

**Patient Blood Management
Guidelines: Module 1**

**Critical
Bleeding
Massive
Transfusion**

Technical Report

Volume 2 – Appendixes

This volume presents appendixes to *Technical report on patient blood management in critical bleeding/massive transfusion: Volume 1 – Review of the evidence and evidence-based recommendations for clinical practice*

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Appendix A Literature searches

A1 Literature search – question 1

Question 1

In patients with critical bleeding requiring massive transfusion, what is the effect of variation of physiologic, biochemical and metabolic (including temperature) parameters on morbidity, mortality and transfusion rate?

Table A1.1 EMBASE.com search conducted 18 June 2009

#	Search	Results
#1	'blood transfusion'/exp	108,083
#2	'transfusion'/de	1,471
#3	#1 OR #2	109,379
#4	'bleeding'/de	92,392
#5	'bleeding tendency'/de	2,883
#6	#4 OR #5	94,927
#7	'postoperative complication'/exp	355,223
#8	'critical illness'/de	16,528
#9	#7 OR #8	371,243
#10	#6 AND #9	12,503
#11	'bleeding'/dm_co	21,672
#12	'bleeding tendency'/dm_co	311
#13	#10 OR #11 OR #12	28,691
#14	#3 AND #13	3,725
#15	'critical bleeding':ab,ti	49
#16	'severe bleeding':ab,ti	1,868
#17	'major bleeding':ab,ti OR 'major blood loss':ab,ti	2,679
#18	'major hemorrhagic complication':ab,ti OR 'major hemorrhagic complications':ab,ti	88
#19	'major haemorrhagic complication':ab,ti OR 'major haemorrhagic complications':ab,ti	24
#20	'massive blood loss':ab,ti OR 'life threatening bleeding':ab,ti	891
#21	'massive hemorrhage':ab,ti OR 'massive haemorrhage':ab,ti	1,963
#22	critical:ti AND bleeding:ti	52
#23	#14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22	10,940
#24	'blood transfusion'/de	58,576
#25	#2 AND #4	167
#26	#24 OR #25	58,738
#27	massive:ab,ti	57,292
#28	#26 AND #27	1,658

#	Search	Results
#29	'massive transfusion':de	3
#30	'massive blood transfusion':de	28
#31	'massive transfusion protocol':de	2
#32	('massive' NEAR/3 'transfusion'):ab,ti OR ('massive' NEAR/3 'transfusions'):ab,ti	1,168
#33	'massive infusion':ab,ti OR 'massively transfused':ab,ti	111
#34	'massive bleeding':ab,ti	2,616
#35	'massive haemorrhage':ab,ti OR 'massive hemorrhage':ab,ti	3,956
#36	#28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35	8,123
#37	#23 OR #36	16,760
#38	'monitoring'/exp	238,408
#39	'physiology'/de	703,569
#40	'pathophysiology'/de	473,040
#41	'hemodynamics'/de	103,241
#42	'pulse rate'/de	12,605
#43	'blood pressure'/exp	268,219
#44	'heart rate'/exp	133,761
#45	'body temperature'/exp	34,199
#46	'thermoregulation'/exp	33,880
#47	'temperature'/de	123,277
#48	'hypothermia'/de	19,473
#49	'body temperature disorder'/de	232
#50	'metabolism'/de	981,908
#51	'metabolic regulation'/exp	82,443
#52	'metabolic balance'/de	556
#53	'fluid balance'/de	5,253
#54	'urine volume'/de	6,470
#55	'biochemistry'/de	31,758
#56	'chemical analysis'/de	53,707
#57	'blood chemistry'/exp	26,875
#58	'metabolic effects':de	390
#59	'physiologic parameters':ab,ti OR 'physiological parameters':ab,ti	4,327
#60	'physiologic effects':ab,ti OR 'physiological effects':ab,ti	6,495
#61	'biochemical parameters':ab,ti OR 'biochemical effects':ab,ti	11,549
#62	'metabolic parameters':ab,ti OR 'metabolic effects':ab,ti	10,657
#63	physiologic*:ti OR biochemical:ti OR metabolic:ti AND parameters:ti	3,484
#64	#38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63	2,708,038

#	Search	Results
#65	#37 AND #64	1,817
#66	'adverse outcome'/exp OR 'outcome assessment'/exp OR 'morbidity'/exp OR 'mortality'/exp OR morbidity:ab,ti OR incidence:ab,ti OR prevalence:ab,ti OR occurrence:ab,ti OR mortality:ab,ti OR death:ab,ti OR survival:ab,ti	1,935,770
#67	#65 AND #66	633
#68	'quality of life'/exp OR qol:ab,ti OR 'quality of life':ab,ti OR 'quality of wellbeing':ab,ti OR 'health related quality':ab,ti OR hrqol:ab,ti OR qaly*:ab,ti OR 'quality adjusted':ab,ti OR 'adjusted life':ab,ti	160,735
#69	#65 AND #68	22
#70	'blood component therapy'/exp AND ('dose response'/exp OR 'drug dose'/exp) OR 'fresh frozen plasma'/exp/dd_do OR 'recombinant erythropoietin'/exp/dd_do OR 'transfusion frequency':ab,ti OR ('frequency' NEAR/5 'transfusion'):ab,ti OR ('frequency' NEAR/5 'transfusions'):ab,ti OR 'transfusion rate':ab,ti OR 'transfusion rates':ab,ti OR ('rate' NEAR/5 'transfusion'):ab,ti OR ('rates' NEAR/5 'transfusion'):ab,ti OR 'transfusion requirement':ab,ti OR 'transfusion requirements':ab,ti OR 'transfusion indication':ab,ti OR 'transfusion indications':ab,ti OR ('indications' NEAR/5 'transfusion'):ab,ti OR ('indications' NEAR/5 'transfusions'):ab,ti OR ('indication' NEAR/5 'transfusion'):ab,ti OR ('indication' NEAR/5 'transfusions'):ab,ti OR 'transfusion interval':ab,ti OR 'transfusion intervals':ab,ti OR ('need' NEAR/3 'transfusion'):ab,ti OR ('need' NEAR/3 'transfusions'):ab,ti OR 'transfusion need':ab,ti OR 'transfusion needs':ab,ti OR ('dose' NEAR/3 'transfusion'):ab,ti OR ('dose' NEAR/3 'transfusions'):ab,ti OR ('dose' NEAR/3 'transfused'):ab,ti OR ('transfusions' NEAR/3 'dose'):ab,ti OR 'transfusion dose':ab,ti OR ('transfused' NEAR/3 'dose'):ab,ti OR 'platelet dose':ab,ti OR ('dose' NEAR/3 'platelets'):ab,ti OR (dose:ab,ti AND transfus*:ab,ti)	17,449
#71	#65 AND #70	152
#72	#67 OR #69 OR #71	727

Table A1.2 Cochrane library database search conducted 19 June 2009

ID	Search	Results
#1	MeSH descriptor Blood Transfusion explode all trees	2,628
#2	MeSH descriptor Hemorrhage explode all trees	7,284
#3	MeSH descriptor Critical Illness , this term only	712
#4	MeSH descriptor Critical Care , this term only	617
#5	MeSH descriptor Postoperative Complications , this term only	10,793
#6	(#3 OR #4 OR #5)	11,991
#7	(#2 AND #6)	888
#8	MeSH descriptor Postoperative Hemorrhage , this term only	485
#9	MeSH descriptor Blood Loss, Surgical , this term only	1,399
#10	(#7 OR #8 OR #9)	2,369
#11	(#1 AND #10)	605
#12	(critical NEAR/1 bleeding)	3
#13	"severe bleeding"	162
#14	"major bleeding" OR "Major blood loss"	892
#15	"major hemorrhagic complication" OR "major hemorrhagic complications"	17

ID	Search	Results
#16	"major haemorrhagic complication" OR "major haemorrhagic complications"	9
#17	"massive blood loss" OR "life threatening bleeding"	31
#18	"massive hemorrhage" OR "massive haemorrhage"	17
#19	(critical AND bleeding):ti	4
#20	(#11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19)	1,704
#21	MeSH descriptor Blood Transfusion , this term only	1,519
#22	(massive)	599
#23	(#21 AND #22)	24
#24	(massive NEAR/3 transfusion*)	20
#25	"massive infusion" OR "massively transfused"	3
#26	(massive NEAR/1 (bleeding OR haemorrhage OR hemorrhage))	47
#27	(#23 OR #24 OR #25 OR #26)	79
#28	(#20 OR #27)	1,757
#29	MeSH descriptor Monitoring, Physiologic explode all trees	6,471
#30	MeSH descriptor Physiological Phenomena explode all trees	72,701
#31	MeSH descriptor Biochemical Phenomena explode all trees	10,154
#32	MeSH descriptor Metabolic Phenomena , this term only	1
#33	MeSH descriptor Hemodynamics , this term only	7,949
#34	MeSH descriptor Blood Pressure , this term only	18,835
#35	MeSH descriptor Heart Rate , this term only	13,287
#36	MeSH descriptor Metabolism , this term only	92
#37	MeSH descriptor Body Temperature Changes explode all trees	1,617
#38	"physiologic parameters" OR "physiological parameters"	338
#39	"physiologic effects" OR "physiological effects"	629
#40	"biochemical parameters" OR "biochemical effects"	878
#41	"metabolic parameters" OR "metabolic effects"	1,488
#42	((physiologic* OR biochemical OR metabolic) AND parameters):ti	225
#43	(#29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42)	104,147
#44	(#28 AND #43)	234
#45	MeSH descriptor Morbidity explode all trees	8,475
#46	MeSH descriptor Mortality explode all trees	7,946
#47	(morbidity OR incidence OR prevalence OR occurrence)	62,784
#48	(mortality OR death OR survival)	55,325
#49	(#45 OR #46 OR #47 OR #48)	99,307
#50	(#44 AND #49)	122
#51	MeSH descriptor Quality of Life , this term only	9,425
#52	MeSH descriptor Quality-Adjusted Life years , this term only	2,062

ID	Search	Results
#53	(qol OR "quality of life" OR "quality of wellbeing")	21,521
#54	"health related quality" or hrqol	2,898
#55	(qaly* or "quality adjusted" or "adjusted life")	3,802
#56	(#51 OR #52 OR #53 OR #54 OR #55)	23,436
#57	(#44 AND #56)	4
#58	MeSH descriptor Blood Component Transfusion explode all trees with qualifier: MT	99
#59	(frequency NEAR/5 transfusion*)	84
#60	(rate* NEAR/5 transfusion*)	324
#61	"transfusion requirement" OR "transfusion requirements"	949
#62	(indication* NEAR/5 transfusion*)	45
#63	"transfusion interval" OR "transfusion intervals"	13
#64	(need NEAR/3 transfusion*) OR "transfusion needs"	623
#65	(dose NEAR/3 transfus*)	86
#66	"platelet dose" OR (dose NEAR/3 platelets)	185
#67	(dose and transfus*):ti	72
#68	(#58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65 OR #66 OR #67)	2,061
#69	(#44 AND #68)	62
#70	(#50 OR #57 OR #69)	163

Table A1.3 PreMedline search conducted 19 June 2009

#	Query	Results
#59	Search #42 OR #47 OR #58	17
#60	Select 17 document(s)	17
#58	Search #38 AND #57	7
#57	Search #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56	33,353
#56	Search dose[ti] AND transfus*[ti]	128
#55	Search "platelet dose"[tw] OR (dose[tw] AND platelets[tw])	8,937
#54	Search dose[tw] AND transfus*[tw]	5,532
#53	Search (need[tw] AND transfusion*[tw]) OR "transfusion needs"[tw]	5,343
#52	Search "transfusion interval"[tw] OR "transfusion intervals"[tw]	34
#51	Search indication*[tw] AND transfusion*[tw]	2,616
#50	Search "transfusion requirement"[tw] OR "transfusion requirements"[tw]	3,107
#49	Search rate*[tw] AND transfusion*[tw]	12,067
#48	Search frequency[tw] AND transfusion*[tw]	2,776
#47	Search #38 AND #46	0
#46	Search #43 OR #44 OR #45	118,552
#45	Search qaly*[tw] or "quality adjusted"[tw] or "adjusted life"[tw]	6,325
#44	Search "health related quality"[tw] or hrqol[tw]	11,507

#	Query	Results
#43	Search qol[tw] OR "quality of life"[tw] OR "quality of wellbeing"[tw]	114,397
#42	Search #38 AND #41	14
#41	Search #39 OR #40	1,901,546
#40	Search mortality[tw] OR death[tw] OR survival[tw]	1,159,420
#39	Search morbidity[tw] OR incidence[tw] OR prevalence[tw] OR occurrence[tw]	966,795
#38	Search #21 AND #37	38
#37	Search #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36	4,110,751
#36	Search metabolism[tw]	3,422,387
#35	Search "urine output"[tw]	3,116
#34	Search "fluid balance"[tw]	3,085
#33	Search hypothermia[tw]	31,617
#32	Search "body temperature"[tw]	60,771
#31	Search "heart rate"[tw]	163,977
#30	Search "blood pressure"[tw]	300,212
#29	Search "pulse rate"[tw]	4,650
#28	Search hemodynamics[tw]	119,919
#27	Search monitoring[tw]	289,919
#26	Search (physiologic*[tw] OR biochemical[tw] OR metabolic[tw]) AND parameters[tw]	55,492
#25	Search "metabolic parameters"[tw] OR "metabolic effects"[tw]	11,388
#24	Search "biochemical parameters"[tw] OR "biochemical effects"[tw]	10,372
#23	Search "physiologic effects"[tw] OR "physiological effects"[tw]	6,487
#22	Search "physiologic parameters"[tw] OR "physiological parameters"[tw]	4,110
#21	Search #18 OR #19 OR #20	570
#20	Search #17 AND pubmednotmedline[sb]	90
#19	Search #17 AND in process[sb]	302
#18	Search #17 NOT (medline[SB] OR oldmedline[sb])	570
#17	Search #9 OR #16	15,398
#16	Search #10 OR #11 OR #12 OR #13 OR #15	11,332
#15	Search massive[tw] AND haemorrhage[tw]	1,183
#14	Search #10 OR #11 OR #12 OR #13 OR #14	0
#13	Search massive[tw] AND hemorrhage[tw]	7,716
#12	Search massive[tw] AND bleeding[tw]	4,967
#11	Search "massive infusion"[tw] OR "massively transfused"[tw]	102
#10	Search massive[tw] AND transfusion*[tw]	2,319
#9	Search #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	6,332
#8	Search critical[title] AND bleeding[title]	44
#7	Search "massive hemorrhage"[tw] OR "massive haemorrhage"[tw]	1,858

#	Query	Results
#6	Search "massive blood loss"[tw] OR "life threatening bleeding"[tw]	370
#5	Search "major haemorrhagic complication"[tw] OR "major haemorrhagic complications"[tw]	23
#4	Search "major hemorrhagic complication"[tw] OR "major hemorrhagic complications"[tw]	74
#3	Search "major bleeding"[tw] OR "Major blood loss"[tw]	2,415
#2	Search "severe bleeding"[tw]	1,628
#1	Search "critical bleeding"[tw]	33

Table A1.4 CINAHL search conducted 19 June 2009

#	Query	Results
S72	S51 or S57 or S71	332
S71	S45 and S70	15
S70	S58 or S59 or S60 or S61 or S62 or S63 or S64 or S65 or S66 or S67 or S68 or S69	807
S69	TI (dose and transfus*)	7
S68	TI (dose N3 platelets) or AB (dose N3 platelets)	3
S67	TI ("platelet dose") or AB ("platelet dose")	3
S66	TI (dose N3 transfus*) or AB (dose N3 transfus*)	14
S65	TI ("transfusion needs") or AB ("transfusion needs")	25
S64	TI (need N3 transfusion*) or AB (need N3 transfusion*)	235
S63	TI ("transfusion interval" OR "transfusion intervals") or AB ("transfusion interval" OR "transfusion intervals")	4
S62	TI (indication* N5 transfusion*) or AB (indication* N5 transfusion*)	34
S61	TI ("transfusion requirement" OR "transfusion requirements") or AB ("transfusion requirement" OR "transfusion requirements")	255
S60	TI (rate* N5 transfusion*) or AB (rate* N5 transfusion*)	168
S59	TI (frequency N5 transfusion*) or AB (frequency N5 transfusion*)	19
S58	(MH "Blood Component Transfusion+/MT")	143
S57	S45 and S56	11
S56	S52 or S53 or S54 or S55	37,309
S55	TI (qaly* or "quality adjusted" or "adjusted life") or AB (qaly* or "quality adjusted" or "adjusted life")	832
S54	TI ("health related quality" or hrqol) or AB ("health related quality" or hrqol)	3,424
S53	TI (qol OR "quality of life" OR "quality of wellbeing") or AB (qol OR "quality of life" OR "quality of wellbeing")	23,709
S52	(MH "Quality of Life+")	26,826
S51	S45 and S50	319
S50	S46 or S47 or S48 or S49	151,997
S49	TI (mortality OR death OR survival) or AB (mortality OR death OR survival)	72,079
S48	TI (morbidity OR incidence OR prevalence OR occurrence) or AB (morbidity OR incidence OR prevalence OR occurrence)	78,574

#	Query	Results
S47	(MH "Mortality+")	18,717
S46	(MH "Morbidity+")	27,983
S45	S30 and S44	786
S44	S31 or S32 or S33 or S34 or S35 or S36 or S37 or S38 or S39 or S40 or S41 or S42	130,278
S43	TI (physiologic* OR biochemical OR metabolic) AND parameters	0
S42	TI ("metabolic parameters" OR "metabolic effects") or AB ("metabolic parameters" OR "metabolic effects")	475
S41	TI ("biochemical parameters" OR "biochemical effects") or AB ("biochemical parameters" OR "biochemical effects")	262
S40	TI ("physiologic effects" OR "physiological effects") or AB ("physiologic effects" OR "physiological effects")	550
S39	TI ("physiologic parameters" OR "physiological parameters") or AB ("physiologic parameters" OR "physiological parameters")	345
S38	(MH "Body Temperature Changes+")	4,109
S37	(MH "Metabolism")	1,258
S36	(MH "Heart Rate")	8,122
S35	(MH "Blood Pressure")	8,490
S34	(MH "Hemodynamics")	3,893
S33	(MH "Biochemical Phenomena+")	9,764
S32	(MH "Physiological Processes+")	91,495
S31	(MH "Monitoring, Physiologic+")	27,608
S30	S22 or S29	5,811
S29	S25 or S26 or S27 or S28	5,201
S28	TI (massive N1 (bleeding OR haemorrhage OR hemorrhage)) or AB (massive N1 (bleeding OR haemorrhage OR hemorrhage))	5,121
S27	TI ("massive infusion" OR "massively transfused") or AB ("massive infusion" OR "massively transfused")	10
S26	TI massive N3 transfusion* or AB massive N3 transfusion*	88
S25	S23 and S24	74
S24	TI massive or AB massive	1,907
S23	(MH "Blood Transfusion")	3,481
S22	S13 or S14 or S15 or S16 or S17 or S18 or S19 or S20 or S21	734
S21	TI critical AND bleeding	11
S20	TI ("massive hemorrhage" OR "massive haemorrhage") or AB ("massive hemorrhage" OR "massive haemorrhage")	34
S19	TI ("massive blood loss" OR "life threatening bleeding") or AB ("massive blood loss" OR "life threatening bleeding")	48
S18	TI ("major haemorrhagic complication" OR "major haemorrhagic complications") or AB ("major haemorrhagic complication" OR "major haemorrhagic complications")	1
S17	TI ("major hemorrhagic complication" OR "major hemorrhagic complications") or AB ("major hemorrhagic complication" OR "major hemorrhagic complications")	1

#	Query	Results
S16	TI ("major bleeding" OR "Major blood loss") or AB ("major bleeding" OR "Major blood loss")	282
S15	TI "severe bleeding" or AB "severe bleeding"	75
S14	TI critical N1 bleeding or AB critical N1 bleeding	3
S13	S1 and S12	299
S12	S9 or S10 or S11	1,822
S11	(MH "Blood Loss, Surgical")	617
S10	(MH "Postoperative Hemorrhage")	498
S9	S2 and S8	1,371
S8	S3 or S4 or S5 or S6 or S7	45,082
S7	(MH "Postoperative Complications+")	21,486
S6	(MH "Critical Care Nursing+")	15,461
S5	(MH "Critical Care")	5,723
S4	(MH "Critically Ill Patients")	4,070
S3	(MH "Critical Illness")	2,210
S2	(MH "Hemorrhage+")	11,980
S1	(MH "Blood Transfusion+")	5,082

Table A1.5 AMI search conducted 19 June 2009

Set	Search terms	Records
#26	(((TI = (massive %1 (bleeding OR haemorrhage OR hemorrhage)) OR AB = (massive %1 (bleeding OR haemorrhage OR hemorrhage))) OR (TI = ("massive infusion" OR "massively transfused") OR AB = ("massive infusion" OR "massively transfused"))) OR (TI = (massive %3 transfusion ^a) OR AB = (massive %3 transfusion ^a)) OR (((TI = (massive) OR AB = (massive)) AND ((MH_PHRASE = "Blood Transfusion"))))) OR (((TI = (critical AND bleeding)) OR (TI = ("massive hemorrhage" OR "massive haemorrhage") OR AB = ("massive hemorrhage" OR "massive haemorrhage"))) OR (TI = ("massive blood loss" OR "life threatening bleeding") OR AB = ("massive blood loss" OR "life threatening bleeding"))) OR (TI = ("major haemorrhagic complication" OR "major haemorrhagic complications") OR AB = ("major haemorrhagic complication" OR "major haemorrhagic complications"))) OR (TI = ("major bleeding" OR "Major blood loss") OR AB = ("major bleeding" OR "Major blood loss"))) OR (TI = ("severe bleeding") OR AB = ("severe bleeding"))) OR (TI = (critical %1 bleeding) OR AB = (critical %1 bleeding)) OR (((((MH_PHRASE = "Blood Loss, Surgical")) OR ((MH_PHRASE = "Postoperative Hemorrhage")))) AND ((MH_PHRASE = "Blood Transfusion"))))))	48
#25	((TI = (massive %1 (bleeding OR haemorrhage OR hemorrhage)) OR AB = (massive %1 (bleeding OR haemorrhage OR hemorrhage))) OR (TI = ("massive infusion" OR "massively transfused") OR AB = ("massive infusion" OR "massively transfused"))) OR (TI = (massive %3 transfusion ^a) OR AB = (massive %3 transfusion ^a)) OR (((TI = (massive) OR AB = (massive)) AND ((MH_PHRASE = "Blood Transfusion")))))	21
#24	TI = (massive %1 (bleeding OR haemorrhage OR hemorrhage)) OR AB = (massive %1 (bleeding OR haemorrhage OR hemorrhage))	11
#23	TI = ("massive infusion" OR "massively transfused") OR AB = ("massive infusion" OR "massively transfused")	1
#22	TI = (massive %3 transfusion ^a) OR AB = (massive %3 transfusion ^a)	9

Set	Search terms	Records
#21	((TI = (massive) OR AB = (massive)) AND ((MH_PHRASE = "Blood Transfusion")))	4
#20	TI = (massive) OR AB = (massive)	237
#19	((TI = (critical AND bleeding)) OR (TI = ("massive hemorrhage" OR "massive haemorrhage") OR AB = ("massive hemorrhage" OR "massive haemorrhage")) OR (TI = ("massive blood loss" OR "life threatening bleeding") OR AB = ("massive blood loss" OR "life threatening bleeding")) OR (TI = ("major haemorrhagic complication" OR "major haemorrhagic complications") OR AB = ("major haemorrhagic complication" OR "major haemorrhagic complications")) OR (TI = ("major bleeding" OR "Major blood loss") OR AB = ("major bleeding" OR "Major blood loss")) OR (TI = ("severe bleeding") OR AB = ("severe bleeding")) OR (TI = (critical %1 bleeding) OR AB = (critical %1 bleeding)) OR (((((MH_PHRASE = "Blood Loss, Surgical")) OR ((MH_PHRASE = "Postoperative Hemorrhage")))) AND ((MH_PHRASE = "Blood Transfusion"))))	31
#18	TI = (critical AND bleeding)	1
#17	TI = ("massive hemorrhage" OR "massive haemorrhage") OR AB = ("massive hemorrhage" OR "massive haemorrhage")	3
#16	TI = ("massive blood loss" OR "life threatening bleeding") OR AB = ("massive blood loss" OR "life threatening bleeding")	4
#15	TI = ("major haemorrhagic complication" OR "major haemorrhagic complications") OR AB = ("major haemorrhagic complication" OR "major haemorrhagic complications")	1
#14	TI = ("major hemorrhagic complication" OR "major hemorrhagic complications") OR AB = ("major hemorrhagic complication" OR "major hemorrhagic complications")	0
#13	TI = ("major bleeding" OR "Major blood loss") OR AB = ("major bleeding" OR "Major blood loss")	14
#12	TI = ("severe bleeding") OR AB = ("severe bleeding")	5
#11	TI = (critical %1 bleeding) OR AB = (critical %1 bleeding)	1
#10	(((((MH_PHRASE = "Blood Loss, Surgical")) OR ((MH_PHRASE = "Postoperative Hemorrhage")))) AND ((MH_PHRASE = "Blood Transfusion")))	5
#9	((MH_PHRASE = "Blood Loss, Surgical")) OR ((MH_PHRASE = "Postoperative Hemorrhage"))	35
#8	(MH_PHRASE = "Blood Loss, Surgical")	30
#7	(MH_PHRASE = "Postoperative Hemorrhage")	5
#6	(((((MH_PHRASE = "Postoperative Complications")) OR ((MH_PHRASE = "Critical Illness")))) AND (MH_PHRASE = "Hemorrhage"))	0
#5	((MH_PHRASE = "Postoperative Complications")) OR ((MH_PHRASE = "Critical Illness"))	573
#4	(MH_PHRASE = "Postoperative Complications")	378
#3	(MH_PHRASE = "Critical Illness")	196
#2	MH_PHRASE = "Hemorrhage"	13
#1	(MH_PHRASE = "Blood Transfusion")	179

a The search was conducted using Informat online platform on 19 June 2009

A2 Literature search – question 2

Question 2

In patients undergoing massive transfusion, does the dose, timing and ratio (algorithm) of red blood cells (RBCs) to blood component therapy (fresh frozen plasma [FFP], platelets, cryoprecipitate or fibrinogen concentrate) influence morbidity, mortality and transfusion rate? (Intervention foreground question)

Table A2.1 EMBASE.com search conducted 22 June 2009

#	Query	Results
#1	"blood transfusion"	108,113
#2	Transfusion	1,471
#3	#1 OR #2	109,409
#4	Bleeding	92,447
#5	"bleeding tendency"	2,883
#6	#4 OR #5	94,982
#7	"postoperative complication"	355,489
#8	"critical illness"	16,537
#9	#7 OR #8	371,518
#10	#6 AND #9	12,514
#11	Bleeding	21,688
#12	"bleeding tendency"	311
#13	#10 OR #11 OR #12	28,710
#14	#3 AND #13	3,725
#15	"critical *1 bleeding"	49
#16	"severe bleeding"	1,870
#17	"major bleeding" OR "Major blood loss"	2,680
#18	"major hemorrhagic complication" OR "major hemorrhagic complications"	88
#19	"major haemorrhagic complication" OR "major haemorrhagic complications"	24
#20	"massive blood loss" OR "life threatening bleeding"	891
#21	"massive hemorrhage" OR "massive haemorrhage"	1,963
#22	critical AND bleeding	52
#23	#14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22	10,943
#24	"blood transfusion"	58,594
#25	#2 AND #4	167
#26	#24 OR #25	58,756
#27	massive	57,324
#28	#26 AND #27	1,660
#29	"massive transfusion"	3
#30	"massive blood transfusion"	28
#31	"massive transfusion protocol"	2

#	Query	Results
#32	"massive *3 transfusion" OR "massive *3 transfusions"	1,170
#33	"massive infusion" OR "massively transfused"	112
#34	"massive *1 bleeding"	2,616
#35	"massive *1 haemorrhage" OR "massive *1 hemorrhage"	3,957
#36	#28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35	8,126
#37	#23 OR #36	16,766
#38	algorithm	86,528
#39	time	359,347
#40	algorithm* OR algorithym OR algorism	78,559
#41	ratio OR ratios	512,091
#42	timing OR interval OR intervals	397,071
#43	"early *1 use" OR immediate	120,775
#44	#38 OR #39 OR #40 OR #41 OR #42 OR #43	1,373,930
#45	#37 AND #44	1,390,696
#46	"blood component therapy"	42,618
#47	"blood component" OR "blood components"	4,114
#48	"blood product" OR "blood products"	6,903
#49	"transfusion product" OR "transfusion products"	83
#50	#46 OR #47 OR #48 OR #49	2,456
#51	#45 AND #50	51,531
#52	"fresh frozen plasma"	3,850
#53	plasma	49,859
#54	"plasma transfusion"	1,482
#55	"fresh frozen plasma" OR FFP	3,540
#56	"plasma transfusion"	238
#57	"plasma infusion" OR "serum transfusion"	386
#58	#52 OR #53 OR #54 OR #55 OR #56 OR #57	262
#59	#45 AND #58	56,413
#60	thrombocyte	53,447
#61	"thrombocyte concentrate"	1,757
#62	"thrombocyte transfusion"	6,552
#63	platelet* OR thrombocyte*	146,108
#64	#60 OR #61 OR #62 OR #63	140
#65	#45 AND #64	160,718
#66	cryoprecipitate	1,124
#67	cryoprecipitate	1,514
#68	#66 OR #67	295
#69	#45 AND #68	2,219

#	Query	Results
#70	fibrinogen	33,658
#71	fibrinogen OR "factor 1" OR "factor I"	69,201
#72	"9001 32 5"	33,668
#73	#70 OR #71 OR #72	82,423
#74	#45 AND #73	71
#75	#59 OR #65 OR #69 OR #74	396
#76	"erythrocyte volume"	1,458
#77	"erythrocyte concentrate"	2,383
#78	"erythrocyte transfusion"	7,201
#79	"packed *2 cell" OR "packed *2 cells"	5,750
#80	"packed erythrocyte" OR "packed erythrocytes"	244
#81	"erythrocyte concentrate" OR "red *1 cell concentrate"	246
#82	PRBC OR RBC	13,921
#83	#76 OR #77 OR #78 OR #79 OR #80 OR #81 OR #82	27,870
#84	#75 AND #83	88
#85	#51 OR #84	279
#86	"adverse outcome"	1,433
#87	"outcome assessment"	67,914
#88	morbidity	110,864
#89	mortality	389,349
#90	comorbidity	63,737
#91	morbidity OR incidence OR prevalence OR occurrence	973,028
#92	mortality OR death OR survival	966,804
#93	#86 OR #87 OR #88 OR #89 OR #90 OR #91 OR #92	1,974,451
#94	#85 AND #93	130
#95	"quality of life"	133,290
#96	qol OR "quality of life" OR "quality of wellbeing"	100,993
#97	"health related quality" or hrqol	12,812
#98	qaly* or "quality adjusted" or "adjusted life"	5,017
#99	#95 OR #96 OR #97 OR #98	160,883
#100	#85 AND #99	2
#101	"blood component therapy"	42,618
#102	"dose response"	320,931
#103	"drug dose"	179,559
#104	#102 OR #103	475,235
#105	#101 AND #104	5,375
#106	"fresh frozen plasma"	30
#107	"recombinant erythropoietin"	2,058

#	Query	Results
#108	"transfusion frequency"	39
#109	"frequency *5 transfusion" OR "frequency *5 transfusions"	339
#110	"transfusion rate" OR "transfusion rates"	870
#111	"rate *5 transfusion" OR "rates *5 transfusion"	622
#112	"transfusion requirement" OR "transfusion requirements"	3,316
#113	"transfusion indication" OR "transfusion indications"	40
#114	"indications *5 transfusion" OR "indications *5 transfusions"	380
#115	"indication *5 transfusion" OR "indication *5 transfusions"	149
#116	"transfusion interval" OR "transfusion intervals"	43
#117	"need *3 transfusion" OR "need *3 transfusions"	2,424
#118	"transfusion need" OR "transfusion needs"	338
#119	"dose *3 transfusion" OR "dose *3 transfusions"	95
#120	"dose *3 transfused" OR "transfusions *3 dose"	72
#121	"transfusion dose" OR "transfused *3 dose"	39
#122	"platelet dose" OR "dose *3 platelets"	85
#123	dose and transfus*	139
#124	#105 OR #106 OR #107 OR #108 OR #109 OR #110 OR #111 OR #112 OR #113 OR #114 OR #115 OR #116 OR #117 OR #118 OR #119 OR #120 OR #121 OR #122 OR #123	14,832
#125	#85 AND #124	130
#126	#94 OR #100 OR #125	166

Table A2.2 Cochrane library: search conducted 19 June 2009

#	Query	Results
#1	Blood Transfusion	2,682
#2	Hemorrhage	7,432
#3	Critical Illness	1,785
#4	Critical Care	8,924
#5	Postoperative Complications	17,922
#6	#3 OR #4 OR #5	1,852
#7	#2 AND #6	1,637
#8	Postoperative Hemorrhage	1,737
#9	Blood Loss, Surgical	3,239
#10	#7 OR #8 OR #9	1,639
#11	#1 AND #10	1,425
#12	critical NEAR/1 bleeding	3
#13	"severe bleeding"	164
#14	"major bleeding" OR "Major blood loss"	918

#	Query	Results
#15	"major hemorrhagic complication" OR "major hemorrhagic complications"	17
#16	"major haemorrhagic complication" OR "major haemorrhagic complications"	9
#17	"massive blood loss" OR "life threatening bleeding"	32
#18	"massive hemorrhage" OR "massive haemorrhage"	18
#19	(critical AND bleeding):ti	4
#20	#11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19	1,435
#21	blood transfusion	5,667
#22	massive	613
#23	#21 AND #22	660
#24	massive NEAR/3 transfusion*	23
#25	"massive infusion" OR "massively transfused"	3
#26	massive NEAR/1 (bleeding OR haemorrhage OR hemorrhage)	50
#27	#23 OR #24 OR #25 OR #26	647
#28	#20 OR #27	774
#29	Algorithms	3,361
#30	Time	147,731
#31	Time Factors	57,421
#32	algorithm* OR algorhythm OR algorism	3,372
#33	ratio OR ratios	38,329
#34	timing OR interval OR intervals	172,090
#35	(early NEAR/1 use) OR immediate	9,147
#36	#29 OR #30 OR #31 OR #32 OR #33 OR #34	502
#37	#28 AND #36	264
#38	Blood Component Transfusion	554
#39	"blood component" OR "blood components"	436
#40	"blood product" OR "blood products"	646
#41	"transfusion product" OR "transfusion products"	7
#42	#38 OR #39 OR #40 OR #41	261
#43	#28 AND #42	188
#44	Plasma	43,582
#45	"fresh frozen plasma" OR FFP	349
#46	"plasma transfusion"	30
#47	"plasma infusion" OR "serum transfusion"	17
#48	#44 OR #45 OR #46 OR #47	191
#49	#28 AND #48	140
#50	Blood Platelets	6,214
#51	Platelet Transfusion	1,405

#	Query	Results
#52	platelet* OR thrombocyte*	9,789
#53	#50 OR #51 OR #52	135
#54	#28 AND #53	98
#55	cryoprecipitate	66
#56	#28 AND #55	87
#57	Fibrinogen	2,875
#58	fibrinogen OR "factor 1" OR "factor I"	4,476
#59	#57 OR #58	83
#60	#28 AND #59	73
#61	#49 OR #54 OR #56 OR #60	148
#62	Erythrocytes	1,628
#63	Erythrocyte Transfusion	640
#64	packed NEAR/2 (cell OR cells)	344
#65	"packed erythrocyte" OR "packed erythrocytes"	25
#66	"erythrocyte concentrate" OR (red NEAR/1 "cell concentrate")	36
#67	PRBC OR RBC	809
#68	#62 OR #63 OR #64 OR #65 OR #66 OR #67	82
#69	#61 AND #68	52
#70	#43 OR #69	186
#71	Morbidity	13,531
#72	Mortality	32,562
#73	morbidity OR incidence OR prevalence OR occurrence	64,044
#74	mortality OR death OR survival	56,680
#75	#71 OR #72 OR #73 OR #74	55
#76	#70 AND #75	46
#77	Quality of Life	26,159
#78	Quality-Adjusted Life years	3,750
#79	qol OR "quality of life" OR "quality of wellbeing"	22,257
#80	"health related quality" or hrqol	3,003
#81	qaly* or "quality adjusted" or "adjusted life"	4,113
#82	#77 OR #78 OR #79 OR #80 OR #81	54
#83	#70 AND #82	39
#84	Blood Component Transfusion	554
#85	frequency NEAR/5 transfusion*	86
#86	rate* NEAR/5 transfusion*	335
#87	"transfusion requirement" OR "transfusion requirements"	962
#88	indication* NEAR/5 transfusion*	45

#	Query	Results
#89	"transfusion interval" OR "transfusion intervals"	13
#90	(need NEAR/3 transfusion*) OR "transfusion needs"	634
#91	dose NEAR/3 transfus*	89
#92	"platelet dose" OR (dose NEAR/3 platelets)	190
#93	(dose and transfus*):ti	76
#94	#84 OR #85 OR #86 OR #87 OR #88 OR #89 OR #90 OR #91 OR #92 OR #93	57
#95	#70 AND #94	23
#96	#76 OR #83 OR #95	49

Table A2.3 PreMedline search conducted 19 June 2009

#	Query	Results
#1	"critical bleeding"[tw]	33
#2	"severe bleeding"[tw]	1,667
#3	"major bleeding"[tw] OR "Major blood loss"[tw]	2,496
#4	"major hemorrhagic complication"[tw] OR "major hemorrhagic complications"[tw]	74
#5	"major haemorrhagic complication"[tw] OR "major haemorrhagic complications"[tw]	24
#6	"massive blood loss"[tw] OR "life threatening bleeding"[tw]	382
#7	"massive hemorrhage"[tw] OR "massive haemorrhage"[tw]	1,888
#8	critical[title] AND bleeding[title]	46
#9	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	6,495
#10	massive[tw] AND transfusion*[tw]	2,369
#11	"massive infusion"[tw] OR "massively transfused"[tw]	107
#12	massive[tw] AND bleeding[tw]	5,052
#13	massive[tw] AND hemorrhage[tw]	7,810
#14	massive[tw] AND haemorrhage[tw]	1,198
#15	#10 OR #11 OR #12 OR #13 OR #14	15,453
#16	#9 OR #15	7,326
#17	#16 NOT (medline[SB] OR oldmedline[sb])	587
#18	#16 AND in process[sb]	324
#19	#16 AND pubmednotmedline[sb]	80
#20	#17 OR #18 OR #19	7,573
#21	algorithm*[tw] OR algorith[m][tw] OR algorism[tw]	144,948
#22	ratio[tw] OR ratios[tw]	549,994
#23	timing[tw] OR interval[tw] OR intervals[tw]	405,415
#24	"early use"[tw] OR immediate[tw]	125,594
#25	#21 OR #22 OR #23 OR #24	1,004,184
#26	#20 AND #25	2

#	Query	Results
#27	"blood component"[tw] OR "blood components"[tw]	8,071
#28	"blood product"[tw] OR "blood products"[tw]	6,164
#29	"transfusion product"[tw] OR "transfusion products"[tw]	70
#30	#27 OR #28 OR #29	13,508
#31	#26 AND #30	7
#32	"fresh frozen plasma"[tw] OR FFP[tw]	3,272
#33	"plasma transfusion"[tw]	252
#34	"plasma infusion"[tw] OR "serum transfusion"[tw]	347
#35	#32 OR #33 OR #34	3,451
#36	#26 AND #35	533
#37	platelet*[tw] OR thrombocyte*[tw]	177,245
#38	#26 AND #37	12,156
#39	cryoprecipitate[tw]	1,459
#40	#26 AND #39	160
#41	fibrinogen[tw] OR "factor 1"[tw] OR "factor I"[tw]	101,216
#42	#26 AND #41	7,605
#43	#36 OR #38 OR #40 OR #42	19,261
#44	packed[tw] AND (cell[tw] OR cells[tw])	10,575
#45	"packed erythrocyte"[tw] OR "packed erythrocytes"[tw]	254
#46	"erythrocyte concentrate"[tw] OR (red[tw] AND "cell concentrate"[tw])	222
#47	PRBC[tw] OR RBC[tw]	13,475
#48	#44 OR #45 OR #46 OR #47	23,827
#49	#43 AND #48	365
#50	#31 AND #49	98
#51	morbidity[tw] OR incidence[tw] OR prevalence[tw] OR occurrence[tw]	985,262
#52	mortality[tw] OR death[tw] OR survival[tw]	1,181,182
#53	#51 OR #52	1,936,897
#54	#50 AND #53	51
#55	qol[tw] OR "quality of life"[tw] OR "quality of wellbeing"[tw]	117,691
#56	"health related quality"[tw] or hrqol[tw]	12,000
#57	qaly*[tw] or "quality adjusted"[tw] or "adjusted life"[tw]	6,538
#58	#55 OR #56 OR #57	121,997
#59	#50 AND #58	0
#60	frequency[tw] AND transfusion*[tw]	2,826
#61	rate*[tw] AND transfusion*[tw]	12,316
#62	"transfusion requirement"[tw] OR "transfusion requirements"[tw]	3,165
#63	indication*[tw] AND transfusion*[tw]	2,665

#	Query	Results
#64	"transfusion interval"[tw] OR "transfusion intervals"[tw]	35
#65	(need[tw] AND transfusion*[tw]) OR "transfusion needs"[tw]	5,461
#66	dose[tw] AND transfus*[tw]	5,596
#67	"platelet dose"[tw] OR (dose[tw] AND platelets[tw])	9,010
#68	dose[title] AND transfus*[title]	128
#69	#60 OR #61 OR #62 OR #63 OR #64 OR #65 OR #66 OR #67 OR #68	33,858
#70	#50 AND #69	53
#71	#54 OR #59 OR #70	75

