Database: Cochrane Central Register of Controlled Trials 2013 to Present

Date searched: Feb 7, 2019
Topic: platelet guidelines published after 2013

APPENDIX A

Cochrane Database of Systematic Reviews 2013 to Present

#	Searches	Results	Type
1	platelet*.mp,kw.	734	Advanced
2	plateletpheres*.mp,kw.	12	Advanced
3	platelet-pheres*.mp,kw.	0	Advanced
4	thrombocyt*.mp,kw.	505	Advanced
5	thrombophores*.mp,kw.	0	Advanced
6	thrombo-phores*.mp,kw.	0	Advanced
7	thrombocytapheres*.mp,kw.	0	Advanced
8	thrombocyta-pheres*.mp,kw.	0	Advanced
9	thrombocytopheres*.mp,kw.	10	Advanced
10	(transfus* adj3 prophyla*).mp,kw.	33	Advanced
11	(transfus* adj3 therap*).mp,kw.	66	Advanced
12	or/1-11	1036	Advanced
13	guideline*.mp,kw.	5464	Advanced
14	guidance*.mp,kw.	2549	Advanced
15	(best adj2 practice?).mp,kw.	383	Advanced
16	consensus*.tw,kw.	5357	Advanced

Database: Cochrane Central Register of Controlled Trials 2013 to Present

Date searched: Feb 7, 2019
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17	recommendation*.mp,kw.	4907	Advanced
18	(position? adj3 statement?).mp,kw.	32	Advanced
19	or/13-18	8442	Advanced
20	12 and 19	933	Advanced
21	limit 20 to protocols	159	Advanced
22	20 not 21	774	Advanced
23	limit 22 to yr="2013 -Current"	447	Advanced

Database: Cochrane Central Register of Controlled Trials 2013 to Present

Date searched: Feb 7, 2019
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Embase Classic+Embase 2013 to 2019 February 06

#	Searches	Results	Type
1	exp thrombocyte/	116818	Advanced
2	exp "thrombocyte function and characteristics"/	93093	Advanced
3	exp thrombocyte function/	91185	Advanced
4	exp blood clotting parameters/	88070	Advanced
5	platelet count/	7859	Advanced
6	exp thrombocyte disorder/	182990	Advanced
7	thrombocyte transfusion/	17583	Advanced
8	thrombocytopheresis/	1765	Advanced
9	exp thrombocytopenia/	168430	Advanced
10	thrombocytosis/	9263	Advanced
11	platelet*.mp,kw.	324925	Advanced
12	plateletpheres*.mp,kw.	854	Advanced
13	platelet-pheres*.mp,kw.	78	Advanced
14	thrombocyt*.mp,kw.	434681	Advanced
15	thrombophores*.mp,kw.	6	Advanced
16	thrombo-phores*.mp,kw.	0	Advanced
17	thrombocytapheres*.mp,kw.	110	Advanced

Database: Cochrane Central Register of Controlled Trials 2013 to Present

Date searched: Feb 7, 2019
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18	thrombocyta-pheres*.mp,kw.	1	Advanced
19	thrombocytopheres*.mp,kw.	1768	Advanced
20	(transfus* adj3 prophyla*).mp,kw.	1184	Advanced
21	(transfus* adj3 therap*).mp,kw.	6305	Advanced
22	or/1-21	604235	Advanced
23	practice guideline/	367525	Advanced
24	consensus/	59607	Advanced
25	guideline*.mp,kw.	664798	Advanced
26	guidance*.mp,kw.	149735	Advanced
27	(best adj2 practice?).mp,kw.	35802	Advanced
28	consensus*.tw,kw.	195905	Advanced
29	recommendation*.mp,kw.	319432	Advanced
30	(position? adj3 statement?).mp,kw.	4614	Advanced
31	or/23-30	1201477	Advanced
32	22 and 31	25706	Advanced
33	(exp animals/ or exp animal experimentation/ or nonhuman/) not ((exp animals/ or exp animal experimentation/ or nonhuman/) and exp human/)	6904627	Advanced
34	32 not 33	25124	Advanced

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Topic: platelet guidelines published after 2013

35	limit 34 to (books or chapter or conference abstract or conference paper or "conference review" or editorial or letter or note or "review")	15890	Advanced
36	34 not 35	9234	Advanced
37	(review* and (practice guideline* or guideline*)).tw,kw.	120856	Advanced
38	22 and 37	3782	Advanced
39	limit 38 to (books or chapter or conference abstract or conference paper or "conference review" or editorial or letter or note)	1275	Advanced
40	38 not 39	2507	Advanced
41	36 or 40	10708	Advanced
42	limit 41 to yr="2013 -Current"	5239	Advanced

