**	**Rh-incompatible**		
Rh alloimmunization									
2	Observational study	very serious[1,2,3,4]	serious[5,6]	serious[5,6]	serious[7]	--	13/118 (11%)	VERY LOW	IMPORTANT

Abbreviation: GRADE, Grades of Recommendation, Assessment, Development and Evaluation

[1] Sample size not determined

[2] Definition of outcomes not clear

[3] Outcomes assessment not blinded

[4] Confounding factors not analyzed

[5] Adult and pediatric populations in two studies and bone marrow transplant patient populations in one study

[6] Difference in interventions, eg, RhD immunoglobulin prophylaxis and platelet products used; difference in duration of follow up to determine outcome

[7] Small sample size

Supplementary Table S15. GRADE evidence profile: HLA selected platelet transfusion for non-refractory patients

Quality assessment						Number of patients		Quality	Importance
Number of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	HLA-matched platelets	Unmatched platelets		
Mortality									
1	Observational study	serious[1]	not serious	not serious	serious[2]	0/11 (0%)	2/31 (6.5%)	LOW	CRITICAL
Hemorrhage									
1	RCT	serious[3]	not serious	not serious	serious[2]	3/15 (20%)	9/18 (50%)	LOW	CRITICAL
Hemorrhage									
1	Observational study	serious[4]	not serious	not serious	serious[2]	0/30 (0%)	5/18 (28%)	LOW	CRITICAL
Refractoriness									
1	RCT	serious[3]	not serious	not serious	serious[2]	2/15 (13%)	5/18 (28%)	LOW	IMPORTANT
Refractoriness									
1	Observational study	serious[1,5]	not serious	not serious	serious[2]	0/11 (0%)	7/31 (22.6%)	LOW	IMPORTANT
HLA alloimmunization									
1	RCT	serious[3]	not serious	not serious	serious[2]	0/15 (0%)	5/18 (28%)	LOW	IMPORTANT
HLA alloimmunization									
1	Observational study	serious[1,5]	not serious	not serious	serious[2]	0/11 (0%)	15/31 (48.4%)	LOW	IMPORTANT
Platelet utilization									
2	Observational study	serious[6]	not serious	not serious	serious[2]	11/61 (18%)[7]	31/61 (51%)[7]	LOW	IMPORTANT
Platelet increment									
8	Observational	very	serious[1]	serious[10]	serious[2]	30/39[11]	9/39[11]	LOW	IMPORTANT

	study	serious[1,6,8]							

Abbreviations: GRADE, Grades of Recommendation, Assessment, Development and Evaluation; RCT, randomized controlled trial

[1] Sample selection unclear, lack of blinded outcome assessment, small sample size

[2] Small sample size

[3] Random sequence generation and blinding of assessor not stated, protocol not available to check inclusion of all outcomes, assessment of bleeding was not standardized

[4] Sample size not predetermined, outcome assessment not blinded, confounding factors not analyzed

[5] Regression techniques for analysis of control for confounding variables not included

[6] Eligibility criteria not well defined

[7] Number of HLA-matched and -unmatched patients transfused with platelets not specified in one study

[8] Missing data not reported, analysis of confounding factors not conducted, small sample size

[9] Reported length of follow up in only one study

[10] Comparisons often indirect

[11] From the study that indicated sample size (number of patients) of HLA-matched platelet group vs HLA-unmatched platelets; other studies with number of matched or unmatched transfusions; platelet increment in eight studies reported variably as qualitative assessment or quantitative values, eg, cut off, mean, median and percent platelet recovery

Supplementary Table S16. GRADE evidence profile: HLA selected platelet transfusion for refractory patients

Quality assessment						Number of patients		Quality	Importance
Number of studies	**Design**	**Limitations**	**Inconsistency**	**Indirectness**	**Imprecision**	**HLA-matched platelets**	**Unmatched platelets**		
Platelet Increment									
18	Observational study	very serious[1,2,3]	serious[1]	serious[4]	serious[5]	25/60[6]	35/60[6]	LOW	IMPORTANT

Abbreviations: GRADE, Grades of Recommendation, Assessment, Development and Evaluation; RCT, randomized controlled trial

