

Online Data Supplement

Table E1: Authors' definition of Cardiovascular Disease

Author	Definition of Cardiovascular disease
Almeida 2013	Arterial coronary artery disease, congestive heart failure, cerebrovascular disease, peripheral arterial disease
Blair 1986	Not discussed
Bush 1997	Patients undergoing elective aortic or infrainguinal arterial reconstruction
Carson 2011	history of ischaemic heart disease, electrocardiographic evidence of previous myocardial infarction, a history or presence of congestive heart failure or peripheral vascular disease, or a history of stroke or transient ischaemic attack
Carson 2013	ST segment elevation myocardial infarction, Non ST segment elevation myocardial infarction, Unstable angina (symptoms of cardiac ischemia at rest with at least one episode lasting 10 minutes AND ST-segment depression of 0.01 mV or more or transient [b30-minute] ST-segment elevation of 0.1 mV or more in two or more contiguous leads), OR prior documented coronary artery disease (myocardial infarction, percutaneous cardiac intervention, coronary artery bypass graft surgery), or age N55 with diabetes mellitus or peripheral arterial disease and no biomarker elevation Stable coronary artery disease undergoing a cardiac catheterization (presence of coronary artery disease (one cardiac artery with at least 70% obstruction by visual inspection based on cardiac catheterization or undergoing a percutaneous cardiac intervention,)during index admission
Cooper 2011	AMI was defined as ischaemic-type chest discomfort lasting 30 minutes and associated with a creatine kinase-MB (CK-MB) or cardiac troponin level above the upper limit of normal (determined locally).
Gregersen 2015	Charlson Comorbidity Index on ICD-10. If a patient was diagnosed with one of the first two boxes (myocardial infarct or congestive cardiac insufficiency/ I21; I22; I23; I50; I11.0; I13.0; I13.2)
Jairath 2015	History of ischaemic heart disease
Hebert 1999	primary or secondary ICU admission diagnosis of a cardiovascular disease, as well as those patients with cardiac disease as an important comorbid illness defined as New York Heart Association class III or IV. As a second step, we examined all patients who were known to have ischemic heart disease. The diagnosis most responsible for the patient's ICU admission was recorded. As many as three secondary diagnoses and up to eight separate comorbid conditions were identified. The cardiovascular disease category included all diagnoses related to ischemic heart disease (myocardial infarct, angina, congestive heart failure, and cardiogenic shock), rhythm disturbances, cardiac arrest, other forms of shock, uncontrolled hypertension, and cardiac and vascular surgical procedures such as abdominal aortic aneurysm repair and peripheral vascular surgical procedures.
Holst 2014	history of myocardial infarction, any history of stable or unstable angina pectoris, previous treatment with nitrates, percutaneous coronary intervention, coronary-artery bypass grafting or noncoronary vascular interventions, any history of chronic heart failure [defined as New York Heart Association class III or IV], or any history of cerebral infarction or transitory cerebral ischemia
Parker 2013	Hypertension Angina Previous myocardial infarction Previous congestive cardiac failure Other cardiac disease
Walsh 2013	Ischaemic heart disease was defined as evidence from the patient's records of a previous history of angina, previous myocardial infarction, or chronic cardiac failure at the time of randomization.

Table E2: Characteristics of all eligible blood transfusion trials not included in quantitative analysis