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Topic: platelet guidelines published after 2013

Ovid MEDLINE® Epub Ahead of Print and In-Process & Other Non-Indexed Citations 2013 to February 06, 2019

#	Searches	Results	Type
1	platelet*.mp,kw.	16776	Advanced
2	plateletpheres*.mp,kw.	43	Advanced
3	platelet-pheres*.mp,kw.	2	Advanced
4	thrombocyt*.mp,kw.	5879	Advanced
5	thrombophores*.mp,kw.	0	Advanced
6	thrombo-phores*.mp,kw.	0	Advanced
7	thrombocytapheres*.mp,kw.	2	Advanced
8	thrombocyta-pheres*.mp,kw.	0	Advanced
9	thrombocytopheres*.mp,kw.	0	Advanced
10	(transfus* adj3 prophyla*).mp,kw.	70	Advanced
11	(transfus* adj3 therap*).mp,kw.	303	Advanced
12	or/1-11	20996	Advanced
13	guideline*.mp,kw.	51169	Advanced
14	guidance*.mp,kw.	16974	Advanced
15	(best adj2 practice?).mp,kw.	4835	Advanced

Database: Cochrane Central Register of Controlled Trials 2013 to Present

Date searched: Feb 7, 2019
Topic: platelet guidelines published after 2013

16	consensus*.tw,kw.	19766	Advanced
17	recommendation*.mp,kw.	34306	Advanced
18	(position? adj3 statement?).mp,kw.	618	Advanced
19	or/13-18	109154	Advanced
20	12 and 19	861	Advanced
21	limit 20 to (case reports or clinical conference or consensus development conference or consensus development conference, nih or editorial or letter or news or newspaper article)	19	Advanced
22	20 not 21	842	Advanced
23	limit 22 to yr="2013 -Current"	687	Advanced

Supplementary table: Summary of recommendations in the studied peer-reviewed platelet evidence-based guidelines		
First author, year	**Guideline group**	**Recommendation**
Prophylactic platelet transfusion for patients with hypoproliferative thrombocytopenia; platelet threshold and dose		
Kaufman 2014	AABB	▪ The AABB recommends that platelets should be transfused prophylactically to reduce the risk for spontaneous bleeding in hospitalized adult patients with therapy- induced hypoproliferative thrombocytopenia. ▪ The AABB recommends transfusing hospitalized adult patients with a platelet count $\leq 10 \times 10^9$ /L or less to reduce the risk for spontaneous bleeding. ▪ The AABB recommends transfusing up to a single apheresis unit or equivalent. Greater doses are not more effective, and lower doses equal to one half of a standard apheresis unit are equally effective. (*Grade: strong recommendation; moderate-quality evidence)*
Nahirniak 2014	ICTMG	▪ Prophylactic platelet transfusion should be given to patients with hypoproliferative thrombocytopenia. (*moderate level of evidence, strong recommendation for adults and weak level of evidence, strong recommendation for pediatric patients*) ▪ A threshold of $\leq 10 \times 10^9$/L should be used for prophylactic platelet transfusion for patients with hypoproliferative thrombocytopenia. (*moderate level of evidence, strong recommendation for adults and weak level of evidence, strong recommendation for pediatric patients)* ▪ Patients with hypoproliferative thrombocytopenia with clinically significant bleeding attributed to thrombocytopenia should probably receive platelet transfusions even if the platelet count is $> 10 \times 10^9$/L. (*very weak level of evidence, weak recommendation*) ▪ Low- or standard-dose platelet transfusion (ie, $1.1 \times 10^{11}/m^2$ or $2.2 \times 10^{11}/m^2$, respectively), as opposed to high-dose platelet transfusion ($4.4 \times 10^{11}/m^2$), should be given to hospitalized patients with