1 Sample selection unclear, lack of blinded outcome assessment, small sample size

2 Eligibility criteria not well defined

3 Missing data not reported, analysis of confounding factors not conducted, small sample size

4 Comparisons often indirect

5 Small sample size

6 From the study that indicated sample size (number of patients) of HLA-matched platelet group vs HLA-unmatched platelets; other studies with number of matched or unmatched transfusions; platelet increment in eighteen studies reported variably as qualitative assessment or quantitative values, eg, cut off, mean, median and percent platelet recovery

Supplementary Table S17. GRADE Evidence Profile: crossmatch-selected platelet transfusion

Quality assessment						Number of patients		Quality	Importance
Number of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Crossmatch-compatible	Crossmatch-incompatible		
Mortality									
1	Observational study	serious[1,2,3]	serious[4]	not serious	serious[5]	1/40 (refractory)	6/440 (non-refractory)	VERY LOW	CRITICAL
Platelet increment									
8	Observational study	very serious[1,2,3,6,7,8,9]	very serious[10]	very serious[10,11]	very serious[12]	210/364	118/305	VERY LOW	IMPORTANT

Abbreviation: GRADE, Grades of Recommendation, Assessment, Development and Evaluation

1 Sample size not determined
2 Outcome assessment not blinded
3 Proportion of missing data not accounted
4 Use of different interventions, eg, SDP and compatible RDP
5 Small number of events and optimal information size not available
6 Sampling method not appropriate
7 Eligibility criteria not defined
8 Quality control measures not instituted
9 Confounding factors not analyzed
10 Heterogeneous populations (eg, pediatric/adult, refractoriness, immune factors), heterogeneous interventions (platelet products used, screening tests used) and different post-transfusion hour CCI measurements
11 Different baseline risks of population subsets (eg, pediatric/adult, refractoriness, immune factors)
12 Small sample size

Supplementary Table S18. Quality assessment of the systematic review comparing single-donor to random-donor platelet transfusion

First author, Year	Heddle NM, 2008[23]
A priori design?	Yes
Duplicate study selection?	Yes
Comprehensive literature search?	Yes
Status of publication disclosed?	Yes
Included grey literature?	Yes
List of included/excluded studies provided?	No
Characteristics of studies provided?	Yes
Quality of studies assessed and documented?	Yes
Scientific quality used appropriately?	Yes
Appropriate method for combining studies?	Yes
Publication bias assessed?	No
Conflict of interest stated?	Yes
Outcomes assessed?	Yes

Supplementary Table S19. Outcomes of the systematic review comparing single-donor to random-donor platelet transfusion

First author, year	Study design included	Number of studies/ abstracts	Transfusion reactions*	Alloimmunization	Platelet increment
Heddle NM, 2008 [23]	RCTs	8/2	Reactions/patient: APC vs WBD, RR= 0.65; 95% CI, 0.44-0.98; APC-LR vs WBD-LR, OR = 1.78; 95% CI, 0.87-3.62 Reaction/product: WBD-PRP non-LR vs APC-LR, OR = 1.87; 95% CI, 1.1-3.1; WBDs-PRP and BC vs APCs-LR, OR = 1.78; 95% CI, 0.87-3.62 Reaction/transfusion: WBD-PRP non-LR vs APC-LR, OR = 0.82; 95% CI, 0.63-1.07; WBD-PRP-LR vs APC-LR, OR = 0.99; 95% CI, 0.63-1.58	Non LR APC vs non LR PRP, RR = 0.63; 95% CI, 0.15-2.54; heterogeneity (I^2 = 65.5%), (n = 3 studies)	APCs vs WBD-PRP, WMD 1-hour CCI = 2.50; 95% CI, 2.19-2.81 APCs vs WBD-BC, WMD 1-hour CCI = 1.80; 95% CI, -0.77-4.38 APCs vs WBD-PRP, WMD 18- to 24-hour CCI = 2.05; 95% CI, 1.44-2.66; APCs vs WBD-BC, WMD 18- to 24-hour CCI = -0.39; 95% CI, -2.95-2.17

Abbreviations: APC, apheresis platelet concentrates; BC, buffy coat; CI, confidence interval; LR, leucoreduced; OR, odds ratio; RCTs, randomized controlled trials; RR, relative risk; WBD-PRP, whole blood derived platelet-rich plasma; WMD, weighted mean difference

* Products not comparable for leucoreduction (ie, pre-storage vs post-storage) and age of platelet product

Supplementary Table S20. Quality of the non controlled studies comparing single-donor vs random-donor platelet transfusion