Author	Journal	Clinical Setting	Trigger	Total n	CV n (%)	Primary endpoint	Reason for exclusion
Bergamin 2014 Brazil (S)	Critical Care	Critical Care	R: 70g/l	73		28 day mortality	CVD not baseline characteristic
			L: 90g/l	63			
Blair 1986 UK (S)	British Journal of Surgery	GI haemorrhage	R: 80g/l or shock	26		Clotting, death	CVD not baseline characteristic
			L: 2 units	24			
Carson 1998 USA/Scotland (M)	Transfusion	Hip fracture patients	R: 80g/l or symptoms of anaemia	42	19 (45.2)	60 day mortality	no reply from authors
			L: 100g/l	42	19 (45.2)		
Colomo 2008 Spain (S)	Hepatology (abstract)	GI haemorrhage in cirrhosis	R: 70g/l	109		mortality	no further information available
			L: 90g/l	105			
Fan 2014 China (S)	Archives of Gerontology and Geriatrics	elective Total hip replacement	R: 80g/l or symptoms of anaemia	41	IHD: 9, BP: 52, CVA:4, CCF: 2	Postoperative Delirium (POD)	No reply from authors
			L: 100g/l	42	IHD: 10, BP: 57, CVA: 3, CCF: 3		
Fortune 1987 USA (S)	Journal of Trauma	Traumatic patients with class 3-4 haemorrhagic shock	R: hct near 30%	12		Metabolic stability	CVD not baseline characteristic
			L: hct near 40%	13			
Foss 2009 Denmark (S)	Transfusion	Hip fracture patients	R: 80g/l	60	28 (46.7)	Postoperative functional mobility	No reply from authors
			L: 100g/l	60	21 (35.0)		
Grover 2006 UK (S)	Vox Sanguinis	orthopaedic surgery	R: 80g/l	109	angina: 6 (5.5) MI: 6 (5.5)	Silent myocardial ischaemia	ECG abnormalities excluded
			L: 100g/l	109	angina: 8 (7.3) MI: 6 (5.5)		
Haberkern 1997 USA (M)	Blood	sickle cell surgery	R: conservative	110		Sickle cell events	pre-operative HbSS transfusion target
			L: aggressive	120			
			Not randomised	134			
Hebert 1995 Canada (M)	JAMA	Critical care	R: 70g/l	33	5 (15.2)	Feasibility Mortality	No reply from authors
			L: 90g/l	36	4 (11.1)		
Hochain 1996	Gut (abstract)	variceal bleeding	R: PCV 25	43		Rebleeding	CVD not mentioned
			L: PCV 32	47			
Park H 2008 South Korea (S)	Cancer Chemo and Pharm	Gastric oncology	R: 100g/l			Response Quality of Life	CVD not mentioned
			L: 120g/l				
Koshy 1988 USA (S)	NEJM	sickle cell pregnancy	R: as required	36		Perinatal mortality	HbSS transfusion target
			Prophylactic transfusion	36			
Liu 2015 China (S)	Chinese Medical Journal	Emergency surgery	R: illness severity score	33		Feasibility	Exc: patients with coronary heart disease
			L: standard care	32			
Lotke 1999 USA (S)	Journal of Arthroplasty	Total knee arthroplasty	R: 90g/l	62		Not explicit Hb, LOS, wellbeing	CVD not baseline characteristic