		hypoproliferative thrombocytopenia who require prophylactic platelet transfusion. (*high level of evidence, strong recommendation)*
Killick 2015	BSCH	▪ Prophylactic platelet transfusions should be given to stable AA patients receiving active treatment. (*1B)* A threshold (pre-transfusion) platelet count of 10 $x10^9$/L should be used. (*1B)* ▪ In patients judged to have additional risk factors for bleeding, such as fever or sepsis, a higher prophylactic transfusion threshold of 20 $x10^9$/L is recommended. *(2C)* ▪ Routine prophylactic platelet transfusions are not recommended for stable AA patients not on active treatment. *(2B)* ▪ Patients with chronic bleeding of WHO grade 2 or above require individual management according to the severity of their symptoms and signs. *(2C)* ▪ Prior to administration of ATG, a daily threshold (pre-transfusion) platelet count of 20 $x10^9$/L should be used for the duration of the ATG course. *(2C)* ▪ Only one adult platelet dose is routinely required. *(1A)* ▪ Supportive care remains the mainstay of treatment of AA in pregnancy, aiming to maintain the platelet count above $20x10^9$/L with platelet transfusions. *(1C)*
Estcourt 2017	BSCH	**<u>Reversible bone marrow failure, recovery anticipated</u>** ▪ Give prophylactic platelet transfusions (platelet transfusions to patients who do not have clinically significant bleeding [WHO grade 0 or 1] and do not require a procedure) to patients with reversible bone marrow failure receiving intensive chemotherapy or undergoing allogeneic HSCT to maintain a platelet count $\geq 10x10^9$/L. (1B) ▪ Use only one adult dose (one unit) routinely for prophylactic platelet transfusions. (*1A)* ▪ Consider not giving prophylactic platelet transfusions to well patients with no evidence of bleeding who have had an autologous stem cell transplant. *(2B)* ▪ 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. *(2C)*

		<u>Chronic bone marrow failure, recovery is not anticipated</u> ▪ Use a 'no prophylactic platelet transfusion' strategy for asymptomatic patients with chronic bone marrow failure (including those taking low dose oral chemotherapy or azacitidine). *(2B)* ▪ Give prophylactic platelet transfusions to patients with chronic bone marrow failure receiving intensive treatment. *(1B)* ▪ Manage patients with chronic bleeding of WHO grade 2 or above individually, according to the severity of their symptoms and signs. Consider a strategy of prophylaxis (e.g. twice a week). *(2C)*
Schiffer 2017	ASCO	▪ Prophylactic platelet transfusion should be administered to patients with thrombocytopenia resulting from impaired bone marrow function to reduce the risk of hemorrhage when the platelet count falls below a predefined threshold level. This threshold level for transfusion varies according to the patient's diagnosis, clinical condition, and treatment modality. (E*vidence based, high evidence quality, Strong recommendation)* ▪ The Panel recommends a threshold of < 10 X 10^9/L for prophylactic platelet transfusion in patients receiving therapy for hematologic malignancies. Transfusion at higher levels may be advisable in patients with signs of hemorrhage, high fever, hyperleukocytosis, rapid fall of platelet count, or coagulation abnormalities (for example, acute promyelocytic leukemia) and in those undergoing invasive procedures or in circumstances in which platelet transfusions may not be readily available in case of emergencies, as might be the case in outpatients who live at a distance from the treatment center. (*Evidence based, high evidence quality, strong recommendation)* ▪ The Panel recommends a threshold of < 10 X 10^9/L for prophylactic platelet transfusion in adult and pediatric patients undergoing allogeneic HSCT. Prophylactic platelet transfusion may be administered at higher counts based on clinician judgement. In adult recipients of autologous HSCT, randomized trials have demonstrated similar rates of bleeding with decreased platelet usage when patients are transfused at the first sign of bleeding rather than prophylactically, and this approach may be used in experienced centers. This recommendation is not generalizable to pediatric patients. (E*vidence based, high evidence quality, moderate recommendation)*

		▪ Patients with chronic, stable, severe thrombocytopenia, such as individuals with myelodysplasia or aplastic anemia, who are not receiving active treatment may be observed without prophylactic transfusion, reserving platelet transfusions for episodes of hemorrhage or during times of active treatment. (*Informal consensus, intermediate evidence quality, moderate recommendation)* ▪ The risk of bleeding in patients with solid tumors during chemotherapy-induced thrombocytopenia is related to the depth and duration of the platelet nadir, although other factors contribute as well. The Panel recommends a threshold < 10 X 10^9/L for prophylactic platelet transfusion, based on extrapolation from studies in hematologic malignancies. Platelet transfusion at higher levels is appropriate in patients with active localized bleeding which can sometimes be seen in patients with necrotic tumors. (*Informal consensus, low evidence quality, moderate recommendation)*
Prophylactic platelet transfusion prior to procedures or surgery		
Kaufman 2014	AABB	▪ The AABB suggests prophylactic platelet transfusion for patients having elective central venous catheter placement with a platelet count < 20 × 10^9 cells/L. (*Grade: weak recommendation; low-quality evidence*) ▪ The AABB suggests prophylactic platelet transfusion for patients having elective diagnostic lumbar puncture with a platelet count < 50 × 10^9 cells/L. (*Grade: weak recommendation; very-low-quality evidence)* ▪ The AABB suggests prophylactic platelet transfusion for patients having major elective nonneuraxial surgery with a platelet count < 50 × 10^9 cells/L. (*Grade: weak recommendation; very-low-quality evidence)* ▪ The AABB recommends against routine prophylactic platelet transfusion for patients who are nonthrombocytopenic and have cardiac surgery with CPB. The AABB suggests platelet transfusion for patients having bypass who exhibit perioperative bleeding with thrombocytopenia and/or evidence of platelet dysfunction. (*Grade: weak recommendation; very-low-quality evidence)*