First author, year	Source of sample appropriate?	Sampling method appropriate?	Sample size pre-determined?	Eligibility criteria clearly defined?	Control group acceptable?	Comparable characteristics?	Clear definitions of outcomes?	Blinded outcome assessment?	Quality control† measures instituted?	Proportion of missing data assessed?	Confound-ing factors analyzed?
Wang RR, 2012 [92]	Yes	Yes	No	Yes	No	NS	No	No	NA	NS	No
Triulzi DJ, 2012 [50]	Yes	No	No	Yes	No	NS	Yes	No	Yes	Yes	No
Tormey CA, 2009 [91]	Yes	No	No	Yes	Yes	NA	Yes	No	NA	NS	No

Abbreviations: NA, not applicable; NS, not stated

† Quality control measures for the collection of data and laboratory tests: accuracy and repeatability of observers, calibration and random calibration and accuracy of instruments, checks for errors in data recording

Supplementary Table S21. Outcomes of the non-controlled studies comparing single-donor to random-donor platelet transfusion

First author, year	Country	Center status	Population	Treatment	Sample size	Total reactions	Allergic reactions	Febrile reactions	Duration of follow up
Wang RR, 2012 [92]	United States	Multi-center	Pediatric patients (organ/stem cell transplant, hematologic/ oncologic malignancy, cardiac surgery or a history of FNHTR)	SDP Pre-storage RDP Post-storage RDP non LR (LR for pediatrics)	9,809 11,380 29.594 19,232 (transfusion episodes)	NS	0.16% 0.17% 0.18% 0.11%	0.07% 0.16%* 0.30%* 0.20*	NS
Triulzi† DJ, 2012 [50]	United States	Multi-center	HT	SDP WBD PRP	552 220	NS	NS	NS	Hospital discharge, 10 days without a platelet transfusion, 30 days after the first platelet transfusion, death, or withdrawal from the study
Tormey ‡ CA, 2009 [91]	United States	Two centers	HT (ITP n = 2)	Pre-storage LRSDP Pre-storage LRRDP	3999 1521 (platelet product)	0.75% (n = 30) 1.38% (n = 21) *P* = ns	0.48% (n = 19) 0.85% (n = 13) *P* = ns	0.25% (n = 10) 0.39% (n = 6) *P* = ns	18 months

Abbreviations: FNHTR, febrile non-hemolytic transfusion reaction; HT, hypoproliferative thrombocytopenia; ITP, immune thrombocytopenia; LR, leucoreduced; LRRDP, leucoreduced random-donor platelets; LRSDP, leucoreduced single-donor platelets; ns, not significant; NS, not stated; RDP, random-donor platelets; SDP, single-donor platelets; WBD PRP, whole blood derived platelet-rich plasma

* SDP vs pre-storage LR, $P = 0.067$; SDP vs post LR, $P < 0.001$; SDP vs non LR, $P = 0.008$, vs pre-storage LR, $P = 0.382$ and vs post-storage LR, $P = 0.045$

† No difference in proportion with WHO grade 2 bleeding, SDP vs WBD 45% vs 47%; time to WHO grade 2 bleeding HR 95% CI 1.15 (0.81–1.65); 4-hr CCI, SDP vs WBD 13051 vs 1667, $P = 0.01$

‡ There were no reported cases of hemolytic transfusion reactions, transfusion related acute lung injury, anaphylaxis or post transfusion purpura in 103 patients. One patient was diagnosed with TACO in the LRRDP group.

Supplementary Table S22. GRADE Evidence Profile: single-donor vs random-donor platelet transfusion

Quality assessment						Number of patients					Effects	Quality	Importance
Number of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	APC		WBD-PRP		WBD-BC	APC vs WBDs PRP		
						Non LR	LR	Non LR	LR				
Hemorrhage													
1	Observa-tional	serious[1,2]	not serious	not serious	serious[3]		251/ 552 (45%)		103/ 220 (47%)		Time to WHO grade ≥ 2 bleeding HR = 1.15; 95% CI, 0.81–1.65	VERY LOW	CRITICAL
Transfusion reactions													
4	RCT	serious[4]	not serious	serious[5]	serious[6,7]		24/ 150 (16%)	107/ 428 (25%)		11/ 344 (3%)	WBD-PRP non-LR vs APC-LR OR = 1.87; 95% CI,1.87,1.1–3.1 WBD (PRP and BC) vs APC OR = 178; 95% CI, 0.87–3.62	LOW	CRITICAL
Transfusion reactions													
1	Observa-tional	serious[8]	serious[9]	not serious	serious[6]		30/ 3999 (0.75%)		21/ 1521 (1.38%)		--	VERY LOW	CRITICAL