Author	Journal	Clinical Setting	Trigger	Total n	CV n (%)	Primary endpoint	Reason for exclusion
			L: 2 units starting in recovery room	65			
Mazza 2015 Brazil (M)		Critical Care	R: 70g/l	22	7 (31.8)	Effect of transfusion on lactate and SvO ₂	No reply from authors
			L: 90g/l	24	10 (41.7)		
Nielsen 2012	Transfusion medicine	Spinal surgery	R: 73g/l	25		subcutaneous oxygen tension	Exc: cardiac disease NYHA II or above
			L: 89g/l	23			
Nielsen 2014 Denmark (S)	BMC Anesthesiology	Elective hip revision	R: 73g/l	33	5 (15.1)	Timed Up and Go-test	No reply from authors
			L: 89g/l	33	7 (21.2)		
Palmer 1998 Scotland (S)	Transfusion Medicine (abstract)	hip fracture					abstract unavailable
Prick 2013 Netherlands (M)	BJOG	postpartum haemorrhage Hb 48-79g/l	R: no transfusion	262		Physical fatigue	Excluded ASA 2-4 patients
			L: transfusion	259			
Robertson 2014 USA (M)	JAMA	Traumatic brain injury	R: 70g/l	99		Glasgow Outcome Scale	CVD not baseline characteristic
			L: 100g/l	101			
So-Osman 2004 Netherlands (S)	Vox Sanguinis (abstract)	hip/knee surgery	unclear			Blood use	CVD not mentioned
So-Osman 2010 Netherlands (M)	Vox Sanguinis	Elective Total knee or hip replacement	R: stratified by risk	299	205 (68.6)	Hospital LOS	30 day mortality not measured
			L: standard care	304	211 (69.4)		
Villanueva 2013 Spain (S)	NEJM	Upper GI bleeding	R: 70g/l	444		Mortality at 45days	CVD not baseline characteristic, many CV patients excluded
			L: 90g/l	445			
Villarejo 1999 Spain (S)	Acta Gastroenterol Latinoam.	GI haemorrhage	R: hct 21%				CVD not mentioned
			L: hct 28%				
Webert 2008 Canada (M)	Transfusion	Leukaemia	R: 80g/l	29		Bleeding	CVD patients excluded
			L: 120g/l	31			
Weiss 1982 USA (S)	Lancet (letter)	Acute leukaemia	R: as needed	12		Marrow recovery	CVD not baseline characteristic
			L: 120g/l	12			
Wu 2011 China (S)	Intensive Care Medicine (abstract only)	liver transplant	R: 70g/l	112		30 day mortality	CVD not mentioned
			L: 100g/l	114			
Zheng 2013 China (S)	Experimental and Therapeutic Medicine	Orthopaedic surgery elderly patients	Standard	52		blood transfusion effectiveness	CVD patients excluded
			Goal directed	54			
Zygun 2009 UK (S)	Critical Care Medicine	traumatic brain injury	R: 8g/dl			Change in brain tissue oxygenation	CVD not baseline characteristic
			Mid: 9g/dl				
			L: 10g/dl				

Table E3: Patients receiving allogenic blood. Mean (SD) or Median (IQR) as quoted in original paper

	Restrictive trigger	Pts receiving blood	%	No. units transfused	Liberal trigger	Pts receiving blood	%	No. units transfused
Bush 1997	90g/l n=49	39	79.6	1.5 (1.7)	100g/l n=50	44	88.0	2.4 (2.5)
Carson 2011	80g/l, Sx anaemia n=1008	413	41.0	0 (0,1)	100g/l n=1007	973	96.6	2(1,2)
Carson 2013 Acute MI	80g/l n=55	15	27.3	0.49 (1.03)	100g/l n=55	52	94.5	1.58(1.13)
Cooper 2011	Hct <24% n=24	13	54.2	1.6 (2.0)	Hct <30% n=21	21	100.0	2.5 (1.3)
Parker	Sx anaemia n=70	11	15.7	0	100g/l n=67	67	100.0	2 (2,2)
Walsh	70g/l n=17	12	70.6	1.5 (0.25,3.5)	90g/l n=15	15	100.0	2 (1,8)

Table E4: Diagnosis of Cardiovascular events:

I: diagnosed by Investigator, C: diagnosed by Clinical team, U: unclear

	Blinded Y/N	Diagnosis
Almeida 2015 (I)	Y	Clinical symptoms suggestive of myocardial ischaemia with ≥ 1 : increase or decrease in cardiac troponin I (≥ 1 value $>99^{\text{th}}$ centile URL) ECG changes: new Q waves, ST-elevation, new LBBB image based evidence of new loss of viable myocardium
Bush 1997 (U)	?	New Q waves and/or CPK elevation (MB fraction $>5\text{ng/ml}$ and relative index >2.0)
Carson 2011 (I)	Y	Detection of rise or fall of cardiac troponin I with at least one value above the 99th percentile of the upper reference limit in the context of myocardial ischemia and at least one of the following: Symptoms of myocardial ischemia; New ECG changes indicative of ischemia (eg ST-T changes or new left bundle branch block [LBBB]) or development of pathological Q waves Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality Autopsy evidence of recent myocardial necrosis
Carson 2013 (I)	Y	Rise and/or fall of cardiac biomarkers (preferably troponin) together with evidence of myocardial ischemia and either symptoms of ischemia or electrocardiogram changes indicative of new ischemia. Unstable angina was defined as: (1) the absence of elevated cardiac biomarkers and (2) presence of ischemic symptoms or electrocardiogram changes indicative of ischemia or (3) chest pain or angina equivalent leading to a coronary artery intervention (e.g., coronary angioplasty) and (4) hospitalization. Congestive heart failure required at least one of the following symptoms or signs, new or worsening including: dyspnea at rest, orthopnea, or paroxysmal nocturnal dyspnea, AND radiological evidence of heart failure or worsening heart failure AND additional/increased therapy.
Cooper 2011 (C)	N	Recurrent ischemic chest discomfort, new ischemic electrocardiographic changes, and CK-MB increase above the upper limit of normal and increased by 50% over the previous value. For patients with percutaneous coronary intervention 24 hours previously, CK-MB >3 times the upper limit of normal and increased by $>50\%$ over the previous value was required. For patients with coronary artery bypass grafting surgery 24 hours previously, CK-MB >5 times the upper limit of normal and increased by $>50\%$ over the previous value was required. New or worsening HF was defined as 1 of the following occurring >6 hours after randomization: cardiogenic shock or a physician's decision to treat HF with an intravenous diuretic or intravenous vasoactive drug and evidence of pulmonary vascular congestion.
Hebert 1999 (I)	?	Unclear
Holst 2014 (I)	Y	Symptoms, electrocardiographic signs, or elevated biomarker levels resulting in an intervention
Parker 2013 (C)	N	Unclear
Walsh 2013 (C)	N	Troponin rise, new ECG change

Table E5: Adverse events – General. Mean (SD)

	Restrictive trigger	Change in MODS	Length of ICU stay (d) LOS Hospital (d)	In-hospital infections	Liberal trigger	MODS	Length of ICU stay (d) LOS Hospital (d)	In-hospital infections
Bush 1997	90g/l		4 (8) days 11 (9) days		100g/l		4 (4) days (p>0.6) 10 (6) days (p>0.6)	
Carson 2011 USA (n=1220) Canada (n=791)	80g/l, Sx anaemia		USA 4.0 (3.9) Canada 12.7 (9.5)				USA 3.7 (3.4) Canada 12.0 (9.3)	
Carson 2013 Acute MI	80g/l			2	100g/l			2
Cooper 2011	Hct <24%		4.3 (3.3) (CCU) 10.4 (7.2)		Hct <30%		3.4 (2.3) (CCU) 4.3 (3.3)	
Gregersen	97g/l		Hosp 7.8 (5.0)	13	113g/l		Hosp 8.4 (8.0)	24
Hebert 1998	70g/l	0.23 +/- 4.2	9.3 (9.7) 28.76 (19.5)		100g/l	1.3 +/- 4.4	10.4 (10.3) 30.6 (18.8)	
Parker	Sx anaemia			3	100g/l			5
Walsh	70g/l		36.5 (26.7) 53.3 (40.1)		90g/l		25.6 (18.1) 36.3 (28.3)	

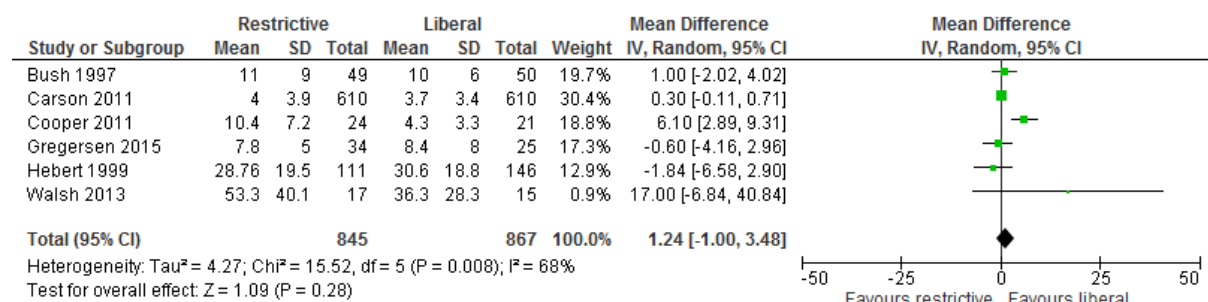


Figure E1: Forest plot with mean difference for hospital length of stay.