		▪ The AABB cannot recommend for or against platelet transfusion for patients receiving antiplatelet therapy who have intracranial hemorrhage (traumatic or spontaneous). (*Grade: uncertain recommendation; very-low-quality evidence)*
Estcourt 2017	BSCH	▪ Whenever possible use a procedure/equipment associated with the lowest bleeding risk. Apply local measures, such as compression, to reduce the risk of bleeding post-procedure. (*1C)* ▪ Do not give platelet transfusions routinely prior to: o Bone marrow aspirate or trephine biopsy *(1B)* o Peripherally inserted central catheters *(2C)* o traction removal of tunnelled central venous catheters *(2C)* o Cataract surgery *(2C)* ▪ Consider performing the following procedures above the platelet count threshold indicated o Venous central lines (both tunnelled and un-tunnelled), inserted by experienced staff using ultrasound guidance techniques, when the platelet count is >20 $x10^9$/L. (*1B)* o Lumbar puncture when the platelet count is ≥40$x10^9$/L. (*2C)* o Insertion/removal of epidural catheter when the platelet count is ≥80$x10^9$/L. (*2C)* o Major surgery – when the platelet count is >50$x10^9$/L. (*1C)* o Neurosurgery or ophthalmic surgery involving the posterior segment of the eye when the platelet count is >100$x10^9$/L. (*1C)* o Percutaneous liver biopsy when the platelet count is >50 $x10^9$/L *(2B).* Consider trans-jugular biopsy if the platelet count is below this level. *(2B)* ▪ Prior to renal biopsy ensure potential risk factors for bleeding are corrected: anaemia (iron and erythropoietin), uraemia (dialysis) (*1B).* If renal biopsy is urgent, consider DDAVP pre-procedure (*1B)* or oestrogen if time allows. (*2B)*

Schiffer 2017	ASCO	▪ The Panel recommends a threshold of 40 X 10^9/L to 50 X 10^9/L for performing major invasive procedures, in the absence of associated coagulation abnormalities. Certain procedures, such as bone marrow aspirations and biopsies, and insertion or removal of central venous catheters can be performed safely at counts > 20 X 10^9/L. There are sparse data, and no randomized trials, addressing the safety of other invasive procedures at much lower count levels. If platelet transfusions are administered before a procedure, it is critical that a posttransfusion platelet count be obtained to prove that the desired platelet count level has been reached. Platelet transfusions should also be available on short notice, in case intraoperative or postoperative bleeding occurs. For alloimmunized patients, histocompatible platelets must be available in these circumstances. (E*vidence based low evidence quality, weak recommendation)*
Prophylactic platelet transfusion to other patient groups		
Estcourt 2017	BSCH	▪ Use the platelet count thresholds for reversible bone marrow failure as a general guide for prophylactic platelet transfusion in patients with critical illness in the absence of bleeding or planned procedures. *(2C)*
Therapeutic platelet transfusion		
Estcourt 2017	BSCH	▪ In severe bleeding, maintain the platelet count > 50x10^9/L. Consider empirical use for the initial management of major haemorrhage. *(1C)* ▪ In patients with multiple trauma, traumatic brain injury or spontaneous intracerebral haemorrhage, maintain the platelet count > 100x 10^9/L. (*2C)* ▪ In patients with bleeding that is not considered severe or life-threatening, consider platelet transfusion if the platelet count is < 30x10^9/L. (*2C)*
Platelet transfusion for platelet dysfunction disorders		
Estcourt 2017	BSCH	Congenital ▪ For first line treatment or prevention of bleeding, consider rFVIIa in Glanzmann thrombasthenia and TXA plus desmopressin in other congenital platelet function disorders. (*2B)*