Alloimmunization													
4	RCT	serious[4]	not serious	serious[5]	serious[6,7]	10/ 53 (19%)		19/ 50 (38%)			APC non-LR vs WBD-PRP non-LR RR = 0.63; 95% CI, 0.15–2.54	LOW	IMPORTANT
Platelet increment (1 hour CCI, 18-24 hour CCI)													
6	RCT	serious[4]	not serious	serious[5]	serious[6,7]	177		455			WMD 1 hour CCI (95% CI): APC vs WBDs, 2.49 (2.21–2.77); APC vs WBD-PRP, 2.50 (2.19–2.81); APC vs WBD-BC 1.80 (-0.77–4.38) WMD 18-24 hour CCI; (95% CI): APC vs WBDs, 1.64 (0.60–2.67); APC vs WBD-PRP, 2.05 (1.44–2.66); APC vs WBD-BC, -0.39 (-2.95–2.17)	LOW	IMPORTANT
Platelet increment (4 hour increment)													
1	Observa-tional	serious[1,2]	not serious	not serious	serious[3]		552		220		--	VERY LOW	IMPORTANT

Abbreviations: APC, Apheresis Platelet Concentrates; BC, Buffy Coat; GRADE, Grades of Recommendation, Assessment, Development and Evaluation; LR, leucoreduced; PRP, platelet-rich plasma; RCT, randomized controlled trial; WBD, Whole blood derived; WMD, weighted mean difference

[1] Sample size not pre-determined

[2] Outcome measurement not blinded

[3] Number of censored observations reduced statistical power for SDP WBD variable

[4] Issues with randomization and blinding: 1 out of 4 studies not described, three out of four did not state method, one out of four a single blind study; one out of four did not describe blinding method, only one study with randomization and blinding method described and description of withdrawals and dropouts
[5] Platelet products age of storage not comparable
[6] Number of events small
[7] Wide OR confidence intervals
[8] Not randomized, outcomes assessment not blinded
[9] Patients investigated for transfusion reactions received multiple blood products

Appendix B. Search Strategies.

ABO

1 exp ABO Blood-Group System/ (12964)
2 exp "Blood Grouping and Crossmatching"/ (3432)
3 abo matching.mp. (34)
4 or/1-3 (15560)
5 ABO-identical.mp. (129)
6 abo unmatched.mp. (24)
7 abo blood group system.mp. or *abo blood-group system/ (13001)
8 abo.mp. (15996)
9 blood group compatibility.mp. or blood group incompatibility/ (5223)
10 blood group antigens.mp. or blood group antigens/ (16186)
11 platelet transfusion.mp. or platelet transfusion/ (5079)
12 platelet refractoriness.mp. (134)
13 platelet count/ or platelet transfusion/ or platelet increment.mp. (19330)
14 or/5-10 (31759)
15 or/11-13 (20170)
16 4 and 14 and 15 (190)
17 exp thrombocytopenia, neonatal alloimmune/ (125)
18 "neonatal alloimmune thrombocytopenia".mp. (451)
19 (FNAIT or NAIT).mp. (176)
20 or/17-19 (537)
21 16 not 20 (185)
22 limit 21 to case reports (28)
23 21 not 22 (157)
24 limit 23 to editorial (7)
25 23 not 24 (150)
26 limit 25 to english language (132)
27 limit 26 to humans (132)
28 limit 27 to yr="2009 -Current" (26)

RhD

1 exp Rh-Hr Blood-Group System/ or exp Blood Group Antigens/ or rh typing.mp. or exp Erythrocytes/ or exp Blood Group Incompatibility/ (190261)

2 rh.mp. (30428)
3 platelet transfusion.mp. or platelet transfusion/ (5075)
4 1 and 2 and 3 (39)
5 exp thrombocytopenia, neonatal alloimmune/ (125)
6 "neonatal alloimmune thrombocytopenia".tw. (451)
7 (FNAIT or NAIT).tw. (168)
8 5 or 6 or 7 (529)
9 4 not 8 (38)
10 limit 9 to case reports (11)
11 9 not 10 (27)
12 limit 11 to editorial (2)
13 11 not 12 (25)
14 limit 13 to english language (22)
15 limit 14 to humans (22)