SEARCH STRATEGIES

CENTRAL

- #1 MeSH descriptor: [Erythrocyte Transfusion] explode all trees
- #2 MeSH descriptor: [Blood Transfusion] this term only
- #3 ((blood or erythrocyte* or "red cell*" or "red blood cell*" or RBC*) near/5 (transfus* or unit* or infus* or therap*))
- #4 ((red cell* or RBC* or erythrocyte* or red blood cell* or whole blood or transfus*) near/5 (use* or usage* or utiliz* or utilis* or requir* or need* or administ* or replac* or support* or strateg* or management or practic* or indicat* or criteri* or standard* or program*)):ab
- #5 ((red cell* or RBC* or erythrocyte* or blood or transfus*) and (use* or usage* or utiliz* or utilis* or requir* or need* or administ* or replac* or support* or strateg* or management or practic* or indicat* or criteri* or standard* or program*)):ti
- #6 (leukodeplet* or leukoreduc* or leucodeplet* or leukoreduc* or leukofiltrat* or leucofiltrat*):ti
- #7 ("allogeneic blood" or (unit* near/2 blood) or "allogenic blood" or (blood near/2 exposure) or "donor blood" or "blood product*" or "blood component*" or "blood support")
- #8 (hemotransfus* or haemotransfus* or hypertransfus* or hemotherap* or haemotherap*)
- #9 (red cell* or erythrocyte* or blood or RBC*) and transfus*:ti
- #10 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9
- #11 MeSH descriptor: [Blood Component Transfusion] this term only
- #12 MeSH descriptor: [Exchange Transfusion, Whole Blood] explode all trees
- #13 MeSH descriptor: [Plasma Exchange] explode all trees
- #14 MeSH descriptor: [Platelet Transfusion] explode all trees
- #15 MeSH descriptor: [Leukocyte Transfusion] explode all trees
- #16 #12 or #13 or #14 or #15
- #17 #11 not #16
- #18 ("red cell*" or "red blood cell*" or erythrocyte* or RBC*)
- #19 MeSH descriptor: [Erythrocytes] this term only
- #20 #18 or #19
- #21 #17 and #20
- #22 #10 or #21
- #23 MeSH descriptor: [Hematocrit] this term only
- #24 ((h?emoglobin or h?emocrit* or HB or HCT) near/5 (level* or concentration* or target* or maintain* or rais* or higher or lower or greater or above or below or equal or transfus*))
- #25 #23 or #24
- #26 #22 and #25
- #27 ((transfus* or "red cell*" or "red blood cell*" or RBC*) near/10 (trigger* or thresh*old* or target* or restrict* or liberal* or aggressive* or conservative* or prophylactic* or limit* or protocol* or policy or policies or practic* or standard*))
- #28 ((transfus* or "red cell*" or "red blood cell*" or RBC* or h?ematocrit*) and (level* or critical* or intensive* or h?emorrhag* or bleed*) or hypertransfus*):ti
- #29 #26 or #27 or #28 Publication Year from 2008 to 2014

MEDLINE (OVID)

- 1. randomized controlled trial.pt.
- 2. controlled clinical trial.pt.
- 3. randomi*.tw.
- 4. placebo.ab.
- 5. clinical trials as topic.sh.
- 6. randomly.ab.
- 7. groups.ab.
- 8. trial.ti.
- 9. or/1-8
- 10. exp animals/ not humans/
- 11. 9 not 10
- 12. BLOOD TRANSFUSION/
- 13. ERYTHROCYTE TRANSFUSION/