Table A2.4 CINAHL search conducted 19 June 2009

#	Query	Results
S71	S44 or S70	62
S70	S62 and S69	20
S69	S63 or S64 or S65 or S66 or S67 or S68	1,680
S68	TI (PRBC OR RBC) or AB (PRBC OR RBC)	612
S67	TI red N1 "cell concentrate" or AB red N1 "cell concentrate"	3
S66	TI "erythrocyte concentrate" or AB "erythrocyte concentrate"	4
S65	TI ("packed erythrocyte" OR "packed erythrocytes") or AB ("packed erythrocyte" OR "packed erythrocytes")	4
S64	TI packed N2 cell ^a and AB packed N2 cell ^a	15
S63	(MH "Erythrocytes")	1,297
S62	S50 or S55 or S57 or S61	103
S61	S38 and S60	15
S60	S58 or S59	1,888
S59	TI (fibrinogen OR "factor 1" OR "factor I") or AB (fibrinogen OR "factor 1" OR "factor I")	1,661
S58	(MH "Fibrinogen")	527
S57	S38 and S56	8
S56	TI cryoprecipitate or AB cryoprecipitate	41
S55	S38 and S54	74
S54	S51 or S52 or S53	4,213
S53	TI (platelet ^a OR thrombocyte ^a) or AB (platelet ^a OR thrombocyte ^a)	3,781
S52	(MH "Platelet Transfusion")	318
S51	(MH "Blood Platelets")	1,338
S50	S38 and S49	35
S49	S45 or S46 or S47 or S48	859
S48	TI ("plasma infusion" OR "serum transfusion") or AB ("plasma infusion" OR "serum transfusion")	6
S47	TI "plasma transfusion" or AB "plasma transfusion"	27
S46	TI ("fresh frozen plasma" OR FFP) or AB ("fresh frozen plasma" OR FFP)	224

#	Query	Results
S45	(MH "Plasma")	705
S44	S38 and S43	56
S43	S39 or S40 or S41 or S42	1,634
S42	TI ("transfusion product" OR "transfusion products") or AB ("transfusion product" OR "transfusion products")	5
S41	TI ("blood product" OR "blood products") or AB ("blood product" OR "blood products")	698
S40	TI ("blood component" OR "blood components") or AB ("blood component" OR "blood components")	298
S39	(MH "Blood Component Transfusion")	838
S38	S30 and S37	1,325
S37	S31 or S32 or S33 or S34 or S35 or S36	107,460
S36	TI ("early N1 use" OR immediate) or AB ("early N1 use" OR immediate)	8,234
S35	TI (timing OR interval OR intervals) or AB (timing OR interval OR intervals)	35,014
S34	TI (ratio OR ratios) or AB (ratio OR ratios)	34,261
S33	TI (algorithm ^a OR algorhythm OR algorism) or AB (algorithm ^a OR algorhythm OR algorism)	4,374
S32	(MH "Time+")	41,886
S31	(MH "Algorithms")	4,449
S30	S22 or S29	5,811
S29	S25 or S26 or S27 or S28	5,201
S28	TI (massive N1 (bleeding OR haemorrhage OR hemorrhage)) or AB (massive N1 (bleeding OR haemorrhage OR hemorrhage))	5,121
S27	TI ("massive infusion" OR "massively transfused") or AB ("massive infusion" OR "massively transfused")	10
S26	TI massive N3 transfusion ^a or AB massive N3 transfusion ^a	88
S25	S23 and S24	74
S24	TI massive or AB massive	1,907
S23	(MH "Blood Transfusion")	3,481
S22	S13 or S14 or S15 or S16 or S17 or S18 or S19 or S20 or S21	734
S21	TI critical AND bleeding	11
S20	TI ("massive hemorrhage" OR "massive haemorrhage") or AB ("massive hemorrhage" OR "massive haemorrhage")	34
S19	TI ("massive blood loss" OR "life threatening bleeding") or AB ("massive blood loss" OR "life threatening bleeding")	48
S18	TI ("major haemorrhagic complication" OR "major haemorrhagic complications") or AB ("major haemorrhagic complication" OR "major haemorrhagic complications")	1
S17	TI ("major hemorrhagic complication" OR "major hemorrhagic complications") or AB ("major hemorrhagic complication" OR "major hemorrhagic complications")	1
S16	TI ("major bleeding" OR "Major blood loss") or AB ("major bleeding" OR "Major blood loss")	282
S15	TI "severe bleeding" or AB "severe bleeding"	75
S14	TI critical N1 bleeding or AB critical N1 bleeding	3

#	Query	Results
S13	S1 and S12	299
S12	S9 or S10 or S11	1,822
S11	(MH "Blood Loss, Surgical")	617
S10	(MH "Postoperative Hemorrhage")	498
S9	S2 and S8	1,371
S8	S3 or S4 or S5 or S6 or S7	45,082
S7	(MH "Postoperative Complications+")	21,486
S6	(MH "Critical Care Nursing+")	15,461
S5	(MH "Critical Care")	5,723
S4	(MH "Critically Ill Patients")	4,070
S3	(MH "Critical Illness")	2,210
S2	(MH "Hemorrhage+")	11,980
S1	(MH "Blood Transfusion+")	5,082

a The search was conducted using EBSCOhost on 19 June 2009

Table A2.5 AMI search conducted 19 June 2009

Set	Search terms	Records
#26	(((TI = (massive %1 (bleeding OR haemorrhage OR hemorrhage)) OR AB = (massive %1 (bleeding OR haemorrhage OR hemorrhage))) OR (TI = ("massive infusion" OR "massively transfused") OR AB = ("massive infusion" OR "massively transfused")) OR (TI = (massive %3 transfusion ^a) OR AB = (massive %3 transfusion ^a)) OR (((TI = (massive) OR AB = (massive)) AND ((MH_PHRASE = "Blood Transfusion"))))) OR (((TI = (critical AND bleeding)) OR (TI = ("massive hemorrhage" OR "massive haemorrhage") OR AB = ("massive hemorrhage" OR "massive haemorrhage")) OR (TI = ("massive blood loss" OR "life threatening bleeding") OR AB = ("massive blood loss" OR "life threatening bleeding")) OR (TI = ("major haemorrhagic complication" OR "major haemorrhagic complications") OR AB = ("major haemorrhagic complication" OR "major haemorrhagic complications")) OR (TI = ("major bleeding" OR "Major blood loss") OR AB = ("major bleeding" OR "Major blood loss")) OR (TI = ("severe bleeding") OR AB = ("severe bleeding")) OR (TI = (critical %1 bleeding) OR AB = (critical %1 bleeding)) OR ((((((MH_PHRASE = "Blood Loss, Surgical")) OR ((MH_PHRASE = "Postoperative Hemorrhage")))) AND ((MH_PHRASE = "Blood Transfusion"))))))))	48
#25	((TI = (massive %1 (bleeding OR haemorrhage OR hemorrhage)) OR AB = (massive %1 (bleeding OR haemorrhage OR hemorrhage))) OR (TI = ("massive infusion" OR "massively transfused") OR AB = ("massive infusion" OR "massively transfused")) OR (TI = (massive %3 transfusion ^a) OR AB = (massive %3 transfusion ^a)) OR (((TI = (massive) OR AB = (massive)) AND ((MH_PHRASE = "Blood Transfusion")))))	21
#24	TI = (massive %1 (bleeding OR haemorrhage OR hemorrhage)) OR AB = (massive %1 (bleeding OR haemorrhage OR hemorrhage))	11
#23	TI = ("massive infusion" OR "massively transfused") OR AB = ("massive infusion" OR "massively transfused")	1
#22	TI = (massive %3 transfusion ^a) OR AB = (massive %3 transfusion ^a)	9
#21	((TI = (massive) OR AB = (massive)) AND ((MH_PHRASE = "Blood Transfusion")))	4
#20	TI = (massive) OR AB = (massive)	237

Set	Search terms	Records
#19	((TI = (critical AND bleeding)) OR (TI = ("massive hemorrhage" OR "massive haemorrhage") OR AB = ("massive hemorrhage" OR "massive haemorrhage"))) OR (TI = ("massive blood loss" OR "life threatening bleeding") OR AB = ("massive blood loss" OR "life threatening bleeding")) OR (TI = ("major haemorrhagic complication" OR "major haemorrhagic complications") OR AB = ("major haemorrhagic complication" OR "major haemorrhagic complications")) OR (TI = ("major bleeding" OR "Major blood loss") OR AB = ("major bleeding" OR "Major blood loss")) OR (TI = ("severe bleeding") OR AB = ("severe bleeding")) OR (TI = (critical %1 bleeding) OR AB = (critical %1 bleeding)) OR (((((MH_PHRASE = "Blood Loss, Surgical")) OR ((MH_PHRASE = "Postoperative Hemorrhage")))) AND ((MH_PHRASE = "Blood Transfusion"))))	31
#18	TI = (critical AND bleeding)	1
#17	TI = ("massive hemorrhage" OR "massive haemorrhage") OR AB = ("massive hemorrhage" OR "massive haemorrhage")	3
#16	TI = ("massive blood loss" OR "life threatening bleeding") OR AB = ("massive blood loss" OR "life threatening bleeding")	4
#15	TI = ("major haemorrhagic complication" OR "major haemorrhagic complications") OR AB = ("major haemorrhagic complication" OR "major haemorrhagic complications")	1
#14	TI = ("major hemorrhagic complication" OR "major hemorrhagic complications") OR AB = ("major hemorrhagic complication" OR "major hemorrhagic complications")	0
#13	TI = ("major bleeding" OR "Major blood loss") OR AB = ("major bleeding" OR "Major blood loss")	14
#12	TI = ("severe bleeding") OR AB = ("severe bleeding")	5
#11	TI = (critical %1 bleeding) OR AB = (critical %1 bleeding)	1
#10	(((MH_PHRASE = "Blood Loss, Surgical")) OR ((MH_PHRASE = "Postoperative Hemorrhage")))) AND ((MH_PHRASE = "Blood Transfusion"))	5
#9	((MH_PHRASE = "Blood Loss, Surgical")) OR ((MH_PHRASE = "Postoperative Hemorrhage"))	35
#8	(MH_PHRASE = "Blood Loss, Surgical")	30
#7	(MH_PHRASE = "Postoperative Hemorrhage")	5
#6	(((MH_PHRASE = "Postoperative Complications")) OR ((MH_PHRASE = "Critical Illness")))) AND (MH_PHRASE = "Hemorrhage")	0
#5	((MH_PHRASE = "Postoperative Complications")) OR ((MH_PHRASE = "Critical Illness"))	573
#4	(MH_PHRASE = "Postoperative Complications")	378
#3	(MH_PHRASE = "Critical Illness")	196
#2	MH_PHRASE = "Hemorrhage"	13
#1	(MH_PHRASE = "Blood Transfusion")	179

aThe search was conducted using Informit online platform on 19 June 2009
These search results were also used for systematic review question 1 (Appendix A1)

A3 Literature search – question 3

In patients with critical bleeding requiring massive transfusion, is anaemia an independent risk factor for adverse outcomes in critical bleeding patients requiring massive transfusion?

Table A3.1 EMBASE.com search conducted 29 April 2009

#	Query	Results
#1	('perioperative period'/exp) OR ('perioperative nursing'/exp) OR ('perioperative complication'/exp) OR ('preoperative period'/exp) OR ('preoperative complication'/exp) OR ('intraoperative period'/exp) OR (perioperative:ab,ti OR 'peri operative':ab,ti) OR (preoperative:ab,ti OR 'pre operative':ab,ti) OR (intraoperative:ab,ti OR 'intra operative':ab,ti) OR (peroperative:ab,ti OR 'per operative':ab,ti)	332,345
#2	'postoperative period'/exp	211,165
#3	postoperative:ab,ti OR 'post operative':ab,ti	279,491
#4	#1 OR #2 OR #3	642,605
#5	((('injury'/exp) OR (injur*:ab,ti OR trauma*:ab,ti)) OR (((('blood transfusion'/exp) OR ('bleeding'/exp) AND ('transfusion'/exp))) AND (massive:ab,ti)) OR ('massive transfusion':de) OR ('massive transfusion protocol':de) OR ('massive *3 transfusion':ab,ti OR 'massive *3 transfusions':ab,ti))	1,259,617
#6	('surgery'/exp) OR ('surgical ward'/exp) OR ('surgical patient'/exp) OR (surgical:ab,ti OR surgery:ab,ti OR operation:ab,ti OR resection:ab,ti)	2,717,431
#7	#4 OR #5 OR #6	3,555,674
#8	'anemia'/exp	145,046
#9	anemia:ab,ti OR anaemia:ab,ti	84,969
#10	#8 OR #9	170,074
#11	#7 AND #10	37,319
#12	((('adverse outcome'/exp) OR ('outcome assessment'/exp) OR ('morbidity'/exp) OR ('mortality'/exp) OR (morbidity:ab,ti OR incidence:ab,ti OR prevalence:ab,ti OR occurrence:ab,ti) OR (mortality:ab,ti OR death:ab,ti OR survival:ab,ti)) OR (('quality of life'/exp) OR (qol:ab,ti OR 'quality of life':ab,ti OR 'quality of wellbeing':ab,ti) OR ('health related quality':ab,ti OR hrqol:ab,ti) OR (qaly*:ab,ti OR 'quality adjusted':ab,ti OR 'adjusted life':ab,ti)) OR (('blood transfusion'/exp) OR ('frequency *5 transfusion':ab,ti OR 'frequency *5 transfusions':ab,ti) OR ('transfusion frequency':ab,ti) OR ('transfusion rate':ab,ti OR 'transfusion rates':ab,ti) OR ('rate *5 transfusion':ab,ti OR 'rates *5 transfusion':ab,ti) OR ('transfusion requirement':ab,ti OR 'transfusion requirements':ab,ti) OR ('transfusion indication':ab,ti OR 'transfusion indications':ab,ti) OR ('indications *5 transfusion':ab,ti OR 'indications *5 transfusions':ab,ti) OR ('indication *5 transfusion':ab,ti OR 'indication *5 transfusions':ab,ti)) OR (('health economics'/exp) OR ('economic aspect'/exp) OR ('biomedical technology assessment'/exp) OR ('economic evaluation'/exp) OR ('health care cost'/exp) OR (economic*:ab,ti OR pharmaco-economic*:ab,ti) OR (cost*:ab,ti OR price*:ab,ti OR pricing:ab,ti) OR ('burden of illness':ab,ti)) OR (('hospitalization'/exp) OR ('length of stay'/exp) OR (hospitaliz*:ab,ti OR hospitalis*:ab,ti) OR ('length *3 stay':ab,ti OR 'hospital stay':ab,ti)) OR (('intensive care unit'/exp) OR ('intensive care unit':ab,ti OR icu:ab,ti OR 'intensive care units':ab,ti) OR ('close attention unit':ab,ti OR 'close attention units':ab,ti) OR ('intensive care department':ab,ti OR 'intensive care departments':ab,ti) OR ('special care unit':ab,ti OR 'special care units':ab,ti) OR ('critical care unit':ab,ti OR 'critical care units':ab,ti)) OR (('hospital admission'/exp) OR ('hospital readmission'/exp) OR ('hospital admission':ab,ti OR 'hospital admittance':ab,ti) OR ('patient admission':ab,ti OR readmission:ab,ti) OR (rehospitalization:ab,ti OR rehospitalisation:ab,ti))	3,114,709

#	Query	Results
#13	#11 AND #12	17,893

Table A3.2 Cochrane library database search conducted 14 May 2009

#	Query	Results
#1	MeSH descriptor Blood Transfusion explode all trees	2,628
#2	blood NEAR/1 transfusion ^a	3,768
#3	"blood exchange" OR "blood infusion"	42
#4	"blood replacement" OR "blood retransfusion"	73
#5	hemotherapy OR hematherapy OR hematotherapy	55
#6	haemotherapy OR haematherapy OR haematotherapy	5
#7	multitransfusion OR polytransfusion OR retransfusion	66
#8	"transfusion blood" OR "transfusion therapy"	224
#9	"exchange transfusion" OR autotransfusion	390
#10	"replacement transfusion" OR "substitution transfusion"	1
#11	"erythrocyte transfusion" OR "leukocyte transfusion"	452
#12	"lymphocyte transfusion" OR "thrombocytic transfusion"	21
#13	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12	1,946
#14	MeSH descriptor Perioperative Care explode all trees	4,254
#15	MeSH descriptor Preoperative Care explode all trees	4,098
#16	MeSH descriptor Postoperative Complications explode all trees	21,418
#17	MeSH descriptor Postoperative Period explode all trees	3,483
#18	MeSH descriptor Intraoperative Complications explode all trees	2,476
#19	MeSH descriptor Intraoperative Period explode all trees	919
#20	perioperative OR "peri operative"	5,196
#21	preoperative OR "pre operative"	11,093
#22	intraoperative OR "intra operative"	8,039
#23	peroperative OR "per operative"	474
#24	postoperative OR "post operative"	40,236
#25	#14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24	1,196
#26	#13 AND #25	512
#27	MeSH descriptor Wounds and Injuries explode all trees	10,953
#28	injur ^a OR trauma ^a	20,750
#29	#27 OR #28	474
#30	#13 AND #29	386
#31	MeSH descriptor Shock explode all trees	930
#32	shock OR "cardiovascular collapse" OR "circulatory collapse"	3,179
#33	#31 OR #32	356
#34	#13 AND #33	286

#	Query	Results
#35	MeSH descriptor Blood Transfusion explode all trees	2,628
#36	massive	599
#37	#35 AND #36	260
#38	massive NEAR/3 transfusion ^a	20
#39	"massive infusion" OR "massively transfused"	3
#40	massive NEAR/1 (bleeding OR haemorrhage OR hemorrhage)	47
#41	#37 OR #38 OR #39 OR #40	274
#42	#13 AND #41	194
#43	MeSH descriptor Thoracic Surgical Procedures explode all trees	10,297
#44	MeSH descriptor Thoracic Surgery explode all trees	130
#45	MeSH descriptor Cardiovascular Surgical Procedures explode all trees	10,930
#46	"cardiothoracic surgery" OR (chest NEAR/1 surgery)	675
#47	cardiothoracic NEAR/1 patient ^a	4
#48	"thoracic operation" OR "thoracic surgery" OR thoracoplasty	2,131
#49	thoracic NEAR/1 procedure ^a	16
#50	#43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49	209
#51	#13 AND #50	117
#52	MeSH descriptor Surgical Procedures, Operative explode all trees	68,578
#53	MeSH descriptor General Surgery explode all trees	167
#54	MeSH descriptor Surgery Department, Hospital explode all trees	68
#55	surgical OR surgery OR operation OR resection	91,783
#56	#52 OR #53 OR #54 OR #55	118
#57	#13 AND #56	82
#58	MeSH descriptor Orthopedic Procedures explode all trees	5,335
#59	MeSH descriptor Orthopedics explode all trees	272
#60	"orthopedic surgery" OR "orthopaedic surgery"	2,339
#61	"bone surgery" OR orthopaedics or orthopedics	7,975
#62	(orthopedic OR orthopaedic) NEAR/1 patient ^a	223
#63	"orthopedic operation" OR "orthopaedic operation"	6
#64	(orthopedic OR orthopaedic) NEAR/1 procedure ^a	638
#65	#58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64	98
#66	#13 AND #65	57
#67	#26 OR #30 OR #34 OR #42 OR #51 OR #57 OR #66	619
#68	MeSH descriptor Morbidity explode all trees	8,475
#69	MeSH descriptor Mortality explode all trees	7,946
#70	morbidity OR incidence OR prevalence OR occurrence	62,784
#71	mortality OR death OR survival	55,325
#72	#68 OR #69 OR #70 OR #71	61

#	Query	Results
#73	#67 AND #72	48
#74	MeSH descriptor Quality of Life explode all trees	9,425
#75	MeSH descriptor Quality-Adjusted Life years explode all trees	2,062
#76	qol OR "quality of life" OR "quality of wellbeing"	21,521
#77	"health related quality" or hrqol	2,898
#78	qaly ^a or "quality adjusted" or "adjusted life"	3,802
#79	#74 OR #75 OR #76 OR #77 OR #78	55
#80	#67 AND #79	39
#81	MeSH descriptor Blood Component Transfusion explode all trees	640
#82	frequency NEAR/5 transfusion ^a	84
#83	rate ^a NEAR/5 transfusion ^a	324
#84	"transfusion requirement" OR "transfusion requirements"	949
#85	indication ^a NEAR/5 transfusion ^a	45
#86	"transfusion interval" OR "transfusion intervals"	13
#87	(need NEAR/3 transfusion ^a) OR "transfusion needs"	623
#88	dose NEAR/3 transfus ^a	86
#89	"platelet dose" OR (dose NEAR/3 platelets)	185
#90	(dose and transfus ^a):ti	72
#91	#81 OR #82 OR #83 OR #84 OR #85 OR #86 OR #87 OR #88 OR #89 OR #90	54
#92	#67 AND #91	25
#93	MeSH descriptor Costs and Cost Analysis explode all trees	26,772
#94	MeSH descriptor Economics explode all trees	28,552
#95	MeSH descriptor Models, Economic explode all trees	1,853
#96	MeSH descriptor Value of Life explode all trees	274
#97	MeSH descriptor Utilization Review explode all trees	420
#98	MeSH descriptor Delivery of Health Care explode all trees with qualifier: UT	762
#99	economic ^a or pharmaco-economic ^a	37,332
#100	cost ^a or price ^a or pricing	48,938
#101	resource ^a near utili ^a	1,537
#102	"burden of illness" or (value NEAR/1 money)	87
#103	#93 or #94 or #95 or #96 or #97 or #98 or #99 OR #100 or #101 OR #102	50
#104	#67 and #103	15
#105	MeSH descriptor Hospitalization explode all trees	10,690
#106	MeSH descriptor Child, Hospitalized explode all trees	82
#107	hospitaliz ^a OR hospitalis ^a	16,298
#108	(length NEAR/3 stay) OR "hospital stay"	11,735
#109	#105 OR #106 OR #107 OR #108	19
#110	#67 AND #109	13

#	Query	Results
#111	MeSH descriptor Intensive Care Units explode all trees	1,978
#112	"intensive care unit" OR icu OR "intensive care units"	6,712
#113	"close attention unit" OR "close attention units"	0
#114	"intensive care department" OR "intensive care departments"	56
#115	"special care unit" OR "special care units"	63
#116	"critical care unit" OR "critical care units"	108
#117	#111 OR #112 OR #113 OR #114 OR #115 OR #116	23
#118	#67 AND #117	11
#119	MeSH descriptor Patient Admission explode all trees	604
#120	MeSH descriptor Patient Readmission explode all trees	593
#121	"hospital admission" OR "hospital admittance"	1,727
#122	"patient admission" OR readmission	2,327
#123	rehospitalization OR rehospitalisation	504
#124	#119 OR #120 OR #121 OR #122 OR #123	23
#125	#67 AND #124	9
#126	#73 OR #80 OR #92 OR #104 OR #110 OR #118 OR #125	56

Table A3.3 PreMedline search conducted 14 May 2009

#	Query	Results
#56	Select 29 document(s)	29
#55	Search #53 AND #54	29
#54	Search anemia[tw] OR anaemia[tw]	125,758
#53	Search #50 OR #51 OR #52	449
#52	Search #49 AND pubmednotmedline[sb]	62
#51	Search #49 AND in process[sb]	246
#50	Search #49 NOT (medline[SB] OR oldmedline[sb])	449
#49	Search #20 OR #22 OR #24 OR #31 OR #37 OR #39 OR #48	24,198
#48	Search #13 AND #47	736
#47	Search #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46	42,676
#46	Search orthopedic[tw] AND procedure ^a [tw]	11,036
#45	Search orthopaedic[tw] AND procedure ^a [tw]	3,340
#44	Search "orthopedic operation"[tw] OR "orthopaedic operation"[tw]	73
#43	Search orthopaedic[tw] AND patient ^a [tw]	8,073
#42	Search orthopedic[tw] AND patient ^a [tw]	15,050
#41	Search "bone surgery"[tw] OR orthopaedics[tw] or orthopedics[tw]	17,574
#40	Search "orthopedic surgery"[tw] OR "orthopaedic surgery"[tw]	5,983
#39	Search #13 AND #38	17,297
#38	Search surgical[tw] OR surgery[tw] OR operation[tw] OR resection[tw]	1,871,038

#	Query	Results
#37	Search #13 AND #36	775
#36	Search #32 OR #33 OR #34 OR #35	53,886
#35	Search thoracic[tw] AND procedure ^a [tw]	19,053
#34	Search "thoracic operation"[tw] OR "thoracic surgery"[tw] OR thoracoplasty[tw]	16,674
#33	Search cardiothoracic[tw] AND patient ^a [tw]	2,265
#32	Search "cardiothoracic surgery"[tw] OR (chest[tw] AND surgery[tw])	24,296
#31	Search #13 AND #30	1,749
#30	Search #25 OR #26 OR #27 OR #28 OR #29	11,274
#29	Search massive[tw] AND haemorrhage[tw]	1,180
#28	Search massive[tw] AND hemorrhage[tw]	7,688
#27	Search massive[tw] AND bleeding[tw]	4,937
#26	Search "massive infusion"[tw] OR "massively transfused"[tw]	100
#25	Search massive[tw] AND transfusion ^a [tw]	2,296
#24	Search #13 AND #23	3,087
#23	Search shock[tw] OR "cardiovascular collapse"[tw] OR "circulatory collapse"[tw]	134,407
#22	Search #13 AND #21	4,592
#21	Search injur ^a [tw] OR trauma ^a [tw]	716,019
#20	Search #13 AND #19	11,631
#19	Search #14 OR #15 OR #16 OR #17 OR #18	609,868
#18	Search postoperative[tw] OR "post operative"[tw]	466,722
#17	Search peroperative[tw] OR "per operative"[tw]	3,704
#16	Search intraoperative[tw] OR "intra operative"[tw]	87,796
#15	Search preoperative[tw] OR "pre operative"[tw]	148,907
#14	Search perioperative[tw] OR "peri operative"[tw]	42,587
#13	Search #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12	76,495
#12	Search "lymphocyte transfusion"[tw] OR "thrombocytic transfusion"	2,968
#11	Search "erythrocyte transfusion"[tw] OR "leukocyte transfusion"[tw]	5,436
#10	Search "replacement transfusion"[tw] OR "substitution transfusion"[tw]	46
#9	Search "exchange transfusion"[tw] OR autotransfusion[tw]	6,690
#8	Search "transfusion blood"[tw] OR "transfusion therapy"[tw]	1,477
#7	Search multitransfusion[tw] OR polytransfusion[tw] OR retransfusion[tw]	476
#6	Search haemotherapy[tw] OR haemotherapy[tw] OR haematotherapy[tw]	67
#5	Search hemotherapy[tw] OR hemotherapy[tw] OR hematotherapy[tw]	511
#4	Search "blood replacement"[tw] OR "blood retransfusion"[tw]	569
#3	Search "blood exchange"[tw] OR "blood infusion"[tw]	482
#2	Search "blood cell transfusion"[tw] OR "blood cell transfusions"[tw]	1,114
#1	Search "blood transfusion"[tw] OR "blood transfusions"[tw]	64,790

Table A3.4 CINAHL search conducted 14 May 2009

#	Query	Results
S138	S134 and S137	109
S137	S135 or S136	7,549
S136	TI (anaemia OR anemia) or AB (anaemia OR anemia)	3,956
S135	(MH "Anemia+")	6,210
S134	S78 or S84 or S98 or S110 or S117 or S126 or S133	1,021
S133	s72 and s132	20
S132	S127 or S128 or S129 or S130 OR S131	7,164
S131	TI (rehospitalization OR rehospitalisation) or AB (rehospitalization OR rehospitalisation)	437
S130	TI ("patient admission" OR readmission) or AB ("patient admission" OR readmission)	1,114
S129	TI ("hospital admission" OR "hospital admittance") or AB ("hospital admission" OR "hospital admittance")	1,894
S128	(MH "Patient Admission")	4,242
S127	(MH "Patient Admission")	4,242
S126	s72 and s125	215
S125	S118 or S119 or S120 or S122 or S123 OR S124	32,219
S124	TI ("critical care unit" OR "critical care units") or AB ("critical care unit" OR "critical care units")	856
S123	TI ("special care unit" OR "special care units") or AB ("special care unit" OR "special care units")	262
S122	TI ("intensive care department" OR "intensive care departments") or AB ("intensive care department" OR "intensive care departments")	33
S121	TI ("close attention unit" OR "close attention units") or AB ("close attention unit" OR "close attention units")	0
S120	TI ("intensive care unit" OR icu OR "intensive care units") or AB ("intensive care unit" OR icu OR "intensive care units")	13,463
S119	(MH "Critical Care Nursing+")	15,220
S118	(MH "Intensive Care Units+")	14,257
S117	S72 AND S116	257
S116	S111 OR S112 OR S113 OR S114 OR S115	41,459
S115	TI ("hospital stay") or AB ("hospital stay")	3,269
S114	TI (length N3 stay) or AB (length N3 stay)	5,750
S113	TI (hospitaliz ^a OR hospitalis ^a) or AB (hospitaliz ^a OR hospitalis ^a)	17,920
S112	(MH "Child, Hospitalized")	2,159
S111	(MH "Hospitalization+")	20,460
S110	s72 and s109	186
S109	S99 or S100 or S101 or S102 or S103 OR S104 OR S105 OR S106 OR S107 OR S108	80,863
S108	TI (value N1 money) or AB (value N1 money)	212
S107	TI ("burden of illness") or AB ("burden of illness")	172
S106	TI (resource ^a and utili ^a) or AB (resource ^a and utili ^a)	3,116

#	Query	Results
S105	TI (cost ^a or price ^a or pricing) or AB (cost ^a or price ^a or pricing)	45,423
S104	TI (economic ^a or pharmacoeconomic ^a) or AB (economic ^a or pharmacoeconomic ^a)	16,024
S103	(MH "Health Care Delivery/UT")	63
S102	(MH "Utilization Review+")	3,370
S101	(MH "Economic Value of Life")	231
S100	(MH "Economics")	2,328
S99	(MH "Costs and Cost Analysis+")	32,259
S98	s72 and s97	397
S97	S85 or S86 or S87 or S88 or S89 or S90 or S91 or S92 OR S93 OR S94 OR S95 OR S96	799
S96	TI (dose and transfus ^a)	7
S95	TI (dose N3 platelets) or AB (dose N3 platelets)	2
S94	TI ("platelet dose") or AB ("platelet dose")	3
S93	TI (dose N3 transfus ^a) or AB (dose N3 transfus ^a)	14
S92	TI ("transfusion needs") or AB ("transfusion needs")	25
S91	TI (need N3 transfusion ^a) or AB (need N3 transfusion ^a)	234
S90	TI ("transfusion interval" OR "transfusion intervals") or AB ("transfusion interval" OR "transfusion intervals")	4
S89	TI (indication ^a N5 transfusion ^a) or AB (indication ^a N5 transfusion ^a)	34
S88	TI ("transfusion requirement" OR "transfusion requirements") or AB ("transfusion requirement" OR "transfusion requirements")	254
S87	TI (rate ^a N5 transfusion ^a) or AB (rate ^a N5 transfusion ^a)	168
S86	TI (frequency N5 transfusion ^a) or AB (frequency N5 transfusion ^a)	19
S85	(MH "Blood Component Transfusion+/MT")	137
S84	s72 and s83	24
S83	S79 or S80 or S81 or S82	36,753
S82	TI (qaly ^a or "quality adjusted" or "adjusted life") or AB (qaly ^a or "quality adjusted" or "adjusted life")	811
S81	TI ("health related quality" or hrqol) or AB ("health related quality" or hrqol)	3,359
S80	TI (qol OR "quality of life" OR "quality of wellbeing") or AB (qol OR "quality of life" OR "quality of wellbeing")	23,338
S79	(MH "Quality of Life+")	26,373
S78	s72 and s77	706
S77	S73 or S74 or S75 or S76	149,826
S76	TI (mortality OR death OR survival) or AB (mortality OR death OR survival)	71,084
S75	TI (morbidity OR incidence OR prevalence OR occurrence) or AB (morbidity OR incidence OR prevalence OR occurrence)	77,393
S74	(MH "Mortality+")	18,436
S73	(MH "Morbidity+")	27,551
S72	S27 OR S33 OR S37 OR S45 OR S54 OR S59 OR S71	2,455

#	Query	Results
S71	s13 and s70	274
S70	S60 or S61 or S62 or S63 or S64 or S65 or S66 OR S67 OR S68 OR S69	25,842
S69	TI (orthopaedic N1 procedure ^a) or AB (orthopaedic N1 procedure ^a)	14
S68	TI (orthopedic N1 procedure ^a) or AB (orthopedic N1 procedure ^a)	115
S67	TI ("orthopedic operation" OR "orthopaedic operation") or AB ("orthopedic operation" OR "orthopaedic operation")	6
S66	TI (orthopaedic N1 patient ^a) or AB (orthopaedic N1 patient ^a)	355
S65	TI (orthopedic N1 patient ^a) or AB (orthopedic N1 patient ^a)	245
S64	TI ("bone surgery" OR orthopaedics or orthopedics) or AB ("bone surgery" OR orthopaedics or orthopedics)	911
S63	TI ("orthopedic surgery" OR "orthopaedic surgery") or AB ("orthopedic surgery" OR "orthopaedic surgery")	790
S62	(MH "Orthopedic Nursing")	1,422
S61	(MH "Orthopedics")	3,289
S60	(MH "Orthopedic Surgery+")	21,259
S59	s13 and s58	1,834
S58	S55 or S56 OR S57	170,781
S57	TI (surgical OR surgery OR operation OR resection) or AB (surgical OR surgery OR operation OR resection)	69,889
S56	(MH "Medical-Surgical Nursing")	2,427
S55	(MH "Surgery, Operative+")	136,639
S54	s13 and s53	325
S53	S46 or S47 or S48 or S49 or S50 or S51 OR S52	23,228
S52	TI (thoracic N1 procedure ^a) or AB (thoracic N1 procedure ^a)	32
S51	TI ("thoracic operation" OR "thoracic surgery" OR thoracoplasty) or AB ("thoracic operation" OR "thoracic surgery" OR thoracoplasty)	253
S50	TI (cardiothoracic N1 patient ^a) or AB (cardiothoracic N1 patient ^a)	56
S49	TI ("cardiothoracic surgery" OR (chest N1 surgery)) or AB ("cardiothoracic surgery" OR (chest N1 surgery))	166
S48	(MH "Cardiovascular Nursing+")	2,655
S47	(MH "Surgery, Cardiovascular+")	16,879
S46	(MH "Thoracic Surgery+")	16,901
S45	s13 and s44	398
S44	S40 or S41 or S42 OR S43	5,209
S43	TI (massive N1 (bleeding OR haemorrhage OR hemorrhage)) or AB (massive N1 (bleeding OR haemorrhage OR hemorrhage))	5,042
S42	TI ("massive infusion" OR "massively transfused") or AB ("massive infusion" OR "massively transfused")	10
S41	TI (massive N3 transfusion ^a) or AB (massive N3 transfusion ^a)	87
S40	S37 and S38	124

#	Query	Results
S39	TI (massive) or AB (massive)	1,888
S38	(MH "Blood Transfusion")	3,427
S37	s13 and s36	215
S36	S34 or S35	6,687
S35	TI (shock OR "cardiovascular collapse" OR "circulatory collapse") or AB (shock OR "cardiovascular collapse" OR "circulatory collapse")	5,193
S34	(MH "Shock+")	3,242
S33	S13 and S32	711
S32	S28 OR S29 or S30 OR S31	121,361
S31	TI (injur ^a OR trauma ^a) or AB (injur ^a OR trauma ^a)	67,640
S30	(MH "Trauma Nursing")	526
S29	(MH "Trauma+")	5,857
S28	(MH "Wounds and Injuries+")	90,837
S27	S13 AND S26	939
S26	S14 OR S15 or S16 or S17 or S18 or S19 or S20 or S21 or S22 or S23 or S24 or S25	54,117
S25	TI (postoperative OR "post operative") or AB (postoperative OR "post operative")	14,379
S24	TI (peroperative OR "per operative") or AB (peroperative OR "per operative")	51
S23	TI (intraoperative OR "intra operative") or AB (intraoperative OR "intra operative")	2,954
S22	TI (preoperative OR "pre operative") or AB (preoperative OR "pre operative")	7,186
S21	TI (perioperative OR "peri operative") or AB (perioperative OR "peri operative")	5,307
S20	(MH "Postoperative Period")	1,898
S19	(MH "Postoperative Complications+")	21,107
S18	(MH "Intraoperative Period")	364
S17	(MH "Intraoperative Complications+")	1,795
S16	(MH "Preoperative Period+")	719
S15	(MH "Perioperative Nursing")	8,787
S14	(MH "Perioperative Care+")	16,023
S13	S1 or S2 or S3 or S4 or S5 or S7 or S8 or S9 or S11 or S12	5,828
S12	TI ("lymphocyte transfusion" OR "thrombocytic transfusion") or AB ("lymphocyte transfusion" OR "thrombocytic transfusion")	1
S11	TI ("erythrocyte transfusion" OR "leukocyte transfusion") or AB ("erythrocyte transfusion" OR "leukocyte transfusion")	11
S10	TI ("replacement transfusion" OR "substitution transfusion") or AB ("replacement transfusion" OR "substitution transfusion")	0
S9	TI ("exchange transfusion" OR autotransfusion) or AB ("exchange transfusion" OR autotransfusion)	216
S8	TI ("transfusion blood" OR "transfusion therapy") or AB ("transfusion blood" OR "transfusion therapy")	142
S7	TI (multitransfusion OR polytransfusion OR retransfusion) OR AB (multitransfusion OR polytransfusion OR retransfusion)	23

#	Query	Results
S6	TI (haemotherapy OR haemotherapy OR haematotherapy) or AB (haemotherapy OR haemotherapy OR haematotherapy)	0
S5	TI (hemotherapy OR hemotherapy OR hematotherapy) or AB (hemotherapy OR hemotherapy OR hematotherapy)	14
S4	TI ("blood replacement" OR "blood retransfusion") or AB ("blood replacement" OR "blood retransfusion")	18
S3	TI ("blood exchange" OR "blood infusion") or AB ("blood exchange" OR "blood infusion")	16
S2	TI (blood N1 transfusion ^a) or AB (blood N1 transfusion ^a)	1,886
S1	(MH "Blood Transfusion+")	5,001

^a The search was conducted using EBSCOhost on 14 May 2009

Table A3.5 AMI search conducted 26 June 2009

Set	Search terms	Records
	#39 OR #43 OR #47 OR #55 OR #64 OR #69 OR #79	251 ^b
#79	(((TI = ((orthopedic OR orthopaedic) %1 procedure ^a)) OR (TI = ("orthopedic operation" OR "orthopaedic operation") OR AB = ("orthopedic operation" OR "orthopaedic operation"))) OR (TI = ((orthopedic OR orthopaedic) %1 patient ^a) OR AB = ((orthopedic OR orthopaedic) %1 patient ^a)) OR (TI = ("bone surgery" OR orthopaedics or orthopedics) OR AB = ("bone surgery" OR orthopaedics or orthopedics)) OR (TI = ("orthopedic surgery" OR "orthopaedic surgery") OR AB = ("orthopedic surgery" OR "orthopaedic surgery")) OR ((MH_PHRASE = "Orthopedic Nursing")) OR (MH_PHRASE = "Orthopedics") OR ((MH_PHRASE = "Orthopedic Procedures")))) AND (((TI = (anaemia OR anemia) OR AB = (anaemia OR anemia)) OR ((MH_PHRASE = "Anemia, Hypochromic")) OR ((MH_PHRASE = "Anemia, Hemolytic, Autoimmune")) OR ((MH_PHRASE = "Anemia, Sickle Cell")) OR ((MH_PHRASE = "Anemia, Hemolytic, Congenital Nonspherocytic")) OR ((MH_PHRASE = "Anemia, Pernicious")) OR ((MH_PHRASE = "Anemia, Diamond-Blackfan")) OR ((MH_PHRASE = "Anemia, Dyserythropoietic, Congenital")) OR ((MH_PHRASE = "Anemia, Macrocytic")) OR ((MH_PHRASE = "Anemia, Refractory")) OR ((MH_PHRASE = "Anemia, Megaloblastic")) OR ((MH_PHRASE = "Anemia, Hypoplastic, Congenital")) OR ((MH_PHRASE = "Anemia, Sideroblastic")) OR ((MH_PHRASE = "Anemia, Neonatal")) OR ((MH_PHRASE = "Anemia, Iron-Deficiency")) OR ((MH_PHRASE = "Anemia, Myelophthisic")) OR ((MH_PHRASE = "Anemia, Aplastic")) OR ((MH_PHRASE = "Anemia, Hemolytic, Congenital")) OR ((MH_PHRASE = "Anemia, Hemolytic")) OR (MH_PHRASE = "Anemia"))))	30
#78	((TI = ((orthopedic OR orthopaedic) %1 procedure ^a)) OR (TI = ("orthopedic operation" OR "orthopaedic operation") OR AB = ("orthopedic operation" OR "orthopaedic operation"))) OR (TI = ((orthopedic OR orthopaedic) %1 patient ^a) OR AB = ((orthopedic OR orthopaedic) %1 patient ^a)) OR (TI = ("bone surgery" OR orthopaedics or orthopedics) OR AB = ("bone surgery" OR orthopaedics or orthopedics)) OR (TI = ("orthopedic surgery" OR "orthopaedic surgery") OR AB = ("orthopedic surgery" OR "orthopaedic surgery")) OR ((MH_PHRASE = "Orthopedic Nursing")) OR (MH_PHRASE = "Orthopedics") OR ((MH_PHRASE = "Orthopedic Procedures")))	140
#77	TI = ((orthopedic OR orthopaedic) %1 procedure ^a)	2
#76	TI = ("orthopedic operation" OR "orthopaedic operation") OR AB = ("orthopedic operation" OR "orthopaedic operation")	1
#75	TI = ((orthopedic OR orthopaedic) %1 patient ^a) OR AB = ((orthopedic OR orthopaedic) %1 patient ^a)	12