		▪ If pharmaceutical therapies are contraindicated, ineffective or if there is high risk of bleeding, consider transfusion of platelets. In Glanzmann thrombasthenia, consider HLA-matched platelets. *(2C)* Acquired ▪ Do not use platelet transfusion pre-procedure when antiplatelet agents have not been discontinued. *(2C)* ▪ Use general haemostatic measures to treat bleeding in patients during treatment with aspirin, $P2Y_{12}$ antagonists or glycoprotein IIa/IIIb inhibitors. If necessary, consider drug cessation and reversal of the effect of co-prescribed anticoagulants.*(2C)* ▪ Use TXA to counteract the effect of anti-platelet agents when a risk/benefit assessment would support this. (*1B)* ▪ Consider the use of platelet transfusion as an additional measure to those suggested above for critical bleeding. (*2C)* ▪ Consider platelet transfusion to prevent bleeding in severe thrombocytopenia (platelet count $<10x10^9$/L) caused by abciximab. (*2C)*
Contraindications for platelet transfusions and situations where transfusion is not recommended		
Estcourt 2017	BSCH	*ITP* ▪ Do not use prophylactic platelet transfusions in patients with ITP. *(1C)* ▪ Only use platelet transfusion prior to a procedure or surgery when other treatment has failed and/or the intervention is urgent. Usual threshold counts may be unachievable or unnecessary and individual case review is required. *(1C)* ▪ Give therapeutic platelet transfusions (more than one dose) to treat serious bleeding *(1C).* Consider co-administration of intravenous immunoglobulin in addition to the platelet transfusion. *(2C)* *PTP*

		▪ In PTP, intravenous immunoglobulin is the treatment of choice. *(1C)* *Thrombotic microangiopathies* ▪ In patients with thrombotic microangiopathies only use platelet transfusions to treat life-threatening bleeding. (*1C)* *Renal failure* ▪ Avoid platelet transfusion in renal failure because infused platelets will acquire a dysfunction similar to the patients' own platelets and platelet transfusion may result in alloimmunisation. (*1B)*
Selection of ABO blood group and selection of special products		
Nahirniak 2014	ICTMG	▪ Platelet concentrates that are ABO identical should probably be used in patients with hypoproliferative thrombocytopenia, if available. (*weak level of evidence, weak recommendation)*
Estcourt 2016	BSCH	▪ Hospitals should establish a strategy to maximise the transfusion of ABO compatible platelets, especially to patients who require regular platelet support. *(2B*) ▪ It is acceptable to use ABO incompatible platelets to reduce wastage. Platelets tested and negative for high titre haemagglutinins and non-group O platelets are associated with a lower risk of haemolysis. Pooled platelets suspended in PAS would also be expected to reduce this risk. (*1B)* ▪ In patients with a history of allergic transfusion reactions, apart from mild, use platelets suspended in PAS. If reactions continue or are severe, washed platelets (re- suspended in 100% PAS) may be required. *(1B)*
Prevention of anti-D alloimmunization		
Nahirniak 2014	ICTMG	▪ Female children and females of child-bearing age/potential, with hypoproliferative thrombocytopenia, who are RhD negative should probably receive Rh immunoglobulin before, immediately after, or within 72 hours of receiving an RhD-positive platelet component (unless antibody testing demonstrates the

		persistence of anti-D from a previous dose of Rh immunoglobulin). (*very weak level of evidence, weak recommendation*). ▪ Males and females who are not of child-bearing age/potential, with hypoproliferative thrombocytopenia, who are RhD negative and are transfused with RhD-positive platelet components probably do not require Rh immunoglobulin. (*very weak level of evidence, weak recommendation*)
Estcourt 2016	BSCH	▪ RhD negative girls or women of childbearing potential should receive RhD negative platelets. If unavailable, RhD positive platelets can be given with anti-D prophylaxis. (*1B)* ▪ For RhD negative boys under 18 years of age, those who already have anti-D antibodies, and transfusion- dependant adults, the platelets of choice are RhD negative. RhD positive platelets should be given if RhD negative platelets are unavailable or to prevent wastage of RhD positive components. Anti-D prophylaxis is not required. (*1B)*
Schiffer 2017	ASCO	▪ Prevention of RhD alloimmunization resulting from platelet transfusions to RhD- negative recipients can be achieved either through the exclusive use of platelet products collected from RhD-negative donors or via anti-D immunoprophylaxis. These approaches may be used for female children and female adults of childbearing potential being treated with curative intent. However, because of the low rate of RhD alloimmunization in cancer patients, these approaches need not be applied universally. (*Evidence based evidence, intermediate quality, moderate recommendation*)
New 2016	BSCH	▪ D-negative paediatric recipients should not receive D-positive platelets because of the risk of allo-immunization to the D antigen. If D-positive platelets must be given in emergency, prophylactic anti-D should be considered if the recipient is female.
Management of platelet refractoriness		