HLA

1 exp Platelet Transfusion/ (3906)
2 Blood Transfusion.mp. (63782)
3 limit 2 to yr="1966 - 1991" (27754)
4 Blood Platelets.mp. (61928)
5 limit 4 to yr="1966 - 1993" (37636)
6 Blood Component Transfusion.mp. (2402)
7 limit 6 to yr="1992 - 1993" (519)
8 Blood Platelets.mp. (61928)
9 transfusion.mp. (93570)
10 8 and 9 (3440)
11 limit 10 to yr="1972 - 1993" (1616)
12 "platelet transfusion*".mp. (5580)
13 1 or 3 or 5 or 7 or 11 or 12 (68462)
14 exp HLA Antigens/ (57905)
15 Histocompatibility.mp. (83517)
16 limit 15 to yr="1970 - 1972" (2546)
17 Histocompatibility Antigens.mp. (43353)
18 limit 17 to yr="1973 - 1974" (1699)
19 exp Antigens, Human Platelet/ (1141)
20 Antigens.mp. (526038)

21 limit 20 to yr="1966 - 1979" (69391)
22 Isoantigens.mp. (8999)
23 limit 22 to yr="1976 - 1991" (3981)
24 (HLA or HL-A or HPA antigen*).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier] (85554)
25 14 or 16 or 18 or 19 or 21 or 23 or 24 (154531)
26 exp Thrombocytopenia/ (34130)
27 Blood Group Incompatibility/ (4984)
28 (alloimmunity or alloimmunization).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier] (1833)
29 (refractory or refractoriness).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier] (70396)
30 26 or 27 or 28 or 29 (109321)
31 13 and 25 and 30 (1118)
32 exp Thrombocytopenia, Neonatal Alloimmune/ (96)
33 "neonatal alloimmune thrombocytopenia".mp. (422)
34 (FNAIT or NAIT).mp. [mp=protocol supplementary concept, rare disease supplementary concept, title, original title, abstract, name of substance word, subject heading word, unique identifier] (158)
35 32 or 33 or 34 (494)
36 31 not 35 (993)
37 limit 36 to "review articles" (146)
38 36 not 37 (847)
39 limit 38 to case reports (171)
40 38 not 39 (676)
41 limit 40 to english language (487)
42 limit 41 to humans (451)

Crossmatch

1 exp platelet transfusion/ (14232)
2 blood transfusion.mp. (168139)
3 limit 2 to yr="1966-1991" (56813)
4 blood platelets.mp. (71381)

5 limit 4 to yr="1966-1993" (41257)
6 blood component transfusion.mp. (2933)
7 limit 6 to yr="1992-1993" (530)
8 transfusion.mp. (258167)
9 4 and 8 (3872)
10 limit 9 to yr="1972-1993" (1662)
11 "platelet transfusion*".mp. (10686)
12 1 or 3 or 5 or 7 or 10 or 11 (112073)
13 exp HLA antigens/ (142446)
14 histocompatibility.mp. (190437)
15 limit 14 to yr="1970-1972" (7066)
16 histocompatibility antigens.mp. (49549)
17 limit 16 to yr="1973-1974" (1911)
18 exp antigens, human platelet/ (2744)
19 antigens.mp. (759346)
20 limit 19 to yr="1966-1979" (94180)
21 isoantigens.mp. (9599)
22 limit 21 to yr="1976-1991" (4167)
23 platelet-specific antigen$.tw. (328)
24 antigen$, platelet-specific.tw. (8)
25 platelet alloantigen$.tw. (451)
26 alloantigen$, platelet.tw. (3)
27 human platelet antigen$.tw. (745)
28 (HLA or HL-A or HPA antigen$).tw. (172226)
29 or/13-28 (959932)
30 exp "Blood Grouping and Crossmatching"/ (7739)
31 typing, blood.tw. (27)
32 blood crossmatching.tw. (14)
33 blood typing.tw. (988)
34 blood grouping.tw. (1320)
35 grouping, blood.tw. (17)
36 blood grouping.mp. and crossmatching.tw. (164)
37 crossmatching, blood.tw. (25)
38 crossmatch.tw. (3548)
39 or/30-38 (12217)
40 exp thrombocytopenia/ (142112)