Set	Search terms	Records
#74	TI = ("bone surgery" OR orthopaedics or orthopedics) OR AB = ("bone surgery" OR orthopaedics or orthopedics)	29
#73	TI = ("orthopedic surgery" OR "orthopaedic surgery") OR AB = ("orthopedic surgery" OR "orthopaedic surgery")	43
#72	(MH_PHRASE = "Orthopedic Nursing")	3
#71	MH_PHRASE = "Orthopedics"	47
#70	(MH_PHRASE = "Orthopedic Procedures")	30
#69	(((TI = (surgical OR surgery OR operation OR resection) OR AB = (surgical OR surgery OR operation OR resection)) OR (MH_PHRASE = "Surgery") OR ((MH_PHRASE = "Surgical Procedures, Operative")))) AND (((TI = (anaemia OR anemia) OR AB = (anaemia OR anemia)) OR ((MH_PHRASE = "Anemia, Hypochromic")) OR ((MH_PHRASE = "Anemia, Hemolytic, Autoimmune")) OR ((MH_PHRASE = "Anemia, Sickle Cell")) OR ((MH_PHRASE = "Anemia, Hemolytic, Congenital Nonspherocytic")) OR ((MH_PHRASE = "Anemia, Pernicious")) OR ((MH_PHRASE = "Anemia, Diamond-Blackfan")) OR ((MH_PHRASE = "Anemia, Dyserythropoietic, Congenital")) OR ((MH_PHRASE = "Anemia, Macrocytic")) OR ((MH_PHRASE = "Anemia, Refractory")) OR ((MH_PHRASE = "Anemia, Megaloblastic")) OR ((MH_PHRASE = "Anemia, Hypoplastic, Congenital")) OR ((MH_PHRASE = "Anemia, Sideroblastic")) OR ((MH_PHRASE = "Anemia, Neonatal")) OR ((MH_PHRASE = "Anemia, Iron-Deficiency")) OR ((MH_PHRASE = "Anemia, Myelophthitic")) OR ((MH_PHRASE = "Anemia, Aplastic")) OR ((MH_PHRASE = "Anemia, Hemolytic, Congenital")) OR ((MH_PHRASE = "Anemia, Hemolytic")) OR (MH_PHRASE = "Anemia"))))	49
#68	((TI = (surgical OR surgery OR operation OR resection) OR AB = (surgical OR surgery OR operation OR resection)) OR (MH_PHRASE = "Surgery") OR ((MH_PHRASE = "Surgical Procedures, Operative")))	6,962
#67	TI = (surgical OR surgery OR operation OR resection) OR AB = (surgical OR surgery OR operation OR resection)	6,890
#66	MH_PHRASE = "Surgery"	119
#65	(MH_PHRASE = "Surgical Procedures, Operative")	63
#64	(((TI = (thoracic %1 procedure ^a) OR AB = (thoracic %1 procedure ^a)) OR (TI = ("thoracic operation" OR "thoracic surgery" OR thoracoplasty) OR AB = ("thoracic operation" OR "thoracic surgery" OR thoracoplasty)) OR (TI = (cardiothoracic %1 patient ^a) OR AB = (cardiothoracic %1 patient ^a)) OR (TI = ("cardiothoracic surgery" OR (chest %1 surgery)) OR AB = ("cardiothoracic surgery" OR (chest %1 surgery))) OR ((MH_PHRASE = "Cardiovascular Surgical Procedures")) OR ((MH_PHRASE = "Thoracic Surgery")) OR ((MH_PHRASE = "Thoracic Surgical Procedures")))) AND (((TI = (anaemia OR anemia) OR AB = (anaemia OR anemia)) OR ((MH_PHRASE = "Anemia, Hypochromic")) OR ((MH_PHRASE = "Anemia, Hemolytic, Autoimmune")) OR ((MH_PHRASE = "Anemia, Sickle Cell")) OR ((MH_PHRASE = "Anemia, Hemolytic, Congenital Nonspherocytic")) OR ((MH_PHRASE = "Anemia, Pernicious")) OR ((MH_PHRASE = "Anemia, Diamond-Blackfan")) OR ((MH_PHRASE = "Anemia, Dyserythropoietic, Congenital")) OR ((MH_PHRASE = "Anemia, Macrocytic")) OR ((MH_PHRASE = "Anemia, Refractory")) OR ((MH_PHRASE = "Anemia, Megaloblastic")) OR ((MH_PHRASE = "Anemia, Hypoplastic, Congenital")) OR ((MH_PHRASE = "Anemia, Sideroblastic")) OR ((MH_PHRASE = "Anemia, Neonatal")) OR ((MH_PHRASE = "Anemia, Iron-Deficiency")) OR ((MH_PHRASE = "Anemia, Myelophthitic")) OR ((MH_PHRASE = "Anemia, Aplastic")) OR ((MH_PHRASE = "Anemia, Hemolytic, Congenital")) OR ((MH_PHRASE = "Anemia, Hemolytic")) OR (MH_PHRASE = "Anemia"))))	29

Set	Search terms	Records
#63	((TI = (thoracic %1 procedure ^a) OR AB = (thoracic %1 procedure ^a)) OR (TI = ("thoracic operation" OR "thoracic surgery" OR thoracoplasty) OR AB = ("thoracic operation" OR "thoracic surgery" OR thoracoplasty)) OR (TI = (cardiothoracic %1 patient ^a) OR AB = (cardiothoracic %1 patient ^a)) OR (TI = ("cardiothoracic surgery" OR (chest %1 surgery)) OR AB = ("cardiothoracic surgery" OR (chest %1 surgery))) OR ((MH_PHRASE = "Cardiovascular Surgical Procedures")) OR ((MH_PHRASE = "Thoracic Surgery")) OR ((MH_PHRASE = "Thoracic Surgical Procedures"))))	86
#62	TI = (thoracic %1 procedure ^a) OR AB = (thoracic %1 procedure ^a)	2
#61	TI = ("thoracic operation" OR "thoracic surgery" OR thoracoplasty) OR AB = ("thoracic operation" OR "thoracic surgery" OR thoracoplasty)	27
#60	TI = (cardiothoracic %1 patient ^a) OR AB = (cardiothoracic %1 patient ^a)	2
#59	TI = ("cardiothoracic surgery" OR (chest %1 surgery)) OR AB = ("cardiothoracic surgery" OR (chest %1 surgery))	37
#58	(MH_PHRASE = "Cardiovascular Surgical Procedures")	7
#57	(MH_PHRASE = "Thoracic Surgery")	19
#56	(MH_PHRASE = "Thoracic Surgical Procedures")	6
#55	(((((TI = (massive %1 (bleeding OR haemorrhage OR hemorrhage)) OR AB = (massive %1 (bleeding OR haemorrhage OR hemorrhage))) OR (TI = ("massive infusion" OR "massively transfused") OR AB = ("massive infusion" OR "massively transfused")) OR (TI = (massive %3 transfusion ^a) OR AB = (massive %3 transfusion ^a)) OR (((TI = (massive) OR AB = (massive)) AND ((MH_PHRASE = "Blood Transfusion"))))) AND (((TI = (anaemia OR anemia) OR AB = (anaemia OR anemia)) OR ((MH_PHRASE = "Anemia, Hypochromic")) OR ((MH_PHRASE = "Anemia, Hemolytic, Autoimmune")) OR ((MH_PHRASE = "Anemia, Sickle Cell")) OR ((MH_PHRASE = "Anemia, Hemolytic, Congenital Nonspherocytic")) OR ((MH_PHRASE = "Anemia, Pernicious")) OR ((MH_PHRASE = "Anemia, Diamond-Blackfan")) OR ((MH_PHRASE = "Anemia, Dyserythropoietic, Congenital")) OR ((MH_PHRASE = "Anemia, Macrocytic")) OR ((MH_PHRASE = "Anemia, Refractory")) OR ((MH_PHRASE = "Anemia, Megaloblastic")) OR ((MH_PHRASE = "Anemia, Hypoplastic, Congenital")) OR ((MH_PHRASE = "Anemia, Sideroblastic")) OR ((MH_PHRASE = "Anemia, Neonatal")) OR ((MH_PHRASE = "Anemia, Iron-Deficiency")) OR ((MH_PHRASE = "Anemia, Myelophthisic")) OR ((MH_PHRASE = "Anemia, Aplastic")) OR ((MH_PHRASE = "Anemia, Hemolytic, Congenital")) OR ((MH_PHRASE = "Anemia, Hemolytic")) OR (MH_PHRASE = "Anemia")))))	32
#54	((TI = (massive %1 (bleeding OR haemorrhage OR hemorrhage)) OR AB = (massive %1 (bleeding OR haemorrhage OR hemorrhage))) OR (TI = ("massive infusion" OR "massively transfused") OR AB = ("massive infusion" OR "massively transfused")) OR (TI = (massive %3 transfusion ^a) OR AB = (massive %3 transfusion ^a)) OR (((TI = (massive) OR AB = (massive)) AND ((MH_PHRASE = "Blood Transfusion")))))	21
#53	TI = (massive %1 (bleeding OR haemorrhage OR hemorrhage)) OR AB = (massive %1 (bleeding OR haemorrhage OR hemorrhage))	11
#52	TI = ("massive infusion" OR "massively transfused") OR AB = ("massive infusion" OR "massively transfused")	1
#51	TI = (massive %3 transfusion ^a) OR AB = (massive %3 transfusion ^a)	9
#50	((TI = (massive) OR AB = (massive)) AND ((MH_PHRASE = "Blood Transfusion")))	4
#49	TI = (massive) OR AB = (massive)	237
#48	(MH_PHRASE = "Blood Transfusion")	179

Set	Search terms	Records
#47	(((TI = (shock OR "cardiovascular collapse" OR "circulatory collapse") OR AB = (shock OR "cardiovascular collapse" OR "circulatory collapse")) OR (MH_PHRASE = "Shock")) AND (((TI = (anaemia OR anemia) OR AB = (anaemia OR anemia)) OR ((MH_PHRASE = "Anemia, Hypochromic")) OR ((MH_PHRASE = "Anemia, Hemolytic, Autoimmune")) OR ((MH_PHRASE = "Anemia, Sickle Cell")) OR ((MH_PHRASE = "Anemia, Hemolytic, Congenital Nonspherocytic")) OR ((MH_PHRASE = "Anemia, Pernicious")) OR ((MH_PHRASE = "Anemia, Diamond-Blackfan")) OR ((MH_PHRASE = "Anemia, Dyserythropoietic, Congenital")) OR ((MH_PHRASE = "Anemia, Macrocytic")) OR ((MH_PHRASE = "Anemia, Refractory")) OR ((MH_PHRASE = "Anemia, Megaloblastic")) OR ((MH_PHRASE = "Anemia, Hypoplastic, Congenital")) OR ((MH_PHRASE = "Anemia, Sideroblastic")) OR ((MH_PHRASE = "Anemia, Neonatal")) OR ((MH_PHRASE = "Anemia, Iron-Deficiency")) OR ((MH_PHRASE = "Anemia, Myelophthisic")) OR ((MH_PHRASE = "Anemia, Aplastic")) OR ((MH_PHRASE = "Anemia, Hemolytic, Congenital")) OR ((MH_PHRASE = "Anemia, Hemolytic")) OR (MH_PHRASE = "Anemia"))))	30
#46	((TI = (shock OR "cardiovascular collapse" OR "circulatory collapse") OR AB = (shock OR "cardiovascular collapse" OR "circulatory collapse")) OR (MH_PHRASE = "Shock"))	465
#45	TI = (shock OR "cardiovascular collapse" OR "circulatory collapse") OR AB = (shock OR "cardiovascular collapse" OR "circulatory collapse")	461
#44	MH_PHRASE = "Shock"	6
#43	(((TI = (injur ^a OR trauma ^a) OR AB = (injur ^a OR trauma ^a)) OR ((MH_PHRASE = "Wounds and Injuries")) AND (((TI = (anaemia OR anemia) OR AB = (anaemia OR anemia)) OR ((MH_PHRASE = "Anemia, Hypochromic")) OR ((MH_PHRASE = "Anemia, Hemolytic, Autoimmune")) OR ((MH_PHRASE = "Anemia, Sickle Cell")) OR ((MH_PHRASE = "Anemia, Hemolytic, Congenital Nonspherocytic")) OR ((MH_PHRASE = "Anemia, Pernicious")) OR ((MH_PHRASE = "Anemia, Diamond-Blackfan")) OR ((MH_PHRASE = "Anemia, Dyserythropoietic, Congenital")) OR ((MH_PHRASE = "Anemia, Macrocytic")) OR ((MH_PHRASE = "Anemia, Refractory")) OR ((MH_PHRASE = "Anemia, Megaloblastic")) OR ((MH_PHRASE = "Anemia, Hypoplastic, Congenital")) OR ((MH_PHRASE = "Anemia, Sideroblastic")) OR ((MH_PHRASE = "Anemia, Neonatal")) OR ((MH_PHRASE = "Anemia, Iron-Deficiency")) OR ((MH_PHRASE = "Anemia, Myelophthisic")) OR ((MH_PHRASE = "Anemia, Aplastic")) OR ((MH_PHRASE = "Anemia, Hemolytic, Congenital")) OR ((MH_PHRASE = "Anemia, Hemolytic")) OR (MH_PHRASE = "Anemia"))))	41
#42	((TI = (injur ^a OR trauma ^a) OR AB = (injur ^a OR trauma ^a)) OR ((MH_PHRASE = "Wounds and Injuries"))	5,555
#41	TI = (injur ^a OR trauma ^a) OR AB = (injur ^a OR trauma ^a)	5,507
#40	(MH_PHRASE = "Wounds and Injuries")	106

Set	Search terms	Records
#39	(((TI = (postoperative OR "post operative") OR AB = (postoperative OR "post operative")) OR (TI = (peroperative OR "per operative") OR AB = (peroperative OR "per operative")) OR (TI = (intraoperative OR "intra operative") OR AB = (intraoperative OR "intra operative")) OR (TI = (preoperative OR "pre operative") OR AB = (preoperative OR "pre operative")) OR (TI = (perioperative OR "peri operative") OR AB = (perioperative OR "peri operative")) OR ((MH_PHRASE = "Intraoperative Care")) OR ((MH_PHRASE = "Intraoperative Complications")) OR ((MH_PHRASE = "Intraoperative Period")) OR ((MH_PHRASE = "Postoperative Hemorrhage")) OR ((MH_PHRASE = "Postoperative Complications")) OR ((MH_PHRASE = "Postoperative Care")) OR ((MH_PHRASE = "Postoperative Period")) OR ((MH_PHRASE = "Preoperative Care")) OR ((MH_PHRASE = "Perioperative Nursing")) OR ((MH_PHRASE = "Perioperative Care")))) AND (((TI = (anaemia OR anemia) OR AB = (anaemia OR anemia)) OR ((MH_PHRASE = "Anemia, Hypochromic")) OR ((MH_PHRASE = "Anemia, Hemolytic, Autoimmune")) OR ((MH_PHRASE = "Anemia, Sickle Cell")) OR ((MH_PHRASE = "Anemia, Hemolytic, Congenital Nonspherocytic")) OR ((MH_PHRASE = "Anemia, Pernicious")) OR ((MH_PHRASE = "Anemia, Diamond-Blackfan")) OR ((MH_PHRASE = "Anemia, Dyserythropoietic, Congenital")) OR ((MH_PHRASE = "Anemia, Macrocytic")) OR ((MH_PHRASE = "Anemia, Refractory")) OR ((MH_PHRASE = "Anemia, Megaloblastic")) OR ((MH_PHRASE = "Anemia, Hypoplastic, Congenital")) OR ((MH_PHRASE = "Anemia, Sideroblastic")) OR ((MH_PHRASE = "Anemia, Neonatal")) OR ((MH_PHRASE = "Anemia, Iron-Deficiency")) OR ((MH_PHRASE = "Anemia, Myelophthisic")) OR ((MH_PHRASE = "Anemia, Aplastic")) OR ((MH_PHRASE = "Anemia, Hemolytic, Congenital")) OR ((MH_PHRASE = "Anemia, Hemolytic")) OR (MH_PHRASE = "Anemia"))))	40
#38	((TI = (postoperative OR "post operative") OR AB = (postoperative OR "post operative")) OR (TI = (peroperative OR "per operative") OR AB = (peroperative OR "per operative")) OR (TI = (intraoperative OR "intra operative") OR AB = (intraoperative OR "intra operative")) OR (TI = (preoperative OR "pre operative") OR AB = (preoperative OR "pre operative")) OR (TI = (perioperative OR "peri operative") OR AB = (perioperative OR "peri operative")) OR ((MH_PHRASE = "Intraoperative Care")) OR ((MH_PHRASE = "Intraoperative Complications")) OR ((MH_PHRASE = "Intraoperative Period")) OR ((MH_PHRASE = "Postoperative Hemorrhage")) OR ((MH_PHRASE = "Postoperative Complications")) OR ((MH_PHRASE = "Postoperative Care")) OR ((MH_PHRASE = "Postoperative Period")) OR ((MH_PHRASE = "Preoperative Care")) OR ((MH_PHRASE = "Perioperative Nursing")) OR ((MH_PHRASE = "Perioperative Care"))	2,443
#37	TI = (postoperative OR "post operative") OR AB = (postoperative OR "post operative")	1,111
#36	TI = (peroperative OR "per operative") OR AB = (peroperative OR "per operative")	7
#35	TI = (intraoperative OR "intra operative") OR AB = (intraoperative OR "intra operative")	251
#34	TI = (preoperative OR "pre operative") OR AB = (preoperative OR "pre operative")	622
#33	TI = (perioperative OR "peri operative") OR AB = (perioperative OR "peri operative")	369
#32	(MH_PHRASE = "Intraoperative Care")	74
#31	(MH_PHRASE = "Intraoperative Complications")	99
#30	(MH_PHRASE = "Intraoperative Period")	77
#29	(MH_PHRASE = "Postoperative Hemorrhage")	5
#28	(MH_PHRASE = "Postoperative Complications")	378
#27	(MH_PHRASE = "Postoperative Care")	197
#26	(MH_PHRASE = "Postoperative Period")	146
#25	(MH_PHRASE = "Preoperative Care")	212

Set	Search terms	Records
#24	(MH_PHRASE = "Perioperative Nursing")	61
#22	(MH_PHRASE = "Perioperative Care")	37
#21	((TI = (anaemia OR anemia) OR AB = (anaemia OR anemia)) OR ((MH_PHRASE = "Anemia, Hypochromic")) OR ((MH_PHRASE = "Anemia, Hemolytic, Autoimmune")) OR ((MH_PHRASE = "Anemia, Sickle Cell")) OR ((MH_PHRASE = "Anemia, Hemolytic, Congenital Nonspherocytic")) OR ((MH_PHRASE = "Anemia, Pernicious")) OR ((MH_PHRASE = "Anemia, Diamond-Blackfan")) OR ((MH_PHRASE = "Anemia, Dyserythropoietic, Congenital")) OR ((MH_PHRASE = "Anemia, Macrocytic")) OR ((MH_PHRASE = "Anemia, Refractory")) OR ((MH_PHRASE = "Anemia, Megaloblastic")) OR ((MH_PHRASE = "Anemia, Hypoplastic, Congenital")) OR ((MH_PHRASE = "Anemia, Sideroblastic")) OR ((MH_PHRASE = "Anemia, Neonatal")) OR ((MH_PHRASE = "Anemia, Iron-Deficiency")) OR ((MH_PHRASE = "Anemia, Myelophthisic")) OR ((MH_PHRASE = "Anemia, Aplastic")) OR ((MH_PHRASE = "Anemia, Hemolytic, Congenital")) OR ((MH_PHRASE = "Anemia, Hemolytic")) OR (MH_PHRASE = "Anemia"))	409
#20	TI = (anaemia OR anemia) OR AB = (anaemia OR anemia)	397
#19	(MH_PHRASE = "Anemia, Hypochromic")	6
#18	(MH_PHRASE = "Anemia, Hemolytic, Autoimmune")	0
#17	(MH_PHRASE = "Anemia, Sickle Cell")	3
#16	(MH_PHRASE = "Anemia, Hemolytic, Congenital Nonspherocytic")	1
#15	(MH_PHRASE = "Anemia, Pernicious")	2
#14	(MH_PHRASE = "Anemia, Diamond-Blackfan")	0
#13	(MH_PHRASE = "Anemia, Dyserythropoietic, Congenital")	0
#12	(MH_PHRASE = "Anemia, Macrocytic")	2
#11	(MH_PHRASE = "Anemia, Refractory")	0
#10	(MH_PHRASE = "Anemia, Megaloblastic")	2
#9	(MH_PHRASE = "Anemia, Hypoplastic, Congenital")	0
#8	(MH_PHRASE = "Anemia, Sideroblastic")	0
#7	(MH_PHRASE = "Anemia, Neonatal")	1
#6	(MH_PHRASE = "Anemia, Iron-Deficiency")	7
#5	(MH_PHRASE = "Anemia, Myelophthisic")	0
#4	(MH_PHRASE = "Anemia, Aplastic")	4
#3	(MH_PHRASE = "Anemia, Hemolytic, Congenital")	2
#2	(MH_PHRASE = "Anemia, Hemolytic")	3
#1	MH_PHRASE = "Anemia"	7

a The search was conducted using Informat online platform on 26 June 2009

b The records from each of these search statements were exported separately owing to technical difficulties experienced with Informat when processing this search statement. Consequently, there were duplicated records in this number. After exclusion of duplicates 66 unique records from AMI were identified

A4 Literature search – question 4

Question 4

In patients with critical bleeding requiring massive transfusion, what is the effect of red blood cell transfusion on patient outcomes in a critical bleeding population requiring massive transfusion?

Tables A4.1 EMBASE.com search conducted 13 May 2009

Table A4.1.1 Red blood cell transfusion

#	Query	Results
#1	'erythrocyte transfusion'/exp	7,121
#2	'erythrocyte transfusion':ab,ti OR 'erythrocyte transfusions':ab,ti	293
#3	'red blood cell *1 transfusion':ab,ti OR 'rbc *1 transfusion':ab,ti	1,089
#4	'red blood cell *1 transfusions':ab,ti OR 'rbc *1 transfusions':ab,ti	928
#5	'red cell *1 transfusion':ab,ti OR 'normocyte transfusion':ab,ti	523
#6	'red cell *1 transfusions':ab,ti OR 'normocyte transfusions':ab,ti	384
#7	'red blood cell *1 exchange':ab,ti OR 'rbc *1 exchange':ab,ti	68
#8	'red cell *3 exchange':ab,ti OR 'red cells *3 exchange':ab,ti	108
#9	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	8,382

Table A4.1.2 Restrictive transfusion trigger

#	Query	Results
#1	'restrictive transfusion trigger':de	1
#2	restrictive:ti AND transfus*:ti	37
#3	'restrictive *3 transfusion':ab,ti OR 'low *3 transfusion':ab,ti	321
#4	'restrictive *3 transfusions':ab,ti OR 'low *3 transfusions':ab,ti	35
#5	#1 OR #2 OR #3 OR #4	357

Table A4.1.3 Liberal transfusion

#	Query	Results
#1	liberal:ti AND transfus*:ti	16
#2	'liberal *3 transfusion':ti,ab OR 'high *3 transfusion':ti,ab	315
#3	'liberal *3 transfusions':ab,ti OR 'high *3 transfusions':ab,ti	46
#4	#1 OR #2 OR #3	362

Table A4.1.4 Transfusion threshold

#	Query	Results
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#1	'transfusion threshold':ab,ti OR 'transfusion thresholds':ab,ti	143
#2	'transfusion trigger':ab,ti OR 'trigger *1 transfusion':ab,ti	208
#3	'transfusion triggers':ab,ti OR 'triggers *1 transfusion':ab,ti	116
#4	'transfusion strategy':ab,ti OR 'transfusion strategies':ab,ti	179
#5	'transfusion policy':ab,ti OR 'transfusion policies':ab,ti	204
#6	'transfusion practice':ab,ti OR 'transfusion practices':ab,ti	915
#7	'transfusion protocol':ti,ab OR 'transfusion protocols':ti,ab	168
#8	'transfusion *1 guideline':ab,ti OR 'transfusion *1 guidelines':ab,ti	166
#9	'hemoglobin threshold':ti,ab OR 'hemoglobin trigger':ti,ab	27
#10	'haemoglobin threshold':ab,ti OR 'haemoglobin trigger':ab,ti	13
#11	'hb threshold':ab,ti OR 'hb trigger':ab,ti	12
#12	'hemoglobin thresholds':ab,ti OR 'hemoglobin triggers':ab,ti	19
#13	'haemoglobin thresholds':ab,ti OR 'haemoglobin triggers':ab,ti	7
#14	'hb thresholds':ab,ti OR 'hb triggers':ab,ti	1
#15	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14	1,839

Table A4.1.5 Haemoglobin

#	Query	Results
#1	'hemoglobin'/de	63,298
#2	'hemoglobin determination'/de	17,180
#3	'hemoglobin blood level'/de	5,457
#4	'mean corpuscular volume'/de	3,287
#5	'blood haemoglobin':ab,ti OR 'blood hemoglobin':ab,ti	1,154
#6	'haemoglobin *1 level':ab,ti OR 'hemoglobin *1 level':ab,ti	4,664
#7	'haemoglobin *1 levels':ab,ti OR 'hemoglobin *1 levels':ab,ti	5,800
#8	'hb level':ab,ti OR 'hb levels':ab,ti	1,621
#9	'haemoglobin determination':ab,ti OR 'hemoglobin determination':ab,ti	178
#10	'hemoglobin assay':ab,ti OR 'haemoglobin assay':ab,ti	92
#11	'hemoglobin estimation':ab,ti OR 'haemoglobin estimation':ab,ti	100
#12	'hb determination':ab,ti OR 'hb estimation':ab,ti OR 'hb assay':ab,ti	47
#13	'hemoglobin *1 content':ab,ti OR 'hemoglobin *1 concentration':ab,ti	5,608
#14	'haemoglobin *1 content':ti,ab OR 'haemoglobin *1 concentration':ti,ab	2,489
#15	'hb content':ab,ti OR 'hb concentration':ab,ti	1,076

#	Query	Results
#16	hemoglobinometry:ab,ti OR haemoglobinometry:ab,ti	114
#17	'plasma haemoglobin':ab,ti OR 'plasma hemoglobin':ab,ti	588
#18	'serum haemoglobin':ab,ti OR 'serum hemoglobin':ab,ti	354
#19	'mean corpuscular volume':ab,ti OR mcv:ab,ti OR mch:ab,ti OR mchc:ab,ti	6,617
#20	'mean corpuscular haemoglobin':ab,ti OR 'mean corpuscular hemoglobin':ab,ti	957
#21	'mean cell *1 haemoglobin':ab,ti OR 'mean cell *1 hemoglobin':ab,ti	285
#22	'erythrocyte indices':ti,ab OR 'erythrocyte index':ti,ab OR 'erythrocyte indexes':ti,ab	167
#23	'red *1 cell indices':ab,ti OR 'red *1 cell index':ab,ti OR 'red *1 cell indexes':ab,ti	436
#24	'rbc indices':ab,ti OR 'rbc index':ab,ti OR 'rbc indexes':ab,ti	75
#25	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #20 OR #21 OR #22 OR #23 OR #24	86,709

Table A4.1.6 Re-operation

#	Query	Results
#1	'reoperation'/de	33,578
#2	'bleeding'/de	91,781
#3	'postoperative hemorrhage'/de	9,331
#4	#2 OR #3	100,287
#5	#1 OR #3	42,145
#6	reoperation*:ti AND (bleeding:ti OR 'blood loss':ti)	14
#7	reoperation*:ti AND (hemorrhag*:ti OR haemorrhag*:ti)	7
#8	('re operation':ti OR 're operations':ti) AND bleeding:ti	3
#9	('re operation':ti OR 're operations':ti) AND 'blood loss':ti	0
#10	('re operation':ti OR 're operations':ti) AND hemorrhag*:ti	1
#11	('re operation':ti OR 're operations':ti) AND haemorrhag*:ti	0
#12	reoperation*:ab AND (bleeding:ab OR 'blood loss':ab)	1,926
#13	reoperation*:ab AND (hemorrhag*:ab OR haemorrhag*:ab)	945
#14	('re operation':ab OR 're operations':ab) AND bleeding:ab	229
#15	('re operation':ab OR 're operations':ab) AND 'blood loss':ab	84
#16	('re operation':ab OR 're operations':ab) AND hemorrhag*:ab	67
#17	('re operation':ab OR 're operations':ab) AND haemorrhag*:ab	58
#18	'repeat surgery':ab,ti OR 'surgical revision':ab,ti	2,033
#19	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18	134,493

Table A4.1.7 Hospital discharge

#	Query	Results
#1	'hospital discharge'/de	29,496
#2	'patient transport'/de	13,541
#3	'hospital discharge':ab,ti OR 'patient discharge':ab,ti	12,048
#4	'discharge planning':ab,ti OR 'discharge plan':ab,ti	1,861
#5	'intra-hospital transfer':ab,ti OR 'patient transfer':ab,ti	399
#6	'patient dumping':ab,ti OR 'discharge home':ab,ti	662
#7	'patients discharged':ab,ti OR 'patient discharged':ab,ti	3,152
#8	'patient discharges':ab,ti OR 'discharge management':ab,ti	180
#9	'discharged patient':ab,ti OR 'discharged patients':ab,ti	864
#10	'discharge program':ab,ti OR 'home discharge':ab,ti	250
#11	'early discharge':ab,ti OR 'admission discharge':ab,ti	1,989
#12	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11	55,207

Table A4.1.8 Disseminated intravascular clotting

#	Query	Results
#1	'disseminated intravascular clotting'/de	14,564
#2	'consumption coagulopathy':ab,ti OR 'consumptive coagulopathy':ab,ti	1,259
#3	'defibrination syndrome':ab,ti OR 'sanarelli shwartzman syndrome':ab,ti	120
#4	'disseminated fibrin thromboembolism':ab,ti	3
#5	'disseminated intravasal thromboembolism':ab,ti	0
#6	'intravasal agglutination':ab,ti OR 'intravasal *1 clotting':ab,ti	5
#7	'intravascular *1 clotting':ab,ti OR 'intravascular *1 coagulation':ab,ti	10,134
#8	'intravascular *1 coagulopathy':ti,ab OR 'intravenous *1 coagulation':ti,ab	669
#9	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	18,446

Table A4.2 Complete EMBASE search

#	Query	Results
#1	('erythrocyte transfusion'/exp) OR ('erythrocyte transfusion':ab,ti OR 'erythrocyte transfusions':ab,ti) OR ('red blood cell *1 transfusion':ab,ti OR 'rbc *1 transfusion':ab,ti) OR ('red blood cell *1 transfusions':ab,ti OR 'rbc *1 transfusions':ab,ti) OR ('red cell *1 transfusion':ab,ti OR 'normocyte transfusion':ab,ti) OR ('red cell *1 transfusions':ab,ti OR 'normocyte transfusions':ab,ti) OR ('red blood cell *1 exchange':ab,ti OR 'rbc *1 exchange':ab,ti) OR ('red cell *3 exchange':ab,ti OR 'red cells *3 exchange':ab,ti)	8,382

#	Query	Results
#2	('restrictive transfusion trigger':de) OR (restrictive:ti AND transfus*:ti) OR ('restrictive *3 transfusion':ab,ti OR 'low *3 transfusion':ab,ti) OR ('restrictive *3 transfusions':ab,ti OR 'low *3 transfusions':ab,ti)	357
#3	(liberal:ti AND transfus*:ti) OR ('liberal *3 transfusion':ti,ab OR 'high *3 transfusion':ti,ab) OR ('liberal *3 transfusions':ab,ti OR 'high *3 transfusions':ab,ti)	362
#4	('transfusion threshold':ab,ti OR 'transfusion thresholds':ab,ti) OR ('transfusion trigger':ab,ti OR 'trigger *1 transfusion':ab,ti) OR ('transfusion triggers':ab,ti OR 'triggers *1 transfusion':ab,ti) OR ('transfusion strategy':ab,ti OR 'transfusion strategies':ab,ti) OR ('transfusion policy':ab,ti OR 'transfusion policies':ab,ti) OR ('transfusion practice':ab,ti OR 'transfusion practices':ab,ti) OR ('transfusion protocol':ti,ab OR 'transfusion protocols':ti,ab) OR ('transfusion *1 guideline':ab,ti OR 'transfusion *1 guidelines':ab,ti) OR ('hemoglobin threshold':ti,ab OR 'hemoglobin trigger':ti,ab) OR ('haemoglobin threshold':ab,ti OR 'haemoglobin trigger':ab,ti) OR ('hb threshold':ab,ti OR 'hb trigger':ab,ti) OR ('hemoglobin thresholds':ab,ti OR 'hemoglobin triggers':ab,ti) OR ('haemoglobin thresholds':ab,ti OR 'haemoglobin triggers':ab,ti) OR ('hb thresholds':ab,ti OR 'hb triggers':ab,ti)	1,839
#5	#1 OR #2 OR #3 OR #4	10,133
#6	('perioperative period'/exp) OR ('perioperative nursing'/exp) OR ('perioperative complication'/exp) OR ('preoperative period'/exp) OR ('preoperative complication'/exp) OR ('intraoperative period'/exp) OR (perioperative:ab,ti OR 'peri operative':ab,ti) OR (preoperative:ab,ti OR 'pre operative':ab,ti) OR (intraoperative:ab,ti OR 'intra operative':ab,ti) OR (peroperative:ab,ti OR 'per operative':ab,ti)	333,328
#7	'postoperative period'/exp	211,781
#8	'postoperative complication'/exp	353,284
#9	postoperative:ab,ti OR 'post operative':ab,ti	280,258
#10	#6 OR #7 OR #8 OR #9	863,981
#11	('injury'/exp) OR (injur*:ab,ti OR trauma*:ab,ti)	1,260,839
#12	('shock'/exp) OR (shock:ab,ti OR 'cardiovascular collapse':ab,ti OR 'circulatory collapse':ab,ti)	135,313
#13	((('blood transfusion'/exp) OR (('bleeding'/exp) AND ('transfusion'/exp))) AND (massive:ab,ti)) OR ('massive transfusion':ab,ti) OR ('massive blood transfusion':ab,ti) OR ('massive transfusion protocol':ab,ti) OR ('massive *3 transfusion':ab,ti OR 'massive *3 transfusions':ab,ti) OR ('massive infusion':ab,ti OR 'massively transfused':ab,ti) OR ('massive *1 bleeding':ab,ti) OR ('massive *1 haemorrhage':ab,ti OR 'massive *1 hemorrhage':ab,ti)	8,395
#14	('thorax surgery'/exp) OR ('heart surgery'/exp) OR ('cardiothoracic surgery':ab,ti OR 'chest *1 surgery':ab,ti) OR ('cardiothoracic *1 patient':ab,ti OR 'cardiothoracic *1 patients':ab,ti) OR ('thoracic operation':ab,ti OR 'thoracic surgery':ab,ti OR thoracoplasty:ab,ti) OR ('thoracic *1 procedure':ab,ti OR 'thoracic *1 procedures':ab,ti)	284,912
#15	('surgery'/exp) OR ('surgical ward'/exp) OR ('surgical patient'/exp) OR (surgical:ab,ti OR surgery:ab,ti OR operation:ab,ti OR resection:ab,ti)	2,723,714

#	Query	Results
#16	('orthopedic surgery'/exp) OR ('orthopedic surgery':ab,ti OR 'orthopaedic surgery':ab,ti) OR ('bone surgery':ab,ti OR orthopaedics:ab,ti OR orthopedics:ab,ti) OR ('orthopedic *1 patient':ab,ti OR 'orthopedic *1 patients':ab,ti) OR ('orthopaedic *1 patient':ab,ti OR 'orthopaedic *1 patients':ab,ti) OR ('orthopedic operation':ab,ti OR 'orthopedic *1 procedures':ab,ti) OR ('orthopaedic operation':ab,ti OR 'orthopaedic *1 procedures':ab,ti) OR ('orthopedic *1 procedure':ab,ti OR 'orthopaedic *1 procedure':ab,ti)	257,834
#17	#10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16	3,678,764
#18	#5 AND #17	5,209
#19	('adverse outcome'/exp) OR ('outcome assessment'/exp) OR ('morbidity'/exp) OR ('mortality'/exp) OR (morbidity:ab,ti OR incidence:ab,ti OR prevalence:ab,ti OR occurrence:ab,ti) OR (mortality:ab,ti OR death:ab,ti OR survival:ab,ti)	1,921,554
#20	('quality of life'/exp) OR (qol:ab,ti OR 'quality of life':ab,ti OR 'quality of wellbeing':ab,ti) OR ('health related quality':ab,ti OR hrqol:ab,ti) OR (qaly*:ab,ti OR 'quality adjusted':ab,ti OR 'adjusted life':ab,ti)	159,310
#21	((('blood component therapy'/exp) AND (('dose response'/exp) OR ('drug dose'/exp))) OR ('fresh frozen plasma'/exp/dd_do) OR ('recombinant erythropoietin'/exp/dd_do) OR ('transfusion frequency':ab,ti) OR ('frequency *5 transfusion':ab,ti OR 'frequency *5 transfusions':ab,ti) OR ('transfusion rate':ab,ti OR 'transfusion rates':ab,ti) OR ('rate *5 transfusion':ab,ti OR 'rates *5 transfusion':ab,ti) OR ('transfusion requirement':ab,ti OR 'transfusion requirements':ab,ti) OR ('transfusion indication':ab,ti OR 'transfusion indications':ab,ti) OR ('indications *5 transfusion':ab,ti OR 'indications *5 transfusions':ab,ti) OR ('indication *5 transfusion':ab,ti OR 'indication *5 transfusions':ab,ti) OR ('transfusion interval':ab,ti OR 'transfusion intervals':ab,ti) OR ('need *3 transfusion':ab,ti OR 'need *3 transfusions':ab,ti) OR ('transfusion need':ab,ti OR 'transfusion needs':ab,ti) OR ('dose *3 transfusion':ab,ti OR 'dose *3 transfusions':ab,ti) OR ('dose *3 transfused':ab,ti OR 'transfusions *3 dose':ab,ti) OR ('transfusion dose':ab,ti OR 'transfused *3 dose':ab,ti) OR ('platelet dose':ab,ti OR 'dose *3 platelets':ab,ti) OR (dose:ab,ti AND transfus*:ab,ti)	17,357
#22	('hemoglobin'/de) OR ('hemoglobin determination'/de) OR ('hemoglobin blood level'/de) OR ('mean corpuscular volume'/de) OR ('blood haemoglobin':ab,ti OR 'blood hemoglobin':ab,ti) OR ('haemoglobin *1 level':ab,ti OR 'hemoglobin *1 level':ab,ti) OR ('haemoglobin *1 levels':ab,ti OR 'hemoglobin *1 levels':ab,ti) OR ('hb level':ab,ti OR 'hb levels':ab,ti) OR ('haemoglobin determination':ab,ti OR 'hemoglobin determination':ab,ti) OR ('hemoglobin assay':ab,ti OR 'haemoglobin assay':ab,ti) OR ('hemoglobin estimation':ab,ti OR 'haemoglobin estimation':ab,ti) OR ('hb determination':ab,ti OR 'hb estimation':ab,ti OR 'hb assay':ab,ti) OR ('hemoglobin *1 content':ab,ti OR 'hemoglobin *1 concentration':ab,ti) OR ('haemoglobin *1 content':ti,ab OR 'haemoglobin *1 concentration':ti,ab) OR ('hb content':ab,ti OR 'hb concentration':ab,ti) OR (hemoglobinometry:ab,ti OR haemoglobinometry:ab,ti) OR ('plasma haemoglobin':ab,ti OR 'plasma hemoglobin':ab,ti) OR ('serum haemoglobin':ab,ti OR 'serum hemoglobin':ab,ti) OR ('mean corpuscular haemoglobin':ab,ti OR 'mean corpuscular hemoglobin':ab,ti) OR ('mean cell *1 haemoglobin':ab,ti OR 'mean cell *1 hemoglobin':ab,ti) OR ('erythrocyte indices':ti,ab OR 'erythrocyte index':ti,ab OR 'erythrocyte indexes':ti,ab) OR ('red *1 cell indices':ab,ti OR 'red *1 cell index':ab,ti OR 'red *1 cell indexes':ab,ti) OR ('rbc indices':ab,ti OR 'rbc index':ab,ti OR 'rbc indexes':ab,ti)	86,709