14. ((blood or erythrocyte* or red cell* or red blood cell* or RBC*) adj5 (transfus* or infus* or unit* or therap*)).ti,ab.
15. ((red cell* or RBC* or erythrocyte* or red blood cell* or whole blood or transfus*) adj5 (use* or usage* or utiliz* or utilis* or requir* or need* or administ* or replac* or support* or strateg* or management or practic* or indicat* or criteri* or standard* or program*)).ab.
16. ((red cell* or RBC* or erythrocyte* or blood or transfus*) and (use* or usage* or utiliz* or utilis* or requir* or need* or administ* or replac* or support* or strateg* or management or practic* or indicat* or criteri* or standard* or program*)).ti.
17. (allogeneic blood or (unit* adj2 blood) or allogenic blood or (blood adj2 exposure) or donor blood or blood product* or blood component* or blood support).ti,ab.
18. (hemotransfus* or haemotransfus* or hypertransfus* or hemotherap* or haemotherap*).tw.
19. (red cell* or erythrocyte* or blood or RBC*).tw. and transfus*.ti.
20. or/12-19
21. BLOOD COMPONENT TRANSFUSION/
22. EXCHANGE TRANSFUSION, WHOLE BLOOD/ or PLASMA EXCHANGE/ or PLATELET TRANSFUSION/ or exp LEUKOCYTE TRANSFUSION/
23. 21 not 22
24. ERYTHROCYTES/
25. (red cell* or red blood cell* or erythrocyte* or RBC*).tw.
26. 24 or 25
27. 23 and 26
28. 20 or 27
29. *HEMATOCRIT/
30. ((h?emoglobin or h?ematocrit* or HB or HCT) adj5 (level* or concentration* or target* or maintain* or rais* or higher or lower or greater or above or below or equal or transfus*)).tw.
31. 29 or 30
32. 28 and 31
33. ((transfus* or red cell* or red blood cell* or RBC*) adj10 (trigger* or thresh?old* or target* or restrict* or liberal* or aggressive* or conservative* or prophylactic* or limit* or protocol* or policy or policies or practice* or standard*)).tw.
34. (((transfus* or red cell* or red blood cell* or RBC* or h?ematocrit*) and (level* or critical* or intensive* or h?emorrhag* or bleed*)) or hypertransfus*).ti.
35. 32 or 33 or 34
36. 11 and 35

EMBASE (OVID)

1. Randomized Controlled Trial/
2. Randomization/
3. Single Blind Procedure/
4. Double Blind Procedure/
5. Crossover Procedure/
6. Placebo/
7. exp Clinical Trial/
8. Prospective Study/
9. (randomi* or double-blind* or single-blind* or RCT*).tw.
10. (random* adj2 (allocat* or assign* or divid* or receiv*)).tw.
11. (crossover* or cross over* or cross-over* or placebo*).tw.
12. ((treble or triple) adj blind*).tw.
13. or/1-12
14. Case Study/
15. case report*.tw.