Nahirniak 2014	ICTMG	▪ Patients with hypoproliferative thrombocytopenia who are refractory to platelet transfusions and have class I HLA antibodies should probably receive class I HLA-selected or crossmatch-selected platelet transfusion to increase the platelet count. (*weak level of evidence, weak recommendation)* ▪ Patients with hypoproliferative thrombocytopenia who are refractory to platelet transfusions and have HPA antibodies should probably receive HPA-selected or crossmatch-selected platelet transfusion to increase the platelet count. (*very weak level of evidence, weak recommendation)* ▪ Patients with hypoproliferative thrombocytopenia who are not refractory to platelet transfusion should probably not receive HLA- selected, HPA-selected, or crossmatch-selected platelets (*weak level of evidence, weak recommendation* for HLA selection and crossmatch selection, v*ery weak level of evidence and weak recommendation* for HPA selection) ▪ Patients with hypoproliferative thrombocytopenia who are refractory to platelet transfusions solely due to nonimmune factors should probably not receive HLA-selected or crossmatch-selected platelets. (*weak level of evidence, weak recommendation*)
Estcourt 2016	BSCH	▪ ABO matched platelets should be used when available to maximise increments. (*2C)* ▪ Patients with hypoproliferative thrombocytopenia who are refractory to platelet transfusions solely due to non- immune factors should not receive HLA-selected platelet transfusion. (*2C)* ▪ Patients with hypoproliferative thrombocytopenia who are refractory to platelet transfusions and have class I HLA antibodies should receive class I HLA-selected platelet transfusion. (*2C)* ▪ Patients with hypoproliferative thrombocytopenia who continue to be refractory to HLA-selected platelet trans- fusions and have HPA antibodies should receive HPA-selected platelet transfusion. (*2C)* ▪ Patients with hypoproliferative thrombocytopenia who are not refractory to platelet transfusion should not receive HLA-selected or HPA-selected platelets. (*2C)*
Schiffer 2017	ASCO	▪ Although there are no empirical data to suggest that monitoring and acting on the post-platelet-transfusion count decreases the incidence of hemorrhagic events, the Panel consensus is that platelet counts performed 10 to 60 minutes posttransfusion should be obtained after all transfusions, when refractoriness is suspected . Because patients may have a poor increment to a single transfusion yet have

		excellent platelet increments with subsequent transfusions, a diagnosis of refractoriness to platelet transfusion should only be made when at least two transfusions of ABO-compatible units, stored < 72 hours, result in poor increments, as defined in the supporting text of the recommendation. (*Informal consensus, insufficient evidence, moderate recommendation)* ▪ Alloimmunization is usually due to antibody against HLA antigens and only rarely to platelet specific antigens. Patients with alloimmune refractory thrombocytopenia, as defined above, are best managed with platelet transfusions from histocompatible donors matched for HLA-A and HLA-B antigens. Many blood suppliers have access to computerized lists of such donors. For patients (a) whose HLA type cannot be determined, (b) who have uncommon HLA types for whom suitable donors cannot be identified, or (c) who do not respond to HLA matched platelets, histocompatible platelet donors can often be identified using platelet cross-matching techniques. In many patients, these two techniques are complementary. (*Evidence based, high Evidence, strong recommendation)*
Alternatives to platelet transfusions		
Estcourt 2016	BSCH	▪ Administer TXA early in trauma patients who are bleeding/at risk of bleeding. (*1A*) ▪ Use TXA in surgical patients expected to have greater than a 500 ml blood loss, unless contraindications exist. (*1A)* ▪ Consider TXA as an alternative or in addition to therapeutic platelet transfusion, in patients with chronic thrombocytopenia caused by bone marrow failure. (*2B)* ▪ In severe perioperative bleeding/bleeding associated with major trauma give fibrinogen (concentrate or cryoprecipitate) if plasma fibrinogen concentration is <15 g/L or if signs of a functional fibrinogen deficit are seen on near patient testing. (*1C)* ▪ Use thrombopoietin receptor agonists in ITP according to international guidelines. At present there is insufficient evidence to recommend these agents in other patient categories. (*1A)*
Pediatrics and Neonates		
New 2016	BSCH	▪ For preterm neonates with very severe thrombocytopenia (platelet count < 25 x10^9/L) platelet transfusions should be administered in addition to treating the underlying cause of the thrombocytopenia

(*2C)*. Suggested threshold counts for platelet transfusions in different situations are given in Table II. *(2C)*

Table II. Suggested thresholds of platelet count for neonatal platelet transfusion.

Platelet count ($\times 10^9$/l)	Indication for platelet transfusion
<25	Neonates with no bleeding (including neonates with NAIT if no bleeding and no family history of ICH)
<50	Neonates with bleeding, current coagulopathy, before surgery, or infants with NAIT if previously affected sibling with ICH
<100	Neonates with major bleeding or requiring major surgery (e.g. neurosurgery)

NAIT, neonatal alloimmune thrombocytopenia; ICH, intracranial haemorrhage.