#	Query	Results
#23	('health economics'/exp) OR ('economic aspect'/exp) OR ('economics'/exp) OR ('finance'/exp) OR ('biomedical technology assessment'/exp) OR ('economic evaluation'/exp) OR ('health care cost'/exp) OR (economic*:ab,ti OR pharmaco-economic*:ab,ti) OR (cost*:ab,ti OR price*:ab,ti OR pricing:ab,ti) OR ('burden of illness':ab,ti OR 'value *1 money':ab,ti) OR (resource*:ab,ti AND utili*:ab,ti) OR (resource*:ab,ti AND utili*:ab,ti) OR ('technology assessment':ab,ti OR 'technology assessments':ab,ti) OR ('technology appraisal':ab,ti OR 'technology appraisals':ab,ti)	994,511
#24	('hospitalization'/exp) OR ('length of stay'/exp) OR (hospitaliz*:ab,ti OR hospitalis*:ab,ti) OR ('length *3 stay':ab,ti OR 'hospital stay':ab,ti)	244,094
#25	('intensive care unit'/exp) OR ('intensive care unit':ab,ti OR icu:ab,ti OR 'intensive care units':ab,ti) OR ('close attention unit':ab,ti OR 'close attention units':ab,ti) OR ('intensive care department':ab,ti OR 'intensive care departments':ab,ti) OR ('special care unit':ab,ti OR 'special care units':ab,ti) OR ('critical care unit':ab,ti OR 'critical care units':ab,ti)	76,464
#26	('reoperation'/de) OR ('bleeding'/de) OR ('postoperative hemorrhage'/de) OR (('bleeding'/de) OR ('postoperative hemorrhage'/de)) OR (('reoperation'/de) OR ('postoperative hemorrhage'/de)) OR (reoperation*:ti AND (bleeding:ti OR 'blood loss':ti)) OR (reoperation*:ti AND (hemorrhag*:ti OR haemorrhag*:ti)) OR (('re operation':ti OR 're operations':ti) AND bleeding:ti) OR (('re operation':ti OR 're operations':ti) AND 'blood loss':ti) OR (('re operation':ti OR 're operations':ti) AND hemorrhag*:ti) OR (('re operation':ti OR 're operations':ti) AND haemorrhag*:ti) OR (reoperation*:ab AND (bleeding:ab OR 'blood loss':ab)) OR (reoperation*:ab AND (hemorrhag*:ab OR haemorrhag*:ab)) OR (('re operation':ab OR 're operations':ab) AND bleeding:ab) OR (('re operation':ab OR 're operations':ab) AND 'blood loss':ab) OR (('re operation':ab OR 're operations':ab) AND hemorrhag*:ab) OR (('re operation':ab OR 're operations':ab) AND haemorrhag*:ab) OR ('repeat surgery':ab,ti OR 'surgical revision':ab,ti)	134,493
#27	('hospital admission'/exp) OR ('hospital readmission'/exp) OR ('hospital admission':ab,ti OR 'hospital admittance':ab,ti) OR ('patient admission':ab,ti OR readmission:ab,ti) OR (rehospitalization:ab,ti OR rehospitalisation:ab,ti)	77,348
#28	('hospital discharge'/de) OR ('patient transport'/de) OR ('hospital discharge':ab,ti OR 'patient discharge':ab,ti) OR ('discharge planning':ab,ti OR 'discharge plan':ab,ti) OR ('intra-hospital transfer':ab,ti OR 'patient transfer':ab,ti) OR ('patient dumping':ab,ti OR 'discharge home':ab,ti) OR ('patients discharged':ab,ti OR 'patient discharged':ab,ti) OR ('patient discharges':ab,ti OR 'discharge management':ab,ti) OR ('discharged patient':ab,ti OR 'discharged patients':ab,ti) OR ('discharge program':ab,ti OR 'home discharge':ab,ti) OR ('early discharge':ab,ti OR 'admission discharge':ab,ti)	55,207
#29	('disseminated intravascular clotting'/de) OR ('consumption coagulopathy':ab,ti OR 'consumptive coagulopathy':ab,ti) OR ('defibrination syndrome':ab,ti OR 'sanarelli shwartzman syndrome':ab,ti) OR ('disseminated fibrin thromboembolism':ab,ti) OR ('disseminated intravasal thromboembolism':ab,ti) OR ('intravasal agglutination':ab,ti OR 'intravasal *1 clotting':ab,ti) OR ('intravascular *1 clotting':ab,ti OR 'intravascular *1 coagulation':ab,ti) OR ('intravascular *1 coagulopathy':ti,ab OR 'intravenous *1 coagulation':ti,ab)	18,446
#30	#19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29	3,242,933
#31	#18 AND #30	3,889

Table A4.3 Cochrane library database search conducted 13 May 2009

No.	Query	Results
#1	MeSH descriptor Erythrocyte Transfusion explode all trees	346
#2	"erythrocyte transfusion" OR "erythrocyte transfusions"	432
#3	("red blood cell" OR rbc) NEAR/1 transfusion*	142
#4	"red cell" NEAR/1 transfusion*	3
#5	"normocyte transfusion" OR "normocyte transfusions"	0
#6	("red blood cell" OR rbc) NEAR/1 exchange	2
#7	("red cell" OR "red cells") NEAR/3 exchange	3
#8	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7	1,916
#9	(restrictive AND transfus*):ti	13
#10	(restrictive OR low) NEAR/3 transfusion*	201
#11	#9 OR #10	1,473
#12	(liberal AND transfus*):ti	6
#13	(liberal OR high) NEAR/3 transfusion*	151
#14	#12 OR #13	1,257
#15	"transfusion threshold" OR "transfusion thresholds"	32
#16	transfusion NEAR/1 trigger*	49
#17	"transfusion strategy" OR "transfusion strategies"	24
#18	"transfusion policy" OR "transfusion policies"	20
#19	"transfusion practice" OR "transfusion practices"	48
#20	"transfusion protocol" OR "transfusion protocols"	43
#21	transfusion NEAR/1 guideline*	29
#22	"hemoglobin threshold" OR "hemoglobin trigger"	4
#23	"haemoglobin threshold" OR "haemoglobin trigger"	5
#24	"hb threshold" OR "hb trigger"	8
#25	"hemoglobin thresholds" OR "hemoglobin triggers"	4
#26	"haemoglobin thresholds" OR "haemoglobin triggers"	1
#27	"hb thresholds" OR "hb triggers"	2
#28	#15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27	1,137
#29	#8 OR #11 OR #14 OR #28	1,541
#30	MeSH descriptor Perioperative Care explode all trees	4,254
#31	MeSH descriptor Preoperative Care explode all trees	4,098

No.	Query	Results
#32	MeSH descriptor Postoperative Complications explode all trees	21,418
#33	Postoperative Period	10,851
#34	MeSH descriptor Intraoperative Complications explode all trees	2,476
#35	MeSH descriptor Intraoperative Period explode all trees	919
#36	(perioperative OR "peri operative")	5,196
#37	preoperative OR "pre operative"	11,093
#38	intraoperative OR "intra operative"	8,039
#39	peroperative OR "per operative"	474
#40	postoperative OR "post operative"	40,236
#41	#30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40	494
#42	#29 AND #41	194
#43	MeSH descriptor Wounds and Injuries explode all trees	10,953
#44	(injur* OR trauma*)	20,750
#45	#43 OR #44	189
#46	#29 AND #45	158
#47	MeSH descriptor Shock explode all trees	930
#48	(shock OR "cardiovascular collapse" OR "circulatory collapse")	3,179
#49	#47 OR #48	149
#50	#29 AND #49	125
#51	MeSH descriptor Blood Transfusion explode all trees	2,628
#52	massive	599
#53	#51 AND #52	107
#54	massive NEAR/3 transfusion*	20
#55	"massive infusion" OR "massively transfused"	3
#56	massive NEAR/1 (bleeding OR haemorrhage OR hemorrhage)	47
#57	#53 OR #54 OR #55 OR #56	106
#58	#29 AND #57	77
#59	MeSH descriptor Thoracic Surgical Procedures explode all trees	10,297
#60	MeSH descriptor Thoracic Surgery explode all trees	130
#61	MeSH descriptor Cardiovascular Surgical Procedures explode all trees	10,930
#62	"cardiothoracic surgery" OR (chest NEAR/1 surgery)	675
#63	cardiothoracic NEAR/1 patient*	4

No.	Query	Results
#64	"thoracic operation" OR "thoracic surgery" OR thoracoplasty	2,131
#65	thoracic NEAR/1 procedure*	16
#66	#59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65	93
#67	#29 AND #66	57
#68	MeSH descriptor Surgical Procedures, Operative explode all trees	68,578
#69	MeSH descriptor General Surgery explode all trees	167
#70	MeSH descriptor Surgery Department, Hospital explode all trees	68
#71	surgical OR surgery OR operation OR resection	91,783
#72	#68 OR #69 OR #70 OR #71	61
#73	#29 AND #72	49
#74	MeSH descriptor Orthopedic Procedures explode all trees	5,335
#75	MeSH descriptor Orthopedics explode all trees	272
#76	"orthopedic surgery" OR "orthopaedic surgery"	2,339
#77	"bone surgery" OR orthopaedics or orthopedics	7,975
#78	(orthopedic OR orthopaedic) NEAR/1 patient*	223
#79	"orthopedic operation" OR "orthopaedic operation"	6
#80	(orthopedic OR orthopaedic) NEAR/1 procedure*	638
#81	#74 OR #75 OR #76 OR #77 OR #78 OR #79 OR #80	59
#82	#29 AND #81	37
#83	#42 OR #46 OR #50 OR #58 OR #67 OR #73 OR #82	244
#84	MeSH descriptor Morbidity explode all trees	8,475
#85	MeSH descriptor Mortality explode all trees	7,946
#86	morbidity OR incidence OR prevalence OR occurrence	62,784
#87	mortality OR death OR survival	55,325
#88	#84 OR #85 OR #86 OR #87	45
#89	#83 AND #88	28
#90	MeSH descriptor Quality of Life explode all trees	9,425
#91	MeSH descriptor Quality-Adjusted Life years explode all trees	2,062
#92	qol OR "quality of life" OR "quality of wellbeing"	21,521
#93	"health related quality" or hrqol	2,898
#94	qaly* or "quality adjusted" or "adjusted life"	3,802
#95	#90 OR #91 OR #92 OR #93 OR #94	38

No.	Query	Results
#96	#83 AND #95	21
#97	MeSH descriptor Blood Component Transfusion explode all trees with qualifier: MT	99
#98	frequency NEAR/5 transfusion*	84
#99	rate* NEAR/5 transfusion*	324
#100	"transfusion requirement" OR "transfusion requirements"	949
#101	indication* NEAR/5 transfusion*	45
#102	"transfusion interval" OR "transfusion intervals"	13
#103	(need NEAR/3 transfusion*) OR "transfusion needs"	623
#104	dose NEAR/3 transfus*	86
#105	"platelet dose" OR (dose NEAR/3 platelets)	185
#106	(dose and transfus*):ti	72
#107	#97 OR #98 OR #99 OR #100 OR #101 OR #102 OR #103 OR #104 OR #105 OR #106	45
#108	#83 AND #107	13
#109	MeSH descriptor Hemoglobins explode all trees	4,487
#110	MeSH descriptor Hemoglobinometry explode all trees	152
#111	MeSH descriptor Erythrocyte Indices explode all trees	110
#112	"blood haemoglobin" OR "blood hemoglobin"	241
#113	(haemoglobin OR hemoglobin) NEAR/1 level*	1,228
#114	"hb level" OR "hb levels"	236
#115	"haemoglobin determination" OR "hemoglobin determination"	120
#116	"hemoglobin assay" OR "haemoglobin assay"	4
#117	"hemoglobin estimation" OR "haemoglobin estimation"	5
#118	"hb determination" OR "hb estimation" OR "hb assay"	2
#119	hemoglobin NEAR/1 (content OR concentration)	904
#120	haemoglobin NEAR/1 (content OR concentration)	904
#121	"hb content" OR "hb concentration"	110
#122	hemoglobinometry OR haemoglobinometry	166
#123	"plasma haemoglobin" OR "plasma hemoglobin"	65
#124	"serum haemoglobin" OR "serum hemoglobin"	47
#125	"mean corpuscular volume" OR mcv OR mch OR mchc	350
#126	"mean corpuscular haemoglobin" OR "mean corpuscular hemoglobin"	41
#127	"Mean Cell" NEAR/1 (Haemoglobin OR Hemoglobin)	2

No.	Query	Results
#128	"erythrocyte indices" OR "Erythrocyte Index" OR "Erythrocyte Indexes"	121
#129	red NEAR/1 ("cell indices" OR "Cell Index" OR "Cell Indexes")	14
#130	"rbc indices" OR "RBC Index" OR "RBC Indexes"	2
#131	#109 OR #110 OR #111 OR #112 OR #113 OR #114 OR #115 OR #116 OR #117 OR #118 OR #119 OR #120 OR #121 OR #122 OR #123 OR #124 OR #125 OR #126 OR #127 OR #128 OR #129 OR #130	49
#132	#83 AND #131	9
#133	MeSH descriptor Costs and Cost Analysis explode all trees	26,772
#134	MeSH descriptor Economics explode all trees	28,552
#135	MeSH descriptor Models, Economic explode all trees	1,853
#136	MeSH descriptor Value of Life explode all trees	274
#137	MeSH descriptor Utilization Review explode all trees	420
#138	MeSH descriptor Delivery of Health Care explode all trees with qualifier: UT	762
#139	economic* or pharmacoeconomic*	37,332
#140	cost* or price* or pricing	48,938
#141	resource* near utili*	1,537
#142	"burden of illness" or (value NEAR/1 money)	87
#143	#133 or #134 or #135 or #136 or #137 or #138 or #139 or #140 or #141 OR #142	15
#144	#83 and #143	7
#145	MeSH descriptor Hospitalization explode all trees	10,690
#146	MeSH descriptor Child, Hospitalized explode all trees	82
#147	hospitaliz* OR hospitalis*	16,298
#148	(length NEAR/3 stay) OR "hospital stay"	11,735
#149	#145 OR #146 OR #147 OR #148	8
#150	#83 AND #149	1
#151	MeSH descriptor Intensive Care Units explode all trees	1,978
#152	"intensive care unit" OR icu OR "intensive care units"	6,712
#153	"close attention unit" OR "close attention units"	0
#154	"intensive care department" OR "intensive care departments"	56
#155	"special care unit" OR "special care units"	63
#156	"critical care unit" OR "critical care units"	108
#157	#151 OR #152 OR #153 OR #154 OR #155 OR #156	3
#158	#83 AND #157	1

No.	Query	Results
#159	MeSH descriptor Reoperation explode all trees	1,199
#160	MeSH descriptor Hemorrhage explode all trees	7,284
#161	MeSH descriptor Postoperative Hemorrhage explode all trees	485
#162	MeSH descriptor Blood Loss, Surgical explode all trees	1,399
#163	#160 OR #161 OR #162	2
#164	#159 AND #163	1
#165	reoperation* NEAR/15 (bleeding or "blood loss")	136
#166	reoperation* NEAR/15 (hemorrhag* OR haemorrhag*)	69
#167	("re operation" OR "re operations") NEAR/15 bleeding	31
#168	("re operation" OR "re operations") NEAR/15 "blood loss"	15
#169	("re operation" OR "re operations") NEAR/15 hemorrhag*	2
#170	("re operation" OR "re operations") NEAR/15 haemorrhag*	9
#171	"Repeat Surgery" OR "Surgical Revision"	110
#172	#164 OR #165 OR #166 OR #167 OR #168 OR #169 OR #170 OR #171	6
#173	#83 AND #172	0
#174	MeSH descriptor Patient Admission explode all trees	604
#175	MeSH descriptor Patient Readmission explode all trees	593
#176	"hospital admission" OR "hospital admittance"	1,727
#177	"patient admission" OR readmission	2,327
#178	rehospitalization OR rehospitalisation	504
#179	#174 OR #175 OR #176 OR #177 OR #178	6
#180	#83 AND #179	0
#181	MeSH descriptor Patient Discharge explode all trees	822
#182	MeSH descriptor Patient Transfer explode all trees	105
#183	"hospital discharge" OR "patient discharge"	2,727
#184	"discharge planning" OR "discharge plan"	312
#185	"intra-hospital transfer" OR "patient transfer"	133
#186	"Patient Dumping" OR "discharge home"	181
#187	"patients discharged" OR "patient discharged"	341
#188	"patient discharges" OR "discharge management"	12
#189	"discharged patient" OR "discharged patients"	73
#190	"discharge program" OR "home discharge"	78

No.	Query	Results
#191	"early discharge" OR "admission discharge"	353
#192	#181 OR #182 OR #183 OR #184 OR #185 OR #186 OR #187 OR #188 OR #189 OR #190 OR #191	7
#193	#83 AND #192	0
#194	MeSH descriptor Disseminated Intravascular Coagulation explode all trees	75
#195	"consumption coagulopathy" OR "consumptive coagulopathy"	12
#196	"defibrination syndrome" OR "sanarelli shwartzman syndrome"	1
#197	"disseminated fibrin thromboembolism"	0
#198	"disseminated intravascular thromboembolism"	0
#199	"intravascular agglutination" OR (intravascular NEAR/1 clotting)	0
#200	intravascular NEAR/1 (clotting OR coagulation OR coagulopathy)	237
#201	intravenous NEAR/1 coagulation	1
#202	#194 OR #195 OR #196 OR #197 OR #198 OR #199 OR #200 OR #201	7
#203	#83 AND #202	0
#204	#89 OR #96 OR #108 OR #132 OR #144 OR #150 OR #158 OR #173 OR #180 OR #193 OR #203	45
#205	#89 OR #96 OR #108 OR #132 OR #144 OR #150 OR #158 OR #173 OR #180 OR #193 OR #203	45

Table A4.4 PreMedline search conducted 18 May 2009

#	Query	Results
#69	Search #66 OR #67 OR #68	314
#68	Search #65 AND pubmednotmedline[sb]	36
#67	Search #65 AND in process[sb]	176
#66	Search #65 NOT (medline[SB] OR oldmedline[sb])	314
#65	Search #36 OR #38 OR #40 OR #47 OR #53 OR #55 OR #64	8,906
#64	Search #29 AND #63	331
#63	Search #56 OR #57 OR #58 OR #59 OR #60 OR #61 OR #62	42,779
#62	Search orthopedic[tw] AND procedure*[tw]	11,073
#61	Search orthopaedic[tw] AND procedure*[tw]	3,355
#60	Search "orthopedic operation"[tw] OR "orthopaedic operation"[tw]	74
#59	Search orthopaedic[tw] AND patient*[tw]	8,103
#58	Search orthopedic[tw] AND patient*[tw]	15,087
#57	Search "bone surgery"[tw] OR orthopaedics[tw] or orthopedics[tw]	17,595
#56	Search "orthopedic surgery"[tw] OR "orthopaedic surgery"[tw]	5,995
#55	Search #29 AND #54	6,746

#	Query	Results
#54	Search surgical[tw] OR surgery[tw] OR operation[tw] OR resection[tw]	1,874,663
#53	Search #29 AND #52	353
#52	Search #48 OR #49 OR #50 OR #51	54,029
#51	Search thoracic[tw] AND procedure*[tw]	19,117
#50	Search "thoracic operation"[tw] OR "thoracic surgery"[tw] OR thoracoplasty[tw]	16,701
#49	Search cardiothoracic[tw] AND patient*[tw]	2,273
#48	Search "cardiothoracic surgery"[tw] OR (chest[tw] AND surgery[tw])	24,366
#47	Search #29 AND #46	713
#46	Search #41 OR #42 OR #43 OR #44 OR #45	11,296
#45	Search massive[tw] AND haemorrhage[tw]	1,180
#44	Search massive[tw] AND hemorrhage[tw]	7,704
#43	Search massive[tw] AND bleeding[tw]	4,946
#42	Search "massive infusion"[tw] OR "massively transfused"[tw]	101
#41	Search massive[tw] AND transfusion*[tw]	2,305
#40	Search #29 AND #39	781
#39	Search shock[tw] OR "cardiovascular collapse"[tw] OR "circulatory collapse"[tw]	134,680
#38	Search #29 AND #37	1,690
#37	Search injur*[tw] OR trauma*[tw]	717,377
#36	Search #29 AND #35	4,687
#35	Search #30 OR #31 OR #32 OR #33 OR #34	611,091
#34	Search postoperative[tw] OR "post operative"[tw]	467,606
#33	Search peroperative[tw] OR "per operative"[tw]	3,707
#32	Search intraoperative[tw] OR "intra operative"[tw]	88,027
#31	Search preoperative[tw] OR "pre operative"[tw]	149,265
#30	Search perioperative[tw] OR "peri operative"[tw]	42,750
#29	Search #7 OR #10 OR #13 OR #28	27,075
#28	Search #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27	3,374
#27	Search "hb thresholds"[tw] OR "hb triggers"[tw]	0
#26	Search "haemoglobin thresholds"[tw] OR "haemoglobin triggers"[tw]	7
#25	Search "hemoglobin thresholds"[tw] OR "hemoglobin triggers"[tw]	14
#24	Search "hb threshold"[tw] OR "hb trigger"[tw]	11
#23	Search "haemoglobin threshold"[tw] OR "haemoglobin trigger"[tw]	8
#22	Search "hemoglobin threshold"[tw] OR "hemoglobin trigger"[tw]	23
#21	Search transfusion[tw] AND guideline*[tw]	1,792
#20	Search "transfusion protocol"[tw] OR "transfusion protocols"[tw]	158
#19	Search "transfusion practice"[tw] OR "transfusion practices"[tw]	819
#18	Search "transfusion policy"[tw] OR "transfusion policies"[tw]	171

#	Query	Results
#17	Search "transfusion strategy"[tw] OR "transfusion strategies"[tw]	153
#16	Search "transfusion trigger"[tw] OR "transfusion triggers"[tw]	252
#15	Search trigger*[tw] AND transfusion[tw]	625
#14	Search "transfusion threshold"[tw] OR "transfusion thresholds"[tw]	131
#13	Search #11 OR #12	10,474
#12	Search (liberal[tw] OR high[tw]) AND transfusion*[tw]	10,474
#11	Search liberal[title] AND transfus*[title]	9
#10	Search #8 OR #9	7,564
#9	Search (restrictive[tw] OR low[tw]) AND transfusion*[tw]	7,564
#8	Search restrictive[title] AND transfus*[title]	28
#7	Search #1 OR #2 OR #3 OR #4 OR #5 OR #6	11,557
#6	Search ("red cell"[tw] OR "red cells"[tw]) AND exchange[tw]	1,734
#5	Search ("red blood cell[tw] OR rbc[tw]) AND exchange	1,021
#4	Search "normocyte transfusion"[tw] OR "normocyte transfusions"[tw]	0
#3	Search "red cell"[tw] AND transfusion*[tw]	3,236
#2	Search ("red blood cell"[tw] OR rbc[tw]) AND transfusion*[tw]	3,870
#1	Search "erythrocyte transfusion"[tw] OR "erythrocyte transfusions"[tw]	4,583

Table A4.5 CINAHL search conducted 28 May 2009

#	Query	Results
S232	s99 OR s105 OR s119 OR s149 OR s161 OR s168 OR s177 OR s198 OR s205 OR s218 OR s231	666 ^b
S231	s93 AND s230	10
S230	s219 OR s220 OR s221 OR s226 OR S227 OR S228	634
S229	TI (intravenous N1 coagulation) OR AB (intravenous N1 coagulation)	0
S228	TI (intravascular N1 coagulopathy) OR AB (intravascular N1 coagulopathy)	36
S227	TI (intravascular N1 coagulation) OR AB (intravascular N1 coagulation)	261
S226	TI (intravascular N1 clotting) OR AB (intravascular N1 clotting)	1
S225	TI (intravascular N1 clotting) OR AB (intravascular N1 clotting)	0
S224	TI ("intravascular agglutination") OR AB ("intravascular agglutination")	0
S223	TI ("disseminated intravascular thromboembolism") OR AB ("disseminated intravascular thromboembolism")	0
S222	TI ("disseminated fibrin thromboembolism") OR AB ("disseminated fibrin thromboembolism")	0
S221	TI ("defibrination syndrome" OR "sanarelli shwartzman syndrome") OR AB ("defibrination syndrome" OR "sanarelli shwartzman syndrome")	1
S220	TI ("consumption coagulopathy" OR "consumptive coagulopathy") OR AB ("consumption coagulopathy" OR "consumptive coagulopathy")	18
S219	(MH "Disseminated Intravascular Coagulation")	492

#	Query	Results
S218	s93 AND s217	9
S217	s206 OR s207 OR s208 OR s209 OR s210 OR s211 OR s212 OR s213 OR s214 OR s215 OR s216	13,207
S216	TI ("early discharge" OR "admission discharge") OR AB ("early discharge" OR "admission discharge")	601
S215	TI ("discharge program" OR "home discharge") OR AB ("discharge program" OR "home discharge")	103
S214	TI ("discharged patient" OR "discharged patients") OR AB ("discharged patient" OR "discharged patients")	184
S213	TI ("patient discharges" OR "discharge management") OR AB ("patient discharges" OR "discharge management")	57
S212	TI ("patients discharged" OR "patient discharged") OR AB ("patients discharged" OR "patient discharged")	601
S211	TI ("Patient Dumping" OR "discharge home") OR AB ("Patient Dumping" OR "discharge home")	248
S210	TI ("intra-hospital transfer" OR "patient transfer") OR AB ("intra-hospital transfer" OR "patient transfer")	131
S209	TI ("discharge planning" OR "discharge plan") OR AB ("discharge planning" OR "discharge plan")	1,274
S208	TI ("hospital discharge" OR "patient discharge") OR AB ("hospital discharge" OR "patient discharge")	2,740
S207	(MH "Patient Dumping")	26
S206	(MH "Patient Discharge+")	9,942
S205	s93 and s204	2
S204	S199 or S200 or S201 or S202 OR S203	8,269
S203	TI (rehospitalization OR rehospitalisation) or AB (rehospitalization OR rehospitalisation)	437
S202	TI ("patient admission" OR readmission) or AB ("patient admission" OR readmission)	1,117
S201	TI ("hospital admission" OR "hospital admittance") or AB ("hospital admission" OR "hospital admittance")	1,910
S200	(MH "Readmission")	1,892
S199	(MH "Patient Admission")	4,267
S198	s93 AND s197	11
S197	s183 OR s184 OR s185 OR s186 OR s187 OR s188 OR S190 OR S192 OR S194 OR S196	211
S196	TI ("Repeat Surgery" OR "Surgical Revision") OR AB ("Repeat Surgery" OR "Surgical Revision")	92
S195	TI ("re operations" N15 haemorrhag ^a) OR AB ("re operations" N15 haemorrhag ^a)	0
S194	TI ("re operation" N15 haemorrhag ^a) OR AB ("re operation" N15 haemorrhag ^a)	1
S193	TI ("re operations" N15 hemorrhag ^a) OR AB ("re operations" N15 hemorrhag ^a)	0
S192	TI ("re operation" N15 hemorrhag ^a) OR AB ("re operation" N15 hemorrhag ^a)	1
S191	TI ("re operations" N15 "blood loss") OR AB ("re operations" N15 "blood loss")	0

#	Query	Results
S190	TI ("re operation" N15 "blood loss") OR AB ("re operation" N15 "blood loss")	4
S189	TI ("re operations" N15 bleeding) OR AB ("re operations" N15 bleeding)	0
S188	TI ("re operation" N15 bleeding) OR AB ("re operation" N15 bleeding)	5
S187	TI (reoperation ^a N15 haemorrhag ^a) OR AB (reoperation ^a N15 haemorrhag ^a)	2
S186	TI (reoperation ^a N15 hemorrhag) OR AB (reoperation ^a N15 hemorrhag ^a)	9
S185	TI (reoperation ^a N15 "blood loss") OR AB (reoperation ^a N15 "blood loss")	5
S184	TI (reoperation ^a N15 bleeding) OR AB (reoperation ^a N15 bleeding)	40
S183	s178 AND s182	62
S182	s179 OR s180 OR s181	4,094
S181	(MH "Blood Loss, Surgical")	612
S180	(MH "postoperative hemorrhage")	493
S179	(MH "hemorrhage")	3,082
S178	(MH "Repeat Procedures+")	3,100
S177	s93 and s176	87
S176	S169 or S170 or S171 or S173 OR S174 OR S175	32,514
S175	TI ("critical care unit" OR "critical care units") or AB ("critical care unit" OR "critical care units")	862
S174	TI ("special care unit" OR "special care units") or AB ("special care unit" OR "special care units")	263
S173	TI ("intensive care department" OR "intensive care departments") or AB ("intensive care department" OR "intensive care departments")	33
S172	TI ("close attention unit" OR "close attention units") or AB ("close attention unit" OR "close attention units")	0
S171	TI ("intensive care unit" OR icu OR "intensive care units") or AB ("intensive care unit" OR icu OR "intensive care units")	13,551
S170	(MH "Critical Care Nursing+")	15,379
S169	(MH "Intensive Care Units+")	14,523
S168	S93 AND S167	68
S167	S162 OR S163 OR S164 OR S165 OR S166	41,714
S166	TI ("hospital stay") or AB ("hospital stay")	3,282
S165	TI (length N3 stay) or AB (length N3 stay)	5,786
S164	TI (hospitaliz ^a OR hospitalis ^a) or AB (hospitaliz ^a OR hospitalis ^a)	18,023
S163	(MH "Child, Hospitalized")	2,168
S162	(MH "Hospitalization+")	20,615
S161	s93 and s160	42
S160	S150 or S151 or S152 or S153 OR S154 OR S155 OR S156 OR S157 OR S158 OR S159	81,392
S159	TI (value N1 money) or AB (value N1 money)	212
S158	TI ("burden of illness") or AB ("burden of illness")	174
S157	TI (resource ^a and utili ^a) or AB (resource ^a and utili ^a)	3,133

#	Query	Results
S156	TI (cost ^a or price ^a or pricing) or AB (cost ^a or price ^a or pricing)	45,635
S155	TI (economic ^a or pharmacoeconomic ^a) or AB (economic ^a or pharmacoeconomic ^a)	16,140
S154	(MH "Health Care Delivery/UT")	63
S153	(MH "Utilization Review+")	3,381
S152	(MH "Economic Value of Life")	236
S151	(MH "Economics")	2,401
S150	(MH "Costs and Cost Analysis+")	32,489
S149	S93 AND S148	72
S148	S120 OR S121 OR S122 OR S123 OR S124 OR S125 OR S126 OR S127 OR S128 OR S129 OR S130 OR S131 OR S132 OR S133 OR S134 OR S135 OR S136 OR S137 OR S138 OR S139 OR S140 OR S141 OR S142 OR S143 OR S144 OR S146 OR S147	3,631
S147	TI ("rbc indices" OR "RBC Index" OR "RBC Indexes") OR AB ("rbc indices" OR "RBC Index" OR "RBC Indexes")	8
S146	TI (red N1 "Cell Indexes") OR AB (red N1 "Cell Indexes")	6
S145	TI (red N1 "Cell Index") OR AB (red N1 "Cell Index")	0
S144	TI (red N1 "cell indices") OR AB (red N1 "cell indices")	24
S143	TI ("erythrocyte indices" OR "Erythrocyte Index" OR "Erythrocyte Indexes") OR AB ("erythrocyte indices" OR "Erythrocyte Index" OR "Erythrocyte Indexes")	8
S142	TI ("Mean Cell" N1 Haemoglobin) OR AB ("Mean Cell" N1 Haemoglobin)	3
S141	TI ("Mean Cell" N1 Hemoglobin) OR AB ("Mean Cell" N1 Hemoglobin)	10
S140	TI ("mean corpuscular haemoglobin" OR "mean corpuscular hemoglobin") OR AB ("mean corpuscular haemoglobin" OR "mean corpuscular hemoglobin")	30
S139	TI ("mean corpuscular volume" OR mcv OR mch OR mchc) OR AB ("mean corpuscular volume" OR mcv OR mch OR mchc)	356
S138	TI ("serum haemoglobin" OR "serum hemoglobin") OR AB ("serum haemoglobin" OR "serum hemoglobin")	14
S137	TI ("plasma haemoglobin" OR "plasma hemoglobin") OR AB ("plasma haemoglobin" OR "plasma hemoglobin")	30
S136	TI (hemoglobinometry OR haemoglobinometry) OR AB (hemoglobinometry OR haemoglobinometry)	2
S135	TI ("hb content" OR "hb concentration") OR AB ("hb content" OR "hb concentration")	50
S134	TI (haemoglobin N1 concentration) OR AB (haemoglobin N1 concentration)	70
S133	TI (haemoglobin N1 content) OR AB (haemoglobin N1 content)	4
S132	TI (hemoglobin N1 concentration) OR AB (hemoglobin N1 concentration)	273
S131	TI (hemoglobin N1 content) OR AB (hemoglobin N1 content)	26
S130	TI ("hb determination" OR "hb estimation" OR "hb assay") OR AB ("hb determination" OR "hb estimation" OR "hb assay")	3
S129	TI ("hemoglobin estimation" OR "haemoglobin estimation") OR AB ("hemoglobin estimation" OR "haemoglobin estimation")	3
S128	TI ("hemoglobin assay" OR "haemoglobin assay") OR AB ("hemoglobin assay" OR "haemoglobin assay")	6

#	Query	Results
S127	TI ("haemoglobin determination" OR "hemoglobin determination") OR AB ("haemoglobin determination" OR "hemoglobin determination")	7
S126	TI ("hb level" OR "hb levels") OR AB ("hb level" OR "hb levels")	171
S125	TI (haemoglobin N1 level ^a) OR AB (haemoglobin N1 level ^a)	150
S124	TI (hemoglobin N1 level ^a) OR AB (hemoglobin N1 level ^a)	670
S123	TI ("blood haemoglobin" OR "blood hemoglobin") OR AB ("blood haemoglobin" OR "blood hemoglobin")	45
S122	(MH "Erythrocyte Indices")	97
S121	(MH "Hemoglobinometry")	21
S120	(MH "Hemoglobins")	2,501
S119	s93 and s118	139
S118	S106 or S107 or S108 OR S109 OR S110 OR S111 OR S112 or S113 or S114 or S115 or S116 or S117	807
S117	TI (dose and transfus ^a)	7
S116	TI (dose N3 platelets) or AB (dose N3 platelets)	2
S115	TI ("platelet dose") or AB ("platelet dose")	3
S114	TI (dose N3 transfus ^a) or AB (dose N3 transfus ^a)	14
S113	TI ("transfusion needs") or AB ("transfusion needs")	25
S112	TI (need N3 transfusion ^a) or AB (need N3 transfusion ^a)	234
S111	TI ("transfusion interval" OR "transfusion intervals") or AB ("transfusion interval" OR "transfusion intervals")	4
S110	TI (indication ^a N5 transfusion ^a) or AB (indication ^a N5 transfusion ^a)	34
S109	TI ("transfusion requirement" OR "transfusion requirements") or AB ("transfusion requirement" OR "transfusion requirements")	254
S108	TI (rate ^a N5 transfusion ^a) or AB (rate ^a N5 transfusion ^a)	170
S107	TI (frequency N5 transfusion ^a) or AB (frequency N5 transfusion ^a)	21
S106	(MH "Blood Component Transfusion+/MT")	141
S105	s93 and s104	7
S104	S100 or S101 or S102 or S103	36,997
S103	TI (qaly ^a or "quality adjusted" or "adjusted life") or AB (qaly ^a or "quality adjusted" or "adjusted life")	824
S102	TI ("health related quality" or hrqol) or AB ("health related quality" or hrqol)	3,387
S101	TI (qol OR "quality of life" OR "quality of wellbeing") or AB (qol OR "quality of life" OR "quality of wellbeing")	23,497
S100	(MH "Quality of Life+")	26,550
S99	s93 and s98	219
S98	S94 or S95 or S96 or S97	150,803
S97	TI (mortality OR death OR survival) or AB (mortality OR death OR survival)	71,523
S96	TI (morbidity OR incidence OR prevalence OR occurrence) or AB (morbidity OR incidence OR prevalence OR occurrence)	77,942

#	Query	Results
S95	(MH "Mortality+")	18,554
S94	(MH "Morbidity+")	27,736
S93	S48 OR S54 OR S58 OR S66 OR S75 OR S80 OR S92	554
S92	s34 and s91	45
S91	S81 or S82 OR S83 OR S84 OR S85 or S86 or S87 or S88 or S89 or S90	26,008
S90	TI (orthopaedic N1 procedure ^a) or AB (orthopaedic N1 procedure ^a)	14
S89	TI (orthopedic N1 procedure ^a) or AB (orthopedic N1 procedure ^a)	115
S88	TI ("orthopedic operation" OR "orthopaedic operation") or AB ("orthopedic operation" OR "orthopaedic operation")	6
S87	TI (orthopaedic N1 patient ^a) or AB (orthopaedic N1 patient ^a)	357
S86	TI (orthopedic N1 patient ^a) or AB (orthopedic N1 patient ^a)	245
S85	TI ("bone surgery" OR orthopaedics or orthopedics) or AB ("bone surgery" OR orthopaedics or orthopedics)	917
S84	TI ("orthopedic surgery" OR "orthopaedic surgery") or AB ("orthopedic surgery" OR "orthopaedic surgery")	801
S83	(MH "Orthopedic Nursing")	1,422
S82	(MH "Orthopedics")	3,339
S81	(MH "Orthopedic Surgery+")	21,376
S80	s34 and s79	360
S79	S76 or S77 or S78	171,915
S78	TI (surgical OR surgery OR operation OR resection) or AB (surgical OR surgery OR operation OR resection)	70,282
S77	(MH "Medical-Surgical Nursing")	2,436
S76	(MH "Surgery, Operative+")	137,624
S75	s34 and s74	87
S74	S67 or S68 or S69 or S70 or S71 or S72 OR S73	23,356
S73	TI (thoracic N1 procedure ^a) or AB (thoracic N1 procedure ^a)	32
S72	TI ("thoracic operation" OR "thoracic surgery" OR thoracoplasty) or AB ("thoracic operation" OR "thoracic surgery" OR thoracoplasty)	253
S71	TI (cardiothoracic N1 patient ^a) or AB (cardiothoracic N1 patient ^a)	57
S70	TI ("cardiothoracic surgery" OR (chest N1 surgery)) or AB ("cardiothoracic surgery" OR (chest N1 surgery))	167
S69	(MH "Cardiovascular Nursing+")	2,667
S68	(MH "Surgery, Cardiovascular+")	16,971
S67	(MH "Thoracic Surgery+")	17,001
S66	s34 and s65	96
S65	S61 or S62 or S63 OR S64	5,151
S64	TI (massive N1 (bleeding OR haemorrhage OR hemorrhage)) or AB (massive N1 (bleeding OR haemorrhage OR hemorrhage))	5,072
S63	TI ("massive infusion" OR "massively transfused") or AB ("massive infusion" OR "massively	10

#	Query	Results
	transfused")	
S62	TI (massive N3 transfusion ^a) or AB (massive N3 transfusion ^a)	87
S61	S59 and S60	74
S60	TI (massive) or AB (massive)	1,894
S59	(MH "Blood Transfusion")	3,449
S58	s34 and s57	57
S57	S55 or S56	6,716
S56	TI (shock OR "cardiovascular collapse" OR "circulatory collapse") or AB (shock OR "cardiovascular collapse" OR "circulatory collapse")	5,211
S55	(MH "Shock+")	3,283
S54	S34 and S53	202
S53	S49 OR S50 or S51 OR S52	121,873
S52	TI (injur ^a OR trauma ^a) or AB (injur ^a OR trauma ^a)	67,919
S51	(MH "Trauma Nursing")	531
S50	(MH "Trauma+")	5,896
S49	(MH "Wounds and Injuries+")	91,270
S48	S34 AND S47	210
S47	S35 or S36 or S37 or S38 or S39 or S40 or S41 or S42 OR S43 or S44 or S45 or S46	54,455
S46	TI (postoperative OR "post operative") or AB (postoperative OR "post operative")	14,432
S45	TI (peroperative OR "per operative") or AB (peroperative OR "per operative")	51
S44	TI (intraoperative OR "intra operative") or AB (intraoperative OR "intra operative")	2,969
S43	TI (preoperative OR "pre operative") or AB (preoperative OR "pre operative")	7,216
S42	TI (perioperative OR "peri operative") or AB (perioperative OR "peri operative")	5,331
S41	(MH "Postoperative Period")	1,907
S40	(MH "Postoperative Complications+")	21,289
S39	(MH "Intraoperative Period")	366
S38	(MH "Intraoperative Complications+")	1,808
S37	(MH "Preoperative Period+")	721
S36	(MH "Perioperative Nursing")	8,844
S35	(MH "Perioperative Care+")	16,111
S34	s11 OR s15 OR s19 OR s33	1,245
S33	s20 OR s21 OR s22 OR s23 OR s24 OR s25 OR s26 OR s27 OR s28 OR s29 OR s30 OR s31	285
S32	TI ("hb thresholds" OR "hb triggers") OR AB ("hb thresholds" OR "hb triggers")	0
S31	TI ("haemoglobin thresholds" OR "haemoglobin triggers") OR AB ("haemoglobin thresholds" OR "haemoglobin triggers")	1
S30	TI ("hemoglobin thresholds" OR "hemoglobin triggers") OR AB ("hemoglobin thresholds" OR "hemoglobin triggers")	3
S29	TI ("hb threshold" OR "hb trigger") OR AB ("hb threshold" OR "hb trigger")	2

#	Query	Results
S28	TI ("haemoglobin threshold" OR "haemoglobin trigger") OR AB ("haemoglobin threshold" OR "haemoglobin trigger")	1
S27	TI ("hemoglobin threshold" OR "hemoglobin trigger") OR AB ("hemoglobin threshold" OR "hemoglobin trigger")	8
S26	TI (transfusion N1 guideline ^a) OR AB (transfusion N1 guideline ^a)	46
S25	TI ("transfusion protocol" OR "transfusion protocols") OR AB ("transfusion protocol" OR "transfusion protocols")	25
S24	TI ("transfusion practice" OR "transfusion practices") OR AB ("transfusion practice" OR "transfusion practices")	126
S23	TI ("transfusion policy" OR "transfusion policies") OR AB ("transfusion policy" OR "transfusion policies")	18
S22	TI ("transfusion strategy" OR "transfusion strategies") OR AB ("transfusion strategy" OR "transfusion strategies")	34
S21	TI (transfusion N1 trigger ^a) OR AB (transfusion N1 trigger ^a)	42
S20	TI ("transfusion threshold" OR "transfusion thresholds") OR AB ("transfusion threshold" OR "transfusion thresholds")	38
S19	s16 OR s17 OR s18	63
S18	TI (high N3 transfusion ^a) OR AB (high N3 transfusion ^a)	43
S17	TI (liberal N3 transfusion ^a) OR AB (liberal N3 transfusion ^a)	20
S16	TI (liberal AND transfus ^a)	8
S15	s12 OR s13 OR s14	79
S14	TI (low N3 transfusion ^a) OR AB (low N3 transfusion ^a)	43
S13	TI (restrictive N3 transfusion ^a) OR AB (restrictive N3 transfusion ^a)	34
S12	TI (restrictive AND transfus ^a)	17
S11	s1 OR s2 OR s3 OR s4 OR s5 OR s7 OR s8 OR s9	1,021
S10	TI ("red cells" N3 exchange) OR AB ("red cells" N3 exchange)	0
S9	TI ("red cell" N3 exchange) OR AB ("red cell" N3 exchange)	5
S8	TI (rbc N1 exchange) OR AB (rbc N1 exchange)	3
S7	TI ("red blood cell" N1 exchange) OR AB ("red blood cell" N1 exchange)	5
S6	TI ("normocyte transfusion" OR "normocyte transfusions") OR AB ("normocyte transfusion" OR "normocyte transfusions")	0
S5	TI ("red cell" N1 transfusion ^a) OR AB ("red cell" N1 transfusion ^a)	64
S4	TI (rbc N1 transfusion ^a) OR AB (rbc N1 transfusion ^a)	121
S3	TI ("red blood cell" N1 transfusion ^a) OR AB ("red blood cell" N1 transfusion ^a)	213
S2	TI ("erythrocyte transfusion" OR "erythrocyte transfusions") OR AB ("erythrocyte transfusion" OR "erythrocyte transfusions")	16
S1	(MH "Blood Component Transfusion")	829

^a The search was conducted using EBSCOhost on 28 May 2009.