16. (note or editorial).pt.
17. or/14-16
18. 13 not 17
19. (animal* or cat or cats or dog or dogs or pig or pigs or sheep or rabbit* or mouse or mice or rat or rats or feline or canine or porcine or ovine or murine).ti.
20. 18 not 19
21. limit 20 to embase
22. BLOOD TRANSFUSION/
23. ERYTHROCYTE TRANSFUSION/
24. ((blood or erythrocyte* or red cell* or red blood cell* or RBC*) adj5 (transfus* or infus* or unit* or therap*)).ti,ab.
25. ((red cell* or RBC* or erythrocyte* or red blood cell* or whole blood or transfus*) adj5 (use* or usage* or utiliz* or utilis* or requir* or need* or administ* or replac* or support* or strateg* or management or practic* or indicat* or criteri* or standard* or program*)).ab.
26. ((red cell* or RBC* or erythrocyte* or blood or transfus*) and (use* or usage* or utiliz* or utilis* or requir* or need* or administ* or replac* or support* or strateg* or management or practic* or indicat* or criteri* or standard* or program*)).ti.
27. (allogeneic blood or (unit* adj2 blood) or allogenic blood or (blood adj2 exposure) or donor blood or blood product* or blood component* or blood support).ti,ab.
28. (hemotransfus* or haemotransfus* or hypertransfus* or hemotherap* or haemotherap*).tw.
29. (red cell* or erythrocyte* or blood or RBC*).tw. and transfus*.ti.
30. 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29
31. BLOOD COMPONENT THERAPY/
32. GRANULOCYTE TRANSFUSION/ or LEUKOCYTE TRANSFUSION/ or LYMPHOCYTE TRANSFUSION/ or PLASMA TRANSFUSION/ or THROMBOCYTE TRANSFUSION/
33. 31 not 32
34. ERYTHROCYTE/
35. (red cell* or red blood cell* or erythrocyte* or RBC*).tw.
36. 34 or 35
37. 33 and 36
38. 30 or 37
39. *HEMATOCRIT/
40. ((h?emoglobin or h?ematocrit* or HB or HCT) adj5 (level* or concentration* or target* or maintain* or rais* or higher or lower or greater or above or below or equal or transfus*)).tw.
41. 39 or 40
42. 38 and 41
43. ((transfus* or red cell* or red blood cell* or RBC*) adj10 (trigger* or thresh?old* or target* or restrict* or liberal* or aggressive* or conservative* or prophylactic* or limit* or protocol* or policy or policies or practice* or standard*)).tw.
44. (((transfus* or red cell* or red blood cell* or RBC* or h?ematocrit*) and (level* or critical* or intensive* or h?emorrhag* or bleed*)) or hypertransfus*).ti.
45. 42 or 43 or 44
46. 21 and 45

CINAHL (EBSCOHost)

- S1 (MH "Blood Transfusion")
- S2 (MH "Erythrocyte Transfusion")
- S3 (erythrocyte* or red cell* or red blood cell* or blood or RBC*) N5 (transfus* or infus* or therap* or unit*)
- S4 AB ((red cell* or RBC* or erythrocyte* or red blood cell* or whole blood or transfus*) N5 (use* or usage* or utiliz* or utilis* or requir* or need* or administ* or replac* or support* or strateg* or management or practic* or indicat* or criteri* or standard* or program*))

S5 TI ((red cell* or RBC* or erythrocyte* or blood or transfus*) and (use* or usage* or utiliz* or utilis* or requir* or need* or administ* or replac* or support* or strateg* or management or practic* or indicat* or criteri* or standard* or program*))

S6 hemotransfus* or haemotransfus* or hemotherap* or haemotherap* or hypertransfus*

S7 TX (red cell* or erythrocyte* or blood or RBC*) and TI (transfus*)

S8 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7

S9 (MM "Hematocrit")

S10 TX ((hemoglobin or haemoglobin or hematocrit* or haematocrit* or HB or HCT) N5 (level* or concentration* or target* or maintain* or rais* or higher or lower or greater or above or below or equal or transfus*))

S11 S9 OR S10

S12 S8 AND S11

S13 TI ((transfus* or red cell* or red blood cell* or RBC* or haematocrit* or hematocrit*) and (level* or critical* or intensive* or haemorrhag* or hemorrhag* or bleed*))

S14 TX ((transfus* or "red cell*" or "red blood cell*" or RBC*) N10 (trigger* or threshold* or target* or restrict* or liberal* or aggressive* or conservative* or prophylactic* or limit* or protocol* or policy or policies or practice* or standard*))

S15 S12 OR S13 OR S14

S16 (MH Clinical Trials+)

S17 PT Clinical Trial

S18 TI ((controlled trial*) or (clinical trial*)) OR AB ((controlled trial*) or (clinical trial*))

S19 TI ((singl* blind*) OR (doubl* blind*) OR (trebl* blind*) OR (tripl* blind*) OR (singl* mask*) OR (doubl* mask*) OR (tripl* mask*)) OR AB ((singl* blind*) OR (doubl* blind*) OR (trebl* blind*) OR (tripl* blind*) OR (singl* mask*) OR (doubl* mask*) OR (tripl* mask*))