- Consider intravenous immunglobulin in NAIT refractory to platelets negative for HPA-1a/5b antigens or if antigen-matched platelets are unavailable. (*1C*)

- Given a lack of studies in paediatrics, recommendations for platelet transfusions in critically ill children or those with haematological/oncological malignancies who develop severe thrombocytopenia are drawn from the wider adult literature and recommendations. (*2C*) (see Table III for suggested thresholds)

Table III. Suggested thresholds of platelet counts for platelet transfusion in children.

Platelet count ($\times 10^9$/l)	Clinical situation to trigger platelet transfusion
<10	Irrespective of signs of haemorrhage (excluding ITP, TTP/HUS, HIT)
<20	Severe mucositis
	Sepsis
	Laboratory evidence of DIC in the absence of bleeding*
	Anticoagulant therapy
	Risk of bleeding due to a local tumour infiltration
	Insertion of a non-tunnelled central venous line
<40	Prior to lumbar puncture†
<50	Moderate haemorrhage (e.g. gastrointestinal bleeding) including bleeding in association with DIC
	Surgery, unless minor (except at critical sites)
	• including tunnelled central venous line insertion
<75–100	Major haemorrhage or significant post-operative bleeding (e.g. post cardiac surgery)
	Surgery at critical sites: central nervous system including eyes

- As pragmatic guidance, it is suggested that for most stable children prophylactic platelet transfusions should be administered when the platelet count is< 10X10^9/L, excluding patients with ITP, thrombotic thrombocytopenic purpura/haemolytic uraemic syndrome and heparin-induced thrombocytopenia who should only be transfused with platelets for life-threatening bleeding. *(2B)*
- For clinically significant bleeding following CPB and platelet count <100X 10^9/L, PT or APTT >15 times midpoint of normal range, fibrinogen <15 g/L specific component replacement may be warranted (*2C).*
- Platelets provided for IUT are HPA compatible with maternal antibody and irradiated. The volume transfused is calculated based on the fetal and concentrate platelet count.

- Platelets should match the recipient ABO blood group wherever possible, but it may be necessary to use alternative groups as in Table IV.

Table IV. Group selection of plasma-based components.

Patient's ABO Group	ABO group of plasma components to be transfused: Platelets	MB FFP & SD FFP‡	MB Cryoprecipitate‡
O			
1st choice	O	O†	O†
2nd choice	A, B or AB	A or B or AB	A or B or AB
A			
1st choice	A	A	A
2nd choice	AB	AB	AB
3rd choice	B*	B‡	B‡
4th choice	O*	–	–
B			
1st choice	B	B	B
2nd choice	AB	AB	AB
3rd choice	A*	A‡	A‡
4th choice	O*	–	–
AB			
1st choice	AB	AB	AB
2nd choice	A*	A‡	A‡
3rd choice	B*	B‡	B‡
4th choice	O*	–	–
Unknown			
1st choice	AB	AB	AB
2nd choice	A*	A‡	A‡
3rd choice	B*	B‡	B‡
4th choice	O*	–	–

- When NAIT is suspected and results of diagnostic tests are not available, order platelets negative for HPA-1a/5b antigens from the Blood Services until the tests either confirm or exclude the presence of NAIT.

Table c. Platelets for fetal/neonatal/infant/paediatric transfusion.

Component type	Component details and administration	Comments
IUT platelets Approx unit volume 75 ml	Group A, D-negative (if ABO D group unknown) or group specific/compatible with maternal antibody HPA compatible with maternal antibody for NAIT (HPA-1a,5b-negative/as required) Obtained by apheresis from a single donor Hyperconcentrated to a platelet count of at least 2000×10^9/l, shelf-life 24 h Irradiated See Section 1.3.1 for administration details	Special order from Blood Services, requiring several days notice • group O platelets should not normally be selected for non-O or unknown group recipients, however the availability of HPA antigen-negative platelets may override ABO group selection considerations • for HPA matched platelets, donors are negative for clinically significant HLA and HPA antibodies • hyperconcentrated to optimise platelet count and minimize volume load Irradiated cellular components are recommended for infants up to 6 months of age post- IUT (BSCH, 2011b)
Neonatal platelets Approx unit volume 45 ml	ABO and D identical or compatible with recipient (see Table IV) HPA compatible with maternal platelet antibody for neonates with NAIT (as for IUT platelets) Obtained by apheresis from a single donor, split into four smaller units Typical transfusion volume: 10–20 ml/kg Transfusion rate: 10–20 ml/kg/h	HPA matched platelets require special order from Blood Services, but HPA-1a/5b-negative usually available 'off the shelf' depending on the geographical location Suitable for neonatal and infant transfusion
Platelets for children from 1 year of age (standard 'adult' apheresis platelets) Approx unit volume 200 ml	ABO and D identical or compatible with recipient (see Table IV) Obtained by apheresis from a single donor where possible Typical transfusion volume: • 10–20 ml/kg for children <15 kg, or a single pack for children ≥15 kg • maximum volume 1 pack Transfusion rate: 10–20 ml/kg/h	These differ from 'neonatal' platelets by not having fetal/neonatal/infant specification. • recipients born on or after 1 January 1996 should be provided with apheresis platelets when possible, as a vCJD risk reduction measure