^b The records from each of these search statements were exported separately owing to technical difficulties experienced with EBSCOhost when processing this search statement. Consequently, there were duplicated records in this number.

Table A4.6 AMI search conducted 11 June 2009

Set	Search terms	Results
#14	((SUBJECT = (blood transfusion)) OR (TI = ("lymphocyte transfusion" OR "thrombocytic transfusion") OR AB = ("lymphocyte transfusion" OR "thrombocytic transfusion"))) OR (TI = ("erythrocyte transfusion" OR "leukocyte transfusion") OR AB = ("erythrocyte transfusion" OR "leukocyte transfusion")) OR (TI = ("replacement transfusion" OR "substitution transfusion") OR AB = ("replacement transfusion" OR "substitution transfusion")) OR (TI = ("exchange transfusion" OR autotransfusion) OR AB = ("exchange transfusion" OR autotransfusion)) OR (TI = ("transfusion blood" OR "transfusion therapy") OR AB = ("transfusion blood" OR "transfusion therapy")) OR (TI = (multitransfusion OR polytransfusion OR retransfusion) OR AB = (multitransfusion OR polytransfusion OR retransfusion)) OR (TI = (haemotherapy OR haemotherapy OR haemotherapy) OR AB = (haemotherapy OR haemotherapy OR haemotherapy)) OR (TI = (hemotherapy OR hemotherapy OR hemotherapy) OR AB = (hemotherapy OR hemotherapy OR hemotherapy)) OR (TI = ("blood replacement" OR "blood retransfusion") OR AB = ("blood replacement" OR "blood retransfusion")) OR (TI = ("blood exchange" OR "blood infusion") OR AB = ("blood exchange" OR "blood infusion")) OR (TI = (blood %1 transfusion ^a) OR AB = (blood %1 transfusion ^a)) OR ((MH_PHRASE = "Blood Transfusion, Intrauterine" OR MH_PHRASE = "Platelet Transfusion" OR MH_PHRASE = "Erythrocyte Transfusion" OR MH_PHRASE = "Leukocyte Transfusion" OR MH_PHRASE = "Blood Transfusion, Autologous" OR MH_PHRASE = "Lymphocyte Transfusion" OR MH_PHRASE = "Blood Transfusion" OR MH_PHRASE = "Blood Component Transfusion" OR MH_PHRASE = "Exchange Transfusion, Whole Blood" OR MH_PHRASE = "Plasma Exchange")))	512
#13	SUBJECT = (blood transfusion)	354
#12	TI = ("lymphocyte transfusion" OR "thrombocytic transfusion") OR AB = ("lymphocyte transfusion" OR "thrombocytic transfusion")	0
#11	TI = ("erythrocyte transfusion" OR "leukocyte transfusion") OR AB = ("erythrocyte transfusion" OR "leukocyte transfusion")	0
#10	TI = ("replacement transfusion" OR "substitution transfusion") OR AB = ("replacement transfusion" OR "substitution transfusion")	0
#9	TI = ("exchange transfusion" OR autotransfusion) OR AB = ("exchange transfusion" OR autotransfusion)	18
#8	TI = ("transfusion blood" OR "transfusion therapy") OR AB = ("transfusion blood" OR "transfusion therapy")	5
#7	TI = (multitransfusion OR polytransfusion OR retransfusion) OR AB = (multitransfusion OR polytransfusion OR retransfusion)	0
#6	TI = (haemotherapy OR haemotherapy OR haemotherapy) OR AB = (haemotherapy OR haemotherapy OR haemotherapy)	0
#5	TI = (hemotherapy OR hemotherapy OR hemotherapy) OR AB = (hemotherapy OR hemotherapy OR hemotherapy)	0
#4	TI = ("blood replacement" OR "blood retransfusion") OR AB = ("blood replacement" OR "blood retransfusion")	1
#3	TI = ("blood exchange" OR "blood infusion") OR AB = ("blood exchange" OR "blood infusion")	0
#2	TI = (blood %1 transfusion ^a) OR AB = (blood %1 transfusion ^a)	194

Set	Search terms	Results
#1	(MH_PHRASE = "Blood Transfusion, Intrauterine" OR MH_PHRASE = "Platelet Transfusion" OR MH_PHRASE = "Erythrocyte Transfusion" OR MH_PHRASE = "Leukocyte Transfusion" OR MH_PHRASE = "Blood Transfusion, Autologous" OR MH_PHRASE = "Lymphocyte Transfusion" OR MH_PHRASE = "Blood Transfusion" OR MH_PHRASE = "Blood Component Transfusion" OR MH_PHRASE = "Exchange Transfusion, Whole Blood" OR MH_PHRASE = "Plasma Exchange")	263

a The search was conducted using Informat online platform on 11 June 2009

A5 Literature search – question 5

Question 5

In patients with critical bleeding requiring massive transfusion, what is the effect of interventions to increase haemoglobin concentration on morbidity, mortality and need for red blood cell transfusion in critical bleeding patients requiring massive transfusion?

Table A5.1 EMBASE.com search conducted 27 May 2009

No.	Query	Results
#1	'anemia'/exp OR anaemia:ab,ti OR anemia:ab,ti	170,860
#2	'perioperative period'/exp OR 'perioperative nursing'/exp OR 'perioperative complication'/exp OR 'preoperative period'/exp OR 'preoperative complication'/exp OR 'intraoperative period'/exp OR perioperative:ab,ti OR 'peri operative':ab,ti OR preoperative:ab,ti OR 'pre operative':ab,ti OR intraoperative:ab,ti OR 'intra operative':ab,ti OR peroperative:ab,ti OR 'per operative':ab,ti OR 'postoperative period'/exp OR 'postoperative complication'/exp OR postoperative:ab,ti OR 'post operative':ab,ti	865,643
#3	'injury'/exp OR injur*:ab,ti OR trauma*:ab,ti	1,263,038
#4	'shock'/exp OR shock:ab,ti OR 'cardiovascular collapse':ab,ti OR 'circulatory collapse':ab,ti	135,548
#5	'blood transfusion'/exp OR ('bleeding'/exp AND 'transfusion'/exp) AND massive:ab,ti OR 'massive transfusion':ab,ti OR 'massive blood transfusion':ab,ti OR 'massive transfusion protocol':ab,ti OR ('massive' NEAR/3 'transfusion'):ab,ti OR ('massive' NEAR/3 'transfusions'):ab,ti OR 'massive infusion':ab,ti OR 'massively transfused':ab,ti OR 'massive bleeding':ab,ti OR 'massive haemorrhage':ab,ti OR 'massive hemorrhage':ab,ti	8,411
#6	'thorax surgery'/exp OR 'heart surgery'/exp OR 'cardiothoracic surgery':ab,ti OR 'chest surgery':ab,ti OR 'cardiothoracic patient':ab,ti OR 'cardiothoracic patients':ab,ti OR 'thoracic operation':ab,ti OR 'thoracic surgery':ab,ti OR thoracoplasty:ab,ti OR 'thoracic procedure':ab,ti OR 'thoracic procedures':ab,ti	285,419
#7	'surgery'/exp OR 'surgical ward'/exp OR 'surgical patient'/exp OR surgical:ab,ti OR surgery:ab,ti OR operation:ab,ti OR resection:ab,ti	2,728,593
#8	'orthopedic surgery'/exp OR 'orthopedic surgery':ab,ti OR 'orthopaedic surgery':ab,ti OR 'bone surgery':ab,ti OR orthopaedics:ab,ti OR orthopedics:ab,ti OR 'orthopedic patient':ab,ti OR 'orthopedic patients':ab,ti OR 'orthopaedic patient':ab,ti OR 'orthopaedic patients':ab,ti OR 'orthopedic operation':ab,ti OR 'orthopedic procedures':ab,ti OR 'orthopaedic operation':ab,ti OR 'orthopaedic procedures':ab,ti OR 'orthopedic procedure':ab,ti OR 'orthopaedic procedure':ab,ti	258,328
#9	'antianemic agent'/exp OR 'antianemic agent':ab,ti OR 'antianemic agents':ab,ti OR 'anti anemic agent':ab,ti OR 'anti anemic agents':ab,ti OR 'antianaemic agent':ab,ti OR 'antianaemic agents':ab,ti OR 'anti anaemic agent':ab,ti OR 'anti anaemic agents':ab,ti OR 'erythropoiesis stimulating agent':ab,ti OR 'hematinics':ab,ti OR 'erythropoiesis stimulating agents':ab,ti OR 'haematinics':ab,ti OR 'hematinic agent':ab,ti OR 'hematinic agents':ab,ti OR 'haematinic agent':ab,ti OR 'haematinic agents':ab,ti OR 'hematopoietic agent':ab,ti OR 'hematopoietic agents':ab,ti OR 'haematopoietic agent':ab,ti OR 'haematopoietic agents':ab,ti OR 'hemopoietic agent':ab,ti OR 'hemopoietic agents':ab,ti OR 'haemopoietic agent':ab,ti OR 'haemopoietic agents':ab,ti	61,198

No.	Query	Results
#10	'erythropoietin'/de OR 'recombinant erythropoietin'/de OR erthropoietin:tn,ab,ti OR 'erythropoiesis stimulating factor':tn,ab,ti OR 'erythropoietic factor':tn,ab,ti OR hematopoietin:tn,ab,ti OR hemopoietin:tn,ab,ti OR haematopoietin:tn,ab,ti OR haemopoietin:tn,ab,ti OR dynepo OR epoch OR epoconn OR epoetin OR epog?n OR epoietin:tn,ab,ti OR epoxitin:tn,ab,ti OR eprex:tn,ab,ti OR erantin:tn,ab,ti OR erypo:tn,ab,ti OR espo:tn,ab,ti OR exprex:tn,ab,ti OR globuren:tn,ab,ti OR hemax:tn,ab,ti OR marogen:tn,ab,ti OR neorecormon:tn,ab,ti OR procrit:tn,ab,ti OR recormon:tn,ab,ti OR recormone:tn,ab,ti OR 'krm 5702':tn,ab,ti OR krn5702:tn,ab,ti OR 'snb 5001':tn,ab,ti OR snb5001:tn,ab,ti OR 'tyb 5220':tn,ab,ti OR tyb5220:tn,ab,ti OR rhuepo:tn,ab,ti OR 'rhu epo':tn,ab,ti OR 'r hu epo':tn,ab,ti OR '11096 26 7':rn OR (113427:rn AND 24:rn AND 0:rn) OR '122312 54 3':rn OR '130455 76 4':rn	32,022
#11	'iron therapy'/de OR 'iron'/dd_dt OR 'iron'/dd_ad OR 'iron therapy':an,ab OR 'iron treatment':an,ab OR 'iron supplement':ab,ti OR 'iron supplements':ab,ti	9,262
#12	'folic acid'/de OR 'cyanocobalamin'/de OR 'ascorbic acid'/exp OR 'folic acid':tn,ab,ti OR folacin:tn,ab,ti OR folate:tn,ab,ti OR foldine:tn,ab,ti OR foliamin:tn,ab,ti OR folicet:tn,ab,ti OR 'folium acid':tn,ab,ti OR folsan:tn,ab,ti OR folvite:tn,ab,ti OR lafol:tn,ab,ti OR 'lactobacillus casei factor':tn,ab,ti OR 'mission prenatal':tn,ab,ti OR 'vitamin bc':tn,ab,ti OR 'vitamin m':tn,ab,ti OR 'pteroyl glutamate':tn,ab,ti OR 'pteroyl l glutamic acid':tn,ab,ti OR 'pteroyl monoglutamate':tn,ab,ti OR pteroylglutamate:tn,ab,ti OR 'pteroylglutamic acid':tn,ab,ti OR pteroylmonoglutamate:tn,ab,ti OR 'pteroylmonoglutamic acid':tn,ab,ti OR cyanobalamin:tn,ab,ti OR cobalamin:tn,ab,ti OR cobalamins:tn,ab,ti OR 'vitamin b12':tn,ab,ti OR 'vitamin b 12':tn,ab,ti OR berubigen:tn,ab,ti OR docibin:tn,ab,ti OR bevidox:tn,ab,ti OR ducobee:tn,ab,ti OR sytobex:ab,ti OR eritron:ab,ti OR 'ascorbic acid':tn,ab,ti OR 'cevitamic acid':tn,ab,ti OR 'vitamin c':tn,ab,ti OR ascorbate:tn,ab,ti OR 'magnesium ascorbicum':tn,ab,ti OR magnorbin:tn,ab,ti OR '59 30 3':rn OR '6484 89 5':rn OR '53570 76 6':rn OR '68 19 9':rn OR '8064 09 3':rn OR '134 03 2':rn OR '15421 15 5':rn OR '50 81 7':rn	107,291
#13	'erythrocyte transfusion'/exp OR 'erythrocyte transfusion':ab,ti OR 'erythrocyte transfusions':ab,ti OR 'red blood cell transfusion':ab,ti OR 'rbc transfusion':ab,ti OR 'red blood cell transfusions':ab,ti OR 'rbc transfusions':ab,ti OR 'red cell transfusion':ab,ti OR 'normocyte transfusion':ab,ti OR 'red cell transfusions':ab,ti OR 'normocyte transfusions':ab,ti OR 'red blood cell exchange':ab,ti OR 'rbc exchange':ab,ti OR ('red cell' NEAR/3 'exchange'):ab,ti OR ('red cells' NEAR/3 'exchange'):ab,ti	8,413
#14	'perioperative complication'/exp	451
#15	'preoperative period'/exp	135,378
#16	preoperative:ab,ti OR 'pre operative':ab,ti	140,998
#17	'adverse outcome'/exp OR 'outcome assessment'/exp OR 'morbidity'/exp OR 'mortality'/exp OR morbidity:ab,ti OR incidence:ab,ti OR prevalence:ab,ti OR occurrence:ab,ti OR mortality:ab,ti OR death:ab,ti OR survival:ab,ti	1,926,742
#18	'quality of life'/exp OR qol:ab,ti OR 'quality of life':ab,ti OR 'quality of wellbeing':ab,ti OR 'health related quality':ab,ti OR hrqol:ab,ti OR qaly*:ab,ti OR 'quality adjusted':ab,ti OR 'adjusted life':ab,ti	159,858

No.	Query	Results
#19	'blood component therapy'/exp AND ('dose response'/exp OR 'drug dose'/exp) OR 'fresh frozen plasma'/exp/dd_do OR 'recombinant erythropoietin'/exp/dd_do OR 'transfusion frequency':ab,ti OR ('frequency' NEAR/5 'transfusion'):ab,ti OR ('frequency' NEAR/5 'transfusions'):ab,ti OR 'transfusion rate':ab,ti OR 'transfusion rates':ab,ti OR ('rate' NEAR/5 'transfusion'):ab,ti OR ('rates' NEAR/5 'transfusion'):ab,ti OR 'transfusion requirement':ab,ti OR 'transfusion requirements':ab,ti OR 'transfusion indication':ab,ti OR 'transfusion indications':ab,ti OR ('indications' NEAR/5 'transfusion'):ab,ti OR ('indications' NEAR/5 'transfusions'):ab,ti OR ('indication' NEAR/5 'transfusion'):ab,ti OR ('indication' NEAR/5 'transfusions'):ab,ti OR 'transfusion interval':ab,ti OR 'transfusion intervals':ab,ti OR ('need' NEAR/3 'transfusion'):ab,ti OR ('need' NEAR/3 'transfusions'):ab,ti OR 'transfusion need':ab,ti OR 'transfusion needs':ab,ti OR ('dose' NEAR/3 'transfusion'):ab,ti OR ('dose' NEAR/3 'transfusions'):ab,ti OR ('dose' NEAR/3 'transfused'):ab,ti OR ('transfusions' NEAR/3 'dose'):ab,ti OR 'transfusion dose':ab,ti OR ('transfused' NEAR/3 'dose'):ab,ti OR 'platelet dose':ab,ti OR ('dose' NEAR/3 'platelets'):ab,ti OR (dose:ab,ti AND transfus*:ab,ti)	17,399
#20	'hemoglobin'/de OR 'hemoglobin determination'/de OR 'hemoglobin blood level'/de OR 'mean corpuscular volume'/de OR 'blood haemoglobin':ab,ti OR 'blood hemoglobin':ab,ti OR 'haemoglobin level':ab,ti OR 'hemoglobin level':ab,ti OR 'haemoglobin levels':ab,ti OR 'hemoglobin levels':ab,ti OR 'hb level':ab,ti OR 'hb levels':ab,ti OR 'haemoglobin determination':ab,ti OR 'hemoglobin determination':ab,ti OR 'hemoglobin assay':ab,ti OR 'haemoglobin assay':ab,ti OR 'hemoglobin estimation':ab,ti OR 'haemoglobin estimation':ab,ti OR 'hb determination':ab,ti OR 'hb estimation':ab,ti OR 'hb assay':ab,ti OR 'hemoglobin content':ab,ti OR 'hemoglobin concentration':ab,ti OR 'haemoglobin content':ab,ti OR 'haemoglobin concentration':ab,ti OR 'hb content':ab,ti OR 'hb concentration':ab,ti OR hemoglobinometry:ab,ti OR haemoglobinometry:ab,ti OR 'plasma haemoglobin':ab,ti OR 'plasma hemoglobin':ab,ti OR 'serum haemoglobin':ab,ti OR 'serum hemoglobin':ab,ti OR 'mean corpuscular haemoglobin':ab,ti OR 'mean corpuscular hemoglobin':ab,ti OR 'mean cell haemoglobin':ab,ti OR 'mean cell hemoglobin':ab,ti OR 'erythrocyte indices':ab,ti OR 'erythrocyte index':ab,ti OR 'erythrocyte indexes':ab,ti OR 'red cell indices':ab,ti OR 'red cell index':ab,ti OR 'red cell indexes':ab,ti OR 'rbc indices':ab,ti OR 'rbc index':ab,ti OR 'rbc indexes':ab,ti	86,870
#21	'health economics'/exp OR 'economic aspect'/exp OR 'economics'/exp OR 'finance'/exp OR 'biomedical technology assessment'/exp OR 'economic evaluation'/exp OR 'health care cost'/exp OR economic*:ab,ti OR pharmacoeconomic*:ab,ti OR cost*:ab,ti OR price*:ab,ti OR pricing:ab,ti OR 'burden of illness':ab,ti OR 'value money':ab,ti OR (resource*:ab,ti AND utili*:ab,ti) OR 'technology assessment':ab,ti OR 'technology assessments':ab,ti OR 'technology appraisal':ab,ti OR 'technology appraisals':ab,ti	996,491
#22	'hospitalization'/exp OR 'length of stay'/exp OR hospitaliz*:ab,ti OR hospitalis*:ab,ti OR ('length' NEAR/3 'stay'):ab,ti OR 'hospital stay':ab,ti	244,661
#23	'intensive care unit'/exp OR 'intensive care unit':ab,ti OR icu:ab,ti OR 'intensive care units':ab,ti OR 'close attention unit':ab,ti OR 'close attention units':ab,ti OR 'intensive care department':ab,ti OR 'intensive care departments':ab,ti OR 'special care unit':ab,ti OR 'special care units':ab,ti OR 'critical care unit':ab,ti OR 'critical care units':ab,ti	76,701
#24	'hospital admission'/exp OR 'hospital readmission'/exp OR 'hospital admission':ab,ti OR 'hospital admittance':ab,ti OR 'patient admission':ab,ti OR readmission:ab,ti OR rehospitalization:ab,ti OR rehospitalisation:ab,ti	77,581
#25	#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	3,685,139
#26	#1 AND #25	38,858
#27	#14 OR #15 OR #16	228,489
#28	#13 AND #27	506

No.	Query	Results
#29	#9 OR #10 OR #11 OR #12 OR #28	171,905
#30	#26 AND #29	5,622
#31	#17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24	3,138,584
#32	#30 AND #31	3,301

Table A5.2 Cochrane library database search conducted 20 May 2009

No.	Query	Results
#1	MeSH descriptor Erythrocyte Transfusion explode all trees	346
#2	"erythrocyte transfusion" OR "erythrocyte transfusions"	432
#3	("red blood cell" OR rbc) NEAR/1 transfusion*	142
#4	"red cell" NEAR/1 transfusion*	3
#5	"normocyte transfusion" OR "normocyte transfusions"	0
#6	("red blood cell" OR rbc) NEAR/1 exchange	2
#7	("red cell" OR "red cells") NEAR/3 exchange	3
#8	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7	1,916
#9	MeSH descriptor Anemia explode all trees	2,505
#10	(anaemia OR anemia)	5,050
#11	#9 or #10	1,473
#12	#8 AND #11	1,296
#13	MeSH descriptor Perioperative Care explode all trees	4,254
#14	MeSH descriptor Preoperative Care explode all trees	4,098
#15	MeSH descriptor Postoperative Complications explode all trees	21,418
#16	MeSH descriptor Postoperative Period explode all trees	3,483
#17	MeSH descriptor Intraoperative Complications explode all trees	2,476
#18	MeSH descriptor Intraoperative Period explode all trees	919
#19	(perioperative OR "peri operative")	5,196
#20	(preoperative OR "pre operative")	11,093
#21	(intraoperative OR "intra operative")	8,039
#22	(peroperative OR "per operative")	474
#23	(postoperative OR "post operative")	40,236
#24	#13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23	1,268
#25	#12 AND #24	550
#26	MeSH descriptor Wounds and Injuries explode all trees	10,953
#27	(injur* OR trauma*)	20,750
#28	#26 OR #27	499
#29	#12 AND #28	417
#30	MeSH descriptor Shock explode all trees	930
#31	(shock OR "cardiovascular collapse" OR "circulatory collapse")	3,179

No.	Query	Results
#32	#30 OR #31	381
#33	#12 AND #32	316
#34	MeSH descriptor Blood Transfusion explode all trees	2,628
#35	(massive)	599
#36	#34 AND #35	265
#37	(massive NEAR/3 transfusion*)	20
#38	"massive infusion" OR "massively transfused"	3
#39	(massive NEAR/1 (bleeding OR haemorrhage OR hemorrhage))	47
#40	#36 OR #37 OR #38 OR #39	284
#41	#12 AND #40	203
#42	MeSH descriptor Thoracic Surgical Procedures explode all trees	10,297
#43	MeSH descriptor Thoracic Surgery explode all trees	130
#44	MeSH descriptor Cardiovascular Surgical Procedures explode all trees	10,930
#45	"cardiothoracic surgery" OR (chest NEAR/1 surgery)	675
#46	(cardiothoracic NEAR/1 patient*)	4
#47	"thoracic operation" OR "thoracic surgery" OR thoracoplasty	2,131
#48	(thoracic NEAR/1 procedure*)	16
#49	#42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48	253
#50	#12 AND #49	127
#51	MeSH descriptor Surgical Procedures, Operative explode all trees	68,578
#52	MeSH descriptor General Surgery explode all trees	167
#53	MeSH descriptor Surgery Department, Hospital explode all trees	68
#54	(surgical OR surgery OR operation OR resection)	91,783
#55	#51 OR #52 OR #53 OR #54	121
#56	#12 AND #55	87
#57	MeSH descriptor Orthopedic Procedures explode all trees	5,335
#58	MeSH descriptor Orthopedics explode all trees	272
#59	"orthopedic surgery" OR "orthopaedic surgery"	2,339
#60	"bone surgery" OR orthopaedics or orthopedics	7,975
#61	(orthopedic OR orthopaedic) NEAR/1 patient*	223
#62	"orthopedic operation" OR "orthopaedic operation"	6
#63	(orthopedic OR orthopaedic) NEAR/1 procedure*	638
#64	#57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63	98
#65	#12 AND #64	63
#66	#25 OR #29 OR #33 OR #41 OR #50 OR #56 OR #65	556
#67	MeSH descriptor Hematinics explode all trees	1,418
#68	"antianemic agent" OR "antianemic agents"	9
#69	"anti anemic agent" OR "anti anemic agents"	0

No.	Query	Results
#70	"antianaemic agent" OR "antianaemic agents"	0
#71	"anti anaemic agent" OR "anti anaemic agents"	0
#72	"erythropoiesis stimulating agent" OR "hematinics"	394
#73	"erythropoiesis stimulating agents" OR "haematinics"	34
#74	"hematinic agent" OR "hematinic agents"	0
#75	"haematinic agent" OR "haematinic agents"	0
#76	"hematopoietic agent" OR "hematopoietic agents"	2
#77	"haematopoietic agent" OR "haematopoietic agents"	0
#78	"hemopoietic agent" OR "hemopoietic agents"	0
#79	"haemopoietic agent" OR "haemopoietic agents"	0
#80	#67 OR #68 OR #69 OR #70 OR #71 OR #72 OR #73 OR #74 OR #75 OR #76 OR #77 OR #78 OR #79	76
#81	#66 AND #80	40
#82	MeSH descriptor Erythropoietin explode all trees	1,234
#83	(erthropoietin OR "erythropoiesis stimulating factor")	4
#84	"erythropoietic NEAR/1 factor"	0
#85	(hematopoietin OR hemopoietin)	2
#86	(haematopoietin OR haemopoietin)	1
#87	(dynepo OR epoch OR epoconn OR epoetin OR epog?n)	789
#88	(epoetin OR epoxitin OR eprex OR erantin OR erypo)	55
#89	(espo OR exprex OR globuren OR hemax OR marogen)	35
#90	(neorecormon OR procrit OR recormon OR recormone)	45
#91	"krm 5702" OR km5702 OR "snb 5001" OR snb5001	10
#92	"tyb 5220" OR tyb5220	3
#93	(rHuEPO OR "rHu EPO" OR "r Hu EPO")	381
#94	#82 OR #83 OR #84 OR #85 OR #86 OR #87 OR #88 OR #89 OR #90 OR #91 OR #92 OR #93	59
#95	#66 AND #94	23
#96	MeSH descriptor Iron explode all trees with qualifier: TU	311
#97	MeSH descriptor Iron explode all trees with qualifier: AD	448
#98	"iron therapy" OR "iron treatment"	320
#99	"iron supplement" OR "iron supplements"	194
#100	#96 OR #97 OR #98 OR #99	29
#101	#66 AND #100	16
#102	MeSH descriptor Folic Acid explode all trees	1,615
#103	MeSH descriptor Vitamin B 12 explode all trees	439
#104	MeSH descriptor Ascorbic Acid explode all trees	1,185
#105	MeSH descriptor Anencephaly explode all trees	8

No.	Query	Results
#106	(folicet OR "folium acid" OR folsan OR folvite OR lafol)	5
#107	"lactobacillus casei factor" OR "mission prenatal"	0
#108	"vitamin bc" OR "vitamin m"	0
#109	"pteroyl glutamate" OR "pteroyl l glutamic acid"	0
#110	"pteroyl monoglutamate" OR pteroylglutamate	0
#111	"pteroylglutamic acid" OR pteroylmonoglutamate	5
#112	"pteroylmonoglutamic acid"	0
#113	(cyanobalamin OR cobalamin OR cobalamins)	89
#114	"vitamin B12" OR "vitamin b 12"	792
#115	(Berubigen OR Docibin OR Bevidox OR Ducobee)	0
#116	(Sytobex OR Eritron)	0
#117	"ascorbic acid" OR "cevitamic acid" OR "vitamin C"	2,183
#118	(ascorbate OR "Magnesium Ascorbicum" OR Magnorbin)	151
#119	#102 OR #103 OR #104 OR #105 OR #106 OR #107 OR #108 OR #109 OR #110 OR #111 OR #112 OR #113 OR #114 OR #115 OR #116 OR #117 OR #118	46
#120	#66 AND #119	9
#121	#14 OR #20	1,116
#122	#8 AND #121	9
#123	#66 AND #122	9
#124	#81 OR #95 OR #101 OR 120 OR #123	14,575
#125	MeSH descriptor Morbidity explode all trees	8,475
#126	MeSH descriptor Mortality explode all trees	7,946
#127	(morbidity OR incidence OR prevalence OR occurrence)	62,784
#128	(mortality OR death OR survival)	55,325
#129	#125 OR #126 OR #127 OR #128	11
#130	#124 AND #129	9
#131	MeSH descriptor Quality of Life explode all trees	9,425
#132	MeSH descriptor Quality-Adjusted Life years explode all trees	2,062
#133	(qol OR "quality of life" OR "quality of wellbeing")	21,521
#134	"health related quality" or hrqol	2,898
#135	(qaly* or "quality adjusted" or "adjusted life")	3,802
#136	#131 OR #132 OR #133 OR #134 OR #135	11
#137	#124 AND #136	8
#138	MeSH descriptor Blood Component Transfusion explode all trees with qualifier: MT	99
#139	(frequency NEAR/5 transfusion*)	84
#140	(rate* NEAR/5 transfusion*)	324
#141	"transfusion requirement" OR "transfusion requirements"	949
#142	(indication* NEAR/5 transfusion*)	45

No.	Query	Results
#143	"transfusion interval" OR "transfusion intervals"	13
#144	(need NEAR/3 transfusion*) OR "transfusion needs"	623
#145	(dose NEAR/3 transfus*)	86
#146	"platelet dose" OR (dose NEAR/3 platelets)	185
#147	(dose and transfus*):ti	72
#148	#138 or #139 or #140 or #141 OR #142 OR #143 OR #144 OR #145 OR #146 OR #147	16
#149	#124 AND #148	2
#150	MeSH descriptor Hemoglobins explode all trees	4,487
#151	MeSH descriptor Hemoglobinometry explode all trees	152
#152	MeSH descriptor Erythrocyte Indices explode all trees	110
#153	"blood haemoglobin" OR "blood hemoglobin"	241
#154	(haemoglobin OR hemoglobin) NEAR/1 level*	1,228
#155	"hb level" OR "hb levels"	236
#156	"haemoglobin determination" OR "hemoglobin determination"	120
#157	"hemoglobin assay" OR "haemoglobin assay"	4
#158	"hemoglobin estimation" OR "haemoglobin estimation"	5
#159	"hb determination" OR "hb estimation" OR "hb assay"	2
#160	(hemoglobin NEAR/1 (content OR concentration))	904
#161	(haemoglobin NEAR/1 (content OR concentration))	904
#162	"hb content" OR "hb concentration"	110
#163	(hemoglobinometry OR haemoglobinometry)	166
#164	"plasma haemoglobin" OR "plasma hemoglobin"	65
#165	"serum haemoglobin" OR "serum hemoglobin"	47
#166	"mean corpuscular volume" OR mcv OR mch OR mchc	350
#167	"mean corpuscular haemoglobin" OR "mean corpuscular hemoglobin"	41
#168	"Mean Cell" NEAR/1 (Haemoglobin OR Hemoglobin)	2
#169	"erythrocyte indices" OR "Erythrocyte Index" OR "Erythrocyte Indexes"	121
#170	(red NEAR/1 ("cell indices" OR "Cell Index" OR "Cell Indexes"))	14
#171	"rbc indices" OR "RBC Index" OR "RBC Indexes"	2
#172	(#150 OR #151 OR #152 OR #153 OR #154 OR #155 OR #156 OR #157 OR #158 OR #159 OR #160 OR #161 OR #162 OR #163 OR #164 OR #165 OR #166 OR #167 OR #168 OR #169 OR #170 OR #171)	6,494
#173	(#124 AND #172)	310
#174	MeSH descriptor Costs and Cost Analysis explode all trees	26,772
#175	MeSH descriptor Economics explode all trees	28,552
#176	MeSH descriptor Models, Economic explode all trees	1,853
#177	MeSH descriptor Value of Life explode all trees	274
#178	MeSH descriptor Utilization Review explode all trees	420

No.	Query	Results
#179	MeSH descriptor Delivery of Health Care explode all trees with qualifiers: EM,UT	762
#180	(economic* or pharmacoeconomic*)	37,332
#181	(cost* or price* or pricing)	48,938
#182	(resource* near utili*)	1,537
#183	"burden of illness" or (value NEAR/1 money)	87
#184	#174 OR #175 OR #176 OR #177 OR #178 OR #179 OR #180 OR #181 OR #182 OR #183	13
#185	#124 AND #184	0
#186	MeSH descriptor Hospitalization explode all trees	10,690
#187	MeSH descriptor Child, Hospitalized explode all trees	82
#188	(hospitaliz* OR hospitalis*)	16,298
#189	(length NEAR/3 stay) OR "hospital stay"	11,735
#190	#186 OR #187 OR #188 OR #189	3
#191	#124 AND #190	0
#192	MeSH descriptor Intensive Care Units explode all trees	1,978
#193	"intensive care unit" OR icu OR "intensive care units"	6,712
#194	"close attention unit" OR "close attention units"	0
#195	"intensive care department" OR "intensive care departments"	56
#196	"special care unit" OR "special care units"	63
#197	"critical care unit" OR "critical care units"	108
#198	#192 OR #193 OR #194 OR #195 OR #196 OR #197	1
#199	#124 AND #198	0
#200	MeSH descriptor Patient Admission explode all trees	604
#201	MeSH descriptor Patient Readmission explode all trees	593
#202	"hospital admission" OR "hospital admittance"	1,727
#203	"patient admission" OR readmission	2,327
#204	(rehospitalization OR rehospitalisation)	504
#205	#200 OR #201 OR #202 OR #203 OR #204	19
#206	#124 AND #205	0
#207	#130 OR #137 OR #149 OR #173 OR #185 OR #191 OR #199 OR #206	15

Table A5.3 PreMedline search conducted 28 May 2009

No	Query	Result
1	"erythrocyte transfusion"[tw] OR "erythrocyte transfusions"[tw]	Note: Search results for individual search strands (1 to 48)
2	("red blood cell"[tw] OR rbc[tw]) AND transfusion*[tw]	
3	"red cell"[tw] AND transfusion*[tw]	
4	"normocyte transfusion"[tw] OR "normocyte transfusions"[tw]	
5	("red blood cell"[tw] OR rbc[tw]) AND exchange	
6	("red cell"[tw] OR "red cells"[tw]) AND exchange[tw]	

No	Query	Result	
7	#1 OR #2 OR #3 OR #4 OR #5 OR #6	were not recorded	
8	anaemia[tw] OR anemia [tw]		
9	#7 AND #8		
10	perioperative[tw] OR "peri operative"[tw]		
11	preoperative[tw] OR "pre operative"[tw]		
12	intraoperative[tw] OR "intra operative"[tw]		
13	peroperative[tw] OR "per operative"[tw]		
14	postoperative[tw] OR "post operative"[tw]		
15	#10 OR #11 OR #12 OR #13 OR #14		
16	#9 AND #15		
17	injur*[tw] OR trauma*[tw]		
18	#9 AND #17		
19	shock[tw] OR "cardiovascular collapse"[tw] OR "circulatory collapse"[tw]		
20	#9 AND #19		
21	massive[tw] AND transfusion*[tw]		
22	"massive infusion"[tw] OR "massively transfused"[tw]		
23	massive[tw] AND bleeding[tw]		
24	massive[tw] AND hemorrhage[tw]		
25	massive[tw] AND haemorrhage[tw]		
26	#21 OR #22 OR #23 OR #24 OR #25		
27	#9 AND #26		
28	"cardiothoracic surgery"[tw] OR (chest[tw] AND surgery[tw])		
29	cardiothoracic[tw] AND patient*[tw]		
30	"thoracic operation"[tw] OR "thoracic surgery"[tw] OR thoracoplasty[tw]		
31	thoracic[tw] AND procedure*[tw]		
32	#28 OR #29 OR #30 OR #31		
33	#9 AND #32		
34	surgical[tw] OR surgery[tw] OR operation[tw] OR resection[tw]		
35	#9 AND #34		
36	"orthopedic surgery"[tw] OR "orthopaedic surgery"[tw]		
37	"bone surgery"[tw] OR orthopaedics[tw] or orthopedics[tw]		
38	orthopedic[tw] AND patient*[tw]		
39	orthopaedic[tw] AND patient*[tw]		
40	"orthopedic operation"[tw] OR "orthopaedic operation"[tw]		
41	orthopaedic[tw] AND procedure*[tw]		
42	orthopedic[tw] AND procedure*[tw]		
43	#36 OR #37 OR #38 OR #39 OR #40		
44	#9 AND #43		
45	#16 OR #18 OR #20 OR #27 OR #33 OR #35 OR #44		
46	#45 NOT (medline[SB] OR oldmedline[sb])		
47	#45 AND in process[sb]		
48	#45 AND pubmednotmedline[sb]		
49	#46 OR #47 OR #48		314

Table A5.4 CINAHL search conducted 14 May 2009

#	Query	Results
S133	s89 OR s103 OR s109 OR s128 OR s132	28
S132	s74 AND s131	11
S131	s11 AND s130	39
S130	s18 OR s24 OR s129	12,618
S129	(MH "Preoperative Care+")	6,893
S128	s74 AND s127	0
S127	s110 OR s111 OR s112 OR s113 OR s114 OR s119 OR s120 OR s121 OR s122 OR s123 OR s125 OR s126	6,054
S126	TI (ascorbate OR "Magnesium Ascorbicum" OR Magnorbin) OR AB (ascorbate OR "Magnesium Ascorbicum" OR Magnorbin)	86
S125	TI ("ascorbic acid" OR "cevitamic acid" OR "vitamin C") OR AB ("ascorbic acid" OR "cevitamic acid" OR "vitamin C")	1,323
S124	TI (Sytobex OR Eritron) OR AB (Sytobex OR Eritron)	0
S123	TI (Berubigen OR Docibin OR Bevidox OR Ducobee) OR AB (Berubigen OR Docibin OR Bevidox OR Ducobee)	1
S122	TI ("vitamin B12" OR "vitamin b 12") OR AB ("vitamin B12" OR "vitamin b 12")	719
S121	TI (cyanobalamin OR cobalamin OR cobalamins) OR AB (cyanobalamin OR cobalamin OR cobalamins)	123
S120	TI ("pteroylmonoglutamic acid") OR AB ("pteroylmonoglutamic acid")	1
S119	TI ("pteroylglutamic acid" OR pteroylmonoglutamate) OR AB ("pteroylglutamic acid" OR pteroylmonoglutamate)	3
S118	TI ("pteroyl monoglutamate" OR pteroylglutamate) OR AB ("pteroyl monoglutamate" OR pteroylglutamate)	0
S117	TI ("pteroyl glutamate" OR "pteroyl l glutamic acid") OR AB ("pteroyl glutamate" OR "pteroyl l glutamic acid")	0
S116	TI ("vitamin bc" OR "vitamin m") OR AB ("vitamin bc" OR "vitamin m")	0
S115	TI ("lactobacillus casei factor" OR "mission prenatal") OR AB ("lactobacillus casei factor" OR "mission prenatal")	0
S114	TI (folicet OR "folium acid" OR folsan OR folvite OR lafol) OR AB (folicet OR "folium acid" OR folsan OR folvite OR lafol)	2
S113	TI ("folic acid" OR folacin OR folate OR foldine OR foliamin) OR AB ("folic acid" OR folacin OR folate OR foldine OR foliamin)	2,168
S112	(MH "Ascorbic Acid")	1,785
S111	(MH "Vitamin B12")	1,181
S110	(MH "Folic Acid+")	2,731
S109	s74 AND s108	3
S108	s104 OR s105 OR s106	429
S107	TI ("iron supplement" OR "iron supplements") OR AB "iron supplement" OR "iron supplements"	0
S106	TI ("iron therapy" OR "iron treatment") OR AB ("iron therapy" OR "iron treatment")	98

#	Query	Results
S105	(MH "Iron/AD")	219
S104	(MH "Iron/TU")	174
S103	s74 AND s102	20
S102	s90 OR s91 OR s95 OR s96 OR s97 OR s98 OR s101	1,711
S101	TI (rHuEPO OR "rHu EPO" OR "r Hu EPO") OR AB (rHuEPO OR "rHu EPO" OR "r Hu EPO")	72
S100	TI ("tyb 5220" OR tyb5220) OR AB ("tyb 5220" OR tyb5220)	0
S99	TI ("krm 5702" OR krm5702 OR "snb 5001" OR snb5001) OR AB ("krm 5702" OR krm5702 OR "snb 5001" OR snb5001)	0
S98	TI (neorecormon OR procrit OR recormon OR recormone) OR AB (neorecormon OR procrit OR recormon OR recormone)	29
S97	TI (espo OR exprex OR globuren OR hemax OR marogen) OR AB (espo OR exprex OR globuren OR hemax OR marogen)	1
S96	TI (epoietin OR epoxitin OR eprex OR erantin OR erypo) OR AB (epoietin OR epoxitin OR eprex OR erantin OR erypo)	12
S95	TI (dynepo OR epoch OR epoconn OR epoetin OR epogen OR epogin) OR AB (dynepo OR epoch OR epoconn OR epoetin OR epogen OR epogin)	475
S94	TI (haematopoiectin OR haemopoiectin) OR AB (haematopoiectin OR haemopoiectin)	0
S93	TI (hematopoiectin OR hemopoiectin) OR AB (hematopoiectin OR hemopoiectin)	0
S92	TI ("erythropoietic N1 factor") OR AB ("erythropoietic N1 factor")	0
S91	TI (erthropoietin OR "erythropoiesis stimulating factor") OR AB (erthropoietin OR "erythropoiesis stimulating factor")	4
S90	(MH "Erythropoietin")	1,592
S89	s74 AND s88	2
S88	S75 OR S80 OR S81 OR S84 OR S85	262
S87	TI ("haemopoietic agent" OR "haemopoietic agents") OR AB ("haemopoietic agent" OR "haemopoietic agents")	0
S86	TI ("hemopoietic agent" OR "hemopoietic agents") OR AB ("hemopoietic agent" OR "hemopoietic agents")	0
S85	TI ("haematopoietic agent" OR "haematopoietic agents") OR AB ("haematopoietic agent" OR "haematopoietic agents")	1
S84	TI ("hematopoietic agent" OR "hematopoietic agents") OR AB ("hematopoietic agent" OR "hematopoietic agents")	2
S83	TI ("haematinic agent" OR "haematinic agents") OR AB ("haematinic agent" OR "haematinic agents")	0
S82	TI ("hematinic agent" OR "hematinic agents") OR AB ("hematinic agent" OR "hematinic agents")	0
S81	TI ("erythropoiesis stimulating agents" OR "haematinics") OR AB ("erythropoiesis stimulating agents" OR "haematinics")	92
S80	TI ("erythropoiesis stimulating agent" OR "hematinics") OR AB ("erythropoiesis stimulating agent" OR "hematinics")	25
S79	TI ("anti anemic agent" OR "anti anemic agents") OR AB ("anti anemic agent" OR "anti anemic agents")	0