S20 TI randomi* OR AB randomi*

S21 MH RANDOM ASSIGNMENT

S22 TI ((phase three) or (phase III) or (phase three)) or AB ((phase three) or (phase III) or (phase three))

S23 (TI (random* N2 (assign* or allocat*))) OR (AB (random* N2 (assign* or allocat*)))

S24 MH PLACEBOS

S25 S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24

S26 S12 AND S25

PUBMED (epublications only)

#1 ("erythrocyte transfusion*" OR "red cell transfusion" OR "red cells" OR "red blood cells" OR "red blood cell transfusion" OR "blood transfusion*" OR RBCs OR "RBC transfusion*" OR hemotransfus* OR haemotransfus* OR hemotherap* OR haemotherap* OR hypertransfus*)

#2 ((hemoglobin OR haemoglobin OR haematocrit* OR hematocrit* OR HB OR HCT) AND (level* or concentration* OR target* OR maintain* OR rais* OR higher OR lower OR greater OR above or below OR equal OR transfus*))

#3 (random* OR blind* OR control group* OR placebo OR controlled trial OR controlled study OR trials OR systematic review OR meta-analysis OR metaanalysis OR literature OR medline OR cochrane OR embase) AND ((publisher[sb] OR inprocess[sb]) NOT pubstatusnihms)

#4 #1 AND #2 AND #3

LILACS

((tw:(transfused OR transfusing OR transfused OR hypertransfusion OR haemoglobin OR hemoglobin OR haematocrit OR hematocrit) AND (instance:"regional") AND (db:("LILACS") AND type of_study:("clinical_trials"))) AND (instance:"regional") AND (year_cluster:("2009" OR "2010" OR "2011" OR "2012" OR "2013" OR "2014"))

TRANSFUSION EVIDENCE LIBRARY

Subject Area: Blood Components/Red Cells

OR

All fields: trigger OR triggers OR threshold OR thresholds OR haemoglobin OR haemoglobin OR haematocrit OR hematocrit OR Hb OR HCT

WEB OF SCIENCE – CPCIS database

#1 TS=((("erythrocyte transfusion*" OR "red cell transfusion" OR "red cells" OR "red blood cells" OR "red blood cell transfusion" OR "blood transfusion*" OR RBCs OR "RBC transfusion*" OR hemotransfus* or haemotransfus* or hemotherap* or haemotherap* or hypertransfus*))

#2 TS=((hemoglobin or haemoglobin or hematocrit* or haematocrit* or HB or HCT) NEAR/1 (level* or concentration* or target* or maintain* or rais* or higher or lower or greater or above or below or equal or transfus*))

#3 #1 AND #2

#4 TS=((transfus* or "red cell*" or "red blood cell*" or RBC*) NEAR/5 (trigger* or threshold* or target* or restrict* or liberal* or aggressive* or conservative* or prophylactic* or limit* or protocol* or policy or policies or practice* or standard*))

#5 #3 OR #4

#6 TS=(randomi* OR randomly OR "random assignment" OR "random allocation" OR blind* OR "control group*" OR controlled trial OR "controlled study")

#7 #5 AND #6

Ongoing Trials:

ClinicalTrials.gov & WHO ICTRP

Search Terms/Title: randomized OR randomised OR randomly

Intervention: red cell transfusion OR RBC transfusion OR blood transfusion

Title: trigger OR threshold OR target OR restrictive OR liberal OR aggressive OR conservative OR prophylactic OR limit OR protocol OR policy OR policies OR practice OR standard OR hemoglobin OR hematocrit

ISRCTN & EUCTR [terms searched in combination and individually]

(red cell transfusion OR red blood cell transfusion OR RBC transfusion OR blood transfusion) AND (trigger OR threshold OR target OR restrictive OR liberal OR aggressive OR conservative OR prophylactic OR limit OR protocol OR policy OR policies OR practice OR standard OR hemoglobin OR hematocrit OR haemoglobin OR haematocrit)

Hong Kong Clinical Trials Registry [terms searched individually]

Disease Group: Blood and blood-forming organs OR Circulatory System

Title: randomized OR randomised OR transfusion