41 blood group incompatibility.mp. (9295)
42 (alloimmunity or alloimmunization).tw. (4954)
43 (refractory or refractoriness).tw. (180309)
44 or/40-43 (327029)
45 12 and 29 and 44 (2644)
46 exp thrombocytopenia, neonatal alloimmune/ (414)
47 "neonatal alloimmune thrombocytopenia".tw. (1119)
48 (FNAIT or NAIT).tw. (481)
49 or/46-48 (1319)
50 45 not 49 (2328)
51 luminex.tw. (4745)
52 elisa.tw. (232853)
53 maipa.tw. (509)
54 sprca.tw. (63)
55 lymphocytotoxic.tw. (2422)
56 or/51-55 (239636)
57 39 or 56 (251015)
58 50 and 57 (365)
59 editorial.mp. (816536)
60 58 not 59 (365)
61 case report.mp. (2108616)
62 60 not 61 (342)
63 case reports.mp. (1689980)
64 62 not 63 (315)
65 letter.mp. (1637209)
66 64 not 65 (314)
67 letters.mp. (76702)
68 66 not 67 (314)
69 abstract.mp. (1922361)
70 68 not 69 (286)
71 abstracts.mp. (66142)
72 70 not 71 (286)
73 review.mp. (4603357)
74 72 not 73 (252)
75 review article.mp. (18989)
76 74 not 75 (252)

77 limit 76 to English language (220)
78 limit 77 to humans (196)
79 remove duplicates from 78 (146)

Apheresis vs WBD Platelets

1 apheres$.tw. (4488)
2 (apheres$ adj4 Single-donor$).tw. (83)
3 apheres$ platelet$.tw. (342)
4 platelet$, apheres$.tw. (96)
5 (apheres$ platelet$ adj4 Single-donor$).tw. (41)
6 plateletpheres$.tw. (453)
7 Single-donor platelet$.tw. (231)
8 platelet$, Single-donor$.tw. (4)
9 Single-donor$ platelet$ transfusion$.tw. (33)
10 platelet$ transfusion$, Single-donor$.tw. (1)
11 ((Single-donor$ or apheres$) adj4 platelet$ transfusion$).tw. (57)
12 ((Single-donor$ or apheres$) adj4 (platelet$ or transfusion$)).tw. (890)
13 (Single-donor$ adj4 (platelet$ or transfus$)).tw. (372)
14 or/1-13 (5047)
15 random-donor$ platelet$.tw. (195)
16 platelet$, random-donor$.tw. (0)
17 pool$ platelet$.tw. (154)
18 platelet$, pool$.tw. (144)
19 random-donor$ platelet$ transfusion$.tw. (43)
20 platelet$ transfusion$, random-donor$.tw. (1)
21 pool$ platelet$ transfusion$.tw. (6)
22 platelet$ transfusion$, pool$.tw. (0)
23 whole blood deriv$ platelet$.tw. (39)
24 platelet$, whole blood derive$.tw. (0)
25 whole blood deriv$ platelet$ transfusion$.tw. (2)
26 platelet$ transfusion$, whole blood deriv$.tw. (0)
27 (random-donor$ adj4 (platelet$ or transfus$)).tw. (248)
28 (whole blood deriv$ adj4 (platelet$ or transfus$)).tw. (54)
29 (pool$ adj4 platelet$).tw. (900)
30 ((random-donor$ or pool$) adj4 (platelet$ or transfus$)).tw. (1155)

31 ((whole blood deriv$ or pool$) adj4 (platelet$ or transfus$)).tw. (991)
32 (random-donor$ pool$ adj4 (platelet$ or transfus$)).tw. (2)
33 (pool$ random-donor$ adj4 (platelet$ or transfus$)).tw. (28)
34 (whole blood deriv$ pool$ adj4 (platelet$ or transfus$)).tw. (1)
35 (pool$ whole blood deriv$ adj4 (platelet$ or transfus$)).tw. (14)
36 (whole blood deriv$ adj2 (platelet$ or concentrate$ or transfus$)).tw. (48)
37 (whole blood adj2 platelet$ transfus$).tw. (6)
38 or/15-37 (1197)
39 14 and 38 (170)
40 exp thrombocytopenia, neonatal alloimmune/ (125)
41 "neonatal alloimmune thrombocytopenia".mp. (451)
42 (FNAIT or NAIT).mp. (176)
43 or/40-42 (537)
44 39 not 43 (169)
45 limit 44 to (case reports or editorial) (5)
46 44 not 45 (164)
47 limit 46 to (english language and humans) (143)
48 limit 47 to yr="2008 -Current" (31)