#	Query	Results
S78	TI ("anti anaemic agent" OR "anti anaemic agents") OR AB ("anti anaemic agent" OR "anti anaemic agents")	0
S77	TI ("antianaemic agent" OR "antianaemic agents") OR AB ("antianaemic agent" OR "antianaemic agents")	0
S76	TI ("antianemic agent" OR "antianemic agents") OR AB ("antianemic agent" OR "antianemic agents")	0
S75	(MH "Hematinics")	175
S74	s29 OR s35 OR s39 OR s47 OR s56 OR s61 OR s73	76
S73	s15 and s72	6
S72	S62 or S63 or S64 or S65 or S66 OR S67 OR S68 OR S69 OR s70 OR s71	25,842
S71	TI (orthopaedic N1 procedure ^a) or AB (orthopaedic N1 procedure ^a)	14
S70	TI (orthopedic N1 procedure ^a) or AB (orthopedic N1 procedure ^a)	115
S69	TI ("orthopedic operation" OR "orthopaedic operation") or AB ("orthopedic operation" OR "orthopaedic operation")	6
S68	TI (orthopaedic N1 patient ^a) or AB (orthopaedic N1 patient ^a)	355
S67	TI (orthopedic N1 patient ^a) or AB (orthopedic N1 patient ^a)	245
S66	TI ("bone surgery" OR orthopaedics or orthopedics) or AB ("bone surgery" OR orthopaedics or orthopedics)	911
S65	TI ("orthopedic surgery" OR "orthopaedic surgery") or AB ("orthopedic surgery" OR "orthopaedic surgery")	790
S64	(MH "Orthopedic Nursing")	1,422
S63	(MH "Orthopedics")	3,289
S62	(MH "Orthopedic Surgery+")	21,259
S61	s15 and s60	53
S60	S57 or S58 OR S59	170,781
S59	TI (surgical OR surgery OR operation OR resection) or AB (surgical OR surgery OR operation OR resection)	69,889
S58	(MH "Medical-Surgical Nursing")	2,427
S57	(MH "Surgery, Operative+")	136,639
S56	s15 and s55	13
S55	S48 or S49 or S50 or S51 or S52 or S53 OR S54	23,228
S54	TI (thoracic N1 procedure ^a) or AB (thoracic N1 procedure ^a)	32
S53	TI ("thoracic operation" OR "thoracic surgery" OR thoracoplasty) or AB ("thoracic operation" OR "thoracic surgery" OR thoracoplasty)	253
S52	TI (cardiothoracic N1 patient ^a) or AB (cardiothoracic N1 patient ^a)	56
S51	TI ("cardiothoracic surgery" OR (chest N1 surgery)) or AB ("cardiothoracic surgery" OR (chest N1 surgery))	166
S50	(MH "Cardiovascular Nursing+")	2,655
S49	(MH "Surgery, Cardiovascular+")	16,879
S48	(MH "Thoracic Surgery+")	16,901

#	Query	Results
S47	s15 and s46	8
S46	S42 or S43 or S44 OR S45	5,121
S45	TI (massive N1 (bleeding OR haemorrhage OR hemorrhage)) or AB (massive N1 (bleeding OR haemorrhage OR hemorrhage))	5,042
S44	TI ("massive infusion" OR "massively transfused") or AB ("massive infusion" OR "massively transfused")	10
S43	TI (massive N3 transfusion ^a) or AB (massive N3 transfusion ^a)	87
S42	S40 and S41	74
S41	TI (massive) or AB (massive)	1,888
S40	(MH "Blood Transfusion")	3,427
S39	s15 and s38	4
S38	S36 or S37	6,687
S37	TI (shock OR "cardiovascular collapse" OR "circulatory collapse") or AB (shock OR "cardiovascular collapse" OR "circulatory collapse")	5,193
S36	(MH "Shock+")	3,242
S35	S15 and S34	18
S34	S30 OR S31 or S32 OR S33	121,361
S33	TI (injur ^a OR trauma ^a) or AB (injur ^a OR trauma ^a)	67,640
S32	(MH "Trauma Nursing")	526
S31	(MH "Trauma+")	5,857
S30	(MH "Wounds and Injuries+")	90,837
S29	S15 AND S28	33
S28	S16 or S17 or S18 or S19 or S20 or S21 or S22 or S23 or S24 or S25 OR S26 OR S27	54,117
S27	TI (postoperative OR "post operative") or AB (postoperative OR "post operative")	14,379
S26	TI (peroperative OR "per operative") or AB (peroperative OR "per operative")	51
S25	TI (intraoperative OR "intra operative") or AB (intraoperative OR "intra operative")	2,954
S24	TI (preoperative OR "pre operative") or AB (preoperative OR "pre operative")	7,186
S23	TI (perioperative OR "peri operative") or AB (perioperative OR "peri operative")	5,307
S22	(MH "Postoperative Period")	1,898
S21	(MH "Postoperative Complications+")	21,107
S20	(MH "Intraoperative Period")	364
S19	(MH "Intraoperative Complications+")	1,795
S18	(MH "Preoperative Period+")	719
S17	(MH "Perioperative Nursing")	8,787
S16	(MH "Perioperative Care+")	16,023
S15	S11 and S14	235
S14	S12 or S13	7,549
S13	TI (anaemia OR anemia) or AB (anaemia OR anemia)	3,956
S12	(MH "Anemia+")	6,210

#	Query	Results
S11	s1 OR s2 OR s3 OR s4 OR s5 OR s7 OR s8 OR s9	1,014
S10	TI ("red cells" N3 exchange) OR AB ("red cells" N3 exchange)	0
S9	TI ("red cell" N3 exchange) OR AB ("red cell" N3 exchange)	5
S8	TI (rbc N1 exchange) OR AB (rbc N1 exchange)	3
S7	TI ("red blood cell" N1 exchange) OR AB ("red blood cell" N1 exchange)	5
S6	TI ("normocyte transfusion" OR "normocyte transfusions") OR AB ("normocyte transfusion" OR "normocyte transfusions")	0
S5	TI ("red cell" N1 transfusion ^a) OR AB ("red cell" N1 transfusion ^a)	63
S4	TI (rbc N1 transfusion ^a) OR AB (rbc N1 transfusion ^a)	121
S3	TI ("red blood cell" N1 transfusion ^a) OR AB ("red blood cell" N1 transfusion ^a)	212
S2	TI ("erythrocyte transfusion" OR "erythrocyte transfusions") OR AB ("erythrocyte transfusion" OR "erythrocyte transfusions")	16
S1	(MH "Blood Component Transfusion")	820

^a The search was conducted using EBSCOhost on 14 May 2009

Table A5.5 AMI search conducted 14 May 2009

Set	Search terms	Results
#13	(((SUBJECT = (anemia)) OR (TI = (anaemia OR anemia) OR AB = (anaemia OR anemia)) OR ((MH_PHRASE = "Anemia" OR MH_PHRASE = "Anemia, Hemolytic" OR MH_PHRASE = "Anemia, Hemolytic, Congenital" OR MH_PHRASE = "Anemia, Aplastic" OR MH_PHRASE = "Anemia, Myelophthisic" OR MH_PHRASE = "Anemia, Iron-Deficiency" OR MH_PHRASE = "Anemia, Neonatal" OR MH_PHRASE = "Anemia, Sideroblastic" OR MH_PHRASE = "Anemia, Hypoplastic, Congenital" OR MH_PHRASE = "Anemia, Megaloblastic" OR MH_PHRASE = "Anemia, Refractory" OR MH_PHRASE = "Anemia, Macrocytic" OR MH_PHRASE = "Anemia, Dyserythropoietic, Congenital" OR MH_PHRASE = "Anemia, Diamond-Blackfan" OR MH_PHRASE = "Anemia, Pernicious" OR MH_PHRASE = "Anemia, Hemolytic, Congenital Nonspherocytic" OR MH_PHRASE = "Fanconi Anemia" OR MH_PHRASE = "Anemia, Sickle Cell" OR MH_PHRASE = "Anemia, Hemolytic, Autoimmune" OR MH_PHRASE = "Anemia, Hypochromic" OR MH_PHRASE = "Anemia, Refractory, with Excess of Blasts")))) AND (((TI = (("red cell" OR "red cells") %3 exchange) OR AB = (("red cell" OR "red cells") %3 exchange)) OR (TI = (("red blood cell" OR rbc) %1 exchange) OR AB = (("red blood cell" OR rbc) %1 exchange)) OR (TI = ("normocyte transfusion" OR "normocyte transfusions") OR AB = ("normocyte transfusion" OR "normocyte transfusions")) OR (TI = ("red cell" %1 transfusion ^a) OR AB = ("red cell" %1 transfusion ^a)) OR (TI = (("red blood cell" OR rbc) %1 transfusion ^a) OR AB = (("red blood cell" OR rbc) %1 transfusion ^a)) OR (TI = ("erythrocyte transfusion" OR "erythrocyte transfusions") OR AB = ("erythrocyte transfusion" OR "erythrocyte transfusions")) OR ((MH_PHRASE = "Erythrocyte Transfusion")))))	41

Set	Search terms	Results
#12	((SUBJECT = (anemia)) OR (TI = (anaemia OR anemia) OR AB = (anaemia OR anemia)) OR ((MH_PHRASE = "Anemia" OR MH_PHRASE = "Anemia, Hemolytic" OR MH_PHRASE = "Anemia, Hemolytic, Congenital" OR MH_PHRASE = "Anemia, Aplastic" OR MH_PHRASE = "Anemia, Myelophthistic" OR MH_PHRASE = "Anemia, Iron-Deficiency" OR MH_PHRASE = "Anemia, Neonatal" OR MH_PHRASE = "Anemia, Sideroblastic" OR MH_PHRASE = "Anemia, Hypoplastic, Congenital" OR MH_PHRASE = "Anemia, Megaloblastic" OR MH_PHRASE = "Anemia, Refractory" OR MH_PHRASE = "Anemia, Macrocytic" OR MH_PHRASE = "Anemia, Dyserythropoietic, Congenital" OR MH_PHRASE = "Anemia, Diamond-Blackfan" OR MH_PHRASE = "Anemia, Pernicious" OR MH_PHRASE = "Anemia, Hemolytic, Congenital Nonspherocytic" OR MH_PHRASE = "Fanconi Anemia" OR MH_PHRASE = "Anemia, Sickle Cell" OR MH_PHRASE = "Anemia, Hemolytic, Autoimmune" OR MH_PHRASE = "Anemia, Hypochromic" OR MH_PHRASE = "Anemia, Refractory, with Excess of Blasts"))))	594
#11	SUBJECT = (anemia)	437
#10	TI = (anaemia OR anemia) OR AB = (anaemia OR anemia)	393
#9	(MH_PHRASE = "Anemia" OR MH_PHRASE = "Anemia, Hemolytic" OR MH_PHRASE = "Anemia, Hemolytic, Congenital" OR MH_PHRASE = "Anemia, Aplastic" OR MH_PHRASE = "Anemia, Myelophthistic" OR MH_PHRASE = "Anemia, Iron-Deficiency" OR MH_PHRASE = "Anemia, Neonatal" OR MH_PHRASE = "Anemia, Sideroblastic" OR MH_PHRASE = "Anemia, Hypoplastic, Congenital" OR MH_PHRASE = "Anemia, Megaloblastic" OR MH_PHRASE = "Anemia, Refractory" OR MH_PHRASE = "Anemia, Macrocytic" OR MH_PHRASE = "Anemia, Dyserythropoietic, Congenital" OR MH_PHRASE = "Anemia, Diamond-Blackfan" OR MH_PHRASE = "Anemia, Pernicious" OR MH_PHRASE = "Anemia, Hemolytic, Congenital Nonspherocytic" OR MH_PHRASE = "Fanconi Anemia" OR MH_PHRASE = "Anemia, Sickle Cell" OR MH_PHRASE = "Anemia, Hemolytic, Autoimmune" OR MH_PHRASE = "Anemia, Hypochromic" OR MH_PHRASE = "Anemia, Refractory, with Excess of Blasts")	34
#8	((TI = (("red cell" OR "red cells") %3 exchange) OR AB = (("red cell" OR "red cells") %3 exchange)) OR (TI = (("red blood cell" OR rbc) %1 exchange) OR AB = (("red blood cell" OR rbc) %1 exchange)) OR (TI = ("normocyte transfusion" OR "normocyte transfusions") OR AB = ("normocyte transfusion" OR "normocyte transfusions")) OR (TI = ("red cell" %1 transfusion ^a) OR AB = ("red cell" %1 transfusion ^a) OR (TI = (("red blood cell" OR rbc) %1 transfusion ^a) OR AB = (("red blood cell" OR rbc) %1 transfusion ^a) OR (TI = ("erythrocyte transfusion" OR "erythrocyte transfusions") OR AB = ("erythrocyte transfusion" OR "erythrocyte transfusions")) OR ((MH_PHRASE = "Erythrocyte Transfusion"))	43
#7	TI = (("red cell" OR "red cells") %3 exchange) OR AB = (("red cell" OR "red cells") %3 exchange)	2
#6	TI = (("red blood cell" OR rbc) %1 exchange) OR AB = (("red blood cell" OR rbc) %1 exchange)	0
#5	TI = ("normocyte transfusion" OR "normocyte transfusions") OR AB = ("normocyte transfusion" OR "normocyte transfusions")	0
#4	TI = ("red cell" %1 transfusion ^a) OR AB = ("red cell" %1 transfusion ^a)	13
#3	TI = (("red blood cell" OR rbc) %1 transfusion ^a) OR AB = (("red blood cell" OR rbc) %1 transfusion ^a)	11
#2	TI = ("erythrocyte transfusion" OR "erythrocyte transfusions") OR AB = ("erythrocyte transfusion" OR "erythrocyte transfusions")	1
#1	(MH_PHRASE = "Erythrocyte Transfusion")	24

^a The search was conducted using Informit online platform on 14 May 2009

A6 Literature search – question 6

Question 6

In patients with critical bleeding requiring massive transfusion, what is the effect of rFVIIa (prophylaxis or treatment) on morbidity, mortality and transfusion rate in patients with critical bleeding requiring massive transfusion?

Table A6.1 EMBASE.com search conducted 24 June 2009

#	Query	Results
#1	'recombinant blood clotting factor 7a'/exp	2,756
#2	'blood clotting factor 7a'/exp	1,850
#3	'recombinant protein'/exp	189,913
#4	#2 AND #3	465
#5	'recombinant fviiia':de	170
#6	'nn 1731':de	12
#7	'recombinant activated factor vii':ab,ti,tn	791
#8	'recombinant *2 viia':ab,ti,tn OR 'recombinant *2 fviiia':ab,ti,tn	1,133
#9	'recombinant f viia':ab,ti,tn	3
#10	rfviiia:ab,ti,tn OR 'r fviiia':ab,ti,tn OR 'r f viia':ab,ti,tn OR rf7a:ab,ti,tn	1,070
#11	'eptacog alfa':ab,ti,tn OR niastase:ab,ti,tn OR 'novo seven':ab,ti,tn OR novoseven:ab,ti,tn	1,272
#12	'nn 1731':ab,ti,tn OR nn1731:ab,ti,tn	12
#13	'blood clotting factor viia':ab,ti,tn OR 'coagulation factor viia':ab,ti,tn	133
#14	'activated *2 factor vii':ab,ti,tn OR 'activated *2 fvii':ab,ti,tn OR acet:ab,ti,tn	1,301
#15	'activated *2 factor 7':ab,ti,tn OR 'activated *2 f7':ab,ti,tn	2
#16	'98982 74 2':rn	1,850
#17	#13 OR #14 OR #15 OR #16	2,949
#18	recombinant:ab,ti	166,319
#19	#17 AND #18	1,275
#20	#1 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #19	3,550
#21	((('perioperative period'/exp) OR ('perioperative nursing'/exp) OR ('perioperative complication'/exp) OR ('preoperative period'/exp) OR ('preoperative complication'/exp) OR ('intraoperative period'/exp) OR (perioperative:ab,ti OR 'peri operative':ab,ti) OR (preoperative:ab,ti OR 'pre operative':ab,ti) OR (intraoperative:ab,ti OR 'intra operative':ab,ti) OR (peroperative:ab,ti OR 'per operative':ab,ti) OR ('postoperative period'/exp) OR ('postoperative complication'/exp) OR (postoperative:ab,ti OR 'post operative':ab,ti))	869,935
#22	('injury'/exp) OR (injur*:ab,ti OR trauma*:ab,ti)	1,268,915
#23	('shock'/exp) OR (shock:ab,ti OR 'cardiovascular collapse':ab,ti OR 'circulatory collapse':ab,ti)	136,163
#24	((('blood transfusion'/exp) OR (('bleeding'/exp) AND ('transfusion'/exp))) AND (massive:ab,ti) OR ('massive transfusion':ab,ti) OR ('massive blood transfusion':ab,ti) OR ('massive transfusion protocol':ab,ti) OR ('massive *3 transfusion':ab,ti OR 'massive *3 transfusions':ab,ti) OR ('massive infusion':ab,ti OR 'massively transfused':ab,ti) OR ('massive *1 bleeding':ab,ti) OR ('massive *1 haemorrhage':ab,ti OR 'massive *1 hemorrhage':ab,ti))	8,445

#	Query	Results
#25	('thorax surgery'/exp) OR ('heart surgery'/exp) OR ('cardiothoracic surgery':ab,ti OR 'chest *1 surgery':ab,ti) OR ('cardiothoracic *1 patient':ab,ti OR 'cardiothoracic *1 patients':ab,ti) OR ('thoracic operation':ab,ti OR 'thoracic surgery':ab,ti OR thoracoplasty:ab,ti) OR ('thoracic *1 procedure':ab,ti OR 'thoracic *1 procedures':ab,ti)	286,765
#26	('surgery'/exp) OR ('surgical ward'/exp) OR ('surgical patient'/exp) OR (surgical:ab,ti OR surgery:ab,ti OR operation:ab,ti OR resection:ab,ti)	2,740,539
#27	('orthopedic surgery'/exp) OR ('orthopedic surgery':ab,ti OR 'orthopaedic surgery':ab,ti) OR ('bone surgery':ab,ti OR orthopaedics:ab,ti OR orthopedics:ab,ti) OR ('orthopedic *1 patient':ab,ti OR 'orthopedic *1 patients':ab,ti) OR ('orthopaedic *1 patient':ab,ti OR 'orthopaedic *1 patients':ab,ti) OR ('orthopedic operation':ab,ti OR 'orthopedic *1 procedures':ab,ti) OR ('orthopaedic operation':ab,ti OR 'orthopaedic *1 procedures':ab,ti) OR ('orthopedic *1 procedure':ab,ti OR 'orthopaedic *1 procedure':ab,ti)	259,726
#28	#21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27	3,700,992
#29	#20 AND #28	2,351
#30	('adverse outcome'/exp) OR ('outcome assessment'/exp) OR ('morbidity'/exp) OR ('mortality'/exp) OR (morbidity:ab,ti OR incidence:ab,ti OR prevalence:ab,ti OR occurrence:ab,ti) OR (mortality:ab,ti OR death:ab,ti OR survival:ab,ti)	1,938,636
#31	('quality of life'/exp) OR (qol:ab,ti OR 'quality of life':ab,ti OR 'quality of wellbeing':ab,ti) OR ('health related quality':ab,ti OR hrqol:ab,ti) OR (qaly*:ab,ti OR 'quality adjusted':ab,ti OR 'adjusted life':ab,ti)	161,033
#31	('quality of life'/exp) OR (qol:ab,ti OR 'quality of life':ab,ti OR 'quality of wellbeing':ab,ti) OR ('health related quality':ab,ti OR hrqol:ab,ti) OR (qaly*:ab,ti OR 'quality adjusted':ab,ti OR 'adjusted life':ab,ti)	161,033
#32	((('blood component therapy'/exp) AND (('dose response'/exp) OR ('drug dose'/exp))) OR ('fresh frozen plasma'/exp/dd_do) OR ('recombinant erythropoietin'/exp/dd_do) OR ('transfusion frequency':ab,ti) OR ('frequency *5 transfusion':ab,ti OR 'frequency *5 transfusions':ab,ti) OR ('transfusion rate':ab,ti OR 'transfusion rates':ab,ti) OR ('rate *5 transfusion':ab,ti OR 'rates *5 transfusion':ab,ti) OR ('transfusion requirement':ab,ti OR 'transfusion requirements':ab,ti) OR ('transfusion indication':ab,ti OR 'transfusion indications':ab,ti) OR ('indications *5 transfusion':ab,ti OR 'indications *5 transfusions':ab,ti) OR ('indication *5 transfusion':ab,ti OR 'indication *5 transfusions':ab,ti) OR ('transfusion interval':ab,ti OR 'transfusion intervals':ab,ti) OR ('need *3 transfusion':ab,ti OR 'need *3 transfusions':ab,ti) OR ('transfusion need':ab,ti OR 'transfusion needs':ab,ti) OR ('dose *3 transfusion':ab,ti OR 'dose *3 transfusions':ab,ti) OR ('dose *3 transfused':ab,ti OR 'transfusions *3 dose':ab,ti) OR ('transfusion dose':ab,ti OR 'transfused *3 dose':ab,ti) OR ('platelet dose':ab,ti OR 'dose *3 platelets':ab,ti) OR (dose:ab,ti AND transfus*:ab,ti)	17,470

#	Query	Results
#33	('hemoglobin'/de) OR ('hemoglobin determination'/de) OR ('hemoglobin blood level'/de) OR ('mean corpuscular volume'/de) OR ('blood haemoglobin':ab,ti OR 'blood hemoglobin':ab,ti) OR ('haemoglobin *1 level':ab,ti OR 'hemoglobin *1 level':ab,ti) OR ('haemoglobin *1 levels':ab,ti OR 'hemoglobin *1 levels':ab,ti) OR ('hb level':ab,ti OR 'hb levels':ab,ti) OR ('haemoglobin determination':ab,ti OR 'hemoglobin determination':ab,ti) OR ('hemoglobin assay':ab,ti OR 'haemoglobin assay':ab,ti) OR ('hemoglobin estimation':ab,ti OR 'haemoglobin estimation':ab,ti) OR ('hb determination':ab,ti OR 'hb estimation':ab,ti OR 'hb assay':ab,ti) OR ('hemoglobin *1 content':ab,ti OR 'hemoglobin *1 concentration':ab,ti) OR ('haemoglobin *1 content':ti,ab OR 'haemoglobin *1 concentration':ti,ab) OR ('hb content':ab,ti OR 'hb concentration':ab,ti) OR (hemoglobinometry:ab,ti OR haemoglobinometry:ab,ti) OR ('plasma haemoglobin':ab,ti OR 'plasma hemoglobin':ab,ti) OR ('serum haemoglobin':ab,ti OR 'serum hemoglobin':ab,ti) OR ('mean corpuscular haemoglobin':ab,ti OR 'mean corpuscular hemoglobin':ab,ti) OR ('mean cell *1 haemoglobin':ab,ti OR 'mean cell *1 hemoglobin':ab,ti) OR ('erythrocyte indices':ti,ab OR 'erythrocyte index':ti,ab OR 'erythrocyte indexes':ti,ab) OR ('red *1 cell indices':ab,ti OR 'red *1 cell index':ab,ti OR 'red *1 cell indexes':ab,ti) OR ('rbc indices':ab,ti OR 'rbc index':ab,ti OR 'rbc indexes':ab,ti)	87,280
#34	('reoperation'/de) OR ('bleeding'/de) OR ('postoperative hemorrhage'/de) OR (('bleeding'/de) OR ('postoperative hemorrhage'/de)) OR (('reoperation'/de) OR ('postoperative hemorrhage'/de)) OR (reoperation*:ti AND (bleeding:ti OR 'blood loss':ti)) OR (reoperation*:ti AND (hemorrhag*:ti OR haemorrhag*:ti)) OR (('re operation':ti OR 're operations':ti) AND bleeding:ti) OR (('re operation':ti OR 're operations':ti) AND 'blood loss':ti) OR (('re operation':ti OR 're operations':ti) AND hemorrhag*:ti) OR (('re operation':ti OR 're operations':ti) AND haemorrhag*:ti) OR (reoperation*:ab AND (bleeding:ab OR 'blood loss':ab)) OR (reoperation*:ab AND (hemorrhag*:ab OR haemorrhag*:ab)) OR (('re operation':ab OR 're operations':ab) AND bleeding:ab) OR (('re operation':ab OR 're operations':ab) AND 'blood loss':ab) OR (('re operation':ab OR 're operations':ab) AND hemorrhag*:ab) OR (('re operation':ab OR 're operations':ab) AND haemorrhag*:ab) OR ('repeat surgery':ab,ti OR 'surgical revision':ab,ti)	135,567
#35	('disseminated intravascular clotting'/de) OR ('consumption coagulopathy':ab,ti OR 'consumptive coagulopathy':ab,ti) OR ('defibrination syndrome':ab,ti OR 'sanarelli shwartzman syndrome':ab,ti) OR ('disseminated fibrin thromboembolism':ab,ti) OR ('disseminated intravasal thromboembolism':ab,ti) OR ('intravasal agglutination':ab,ti OR 'intravasal *1 clotting':ab,ti) OR ('intravascular *1 clotting':ab,ti OR 'intravascular *1 coagulation':ab,ti) OR ('intravascular *1 coagulopathy':ti,ab OR 'intravenous *1 coagulation':ti,ab)	18,502
#36	('health economics'/exp) OR ('economic aspect'/exp) OR ('economics'/exp) OR ('finance'/exp) OR ('biomedical technology assessment'/exp) OR ('economic evaluation'/exp) OR ('health care cost'/exp) OR (economic*:ab,ti OR pharmaco-economic*:ab,ti) OR (cost*:ab,ti OR price*:ab,ti OR pricing:ab,ti) OR ('burden of illness':ab,ti OR 'value *1 money':ab,ti) OR (resource*:ab,ti AND utili*:ab,ti) OR (resource*:ab,ti AND utili*:ab,ti) OR ('technology assessment':ab,ti OR 'technology assessments':ab,ti) OR ('technology appraisal':ab,ti OR 'technology appraisals':ab,ti)	1,001,267
#37	('hospitalization'/exp) OR ('length of stay'/exp) OR (hospitaliz*:ab,ti OR hospitalis*:ab,ti) OR ('length *3 stay':ab,ti OR 'hospital stay':ab,ti)	246,178
#38	('intensive care unit'/exp) OR ('intensive care unit':ab,ti OR icu:ab,ti OR 'intensive care units':ab,ti) OR ('close attention unit':ab,ti OR 'close attention units':ab,ti) OR ('intensive care department':ab,ti OR 'intensive care departments':ab,ti) OR ('special care unit':ab,ti OR 'special care units':ab,ti) OR ('critical care unit':ab,ti OR 'critical care units':ab,ti)	77,229
#39	('hospital admission'/exp) OR ('hospital readmission'/exp) OR ('hospital admission':ab,ti OR 'hospital admittance':ab,ti) OR ('patient admission':ab,ti OR readmission:ab,ti) OR (rehospitalization:ab,ti OR rehospitalisation:ab,ti)	78,138

#	Query	Results
#40	#30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39	3,250,321
#41	#29 AND #40	1,835

Table A6.2 Cochrane library database search conducted 24 June 2009

#	Query	Results
#1	MeSH descriptor Factor VIIa explode all trees	126
#2	MeSH descriptor Recombinant Proteins explode all trees	5,962
#3	#1 AND #2	1,738
#4	"recombinant activated factor VII"	69
#5	"recombinant *2 VIIa" OR "Recombinant *2 FVIIa"	0
#6	"recombinant F VIIa"	0
#7	rFVIIa OR "r FVIIa" OR "r F VIIa" OR rf7a	111
#8	"eptacog alfa" OR niastase OR "Novo Seven" OR Novoseven	60
#9	"nn 1731" OR nn1731	0
#10	"blood clotting factor viia" OR "coagulation factor viia"	3
#11	Activated NEAR/2 ("Factor VII" OR FVII)	142
#12	Activated NEAR/2 ("Factor 7" OR "F7")	1
#13	acset	1
#14	#10 OR #11 OR #12 OR #13	1,422
#15	recombinant	8,146
#16	#14 AND #15	1,020
#17	#3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #16	1,836
#18	MeSH descriptor Perioperative Care explode all trees	4,254
#19	MeSH descriptor Preoperative Care explode all trees	4,098
#20	MeSH descriptor Postoperative Complications explode all trees	21,418
#21	MeSH descriptor Postoperative Period explode all trees	3,483
#22	MeSH descriptor Intraoperative Complications explode all trees	2,476
#23	MeSH descriptor Intraoperative Period explode all trees	919
#24	perioperative OR "peri operative"	5,196
#25	preoperative OR "pre operative"	11,093
#26	intraoperative OR "intra operative"	8,039
#27	peroperative OR "per operative"	474
#28	postoperative OR "post operative"	40,236
#29	#18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28	933
#30	#17 AND #29	385
#31	MeSH descriptor Wounds and Injuries explode all trees	10,953
#32	injur* OR trauma*	20,750
#33	#31 OR #32	356

#	Query	Results
#34	#17 AND #33	284
#35	MeSH descriptor Shock explode all trees	930
#36	shock OR "cardiovascular collapse" OR "circulatory collapse"	3,179
#37	#35 OR #36	281
#38	#17 AND #37	241
#39	MeSH descriptor Blood Transfusion explode all trees	2,628
#40	massive	599
#41	#39 AND #40	205
#42	massive NEAR/3 transfusion*	20
#43	"massive infusion" OR "massively transfused"	3
#44	massive NEAR/1 (bleeding OR haemorrhage OR hemorrhage)	47
#45	#41 OR #42 OR #43 OR #44	254
#46	#17 AND #45	159
#47	MeSH descriptor Thoracic Surgical Procedures explode all trees	10,297
#48	MeSH descriptor Thoracic Surgery explode all trees	130
#49	MeSH descriptor Cardiovascular Surgical Procedures explode all trees	10,930
#50	"cardiothoracic surgery" OR (chest NEAR/1 surgery)	675
#51	cardiothoracic NEAR/1 patient*	4
#52	"thoracic operation" OR "thoracic surgery" OR thoracoplasty	2,131
#53	thoracic NEAR/1 procedure*	16
#54	#47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53	164
#55	#17 AND #54	91
#56	MeSH descriptor Surgical Procedures, Operative explode all trees	68,578
#57	MeSH descriptor General Surgery, this term only	167
#58	MeSH descriptor Surgery Department, Hospital, this term only	68
#59	surgical OR surgery OR operation OR resection	91,783
#60	#56 OR #57 OR #58 OR #59	88
#61	#17 AND #60	69
#62	MeSH descriptor Orthopedic Procedures explode all trees	5,335
#63	MeSH descriptor Orthopedics, this term only	272
#64	"orthopedic surgery" OR "orthopaedic surgery"	2,339
#65	"bone surgery" OR orthopaedics or orthopedics	7,975
#66	(orthopedic OR orthopaedic) NEAR/1 patient*	223
#67	"orthopedic operation" OR "orthopaedic operation"	6
#68	(orthopedic OR orthopaedic) NEAR/1 procedure*	638
#69	#62 OR #63 OR #64 OR #65 OR #66 OR #67 OR #68	79
#70	#17 AND #69	51
#71	#30 OR #34 OR #38 OR #46 OR #55 OR #61 OR #70	466

#	Query	Results
#72	MeSH descriptor Morbidity explode all trees	8,475
#73	MeSH descriptor Mortality explode all trees	7,946
#74	morbidity OR incidence OR prevalence OR occurrence	62,784
#75	mortality OR death OR survival	55,325
#76	#72 OR #73 OR #74 OR #75	54
#77	#71 AND #76	43
#78	MeSH descriptor Quality of Life, this term only	9,425
#79	MeSH descriptor Quality-Adjusted Life years, this term only	2,062
#80	qol OR "quality of life" OR "quality of wellbeing"	21,521
#81	"health related quality" or hrqol	2,898
#82	qaly* or "quality adjusted" or "adjusted life"	3,802
#83	#78 OR #79 OR #80 OR #81 OR #82	49
#84	#71 AND #83	37
#85	MeSH descriptor Blood Component Transfusion explode all trees with qualifier: MT	99
#86	frequency NEAR/5 transfusion*	84
#87	rate* NEAR/5 transfusion*	324
#88	"transfusion requirement" OR "transfusion requirements"	949
#89	indication* NEAR/5 transfusion*	45
#90	"transfusion interval" OR "transfusion intervals"	13
#91	(need NEAR/3 transfusion*) OR "transfusion needs"	623
#92	dose NEAR/3 transfus*	86
#93	"platelet dose" OR (dose NEAR/3 platelets)	185
#94	(dose and transfus*):ti	72
#95	#85 OR #86 OR #87 OR #88 OR #89 OR #90 OR #91 OR #92 OR #93 OR #94	56
#96	#71 AND #95	22
#97	MeSH descriptor Hemoglobins, this term only	1,990
#98	MeSH descriptor Hemoglobinometry, this term only	152
#99	MeSH descriptor Erythrocyte Indices, this term only	110
#100	"blood haemoglobin" OR "blood hemoglobin"	241
#101	(haemoglobin OR hemoglobin) NEAR/1 level*	1,228
#102	"hb level" OR "hb levels"	236
#103	"haemoglobin determination" OR "hemoglobin determination"	120
#104	"hemoglobin assay" OR "haemoglobin assay"	4
#105	"hemoglobin estimation" OR "haemoglobin estimation"	5
#106	"hb determination" OR "hb estimation" OR "hb assay"	2
#107	hemoglobin NEAR/1 (content OR concentration)	904
#108	haemoglobin NEAR/1 (content OR concentration)	904
#109	"hb content" OR "hb concentration"	110

#	Query	Results
#110	hemoglobinometry OR haemoglobinometry	166
#111	"plasma haemoglobin" OR "plasma hemoglobin"	65
#112	"serum haemoglobin" OR "serum hemoglobin"	47
#113	"mean corpuscular volume" OR mcv OR mch OR mchc	350
#114	"mean corpuscular haemoglobin" OR "mean corpuscular hemoglobin"	41
#115	"Mean Cell" NEAR/1 (Haemoglobin OR Hemoglobin)	2
#116	"erythrocyte indices" OR "Erythrocyte Index" OR "Erythrocyte Indexes"	121
#117	red NEAR/1 ("cell indices" OR "Cell Index" OR "Cell Indexes")	14
#118	"rbc indices" OR "RBC Index" OR "RBC Indexes"	2
#119	#97 OR #98 OR #99 OR #100 OR #101 OR #102 OR #103 OR #104 OR #105 OR #106 OR #107 OR #108 OR #109 OR #110 OR #111 OR #112 OR #113 OR #114 OR #115 OR #116 OR #117 OR #118	62
#120	#71 AND #119	9
#121	MeSH descriptor Reoperation, this term only	1,199
#122	MeSH descriptor Hemorrhage, this term only	1,471
#123	MeSH descriptor Postoperative Hemorrhage, this term only	485
#124	MeSH descriptor Blood Loss, Surgical, this term only	1,399
#125	#122 OR #123 OR #124	13
#126	#121 AND #125	9
#127	reoperation* NEAR/15 (bleeding or "blood loss")	136
#128	reoperation* NEAR/15 (hemorrhag* OR haemorrhag*)	69
#129	("re operation" OR "re operations") NEAR/15 bleeding	31
#130	("re operation" OR "re operations") NEAR/15 "blood loss"	15
#131	("re operation" OR "re operations") NEAR/15 hemorrhag*	2
#132	("re operation" OR "re operations") NEAR/15 haemorrhag*	9
#133	"Repeat Surgery" OR "Surgical Revision"	110
#134	#126 OR #127 OR #128 OR #129 OR #130 OR #131 OR #132 OR #133	13
#135	#71 AND #134	8
#136	MeSH descriptor Disseminated Intravascular Coagulation, this term only	75
#137	"consumption coagulopathy" OR "consumptive coagulopathy"	12
#138	"defibrination syndrome" OR "sanarelli shwartzman syndrome"	1
#139	"disseminated fibrin thromboembolism"	0
#140	"disseminated intravasal thromboembolism"	0
#141	"intravasal agglutination" OR (intravasal NEAR/1 clotting)	0
#142	intravascular NEAR/1 (clotting OR coagulation OR coagulopathy)	237
#143	intravenous NEAR/1 coagulation	1
#144	#136 OR #137 OR #138 OR #139 OR #140 OR #141 OR #142 OR #143	14
#145	#71 AND #144	7

#	Query	Results
#146	MeSH descriptor Costs and Cost Analysis explode all trees	26,772
#147	MeSH descriptor Economics, this term only	65
#148	MeSH descriptor Models, Economic explode all trees	1,853
#149	MeSH descriptor Value of Life, this term only	274
#150	MeSH descriptor Utilization Review explode all trees	420
#151	MeSH descriptor Delivery of Health Care, this term only with qualifier: UT	62
#152	economic* OR pharmacoeconomic*	37,332
#153	cost* OR price* OR pricing	48,938
#154	resource* NEAR utili*	1,537
#155	"burden of illness" OR (value NEAR/1 money)	87
#156	#146 OR #147 OR #148 OR #149 OR #150 OR #151 OR #152 OR #153 OR #154 OR #155	8
#157	#71 AND #156	1
#158	MeSH descriptor Hospitalization explode all trees	10,690
#159	MeSH descriptor Child, Hospitalized, this term only	82
#160	hospitaliz* OR hospitalis*	16,298
#161	(length NEAR/3 stay) OR "hospital stay"	11,735
#162	#158 OR #159 OR #160 OR #161	1
#163	#71 AND #162	1
#164	MeSH descriptor Intensive Care Units explode all trees	1,978
#165	"intensive care unit" OR icu OR "intensive care units"	6,712
#166	"close attention unit" OR "close attention units"	0
#167	"intensive care department" OR "intensive care departments"	56
#168	"special care unit" OR "special care units"	63
#169	"critical care unit" OR "critical care units"	108
#170	#164 OR #165 OR #166 OR #167 OR #168 OR #169	5
#171	#71 AND #170	0
#172	MeSH descriptor Patient Admission, this term only	604
#173	MeSH descriptor Patient Readmission, this term only	593
#174	"hospital admission" OR "hospital admittance"	1,727
#175	"patient admission" OR readmission	2,327
#176	rehospitalization OR rehospitalisation	504
#177	#172 OR #173 OR #174 OR #175 OR #176	9
#178	#71 AND #177	0
#179	#77 OR #84 OR #96 OR #120 OR #135 OR #145 OR #157 OR #163 OR #171 OR #178	55

Table A6.3 PreMedline search conducted 24 June 2009

Search	Query	Results
#54	Search #51 OR #52 OR #53	57
#53	Search #50 AND pubmednotmedline[sb]	5
#52	Search #50 AND in process[sb]	34
#51	Search #50 NOT (medline[SB] OR oldmedline[sb])	57
#50	Search #21 OR #23 OR #25 OR #32 OR #38 OR #40 OR #49	812
#49	Search #14 AND #48	47
#48	Search #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47	43,020
#47	Search orthopedic[tw] AND procedure*[tw]	11,166
#46	Search orthopaedic[tw] AND procedure*[tw]	3,376
#45	Search "orthopedic operation"[tw] OR "orthopaedic operation"[tw]	75
#44	Search orthopaedic[tw] AND patient*[tw]	8,162
#43	Search orthopedic[tw] AND patient*[tw]	15,187
#42	Search "bone surgery"[tw] OR orthopaedics[tw] or orthopedics[tw]	17,665
#41	Search "orthopedic surgery"[tw] OR "orthopaedic surgery"[tw]	6,028
#40	Search #14 AND #39	585
#39	Search surgical[tw] OR surgery[tw] OR operation[tw] OR resection[tw]	1,882,022
#38	Search #14 AND #37	32
#37	Search #33 OR #34 OR #35 OR #36	54,299
#36	Search thoracic[tw] AND procedure*[tw]	19,240
#35	Search "thoracic operation"[tw] OR "thoracic surgery"[tw] OR thoracoplasty[tw]	16,763
#34	Search cardiothoracic[tw] AND patient*[tw]	2,288
#33	Search "cardiothoracic surgery"[tw] OR (chest[tw] AND surgery[tw])	24,500
#32	Search #14 AND #31	149
#31	Search #26 OR #27 OR #28 OR #29 OR #30	11,339
#30	Search "massive infusion"[tw] OR "massively transfused"[tw]	102
#29	Search massive[tw] AND haemorrhage[tw]	1,184
#28	Search massive[tw] AND hemorrhage[tw]	7,719
#27	Search massive[tw] AND bleeding[tw]	4,968
#26	Search massive[tw] AND transfusion*[tw]	2,323
#25	Search #14 AND #24	70
#24	Search shock[tw] OR "cardiovascular collapse"[tw] OR "circulatory collapse"[tw]	135,235
#23	Search #14 AND #22	293
#22	Search injur*[tw] OR trauma*[tw]	720,615
#21	Search #14 AND #20	293
#20	Search #15 OR #16 OR #17 OR #18 OR #19	613,621
#19	Search postoperative[tw] OR "post operative"[tw]	469,400
#18	Search peroperative[tw] OR "per operative"[tw]	3,711