Apheresis versus whole blood platelets		
Nahirniak 2014	ICTMG	▪ When leukoreduced platelet products are available, whole blood derived platelets (from buffy coat or platelet rich plasma methods) should be used as equivalent products to apheresis platelets. (*moderate level of evidence, strong recommendation*)

Schiffer 2017	ASCO	▪ Platelets for transfusion can be prepared either by separation of units of platelet concentrates from whole blood using either the buffy coat or platelet-rich plasma method, which can be pooled before administration, or by apheresis from single donors. Comparative studies have shown that the posttransfusion increments, hemostatic benefit, and side effects are similar with any of these platelet products. Thus, in routine circumstances, they can be used interchangeably. In most centers, pooled platelet concentrates are less costly. Single-donor platelets from selected donors are necessary when histocompatible platelet transfusions are needed. (*Evidence based, high evidence quality, strong recommendation)*
Leukoreduction		
Schiffer 2017	ASCO	▪ The incidence of alloantibody mediated refractoriness to platelet transfusion can be decreased in patients with acute myeloid leukemia receiving induction chemotherapy when both platelet and red blood cell products are leukoreduced before transfusion. It is therefore appropriate to provide leukoreduced blood products to patients with AML from the time of diagnosis to ameliorate this important clinical problem. Although randomized trials have not been conducted in other patient groups, it is likely that alloimmunization can also be decreased in patients with other types of leukemia and in other cancer patients receiving chemotherapy. There are less data in patients who are not receiving chemotherapy in the same time periods that the transfusions are being administered (for example, aplastic anemia, myelodysplasia), although the consensus would favor its use in these patients as well. In the United States and several other countries, the overwhelming majority of blood products are now leukoreduced at the time of blood collection and component preparation. Other advantages of prestorage leukoreduction include a substantial reduction in transfusion reactions and transmission of cytomegalovirus infection. (*Evidence based, high evidence quality, strong recommendation*)
Irradiation		
Killick		▪ All patients undergoing treatment with immunosuppressive therapy (ATG or Alemtuzumab) should receive irradiated blood products. (*Grade 1C)*

2016		▪ All patients undergoing HSCT should receive irradiated blood products. (*Grade 1A*)
Platelet additive solution		
Estcourt 2016	BSCH	▪ In patients with a history of allergic transfusion reactions, apart from mild, use platelets suspended in PAS. If reactions continue or are severe, washed platelets (re- suspended in 100% PAS) may be required. (*1B)*

A AA: aplastic anemia, AABB; formerly American Association of Blood Banks, APC: Apheresis Platelet Concentrate , ASCO; American Society of Clinical Oncology, ATG: antithymocyte globulin, BCSH; British Committee for Standards in Hematology, CPB; cardiopulmonary bypass, DDAVP: desmopressin, DIC: Dissaminated intravascular coagulation, ECMO: Extra-Corporeal Membrane Oxygenation, HIT: heparin induced thrombocytopenia, HLA: human leucocyte antigen, HPA; human platelet antigen, HSCT: Hematopoietic stem cell transplantation, ICTMG; International Collaboration for Transfusion Medicine Guidelines, IUT; intrauterine transfusion, SSC of the ISTH; Scientific and Standardization Committee of the ISTH, MT; massive transfusion, NAIT ; Neonatal alloimmune thrombocytopenia, PAS; platelet additive solution, PTP; post transfusion purpura, TPO; thrombopoietin receptor, TXA; tranexamic acid, rFVIIa; recombinant factor VIIa, ITP; autoimmune thrombocytopenia, PAS; Platelet Additive Solution, PCM; platelet concentrate mixture, WHO; World Health Organization

**One guideline is not included in this table as it lacks recommendations with regard to platelet transfusion.