Search	Query	Results
#17	Search intraoperative[tw] OR "intra operative"[tw]	88,480
#16	Search preoperative[tw] OR "pre operative"[tw]	149,999
#15	Search perioperative[tw] OR "peri operative"[tw]	43,061
#14	Search #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #13	1,479
#13	Search #11 AND #12	1,076
#12	Search recombinant[tw]	314,925
#11	Search #7 OR #8 OR #9 OR #10	2,061
#10	Search acset[tw]	0
#9	Search Activated[tw] AND ("Factor 7"[tw] OR "F7"[tw])	178
#8	Search Activated[tw] AND ("Factor VII"[tw] OR "FVII"[tw])	1,775
#7	Search "blood clotting factor viia"[tw] OR "coagulation factor viia"[tw]	132
#6	Search "nn 1731"[tw] OR nn1731[tw]	8
#5	Search "eptacog alfa"[tw] OR niastase[tw] OR "Novo Seven"[tw] OR Novoseven[tw]	335
#4	Search rFVIIa[tw] OR "r FVIIa"[tw] OR "r F VIIa"[tw] OR rf7a[tw]	921
#3	Search "recombinant F VIIa" [tw]	0
#2	Search "recombinant *2 VIIa"[tw] OR "Recombinant *2 FVIIa"[tw]	0
#1	Search "recombinant activated factor VII"[tw]	679

Table A6.4 CINAHL search conducted 23 June 2009

#	Query	Results
S14	S1 or S2 or S3 or S4 or S5 or S6 or S13	199
S13	S11 and S12	84
S12	TI recombinant or AB recombinant	2,345
S11	S7 or S8 or S9 or S10	145
S10	TI acset or AB acset	0
S9	TI (Activated N2 ("Factor 7" OR F7)) or AB (Activated N2 ("Factor 7" OR F7))	37
S8	TI (Activated N2 ("Factor VII" OR FVII)) or AB (Activated N2 ("Factor VII" OR FVII))	105
S7	TI ("blood clotting factor viia" OR "coagulation factor viia") or AB ("blood clotting factor viia" OR "coagulation factor viia")	3
S6	TI ("nn 1731" OR nn1731) or AB ("nn 1731" OR nn1731)	0
S5	TI ("eptacog alfa" OR niastase OR "Novo Seven" OR Novoseven) or AB ("eptacog alfa" OR niastase OR "Novo Seven" OR Novoseven)	14
S4	TI (rFVIIa OR "r FVIIa" OR "r F VIIa" OR rf7a) or AB (rFVIIa OR "r FVIIa" OR "r F VIIa" OR rf7a)	72
S3	TI "recombinant F VIIa" or AB "recombinant F VIIa"	0
S2	TI (recombinant N2 (VIIa OR FVIIa)) or AB (recombinant N2 (VIIa OR FVIIa))	117
S1	TI "recombinant activated factor VII" or AB "recombinant activated factor VII"	71

The search was conducted using EBSCOhost on 23 June 2009

Table A6.5 AMI search conducted 23 June 2009

Set	Search terms	Records
#17	((((TI = (recombinant) OR AB = (recombinant)) AND (((TI = (acset) OR AB = (acset)) OR (TI = (Activated %2 ("Factor 7" OR F7)) OR AB = (Activated %2 ("Factor 7" OR F7))) OR (TI = (Activated %2 ("Factor VII" OR FVII)) OR AB = (Activated %2 ("Factor VII" OR FVII))) OR (TI = ("blood clotting factor viia" OR "coagulation factor viia") OR AB = ("blood clotting factor viia" OR "coagulation factor viia")))))) OR (TI = ("nn 1731" OR nn1731) OR AB = ("nn 1731" OR nn1731)) OR (TI = ("eptacog alfa" OR niastase OR "Novo Seven" OR Novoseven) OR AB = ("eptacog alfa" OR niastase OR "Novo Seven" OR Novoseven)) OR (TI = (rFVIIa OR "r FVIIa" OR "r F VIIa" OR rf7a) OR AB = (rFVIIa OR "r FVIIa" OR "r F VIIa" OR rf7a)) OR (TI = ("recombinant F VIIa") OR AB = ("recombinant F VIIa")) OR (TI = (recombinant %2 (VIIa OR FVIIa)) OR AB = (recombinant %2 (VIIa OR FVIIa))) OR (TI = ("recombinant activated factor VII") OR AB = ("recombinant activated factor VII")) OR (((MH_PHRASE = "Recombinant Proteins")) AND ((MH_PHRASE = "Factor VIIa")))))	15
#16	((TI = (recombinant) OR AB = (recombinant)) AND (((TI = (acset) OR AB = (acset)) OR (TI = (Activated %2 ("Factor 7" OR F7)) OR AB = (Activated %2 ("Factor 7" OR F7))) OR (TI = (Activated %2 ("Factor VII" OR FVII)) OR AB = (Activated %2 ("Factor VII" OR FVII))) OR (TI = ("blood clotting factor viia" OR "coagulation factor viia") OR AB = ("blood clotting factor viia" OR "coagulation factor viia")))))	10
#15	TI = (recombinant) OR AB = (recombinant)	379
#14	((TI = (acset) OR AB = (acset)) OR (TI = (Activated %2 ("Factor 7" OR F7)) OR AB = (Activated %2 ("Factor 7" OR F7))) OR (TI = (Activated %2 ("Factor VII" OR FVII)) OR AB = (Activated %2 ("Factor VII" OR FVII))) OR (TI = ("blood clotting factor viia" OR "coagulation factor viia") OR AB = ("blood clotting factor viia" OR "coagulation factor viia")))	10
#13	TI = (acset) OR AB = (acset)	0
#12	TI = (Activated %2 ("Factor 7" OR F7)) OR AB = (Activated %2 ("Factor 7" OR F7))	0
#11	TI = (Activated %2 ("Factor VII" OR FVII)) OR AB = (Activated %2 ("Factor VII" OR FVII))	10
#10	TI = ("blood clotting factor viia" OR "coagulation factor viia") OR AB = ("blood clotting factor viia" OR "coagulation factor viia")	0
#9	TI = ("nn 1731" OR nn1731) OR AB = ("nn 1731" OR nn1731)	0
#8	TI = ("eptacog alfa" OR niastase OR "Novo Seven" OR Novoseven) OR AB = ("eptacog alfa" OR niastase OR "Novo Seven" OR Novoseven)	5
#7	TI = (rFVIIa OR "r FVIIa" OR "r F VIIa" OR rf7a) OR AB = (rFVIIa OR "r FVIIa" OR "r F VIIa" OR rf7a)	8
#6	TI = ("recombinant F VIIa") OR AB = ("recombinant F VIIa")	0
#5	TI = (recombinant %2 (VIIa OR FVIIa)) OR AB = (recombinant %2 (VIIa OR FVIIa))	6
#4	TI = ("recombinant activated factor VII") OR AB = ("recombinant activated factor VII")	10
#3	((((MH_PHRASE = "Recombinant Proteins")) AND ((MH_PHRASE = "Factor VIIa"))))	0
#2	(MH_PHRASE = "Recombinant Proteins")	109
#1	(MH_PHRASE = "Factor VIIa")	1

The search was conducted using Informit online platform on 23 June 2009

A7 Literature search – question 7

Question 7

In patients with critical bleeding requiring massive transfusion, what is the effect of fresh frozen plasma, cryoprecipitate, fibrinogen concentrate, and/or platelet transfusion on patient outcomes?

Table A7.1 EMBASE.com search conducted 25 June 2009

Table A7.1.1 Transfusion therapy

#	Query	Results
#1	'blood component therapy'/exp	42,649
#2	'blood transfusion'/exp	108,198
#3	'transfusion'/exp	171,322
#4	transfusion:ab,ti	52,679
#5	'blood exchange':ab,ti OR 'blood infusion':ab,ti	512
#6	'blood replacement':ab,ti OR 'blood retransfusion':ab,ti	645
#7	hemotherapy:ab,ti OR hematherapy:ab,ti OR hematotherapy:ab,ti	449
#8	haemotherapy:ab,ti OR haematherapy:ab,ti OR haematotherapy:ab,ti	109
#9	multitransfusion:ab,ti OR polytransfusion:ab,ti OR retransfusion:ab,ti	536
#10	'transfusion blood':ab,ti OR 'transfusion therapy':ab,ti	1,732
#11	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10	188,592

Table A7.1.2 Blood component

#	Query	Results
#1	'blood component'/exp	1,318
#2	'blood component':ab,ti OR 'blood components':ab,ti	4,118
#3	'blood product':ab,ti OR 'blood products':ab,ti	6,910
#4	'transfusion product':ab,ti OR 'transfusion products':ab,ti	83
#5	'blood constituent':ab,ti OR 'blood constituents':ab,ti	679
#6	#1 OR #2 OR #3 OR #4 OR #5	11,898

Table A7.1.3 Fresh frozen plasma

#	Query	Results
#1	'fresh frozen plasma'/exp	3,856
#2	'plasma'/exp	51,785
#3	'fresh frozen plasma':ab,ti OR ffp:ab,ti	3,545
#4	#1 OR #2 OR #3	57,199

Table A7.1.4 Plasma transfusion

#	Query	Results
#1	'plasma transfusion'/exp	1,485
#2	'plasma transfusion':ab,ti	240
#3	'plasma infusion':ab,ti OR 'serum transfusion':ab,ti	386
#4	#1 OR #2 OR #3	1,886

Table A7.1.5 Cryoprecipitate

#	Query	Results
#1	'cryoprecipitate'/exp	1,125
#2	'cryoprecipitate coagulum':de	75
#3	cryoprecipitate:ab,ti OR 'cryo precipitate':ab,ti	1,521
#4	#1 OR #2 OR #3	2,268

Table A7.1.6 Fibrinogen

#	Query	Results
#1	'fibrinogen'/exp	33,677
#2	fibrinogen:ab,ti OR 'factor 1':ab,ti OR 'factor i':ab,ti	69,267
#3	'9001 32 5':rn	33,687
#4	#1 OR #2 OR #3	82,495

Tabel A7.1.7 Platelet

#	Query	Results
#1	'thrombocyte transfusion'/exp	6,564
#2	'thrombocyte'/exp	53,469
#3	'blood transfusion'/exp	108,198
#4	'transfusion'/exp	171,322
#5	#3 OR #4	171,322
#6	#2 AND #5	3,307
#7	'platelet *1 transfusion':ab,ti OR 'platelet *1 transfusions':ab,ti	2,966
#8	'transfusion *3 platelet':ab,ti OR 'transfusion *3 platelets':ab,ti	700
#9	'thrombocyte transfusion':ab,ti OR 'thrombocytic transfusion':ab,ti	42
#10	#1 OR #6 OR #7 OR #8 OR #9	10,225

Table A7.2 Complete EMBASE search

#	Query	Results
#1	('blood component therapy'/exp) OR ('blood transfusion'/exp) OR ('transfusion'/exp) OR (transfusion:ab,ti) OR ('blood exchange':ab,ti OR 'blood infusion':ab,ti) OR ('blood replacement':ab,ti OR 'blood retransfusion':ab,ti) OR (hemotherapy:ab,ti OR hematherapy:ab,ti OR hematotherapy:ab,ti) OR (haemotherapy:ab,ti OR haematherapy:ab,ti OR haematotherapy:ab,ti) OR (multitransfusion:ab,ti OR polytransfusion:ab,ti OR retransfusion:ab,ti) OR ('transfusion blood':ab,ti OR 'transfusion therapy':ab,ti)	188,592
#2	('blood component'/exp) OR ('blood component':ab,ti OR 'blood components':ab,ti) OR ('blood product':ab,ti OR 'blood products':ab,ti) OR ('transfusion product':ab,ti OR 'transfusion products':ab,ti) OR ('blood constituent':ab,ti OR 'blood constituents':ab,ti)	11,898
#3	('fresh frozen plasma'/exp) OR ('plasma'/exp) OR ('fresh frozen plasma':ab,ti OR ffp:ab,ti)	57,199
#4	('plasma transfusion'/exp) OR ('plasma transfusion':ab,ti) OR ('plasma infusion':ab,ti OR 'serum transfusion':ab,ti)	1,886
#5	('cryoprecipitate'/exp) OR ('cryoprecipitate coagulum':de) OR (cryoprecipitate:ab,ti OR 'cryo precipitate':ab,ti)	2,268
#6	('fibrinogen'/exp) OR (fibrinogen:ab,ti OR 'factor 1':ab,ti OR 'factor i':ab,ti) OR ('9001 32 5':rn)	82,495
#7	('thrombocyte transfusion'/exp) OR (('thrombocyte'/exp) AND (('blood transfusion'/exp) OR ('transfusion'/exp))) OR ('platelet *1 transfusion':ab,ti OR 'platelet *1 transfusions':ab,ti) OR ('transfusion *3 platelet':ab,ti OR 'transfusion *3 platelets':ab,ti) OR ('thrombocyte transfusion':ab,ti OR 'thrombocytic transfusion':ab,ti)	10,225
#8	#2 OR #3 OR #5 OR #6	149,046
#9	#1 AND #8	12,970
#10	#4 OR #7 OR #9	21,876
#11	((('perioperative period'/exp) OR ('perioperative nursing'/exp) OR ('perioperative complication'/exp) OR ('preoperative period'/exp) OR ('preoperative complication'/exp) OR ('intraoperative period'/exp) OR (perioperative:ab,ti OR 'peri operative':ab,ti) OR (preoperative:ab,ti OR 'pre operative':ab,ti) OR (intraoperative:ab,ti OR 'intra operative':ab,ti) OR (peroperative:ab,ti OR 'per operative':ab,ti)) OR ('postoperative period'/exp) OR ('postoperative complication'/exp) OR (postoperative:ab,ti OR 'post operative':ab,ti))	870,294
#12	injur*:ab,ti OR trauma*:ab,ti	554,730
#13	('shock'/exp) OR (shock:ab,ti OR 'cardiovascular collapse':ab,ti OR 'circulatory collapse':ab,ti)	136,201
#14	((('blood transfusion'/exp) OR (('bleeding'/exp) AND ('transfusion'/exp))) AND (massive:ab,ti) OR ('massive transfusion':ab,ti) OR ('massive blood transfusion':ab,ti) OR ('massive transfusion protocol':ab,ti) OR ('massive *3 transfusion':ab,ti OR 'massive *3 transfusions':ab,ti) OR ('massive infusion':ab,ti OR 'massively transfused':ab,ti) OR ('massive *1 bleeding':ab,ti) OR ('massive *1 haemorrhage':ab,ti OR 'massive *1 hemorrhage':ab,ti))	8,451

#	Query	Results
#15	('thorax surgery'/exp) OR ('heart surgery'/exp) OR ('cardiothoracic surgery':ab,ti OR 'chest *1 surgery':ab,ti) OR ('cardiothoracic *1 patient':ab,ti OR 'cardiothoracic *1 patients':ab,ti) OR ('thoracic operation':ab,ti OR 'thoracic surgery':ab,ti OR 'thoracoplasty':ab,ti) OR ('thoracic *1 procedure':ab,ti OR 'thoracic *1 procedures':ab,ti)	286,869
#16	('surgery'/exp) OR ('surgical ward'/exp) OR ('surgical patient'/exp) OR (surgical:ab,ti OR surgery:ab,ti OR operation:ab,ti OR resection:ab,ti)	2,741,599
#17	('orthopedic surgery'/exp) OR ('orthopedic surgery':ab,ti OR 'orthopaedic surgery':ab,ti) OR ('bone surgery':ab,ti OR orthopaedics:ab,ti OR orthopedics:ab,ti) OR ('orthopedic *1 patient':ab,ti OR 'orthopedic *1 patients':ab,ti) OR ('orthopaedic *1 patient':ab,ti OR 'orthopaedic *1 patients':ab,ti) OR ('orthopedic operation':ab,ti OR 'orthopedic *1 procedures':ab,ti) OR ('orthopaedic operation':ab,ti OR 'orthopaedic *1 procedures':ab,ti) OR ('orthopedic *1 procedure':ab,ti OR 'orthopaedic *1 procedure':ab,ti)	259,925
#18	#11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17	3,294,948
#19	#10 AND #18	10,104
#20	('adverse outcome'/exp) OR ('outcome assessment'/exp) OR ('morbidity'/exp) OR ('mortality'/exp) OR (morbidity:ab,ti OR incidence:ab,ti OR prevalence:ab,ti OR occurrence:ab,ti) OR (mortality:ab,ti OR death:ab,ti OR survival:ab,ti)	1,939,842
#21	('quality of life'/exp) OR (qol:ab,ti OR 'quality of life':ab,ti OR 'quality of wellbeing':ab,ti) OR ('health related quality':ab,ti OR 'hrqol':ab,ti) OR (qaly*:ab,ti OR 'quality adjusted':ab,ti OR 'adjusted life':ab,ti)	161,171
#22	((('blood component therapy'/exp) AND (('dose response'/exp) OR ('drug dose'/exp))) OR ('fresh frozen plasma'/exp/dd_do) OR ('recombinant erythropoietin'/exp/dd_do) OR ('transfusion frequency':ab,ti) OR ('frequency *5 transfusion':ab,ti OR 'frequency *5 transfusions':ab,ti) OR ('transfusion rate':ab,ti OR 'transfusion rates':ab,ti) OR ('rate *5 transfusion':ab,ti OR 'rates *5 transfusion':ab,ti) OR ('transfusion requirement':ab,ti OR 'transfusion requirements':ab,ti) OR ('transfusion indication':ab,ti OR 'transfusion indications':ab,ti) OR ('indications *5 transfusion':ab,ti OR 'indications *5 transfusions':ab,ti) OR ('indication *5 transfusion':ab,ti OR 'indication *5 transfusions':ab,ti) OR ('transfusion interval':ab,ti OR 'transfusion intervals':ab,ti) OR ('need *3 transfusion':ab,ti OR 'need *3 transfusions':ab,ti) OR ('transfusion need':ab,ti OR 'transfusion needs':ab,ti) OR ('dose *3 transfusion':ab,ti OR 'dose *3 transfusions':ab,ti) OR ('dose *3 transfused':ab,ti OR 'transfusions *3 dose':ab,ti) OR ('transfusion dose':ab,ti OR 'transfused *3 dose':ab,ti) OR ('platelet dose':ab,ti OR 'dose *3 platelets':ab,ti) OR (dose:ab,ti AND transfus*:ab,ti)	17,482

#	Query	Results
#23	('hemoglobin'/de) OR ('hemoglobin determination'/de) OR ('hemoglobin blood level'/de) OR ('mean corpuscular volume'/de) OR ('blood haemoglobin':ab,ti OR 'blood hemoglobin':ab,ti) OR ('haemoglobin *1 level':ab,ti OR 'hemoglobin *1 level':ab,ti) OR ('haemoglobin *1 levels':ab,ti OR 'hemoglobin *1 levels':ab,ti) OR ('hb level':ab,ti OR 'hb levels':ab,ti) OR ('haemoglobin determination':ab,ti OR 'hemoglobin determination':ab,ti) OR ('hemoglobin assay':ab,ti OR 'haemoglobin assay':ab,ti) OR ('hemoglobin estimation':ab,ti OR 'haemoglobin estimation':ab,ti) OR ('hb determination':ab,ti OR 'hb estimation':ab,ti OR 'hb assay':ab,ti) OR ('hemoglobin *1 content':ab,ti OR 'hemoglobin *1 concentration':ab,ti) OR ('haemoglobin *1 content':ti,ab OR 'haemoglobin *1 concentration':ti,ab) OR ('hb content':ab,ti OR 'hb concentration':ab,ti) OR (hemoglobinometry:ab,ti OR haemoglobinometry:ab,ti) OR ('plasma haemoglobin':ab,ti OR 'plasma hemoglobin':ab,ti) OR ('serum haemoglobin':ab,ti OR 'serum hemoglobin':ab,ti) OR ('mean corpuscular haemoglobin':ab,ti OR 'mean corpuscular hemoglobin':ab,ti) OR ('mean cell *1 haemoglobin':ab,ti OR 'mean cell *1 hemoglobin':ab,ti) OR ('erythrocyte indices':ti,ab OR 'erythrocyte index':ti,ab OR 'erythrocyte indexes':ti,ab) OR ('red *1 cell indices':ab,ti OR 'red *1 cell index':ab,ti OR 'red *1 cell indexes':ab,ti) OR ('rbc indices':ab,ti OR 'rbc index':ab,ti OR 'rbc indexes':ab,ti)	87,312
#24	('reoperation'/de) OR ('bleeding'/de) OR ('postoperative hemorrhage'/de) OR (('bleeding'/de) OR ('postoperative hemorrhage'/de)) OR (('reoperation'/de) OR ('postoperative hemorrhage'/de)) OR (reoperation*:ti AND (bleeding:ti OR 'blood loss':ti)) OR (reoperation*:ti AND (hemorrhag*:ti OR haemorrhag*:ti)) OR (('re operation':ti OR 're operations':ti) AND bleeding:ti) OR (('re operation':ti OR 're operations':ti) AND 'blood loss':ti) OR (('re operation':ti OR 're operations':ti) AND hemorrhag*:ti) OR (('re operation':ti OR 're operations':ti) AND haemorrhag*:ti) OR (reoperation*:ab AND (bleeding:ab OR 'blood loss':ab)) OR (reoperation*:ab AND (hemorrhag*:ab OR haemorrhag*:ab)) OR (('re operation':ab OR 're operations':ab) AND bleeding:ab) OR (('re operation':ab OR 're operations':ab) AND 'blood loss':ab) OR (('re operation':ab OR 're operations':ab) AND hemorrhag*:ab) OR (('re operation':ab OR 're operations':ab) AND haemorrhag*:ab) OR ('repeat surgery':ab,ti OR 'surgical revision':ab,ti)	135,633
#25	('disseminated intravascular clotting'/de) OR ('consumption coagulopathy':ab,ti OR 'consumptive coagulopathy':ab,ti) OR ('defibrination syndrome':ab,ti OR 'sanarelli shwartzman syndrome':ab,ti) OR ('disseminated fibrin thromboembolism':ab,ti) OR ('disseminated intravasal thromboembolism':ab,ti) OR ('intravasal agglutination':ab,ti OR 'intravasal *1 clotting':ab,ti) OR ('intravascular *1 clotting':ab,ti OR 'intravascular *1 coagulation':ab,ti) OR ('intravascular *1 coagulopathy':ti,ab OR 'intravenous *1 coagulation':ti,ab)	18,505
#26	('health economics'/exp) OR ('economic aspect'/exp) OR ('economics'/exp) OR ('finance'/exp) OR ('biomedical technology assessment'/exp) OR ('economic evaluation'/exp) OR ('health care cost'/exp) OR (economic*:ab,ti OR pharmaco-economic*:ab,ti) OR (cost*:ab,ti OR price*:ab,ti OR pricing:ab,ti) OR ('burden of illness':ab,ti OR 'value *1 money':ab,ti) OR (resource*:ab,ti AND utili*:ab,ti) OR (resource*:ab,ti AND utili*:ab,ti) OR ('technology assessment':ab,ti OR 'technology assessments':ab,ti) OR ('technology appraisal':ab,ti OR 'technology appraisals':ab,ti)	1,001,779
#27	('hospitalization'/exp) OR ('length of stay'/exp) OR (hospitaliz*:ab,ti OR hospitalis*:ab,ti) OR ('length *3 stay':ab,ti OR 'hospital stay':ab,ti)	246,361

#	Query	Results
#28	('intensive care unit'/exp) OR ('intensive care unit':ab,ti OR icu:ab,ti OR 'intensive care units':ab,ti) OR ('close attention unit':ab,ti OR 'close attention units':ab,ti) OR ('intensive care department':ab,ti OR 'intensive care departments':ab,ti) OR ('special care unit':ab,ti OR 'special care units':ab,ti) OR ('critical care unit':ab,ti OR 'critical care units':ab,ti)	77,297
#29	('hospital admission'/exp) OR ('hospital readmission'/exp) OR ('hospital admission':ab,ti OR 'hospital admittance':ab,ti) OR ('patient admission':ab,ti OR 'readmission':ab,ti) OR (rehospitalization:ab,ti OR rehospitalisation:ab,ti)	78,194
#30	#20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29	3,252,157
#31	#19 AND #30	6,327

Table A7.3 Cochrane library database search conducted 25 June 2009

#	Query	Results
#1	MeSH descriptor Blood Component Transfusion, this term only	94
#2	MeSH descriptor Blood Transfusion, this term only	1,519
#3	transfusion	6,598
#4	"blood exchange" OR "blood infusion"	42
#5	"blood replacement" OR "blood retransfusion"	73
#6	hemotherapy OR hematherapy OR hematotherapy	55
#7	haemotherapy OR haematherapy OR haematotherapy	5
#8	multitransfusion OR polytransfusion OR retransfusion	66
#9	"transfusion blood" OR "transfusion therapy"	224
#10	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9	1,930
#11	"blood component" OR "blood components"	429
#12	"blood product" OR "blood products"	639
#13	"transfusion product" OR "transfusion products"	6
#14	"blood constituent" OR "blood constituents"	14
#15	#11 OR #12 OR #13 OR #14	1,340
#16	#10 AND #15	1,020
#17	MeSH descriptor Plasma, this term only	236
#18	"fresh frozen plasma" OR FFP	348
#19	#17 OR #18	924
#20	#10 AND #19	762
#21	"plasma transfusion"	30
#22	"plasma infusion" OR "serum transfusion"	17
#23	#20 OR #21 OR #22	761
#24	cryoprecipitate	65
#25	cryoprecipitate OR "cryo precipitate"	65
#26	#24 OR #25	580
#27	#10 AND #26	477

#	Query	Results
#28	Fibrinogen	2,831
#29	fibrinogen OR "factor 1" OR "factor I"	4,401
#30	#28 OR #29	437
#31	#10 AND #30	360
#32	MeSH descriptor Platelet Transfusion, this term only	208
#33	MeSH descriptor Blood Platelets, this term only	1,366
#34	#2 AND #33	286
#35	platelet* NEAR/3 transfusion*	552
#36	"thrombocyte transfusion" OR "thrombocytic transfusion"	40
#37	#32 OR #34 OR #35 OR #36	412
#38	#16 OR #23 OR #27 OR #31 OR #37	1,004
#39	MeSH descriptor Perioperative Care explode all trees	4,254
#40	MeSH descriptor Preoperative Care explode all trees	4,098
#41	MeSH descriptor Postoperative Complications explode all trees	21,418
#42	MeSH descriptor Postoperative Period explode all trees	3,483
#43	MeSH descriptor Intraoperative Complications explode all trees	2,476
#44	MeSH descriptor Intraoperative Period, this term only	919
#45	perioperative OR "peri operative"	5,196
#46	preoperative OR "pre operative"	11,093
#47	intraoperative OR "intra operative"	8,039
#48	peroperative OR "per operative"	474
#49	postoperative OR "post operative"	40,236
#50	#39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49	303
#51	#38 AND #50	117
#52	MeSH descriptor Wounds and Injuries explode all trees	10,953
#53	injur* OR trauma*	20,750
#54	#52 OR #53	113
#55	#38 AND #54	89
#56	MeSH descriptor Shock explode all trees	930
#57	shock OR "cardiovascular collapse" OR "circulatory collapse"	3,179
#58	#56 OR #57	86
#59	#38 AND #58	75
#60	MeSH descriptor Blood Transfusion, this term only	1,519
#61	massive	599
#62	#60 AND #61	66
#63	massive NEAR/3 transfusion*	20
#64	"massive infusion" OR "massively transfused"	3
#65	massive NEAR/1 (bleeding OR haemorrhage OR hemorrhage)	47

#	Query	Results
#66	#62 OR #63 OR #64 OR #65	74
#67	#38 AND #66	56
#68	MeSH descriptor Thoracic Surgical Procedures explode all trees	10,297
#69	MeSH descriptor Thoracic Surgery, this term only	130
#70	MeSH descriptor Cardiovascular Surgical Procedures explode all trees	10,930
#71	"cardiothoracic surgery" OR (chest NEAR/1 surgery)	675
#72	cardiothoracic NEAR/1 patient*	4
#73	"thoracic operation" OR "thoracic surgery" OR thoracoplasty	2,131
#74	thoracic NEAR/1 procedure*	16
#75	#68 OR #69 OR #70 OR #71 OR #72 OR #73 OR #74	62
#76	#38 AND #75	45
#77	MeSH descriptor Surgical Procedures, Operative explode all trees	68,578
#78	MeSH descriptor General Surgery, this term only	167
#79	MeSH descriptor Surgery Department, Hospital, this term only	68
#80	surgical OR surgery OR operation OR resection	91,783
#81	#77 OR #78 OR #79 OR #80	51
#82	#38 AND #81	37
#83	MeSH descriptor Orthopedic Procedures explode all trees	5,335
#84	MeSH descriptor Orthopedics, this term only	272
#85	"orthopedic surgery" OR "orthopaedic surgery"	2,339
#86	"bone surgery" OR orthopaedics or orthopedics	7,975
#87	(orthopedic OR orthopaedic) NEAR/1 patient*	223
#88	"orthopedic operation" OR "orthopaedic operation"	6
#89	(orthopedic OR orthopaedic) NEAR/1 procedure*	638
#90	#83 OR #84 OR #85 OR #86 OR #87 OR #88 OR #89	51
#91	#38 AND #90	26
#92	#51 OR #55 OR #59 OR #67 OR #76 OR #82 OR #91	122
#93	MeSH descriptor Morbidity explode all trees	8,475
#94	MeSH descriptor Mortality explode all trees	7,946
#95	morbidity OR incidence OR prevalence OR occurrence	62,784
#96	mortality OR death OR survival	55,325
#97	#93 OR #94 OR #95 OR #96	34
#98	#92 AND #97	20
#99	MeSH descriptor Quality of Life, this term only	9,425
#100	MeSH descriptor Quality-Adjusted Life years, this term only	2,062
#101	qol OR "quality of life" OR "quality of wellbeing"	21,521
#102	"health related quality" or hrqol	2,898
#103	qaly* or "quality adjusted" or "adjusted life"	3,802

#	Query	Results
#104	#99 OR #100 OR #101 OR #102 OR #103	34
#105	#92 AND #104	15
#106	MeSH descriptor Blood Component Transfusion explode all trees with qualifier: MT	99
#107	frequency NEAR/5 transfusion*	84
#108	rate* NEAR/5 transfusion*	324
#109	"transfusion requirement" OR "transfusion requirements"	949
#110	indication* NEAR/5 transfusion*	45
#111	"transfusion interval" OR "transfusion intervals"	13
#112	(need NEAR/3 transfusion*) OR "transfusion needs"	623
#113	dose NEAR/3 transfus*	86
#114	"platelet dose" OR (dose NEAR/3 platelets)	185
#115	(dose and transfus*):ti	72
#116	#106 OR #107 OR #108 OR #109 OR #110 OR #111 OR #112 OR #113 OR #114 OR #115	29
#117	#92 AND #116	11
#118	MeSH descriptor Hemoglobins, this term only	1,990
#119	MeSH descriptor Hemoglobinometry, this term only	152
#120	MeSH descriptor Erythrocyte Indices, this term only	110
#121	"blood haemoglobin" OR "blood hemoglobin"	241
#122	(haemoglobin OR hemoglobin) NEAR/1 level*	1,228
#123	"hb level" OR "hb levels"	236
#124	"haemoglobin determination" OR "hemoglobin determination"	120
#125	"hemoglobin assay" OR "haemoglobin assay"	4
#126	"hemoglobin estimation" OR "haemoglobin estimation"	5
#127	"hb determination" OR "hb estimation" OR "hb assay"	2
#128	hemoglobin NEAR/1 (content OR concentration)	904
#129	haemoglobin NEAR/1 (content OR concentration)	904
#130	"hb content" OR "hb concentration"	110
#131	hemoglobinometry OR haemoglobinometry	166
#132	"plasma haemoglobin" OR "plasma hemoglobin"	65
#133	"serum haemoglobin" OR "serum hemoglobin"	47
#134	"mean corpuscular volume" OR mcv OR mch OR mchc	350
#135	"mean corpuscular haemoglobin" OR "mean corpuscular hemoglobin"	41
#136	"Mean Cell" NEAR/1 (Haemoglobin OR Hemoglobin)	2
#137	"erythrocyte indices" OR "Erythrocyte Index" OR "Erythrocyte Indexes"	121
#138	red NEAR/1 ("cell indices" OR "Cell Index" OR "Cell Indexes")	14
#139	"rbc indices" OR "RBC Index" OR "RBC Indexes"	2

#	Query	Results
#140	#118 OR #119 OR #120 OR #121 OR #122 OR #123 OR #124 OR #125 OR #126 OR #127 OR #128 OR #129 OR #130 OR #131 OR #132 OR #133 OR #134 OR #135 OR #136 OR #137 OR #138 OR #139	33
#141	#92 AND #140	8
#142	MeSH descriptor Reoperation, this term only	1,199
#143	MeSH descriptor Hemorrhage, this term only	1,471
#144	MeSH descriptor Postoperative Hemorrhage, this term only	485
#145	MeSH descriptor Blood Loss, Surgical, this term only	1,399
#146	#143 OR #144 OR #145	10
#147	#142 AND #146	5
#148	reoperation* NEAR/15 (bleeding or "blood loss")	136
#149	reoperation* NEAR/15 (hemorrhag* OR haemorrhag*)	69
#150	("re operation" OR "re operations") NEAR/15 bleeding	31
#151	("re operation" OR "re operations") NEAR/15 "blood loss"	15
#152	("re operation" OR "re operations") NEAR/15 hemorrhag*	2
#153	("re operation" OR "re operations") NEAR/15 haemorrhag*	9
#154	"Repeat Surgery" OR "Surgical Revision"	110
#155	#147 OR #148 OR #149 OR #150 OR #151 OR #152 OR #153 OR #154	5
#156	#92 AND #155	1
#157	MeSH descriptor Disseminated Intravascular Coagulation, this term only	75
#158	"consumption coagulopathy" OR "consumptive coagulopathy"	12
#159	"defibrination syndrome" OR "sanarelli shwartzman syndrome"	1
#160	"disseminated fibrin thromboembolism"	0
#161	"disseminated intravasal thromboembolism"	0
#162	"intravasal agglutination" OR (intravasal NEAR/1 clotting)	0
#163	intravascular NEAR/1 (clotting OR coagulation OR coagulopathy)	237
#164	intravenous NEAR/1 coagulation	1
#165	#157 OR #158 OR #159 OR #160 OR #161 OR #162 OR #163 OR #164	2
#166	#92 AND #165	1
#167	MeSH descriptor Costs and Cost Analysis explode all trees	26,772
#168	MeSH descriptor Economics, this term only	65
#169	MeSH descriptor Models, Economic explode all trees	1,853
#170	MeSH descriptor Value of Life, this term only	274
#171	MeSH descriptor Utilization Review explode all trees	420
#172	MeSH descriptor Delivery of Health Care, this term only with qualifier: UT	62
#173	economic* or pharmaco-economic*	37,332
#174	cost* or price* or pricing	48,938
#175	resource* near utili*	1,537

#	Query	Results
#176	"burden of illness" or (value NEAR/1 money)	87
#177	#167 OR #168 OR #169 OR #170 OR #171 OR #172 OR #173 OR #174 OR #175 OR #176	13
#178	#92 and #177	0
#179	MeSH descriptor Hospitalization explode all trees	10,690
#180	MeSH descriptor Hospitalization, this term only	4,328
#181	hospitaliz* OR hospitalis*	16,298
#182	(length NEAR/3 stay) OR "hospital stay"	11,735
#183	#179 OR #180 OR #181 OR #182	6
#184	#92 AND #183	0
#185	MeSH descriptor Intensive Care Units explode all trees	1,978
#186	"intensive care unit" OR icu OR "intensive care units"	6,712
#187	"close attention unit" OR "close attention units"	0
#188	"intensive care department" OR "intensive care departments"	56
#189	"special care unit" OR "special care units"	63
#190	"critical care unit" OR "critical care units"	108
#191	#185 OR #186 OR #187 OR #188 OR #189 OR #190	3
#192	#92 AND #191	0
#193	MeSH descriptor Patient Admission, this term only	604
#194	MeSH descriptor Patient Readmission, this term only	593
#195	"hospital admission" OR "hospital admittance"	1,727
#196	"patient admission" OR readmission	2,327
#197	rehospitalization OR rehospitalisation	504
#198	#193 OR #194 OR #195 OR #196 OR #197	1
#199	#92 AND #198	0
#200	#98 OR #105 OR #117 OR #141 OR #156 OR #166 OR #178 OR #184 OR #192 OR #199	23

Table A7.4 PreMedline search conducted 25 June 2009

Search	Query	Results
#66	Search #37 OR #39 OR #41 OR #48 OR #54 OR #56 OR #65	168
#65	Search #30 AND #64	3
#64	Search #57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63	43,030
#63	Search orthopedic[tw] AND procedure*[tw]	11,166
#62	Search orthopaedic[tw] AND procedure*[tw]	3,378
#61	Search "orthopedic operation"[tw] OR "orthopaedic operation"[tw]	75
#60	Search orthopaedic[tw] AND patient*[tw]	8,166
#59	Search orthopedic[tw] AND patient*[tw]	15,190
#58	Search "bone surgery"[tw] OR orthopaedics[tw] or orthopedics[tw]	17,668
#57	Search "orthopedic surgery"[tw] OR "orthopaedic surgery"[tw]	6,029

Search	Query	Results
#56	Search #30 AND #55	114
#55	Search surgical[tw] OR surgery[tw] OR operation[tw] OR resection[tw]	1,882,237
#54	Search #30 AND #53	9
#53	Search #49 OR #50 OR #51 OR #52	54,307
#52	Search thoracic[tw] AND procedure*[tw]	19,247
#51	Search "thoracic operation"[tw] OR "thoracic surgery"[tw] OR thoracoplasty[tw]	16,764
#50	Search cardiothoracic[tw] AND patient*[tw]	2,289
#49	Search "cardiothoracic surgery"[tw] OR (chest[tw] AND surgery[tw])	24,504
#48	Search #30 AND #47	27
#47	Search #42 OR #43 OR #44 OR #45 OR #46	11,341
#46	Search "massive infusion"[tw] OR "massively transfused"[tw]	102
#45	Search massive[tw] AND haemorrhage[tw]	1,185
#44	Search massive[tw] AND hemorrhage[tw]	7,720
#43	Search massive[tw] AND bleeding[tw]	4,969
#42	Search massive[tw] AND transfusion*[tw]	2,325
#41	Search #30 AND #40	17
#40	Search shock[tw] OR "cardiovascular collapse"[tw] OR "circulatory collapse"[tw]	135,260
#39	Search #30 AND #38	49
#38	Search injur*[tw] OR trauma*[tw]	720,728
#37	Search #30 AND #36	73
#36	Search #31 OR #32 OR #33 OR #34 OR #35	613,700
#35	Search postoperative[tw] OR "post operative"[tw]	469,454
#34	Search peroperative[tw] OR "per operative"[tw]	3,712
#33	Search intraoperative[tw] OR "intra operative"[tw]	88,495
#32	Search preoperative[tw] OR "pre operative"[tw]	150,018
#31	Search perioperative[tw] OR "peri operative"[tw]	43,074
#30	Search #27 OR #28 OR #29	391
#29	Search #26 AND pubmednotmedline[sb]	59
#28	Search #26 AND in process[sb]	216
#27	Search #26 NOT (medline[SB] OR oldmedline[sb])	391
#26	Search #14 OR #19 OR #21 OR #23 OR #24 OR #25	17,790
#25	Search "thrombocyte transfusion"[tw] OR "thrombocytic transfusion"[tw]	37
#24	Search platelet*[tw] AND transfusion*[tw]	11,149
#23	Search #8 AND #22	1,327
#22	Search fibrinogen[tw] OR "factor 1"[tw] OR "factor I"[tw]	99,755
#21	Search #8 AND #20	423
#20	Search cryoprecipitate[tw] OR "cryo precipitate"[tw]	1,449
#19	Search #16 OR #17 OR #18	1,957

Search	Query	Results
#18	Search "plasma infusion"[tw] OR "serum transfusion"[tw]	344
#17	Search "plasma transfusion"[tw]	243
#16	Search #8 AND #15	1,477
#15	Search "fresh frozen plasma"[tw] OR FFP[tw]	3,202
#14	Search #8 AND #13	7,052
#13	Search #9 OR #10 OR #11 OR #12	14,015
#12	Search "blood constituent"[tw] OR "blood constituents"[tw]	683
#11	Search "transfusion product"[tw] OR "transfusion products"[tw]	67
#10	Search "blood product"[tw] OR "blood products"[tw]	6,061
#9	Search "blood component"[tw] OR "blood components"[tw]	7,960
#8	Search #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7	89,994
#7	Search "transfusion blood"[tw] OR "transfusion therapy"[tw]	1,482
#6	Search multitransfusion[tw] OR polytransfusion[tw] OR retransfusion[tw]	478
#5	Search haemotherapy[tw] OR haematherapy[tw] OR haematotherapy[tw]	67
#4	Search hemotherapy[tw] OR hematherapy[tw] OR hematotherapy[tw]	513
#3	Search "blood replacement"[tw] OR "blood retransfusion"[tw]	569
#2	Search "blood exchange"[tw] OR "blood infusion"[tw]	485
#1	Search transfusion[tw]	89,172

Table A7.5 CINAHL search conducted 26 June 2009

#	Query	Results
S221	S101 or S107 or S121 or S151 or S172 or S185 or S197 or S204 or S213 or S220	529 ^b
S220	S95 and S219	6
S219	S214 or S215 or S216 or S217 or S218	8367
S218	TI (rehospitalization OR rehospitalisation) or AB (rehospitalization OR rehospitalisation)	440
S217	TI ("patient admission" OR readmission) or AB ("patient admission" OR readmission)	1,129
S216	TI ("hospital admission" OR "hospital admittance") or AB ("hospital admission" OR "hospital admittance")	1,934
S215	(MH "Readmission")	1,926
S214	(MH "Patient Admission")	4,308
S213	S95 and S212	57
S212	S205 or S206 or S207 or S208 or S209 or S210 or S211	32,811
S211	TI ("critical care unit" OR "critical care units") or AB ("critical care unit" OR "critical care units")	868
S210	TI ("special care unit" OR "special care units") or AB ("special care unit" OR "special care units")	264
S209	TI ("intensive care department" OR "intensive care departments") or AB ("intensive care department" OR "intensive care departments")	33

#	Query	Results
S208	TI ("close attention unit" OR "close attention units") or AB ("close attention unit" OR "close attention units")	0
S207	TI ("intensive care unit" OR icu OR "intensive care units") or AB ("intensive care unit" OR icu OR "intensive care units")	13,701
S206	(MH "Critical Care Nursing+")	15,472
S205	(MH "Intensive Care Units+")	14,710
S204	S95 and S203	46
S203	S198 or S199 or S200 or S201 or S202	42,095
S202	TI ("hospital stay") or AB ("hospital stay")	3,313
S201	TI (length N3 stay) or AB (length N3 stay)	5,843
S200	TI (hospitaliz ^a OR hospitalis ^a) or AB (hospitaliz ^a OR hospitalis ^a)	18,171
S199	(MH "Child, Hospitalized")	2,176
S198	(MH "Hospitalization+")	20,839
S197	S95 and S196	40
S196	S186 or S187 or S188 or S189 or S190 or S191 or S192 or S193 or S194 or S195	82,178
S195	TI (value N1 money) or AB (value N1 money)	214
S194	TI ("burden of illness") or AB ("burden of illness")	175
S193	TI (resource ^a and utili ^a) or AB (resource ^a and utili ^a)	3,155
S192	TI (cost ^a or price ^a or pricing) or AB (cost ^a or price ^a or pricing)	45,979
S191	TI (economic ^a or pharmaco-economic ^a) or AB (economic ^a or pharmaco-economic ^a)	16,293
S190	(MH "Health Care Delivery/UT")	65
S189	(MH "Utilization Review+")	3,417
S188	(MH "Economic Value of Life")	236
S187	(MH "Economics")	2,517
S186	(MH "Costs and Cost Analysis+")	32,852
S185	S95 and S184	19
S184	S173 or S174 or S175 or S180 or S181 or S182	636
S183	TI (intravenous N1 coagulation) OR AB (intravenous N1 coagulation)	0
S182	TI (intravascular N1 coagulopathy) OR AB (intravascular N1 coagulopathy)	36
S181	TI (intravascular N1 coagulation) OR AB (intravascular N1 coagulation)	262
S180	TI (intravascular N1 clotting) OR AB (intravascular N1 clotting)	1
S179	TI (intravascular N1 clotting) OR AB (intravascular N1 clotting)	0
S178	TI ("intravascular agglutination") OR AB ("intravascular agglutination")	0
S177	TI ("disseminated intravascular thromboembolism") OR AB ("disseminated intravascular thromboembolism")	0
S176	TI ("disseminated fibrin thromboembolism") OR AB ("disseminated fibrin thromboembolism")	0
S175	TI ("defibrination syndrome" OR "sanarelli shwartzman syndrome") OR AB ("defibrination syndrome" OR "sanarelli shwartzman syndrome")	1

#	Query	Results
S174	TI ("consumption coagulopathy" OR "consumptive coagulopathy") OR AB ("consumption coagulopathy" OR "consumptive coagulopathy")	18
S173	(MH "Disseminated Intravascular Coagulation")	494
S172	S95 and S171	7
S171	S157 or S158 or S159 or S160 or S161 or S162 or S164 or S166 or S168 or S170	213
S170	TI ("Repeat Surgery" OR "Surgical Revision") OR AB ("Repeat Surgery" OR "Surgical Revision")	92
S169	TI ("re operations" N15 haemorrhag ^a) OR AB ("re operations" N15 haemorrhag ^a)	0
S168	TI ("re operation" N15 haemorrhag ^a) OR AB ("re operation" N15 haemorrhag ^a)	1
S167	TI ("re operations" N15 hemorrhag ^a) OR AB ("re operations" N15 hemorrhag ^a)	0
S166	TI ("re operation" N15 hemorrhag ^a) OR AB ("re operation" N15 hemorrhag ^a)	1
S165	TI ("re operations" N15 "blood loss") OR AB ("re operations" N15 "blood loss")	0
S164	TI ("re operation" N15 "blood loss") OR AB ("re operation" N15 "blood loss")	4
S163	TI ("re operations" N15 bleeding) OR AB ("re operations" N15 bleeding)	0
S162	TI ("re operation" N15 bleeding) OR AB ("re operation" N15 bleeding)	5
S161	TI (reoperation ^a N15 haemorrhag ^a) OR AB (reoperation ^a N15 haemorrhag ^a)	2
S160	TI (reoperation ^a N15 hemorrhag) OR AB (reoperation ^a N15 hemorrhag ^a)	9
S159	TI (reoperation ^a N15 "blood loss") OR AB (reoperation ^a N15 "blood loss")	5
S158	TI (reoperation ^a N15 bleeding) OR AB (reoperation ^a N15 bleeding)	41
S157	S152 and S156	63
S156	S153 or S154 or S155	4,145
S155	(MH "Blood Loss, Surgical")	626
S154	(MH "postoperative hemorrhage")	501
S153	(MH "hemorrhage")	3,116
S152	(MH "Repeat Procedures+")	3,142
S151	S95 and S150	37
S150	S122 or S123 or S124 or S125 or S126 or S127 or S128 or S129 or S130 or S131 or S132 or S133 or S134 or S135 or S136 or S137 or S138 or S139 or S140 or S141 or S142 or S143 or S144 or S145 or S146 or S148 or S149	3,661
S149	TI ("rbc indices" OR "RBC Index" OR "RBC Indexes") OR AB ("rbc indices" OR "RBC Index" OR "RBC Indexes")	8
S148	TI (red N1 "Cell Indexes") OR AB (red N1 "Cell Indexes")	6
S147	TI (red N1 "Cell Index") OR AB (red N1 "Cell Index")	0
S146	TI (red N1 "cell indices") OR AB (red N1 "cell indices")	24
S145	TI ("erythrocyte indices" OR "Erythrocyte Index" OR "Erythrocyte Indexes") OR AB ("erythrocyte indices" OR "Erythrocyte Index" OR "Erythrocyte Indexes")	8
S144	TI ("Mean Cell" N1 Haemoglobin) OR AB ("Mean Cell" N1 Haemoglobin)	3
S143	TI ("Mean Cell" N1 Hemoglobin) OR AB ("Mean Cell" N1 Hemoglobin)	10
S142	TI ("mean corpuscular haemoglobin" OR "mean corpuscular hemoglobin") OR AB ("mean corpuscular haemoglobin" OR "mean corpuscular hemoglobin")	30

#	Query	Results
S141	TI ("mean corpuscular volume" OR mcv OR mch OR mchc) OR AB ("mean corpuscular volume" OR mcv OR mch OR mchc)	358
S140	TI ("serum haemoglobin" OR "serum hemoglobin") OR AB ("serum haemoglobin" OR "serum hemoglobin")	15
S139	TI ("plasma haemoglobin" OR "plasma hemoglobin") OR AB ("plasma haemoglobin" OR "plasma hemoglobin")	30
S138	TI (hemoglobinometry OR haemoglobinometry) OR AB (hemoglobinometry OR haemoglobinometry)	2
S137	TI ("hb content" OR "hb concentration") OR AB ("hb content" OR "hb concentration")	50
S136	TI (haemoglobin N1 concentration) OR AB (haemoglobin N1 concentration)	70
S135	TI (haemoglobin N1 content) OR AB (haemoglobin N1 content)	4
S134	TI (hemoglobin N1 concentration) OR AB (hemoglobin N1 concentration)	275
S133	TI (hemoglobin N1 content) OR AB (hemoglobin N1 content)	26
S132	TI ("hb determination" OR "hb estimation" OR "hb assay") OR AB ("hb determination" OR "hb estimation" OR "hb assay")	3
S131	TI ("hemoglobin estimation" OR "haemoglobin estimation") OR AB ("hemoglobin estimation" OR "haemoglobin estimation")	3
S130	TI ("hemoglobin assay" OR "haemoglobin assay") OR AB ("hemoglobin assay" OR "haemoglobin assay")	6
S129	TI ("haemoglobin determination" OR "hemoglobin determination") OR AB ("haemoglobin determination" OR "hemoglobin determination")	7
S128	TI ("hb level" OR "hb levels") OR AB ("hb level" OR "hb levels")	170
S127	TI (haemoglobin N1 level ^a) OR AB (haemoglobin N1 level ^a)	152
S126	TI (hemoglobin N1 level ^a) OR AB (hemoglobin N1 level ^a)	673
S125	TI ("blood haemoglobin" OR "blood hemoglobin") OR AB ("blood haemoglobin" OR "blood hemoglobin")	45
S124	(MH "Erythrocyte Indices")	97
S123	(MH "Hemoglobinometry")	22
S122	(MH "Hemoglobins")	2,525
S121	S95 and S120	121
S120	S108 or S109 or S110 or S111 or S112 or S113 or S114 or S115 or S116 or S117 or S118 or S119	809
S119	TI (dose and transfus ^a)	7
S118	TI (dose N3 platelets) or AB (dose N3 platelets)	3
S117	TI ("platelet dose") or AB ("platelet dose")	3
S116	TI (dose N3 transfus ^a) or AB (dose N3 transfus ^a)	14
S115	TI ("transfusion needs") or AB ("transfusion needs")	25
S114	TI (need N3 transfusion ^a) or AB (need N3 transfusion ^a)	236
S113	TI ("transfusion interval" OR "transfusion intervals") or AB ("transfusion interval" OR "transfusion intervals")	4
S112	TI (indication ^a N5 transfusion ^a) or AB (indication ^a N5 transfusion ^a)	34

#	Query	Results
S111	TI ("transfusion requirement" OR "transfusion requirements") or AB ("transfusion requirement" OR "transfusion requirements")	255
S110	TI (rate ^a N5 transfusion ^a) or AB (rate ^a N5 transfusion ^a)	169
S109	TI (frequency N5 transfusion ^a) or AB (frequency N5 transfusion ^a)	19
S108	(MH "Blood Component Transfusion+/MT")	143
S107	S95 and S106	2
S106	S102 or S103 or S104 or S105	37,397
S105	TI (qaly ^a or "quality adjusted" or "adjusted life") or AB (qaly ^a or "quality adjusted" or "adjusted life")	834
S104	TI ("health related quality" or hrqol) or AB ("health related quality" or hrqol)	3,433
S103	TI (qol OR "quality of life" OR "quality of wellbeing") or AB (qol OR "quality of life" OR "quality of wellbeing")	23,773
S102	(MH "Quality of Life+")	26,875
S101	S95 and S100	194
S100	S96 or S97 or S98 or S99	152,334
S99	TI (mortality OR death OR survival) or AB (mortality OR death OR survival)	72,235
S98	TI (morbidity OR incidence OR prevalence OR occurrence) or AB (morbidity OR incidence OR prevalence OR occurrence)	78,734
S97	(MH "Mortality+")	18,757
S96	(MH "Morbidity+")	28,062
S95	S50 or S56 or S60 or S68 or S77 or S82 or S94	505
S94	S36 and S93	32
S93	S83 or S84 or S85 or S86 or S87 or S88 or S89 or S90 or S91 or S92	26,353
S92	TI (orthopaedic N1 procedure ^a) or AB (orthopaedic N1 procedure ^a)	88
S91	TI (orthopedic N1 procedure ^a) or AB (orthopedic N1 procedure ^a)	116
S90	TI ("orthopedic operation" OR "orthopaedic operation") or AB ("orthopedic operation" OR "orthopaedic operation")	6
S89	TI (orthopaedic N1 patient ^a) or AB (orthopaedic N1 patient ^a)	359
S88	TI (orthopedic N1 patient ^a) or AB (orthopedic N1 patient ^a)	247
S87	TI ("bone surgery" OR orthopaedics or orthopedics) or AB ("bone surgery" OR orthopaedics or orthopedics)	924
S86	TI ("orthopedic surgery" OR "orthopaedic surgery") or AB ("orthopedic surgery" OR "orthopaedic surgery")	803
S85	(MH "Orthopedic Nursing")	1,426
S84	(MH "Orthopedics")	3,401
S83	(MH "Orthopedic Surgery+")	21,657
S82	S36 and S81	344
S81	S78 or S79 or S80	173,634
S80	TI (surgical OR surgery OR operation OR resection) or AB (surgical OR surgery OR operation OR resection)	70,928

#	Query	Results
S79	(MH "Medical-Surgical Nursing")	2,449
S78	(MH "Surgery, Operative+")	139,091
S77	S36 and S76	85
S76	S69 or S70 or S71 or S72 or S73 or S74 or S75	23,580
S75	TI (thoracic N1 procedure ^a) or AB (thoracic N1 procedure ^a)	34
S74	TI ("thoracic operation" OR "thoracic surgery" OR thoracoplasty) or AB ("thoracic operation" OR "thoracic surgery" OR thoracoplasty)	255
S73	TI (cardiothoracic N1 patient ^a) or AB (cardiothoracic N1 patient ^a)	57
S72	TI ("cardiothoracic surgery" OR (chest N1 surgery)) or AB ("cardiothoracic surgery" OR (chest N1 surgery))	170
S71	(MH "Cardiovascular Nursing+")	2,682
S70	(MH "Surgery, Cardiovascular+")	17,133
S69	(MH "Thoracic Surgery+")	17,176
S68	S36 and S67	96
S67	S63 or S64 or S65 or S66	5,213
S66	TI (massive N1 (bleeding OR haemorrhage OR hemorrhage)) or AB (massive N1 (bleeding OR haemorrhage OR hemorrhage))	5,133
S65	TI ("massive infusion" OR "massively transfused") or AB ("massive infusion" OR "massively transfused")	10
S64	TI (massive N3 transfusion ^a) or AB (massive N3 transfusion ^a)	88
S63	S61 and S62	74
S62	TI (massive) or AB (massive)	1,910
S61	(MH "Blood Transfusion")	3,485
S60	S36 and S59	43
S59	S57 or S58	6,769
S58	TI (shock OR "cardiovascular collapse" OR "circulatory collapse") or AB (shock OR "cardiovascular collapse" OR "circulatory collapse")	5,247
S57	(MH "Shock+")	3,312
S56	S36 and S55	179
S55	S51 or S52 or S53 or S54	122,929
S54	TI (injur ^a OR trauma ^a) or AB (injur ^a OR trauma ^a)	68,513
S53	(MH "Trauma Nursing")	532
S52	(MH "Trauma+")	5,939
S51	(MH "Wounds and Injuries+")	91,987
S50	S36 and S49	192
S49	S37 or S38 or S39 or S40 or S41 or S42 or S43 or S44 or S45 or S46 or S47 or S48	54,968
S48	TI (postoperative OR "post operative") or AB (postoperative OR "post operative")	14,568
S47	TI (peroperative OR "per operative") or AB (peroperative OR "per operative")	51
S46	TI (intraoperative OR "intra operative") or AB (intraoperative OR "intra operative")	3,001

#	Query	Results
S45	TI (preoperative OR "pre operative") or AB (preoperative OR "pre operative")	7,282
S44	TI (perioperative OR "peri operative") or AB (perioperative OR "peri operative")	5,369
S43	(MH "Postoperative Period")	1,926
S42	(MH "Postoperative Complications+")	21,543
S41	(MH "Intraoperative Period")	367
S40	(MH "Intraoperative Complications+")	1,832
S39	(MH "Preoperative Period+")	726
S38	(MH "Perioperative Nursing")	8,865
S37	(MH "Perioperative Care+")	16,246
S36	S16 or S23 or S25 or S29 or S35	1,186
S35	S30 or S32 or S33 or S34	482
S34	TI ("thrombocyte transfusion" OR "thrombocytic transfusion") or AB ("thrombocyte transfusion" OR "thrombocytic transfusion")	0
S33	TI platelet ^a N3 transfusion ^a or AB platelet ^a N3 transfusion ^a	186
S32	S2 and S31	86
S31	(MH "Blood Platelets")	1,345
S30	(MH "Platelet Transfusion")	320
S29	S10 and S28	53
S28	S26 or S27	1,893
S27	TI (fibrinogen OR "factor 1" OR "factor I") or AB (fibrinogen OR "factor 1" OR "factor I")	1,665
S26	(MH "Fibrinogen")	529
S25	S10 and S24	27
S24	TI (cryoprecipitate OR "cryo precipitate") or AB (cryoprecipitate OR "cryo precipitate")	41
S23	S20 or S21 or S22	273
S22	TI ("plasma infusion" OR "serum transfusion") or AB ("plasma infusion" OR "serum transfusion")	6
S21	TI "plasma transfusion"	14
S20	S10 and S19	267
S19	S17 or S18	856
S18	TI ("fresh frozen plasma" OR FFP) or AB ("fresh frozen plasma" OR FFP)	224
S17	(MH "Plasma")	709
S16	S10 and S15	583
S15	S11 or S12 or S13 or S14	966
S14	TI ("blood constituent" OR "blood constituents") or AB ("blood constituent" OR "blood constituents")	11
S13	TI ("transfusion product" OR "transfusion products") or AB ("transfusion product" OR "transfusion products")	5
S12	TI ("blood product" OR "blood products") or AB ("blood product" OR "blood products")	700

#	Query	Results
S11	TI ("blood component" OR "blood components") or AB ("blood component" OR "blood components")	298
S10	S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9	5,951
S9	TI ("transfusion blood" OR "transfusion therapy") or AB ("transfusion blood" OR "transfusion therapy")	143
S8	TI (multitransfusion OR polytransfusion OR retransfusion) or AB (multitransfusion OR polytransfusion OR retransfusion)	23
S7	TI (haemotherapy OR haemotherapy OR haemotherapy) or AB (haemotherapy OR haemotherapy OR haemotherapy)	0
S6	TI (hemotherapy OR hemotherapy OR hemotherapy) or AB (hemotherapy OR hemotherapy OR hemotherapy)	14
S5	TI ("blood replacement" OR "blood retransfusion") or AB ("blood replacement" OR "blood retransfusion")	18
S4	TI ("blood exchange" OR "blood infusion") or AB ("blood exchange" OR "blood infusion")	16
S3	TI transfusion or AB transfusion	3,686
S2	(MH "Blood Transfusion")	3,485
S1	(MH "Blood Component Transfusion")	843

a The search was conducted using EBSCOhost on 26 June 2009

b The records from each of these search statements were exported separately owing to technical difficulties experienced with EBSCOhost when processing this search statement. Consequently there were duplicated records in this number

Table A7.6 AMI search conducted 30 June 2009

Set	Search terms	Records
#18	((TI = ("thrombocyte transfusion" OR "thrombocytic transfusion") OR AB = ("thrombocyte transfusion" OR "thrombocytic transfusion")) OR (TI = (platelet ^a %3 transfusion ^a) OR AB = (platelet ^a %3 transfusion ^a)) OR ((MH_PHRASE = "Platelet Transfusion")) OR (((TI = (concentrat ^a) OR AB = (concentrat ^a)) AND (((TI = (fibrinogen OR "factor 1" OR "factor I") OR AB = (fibrinogen OR "factor 1" OR "factor I")) OR (MH_PHRASE = "Fibrinogen")))) OR (TI = ("plasma infusion" OR "serum transfusion") OR AB = ("plasma infusion" OR "serum transfusion")) OR (TI = ("plasma transfusion") OR AB = ("plasma transfusion")) OR (TI = ("fresh frozen plasma" OR FFP) OR AB = ("fresh frozen plasma" OR FFP)) OR (TI = ("blood constituent" OR "blood constituents") OR AB = ("blood constituent" OR "blood constituents")) OR (TI = ("transfusion product" OR "transfusion products") OR AB = ("transfusion product" OR "transfusion products")) OR (TI = ("blood product" OR "blood products") OR AB = ("blood product" OR "blood products")) OR (TI = ("blood component" OR "blood components") OR AB = ("blood component" OR "blood components")) OR ((MH_PHRASE = "Blood Component Transfusion"))	191
#17	TI = ("thrombocyte transfusion" OR "thrombocytic transfusion") OR AB = ("thrombocyte transfusion" OR "thrombocytic transfusion")	0
#16	TI = (platelet ^a %3 transfusion ^a) OR AB = (platelet ^a %3 transfusion ^a)	13
#15	(MH_PHRASE = "Platelet Transfusion")	9
#14	((TI = (concentrat ^a) OR AB = (concentrat ^a)) AND (((TI = (fibrinogen OR "factor 1" OR "factor I") OR AB = (fibrinogen OR "factor 1" OR "factor I")) OR (MH_PHRASE = "Fibrinogen"))))	31
#13	TI = (concentrat ^a) OR AB = (concentrat ^a)	2,952

Set	Search terms	Records
#12	((TI = (fibrinogen OR "factor 1" OR "factor I") OR AB = (fibrinogen OR "factor 1" OR "factor I")) OR (MH_PHRASE = "Fibrinogen"))	206
#11	TI = (fibrinogen OR "factor 1" OR "factor I") OR AB = (fibrinogen OR "factor 1" OR "factor I")	204
#10	MH_PHRASE = "Fibrinogen"	4
#9	TI = (cryoprecipitate OR "cryo precipitate") OR AB = (cryoprecipitate OR "cryo precipitate")	14
#8	TI = ("plasma infusion" OR "serum transfusion") OR AB = ("plasma infusion" OR "serum transfusion")	3
#7	TI = ("plasma transfusion") OR AB = ("plasma transfusion")	0
#6	TI = ("fresh frozen plasma" OR FFP) OR AB = ("fresh frozen plasma" OR FFP)	29
#5	TI = ("blood constituent" OR "blood constituents") OR AB = ("blood constituent" OR "blood constituents")	2
#4	TI = ("transfusion product" OR "transfusion products") OR AB = ("transfusion product" OR "transfusion products")	0
#3	TI = ("blood product" OR "blood products") OR AB = ("blood product" OR "blood products")	100
#2	TI = ("blood component" OR "blood components") OR AB = ("blood component" OR "blood components")	18
#1	(MH_PHRASE = "Blood Component Transfusion")	23

^a The search was conducted using Informat online platform on 30 June 2009

A8 Literature search – question 8

Question 8

In patients with critical bleeding requiring massive transfusion, at what INR (or PT/APTT) for fresh frozen plasma, fibrinogen level for cryoprecipitate, platelet count for platelet concentrates should patients be transfused to avoid risks of significant adverse events in patients with critical bleeding requiring massive transfusion?

Table A8.1 EMBASE.com search conducted 28 June 2009

#	Query	Results
#1	'transfusion'/exp	171,390
#2	'blood transfusion'/exp	108,244
#3	transfus*:ab,ti	68,100
#4	'blood exchange':ab,ti OR 'blood infusion':ab,ti	512
#5	'blood replacement':ab,ti OR 'blood retransfusion':ab,ti	646
#6	hemotherapy:ab,ti OR hematherapy:ab,ti OR hematotherapy:ab,ti	449
#7	haemotherapy:ab,ti OR haematherapy:ab,ti OR haematotherapy:ab,ti	109
#8	multitransfusion:ab,ti OR polytransfusion:ab,ti OR retransfusion:ab,ti	536
#9	'transfusion blood':ab,ti OR 'transfusion therapy':ab,ti	1,732
#10	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9	195,155
#11	'fresh frozen plasma'/exp	3,863
#12	'plasma'/exp	51,796
#13	'plasma transfusion'/exp	1,487
#14	'fresh frozen plasma':ab,ti OR ffp:ab,ti	3,549
#15	'plasma infusion':ab,ti OR 'serum transfusion':ab,ti	386
#16	#11 OR #12 OR #13 OR #14 OR #15	58,271
#17	'international normalized ratio'/exp	2,883
#18	'prothrombin time'/exp	11,644
#19	'partial thromboplastin time'/exp	8,140
#20	'thromboplastin time'/exp	984
#21	'thrombotest'/exp	182
#22	'international standard unit'/exp	2,270
#23	'international sensitivity index':de	4
#24	'dilute russell viper venom time test':de	1
#25	'russell viper venom time':de	8
#26	'dilute russell viper venom time':de	4
#27	'diluted russell viper venom time':de	1
#28	'russell viper venom':de	127
#29	'international normalized ratio':ab,ti OR inr:ab,ti	4,786
#30	'international normalised ratio':ab,ti	320

#	Query	Results
#31	'international sensitivity index':ab,ti OR isi:ab,ti	2,871
#32	'prothrombin *1 time':ab,ti OR pt:ab,ti OR thrombotest:ab,ti	28,896
#33	'prothrombin test':ab,ti OR 'prothrombine time':ab,ti OR 'protrombin time':ab,ti	91
#34	'howell test':ab,ti OR 'smith test':ab,ti OR 'quick test':ab,ti	345
#35	'russell viper venom time':ab,ti OR drvvt:ab,ti OR rvvt:ab,ti	197
#36	'partial thromboplastin time':ab,ti OR ptt:ab,ti OR aptt:ab,ti	8,527
#37	#17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36	52,753
#38	#16 AND #37	1,674
#39	#10 AND #38	638
#40	'cryoprecipitation'/exp	1,839
#41	'cryoprecipitate coagulum':de	75
#42	cryoprecipitate:ab,ti OR 'cryo precipitate':ab,ti	1,521
#43	#16 OR #40 OR #41 OR #42	60,043
#44	'fibrinogen'/exp	33,692
#45	'fibrinogen blood level'/exp	4,032
#46	fibrinogen:ab,ti OR 'factor 1':ab,ti OR 'factor i':ab,ti	69,316
#47	'9001 32 5':rn	33,702
#48	#44 OR #45 OR #46 OR #47	82,850
#49	#43 AND #48	2,384
#50	#10 AND #49	615
#51	'thrombocyte concentrate'/exp	1,760
#52	'thrombocyte transfusion'/exp	6,565
#53	'thrombocyte'/exp	53,484
#54	#2 OR #3	133,476
#55	#53 AND #54	3,041
#56	'thrombocyte concentrate':ab,ti OR 'thrombocyte concentrates':ab,ti	100
#57	'platelet concentrate':ab,ti OR 'platelet concentrates':ab,ti	2,198
#58	'platelet *1 transfusion':ab,ti OR 'platelet *1 transfusions':ab,ti	2,968
#59	'transfusion *3 platelet':ab,ti OR 'transfusion *3 platelets':ab,ti	701
#60	'thrombocyte transfusion':ab,ti OR 'thrombocytic transfusion':ab,ti	42
#61	#51 OR #52 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60	134,760
#62	'thrombocyte count'/exp	21,426
#63	'thrombocyte count':ab,ti OR 'thrombocytic count':ab,ti	414
#64	'thrombocyte counts':ab,ti OR 'thrombocytic counts':ab,ti	236
#65	'thrombocyte number':ab,ti OR 'thrombocyte numbers':ab,ti	56
#66	'thrombocyte counting':ab,ti OR 'platelet counting':ab,ti	237
#67	'platelet count':ab,ti OR 'platelet counts':ab,ti	16,635

#	Query	Results
#68	'platelet number':ab,ti OR 'platelet numbers':ab,ti	906
#69	#62 OR #63 OR #64 OR #65 OR #66 OR #67 OR #68	30,335
#70	#61 AND #69	4,484
#71	#10 AND #70	4,336
#72	#39 OR #50 OR #71	5,178
#73	((('perioperative period'/exp) OR ('perioperative nursing'/exp) OR ('perioperative complication'/exp) OR ('preoperative period'/exp) OR ('preoperative complication'/exp) OR ('intraoperative period'/exp) OR (perioperative:ab,ti OR 'peri operative':ab,ti) OR (preoperative:ab,ti OR 'pre operative':ab,ti) OR (intraoperative:ab,ti OR 'intra operative':ab,ti) OR (peroperative:ab,ti OR 'per operative':ab,ti)) OR ('postoperative period'/exp) OR ('postoperative complication'/exp) OR (postoperative:ab,ti OR 'post operative':ab,ti)	870,712
#74	('injury'/exp) OR (injur*:ab,ti OR trauma*:ab,ti)	1,270,020
#75	('shock'/exp) OR (shock:ab,ti OR 'cardiovascular collapse':ab,ti OR 'circulatory collapse':ab,ti)	136,258
#76	((('blood transfusion'/exp) OR (('bleeding'/exp) AND ('transfusion'/exp))) AND (massive:ab,ti) OR ('massive transfusion':ab,ti) OR ('massive blood transfusion':ab,ti) OR ('massive transfusion protocol':ab,ti) OR ('massive *3 transfusion':ab,ti OR 'massive *3 transfusions':ab,ti) OR ('massive infusion':ab,ti OR 'massively transfused':ab,ti) OR ('massive *1 bleeding':ab,ti) OR ('massive *1 haemorrhage':ab,ti OR 'massive *1 hemorrhage':ab,ti)	8,454
#77	('thorax surgery'/exp) OR ('heart surgery'/exp) OR ('cardiothoracic surgery':ab,ti OR 'chest *1 surgery':ab,ti) OR ('cardiothoracic *1 patient':ab,ti OR 'cardiothoracic *1 patients':ab,ti) OR ('thoracic operation':ab,ti OR 'thoracic surgery':ab,ti OR thoracoplasty:ab,ti) OR ('thoracic *1 procedure':ab,ti OR 'thoracic *1 procedures':ab,ti)	286,978
#78	('surgery'/exp) OR ('surgical ward'/exp) OR ('surgical patient'/exp) OR (surgical:ab,ti OR surgery:ab,ti OR operation:ab,ti OR resection:ab,ti)	2,742,947
#79	('orthopedic surgery'/exp) OR ('orthopedic surgery':ab,ti OR 'orthopaedic surgery':ab,ti) OR ('bone surgery':ab,ti OR orthopaedics:ab,ti OR orthopedics:ab,ti) OR ('orthopedic *1 patient':ab,ti OR 'orthopedic *1 patients':ab,ti) OR ('orthopaedic *1 patient':ab,ti OR 'orthopaedic *1 patients':ab,ti) OR ('orthopedic operation':ab,ti OR 'orthopedic *1 procedures':ab,ti) OR ('orthopaedic operation':ab,ti OR 'orthopaedic *1 procedures':ab,ti) OR ('orthopedic *1 procedure':ab,ti OR 'orthopaedic *1 procedure':ab,ti)	260,054
#80	#73 OR #74 OR #75 OR #76 OR #77 OR #78 OR #79	3,704,145
#81	#72 AND #80	3,018
#82	('adverse outcome'/exp) OR ('outcome assessment'/exp) OR ('morbidity'/exp) OR ('mortality'/exp) OR (morbidity:ab,ti OR incidence:ab,ti OR prevalence:ab,ti OR occurrence:ab,ti) OR (mortality:ab,ti OR death:ab,ti OR survival:ab,ti)	1,941,273
#83	('quality of life'/exp) OR (qol:ab,ti OR 'quality of life':ab,ti OR 'quality of wellbeing':ab,ti) OR ('health related quality':ab,ti OR hrqol:ab,ti) OR (qaly*:ab,ti OR 'quality adjusted':ab,ti OR 'adjusted life':ab,ti)	161,320

#	Query	Results
#84	((('blood component therapy'/exp) AND (('dose response'/exp) OR ('drug dose'/exp))) OR ('fresh frozen plasma'/exp/dd_do) OR ('recombinant erythropoietin'/exp/dd_do) OR ('transfusion frequency':ab,ti) OR ('frequency *5 transfusion':ab,ti OR 'frequency *5 transfusions':ab,ti) OR ('transfusion rate':ab,ti OR 'transfusion rates':ab,ti) OR ('rate *5 transfusion':ab,ti OR 'rates *5 transfusion':ab,ti) OR ('transfusion requirement':ab,ti OR 'transfusion requirements':ab,ti) OR ('transfusion indication':ab,ti OR 'transfusion indications':ab,ti) OR ('indications *5 transfusion':ab,ti OR 'indications *5 transfusions':ab,ti) OR ('indication *5 transfusion':ab,ti OR 'indication *5 transfusions':ab,ti) OR ('transfusion interval':ab,ti OR 'transfusion intervals':ab,ti) OR ('need *3 transfusion':ab,ti OR 'need *3 transfusions':ab,ti) OR ('transfusion need':ab,ti OR 'transfusion needs':ab,ti) OR ('dose *3 transfusion':ab,ti OR 'dose *3 transfusions':ab,ti) OR ('dose *3 transfused':ab,ti OR 'transfusions *3 dose':ab,ti) OR ('transfusion dose':ab,ti OR 'transfused *3 dose':ab,ti) OR ('platelet dose':ab,ti OR 'dose *3 platelets':ab,ti) OR (dose:ab,ti AND transfus*:ab,ti)	17,493
#85	#82 OR #83 OR #84	2,063,307
#86	#81 AND #85	1,366

Table A8.2 Cochrane library database search conducted 28 June 2009

#	Query	Results
#1	MeSH descriptor Blood Transfusion explode all trees	2,628
#2	transfus*	6,897
#3	"blood exchange" OR "blood infusion"	42
#4	"blood replacement" OR "blood retransfusion"	73
#5	hemotherapy OR hematherapy OR hematotherapy	55
#6	haemotherapy OR haematherapy OR haematotherapy	5
#7	multitransfusion OR polytransfusion OR retransfusion	66
#8	"transfusion blood" OR "transfusion therapy"	224
#9	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	1,922
#10	MeSH descriptor Plasma, this term only	236
#11	"fresh frozen plasma" OR FFP	348
#12	"plasma transfusion"	30
#13	"plasma infusion" OR "serum transfusion"	17
#14	#10 OR #11 OR #12 OR #13	1,422
#15	MeSH descriptor International Normalized Ratio, this term only	263
#16	MeSH descriptor Prothrombin Time, this term only	362
#17	MeSH descriptor Partial Thromboplastin Time, this term only	376
#18	"international normalized ratio" OR inr	728
#19	"international normalised ratio"	123
#20	"International Sensitivity Index" OR isi	723
#21	(prothrombin NEAR/1 time) OR pt OR Thrombotest	13,024
#22	"prothrombin test" OR "prothrombine time" OR "protrombin time"	13
#23	"howell test" OR "smith test" OR "Quick Test"	19

#	Query	Results
#24	"Russell Viper Venom Time" OR dRVVT OR RVVT	9
#25	"partial thromboplastin time" OR ptt OR aptt	1,096
#26	#15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25	1,129
#27	#14 AND #26	479
#28	#9 AND #27	452
#29	cryoprecipitate	65
#30	cryoprecipitate OR "cryo precipitate"	65
#31	#14 OR #29 OR #30	1,122
#32	MeSH descriptor Fibrinogen, this term only	954
#33	fibrinogen OR "factor 1" OR "factor I"	4,401
#34	#32 OR #33	335
#35	#31 AND #34	280
#36	#9 AND #35	260
#37	MeSH descriptor Platelet Transfusion, this term only	208
#38	MeSH descriptor Blood Platelets, this term only	1,366
#39	MeSH descriptor Blood Transfusion, this term only	1,519
#40	#38 AND #39	217
#41	"thrombocyte concentrate" OR "thrombocyte concentrates"	16
#42	"platelet concentrate" OR "platelet concentrates"	176
#43	platelet* NEAR/3 transfusion*	552
#44	"thrombocyte transfusion" OR "thrombocytic transfusion"	40
#45	#37 OR #40 OR #41 OR #42 OR #43 OR #44	317
#46	MeSH descriptor Platelet Count, this term only	955
#47	"thrombocyte count" OR "thrombocytic count"	133
#48	"thrombocyte counts" OR "thrombocytic counts"	11
#49	"thrombocyte number" OR "thrombocyte numbers"	1
#50	"thrombocyte counting" OR "platelet counting"	9
#51	"platelet count" OR "platelet counts"	2,114
#52	"platelet number" OR "platelet numbers"	75
#53	#46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52	177
#54	#45 AND #53	99
#55	#9 AND #54	92
#56	#28 OR #36 OR #55	442
#57	MeSH descriptor Perioperative Care explode all trees	4,254
#58	MeSH descriptor Preoperative Care explode all trees	4,098
#59	MeSH descriptor Postoperative Complications explode all trees	21,418
#60	MeSH descriptor Postoperative Period explode all trees	3,483
#61	MeSH descriptor Intraoperative Complications explode all trees	2,476

#	Query	Results
#62	MeSH descriptor Intraoperative Period, this term only	919
#63	perioperative OR "peri operative"	5,196
#64	preoperative OR "pre operative"	11,093
#65	intraoperative OR "intra operative"	8,039
#66	peroperative OR "per operative"	474
#67	postoperative OR "post operative"	40,236
#68	#57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65 OR #66 OR #67	106
#69	#56 AND #68	51
#70	MeSH descriptor Wounds and Injuries explode all trees	10,953
#71	injur* OR trauma*	20,750
#72	#70 OR #71	54
#73	#56 AND #72	48
#74	MeSH descriptor Shock explode all trees	930
#75	shock OR "cardiovascular collapse" OR "circulatory collapse"	3,179
#76	#74 OR #75	50
#77	#56 AND #76	41
#78	MeSH descriptor Blood Transfusion, this term only	1,519
#79	massive	599
#80	#78 AND #79	39
#81	massive NEAR/3 transfusion*	20
#82	"massive infusion" OR "massively transfused"	3
#83	massive NEAR/1 (bleeding OR haemorrhage OR hemorrhage)	47
#84	#80 OR #81 OR #82 OR #83	43
#85	#56 AND #84	35
#86	MeSH descriptor Thoracic Surgical Procedures explode all trees	10,297
#87	MeSH descriptor Thoracic Surgery, this term only	130
#88	MeSH descriptor Cardiovascular Surgical Procedures explode all trees	10,930
#89	"cardiothoracic surgery" OR (chest NEAR/1 surgery)	675
#90	cardiothoracic NEAR/1 patient*	4
#91	"thoracic operation" OR "thoracic surgery" OR thoracoplasty	2,131
#92	thoracic NEAR/1 procedure*	16
#93	#86 OR #87 OR #88 OR #89 OR #90 OR #91 OR #92	47
#94	#56 AND #93	24
#95	MeSH descriptor Surgical Procedures, Operative explode all trees	68,578
#96	MeSH descriptor General Surgery, this term only	167
#97	MeSH descriptor Surgery Department, Hospital, this term only	68
#98	surgical OR surgery OR operation OR resection	91,783
#99	#95 OR #96 OR #97 OR #98	27

#	Query	Results
#100	#56 AND #99	17
#101	MeSH descriptor Orthopedic Procedures explode all trees	5,335
#102	MeSH descriptor Orthopedics, this term only	272
#103	"orthopedic surgery" OR "orthopaedic surgery"	2,339
#104	"bone surgery" OR orthopaedics or orthopedics	7,975
#105	(orthopedic OR orthopaedic) NEAR/1 patient*	223
#106	"orthopedic operation" OR "orthopaedic operation"	6
#107	(orthopedic OR orthopaedic) NEAR/1 procedure*	638
#108	#101 OR #102 OR #103 OR #104 OR #105 OR #106 OR #107	30
#109	#56 AND #108	13
#110	#69 OR #73 OR #77 OR #85 OR #94 OR #100 OR #109	74
#111	MeSH descriptor Morbidity explode all trees	8,475
#112	MeSH descriptor Mortality explode all trees	7,946
#113	morbidity OR incidence OR prevalence OR occurrence	62,784
#114	mortality OR death OR survival	55,325
#115	#111 OR #112 OR #113 OR #114	20
#116	#110 AND #115	11
#117	MeSH descriptor Quality of Life, this term only	9,425
#118	MeSH descriptor Quality-Adjusted Life years, this term only	2,062
#119	qol OR "quality of life" OR "quality of wellbeing"	21,521
#120	"health related quality" or hrqol	2,898
#121	qaly* or "quality adjusted" or "adjusted life"	3,802
#122	#117 OR #118 OR #119 OR #120 OR #121	25
#123	#110 AND #122	9
#124	MeSH descriptor Blood Component Transfusion explode all trees with qualifier: MT	99
#125	frequency NEAR/5 transfusion*	84
#126	rate* NEAR/5 transfusion*	324
#127	"transfusion requirement" OR "transfusion requirements"	949
#128	indication* NEAR/5 transfusion*	45
#129	"transfusion interval" OR "transfusion intervals"	13
#130	(need NEAR/3 transfusion*) OR "transfusion needs"	623
#131	dose NEAR/3 transfus*	86
#132	"platelet dose" OR (dose NEAR/3 platelets)	185
#133	(dose and transfus*):ti	72
#134	#124 OR #125 OR #126 OR #127 OR #128 OR #129 OR #130 OR #131 OR #132 OR #133	15
#135	#110 AND #134	8
#136	#116 OR #123 OR #135	15

Table A8.3 PreMedline search conducted 28 June 2009

#	Query	Results
#48	Search #45 OR #46 OR #47	86
#47	Search #44 AND pubmednotmedline[sb]	9
#46	Search #44 AND in process[sb]	53
#45	Search #44 NOT (medline[SB] OR oldmedline[sb])	86
#44	Search #24 OR #29 OR #43	3,463
#43	Search #8 AND #42	3,081
#42	Search #34 AND #41	3,311
#41	Search #35 OR #36 OR #37 OR #38 OR #39 OR #40	26,433
#40	Search "platelet number"[tw] OR "platelet numbers"[tw]	924
#39	Search "platelet count"[tw] OR "platelet counts"[tw]	25,512
#38	Search "thrombocyte counting"[tw] OR "platelet counting"[tw]	214
#37	Search "thrombocyte number"[tw] OR "thrombocyte numbers"[tw]	48
#36	Search "thrombocyte counts"[tw] OR "thrombocytic counts"[tw]	200
#35	Search "thrombocyte count"[tw] OR "thrombocytic count"[tw]	377
#34	Search #30 OR #31 OR #32 OR #33	12,050
#33	Search "thrombocyte transfusion"[tw] OR "thrombocytic transfusion"[tw]	37
#32	Search platelet*[tw] AND transfusion*[tw]	11,154
#31	Search "platelet concentrate"[tw] OR "platelet concentrates"[tw]	2,075
#30	Search "thrombocyte concentrate"[tw] OR "thrombocyte concentrates"[tw]	93
#29	Search #8 AND #28	294
#28	Search #26 AND #27	726
#27	Search fibrinogen[tw] OR "factor 1"[tw] OR "factor I"[tw]	99,797
#26	Search #12 OR #25	4,787
#25	Search cryoprecipitate[tw] OR "cryo precipitate"[tw]	1,449
#24	Search #8 AND #23	272
#23	Search #12 AND #22	529
#22	Search #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21	43,935
#21	Search "partial thromboplastin time"[tw] OR ptt[tw] OR aptt[tw]	9,935
#20	Search "Russell Viper Venom Time"[tw] OR dRVVT[tw] OR RVVT[tw]	198
#19	Search "howell test"[tw] OR "smith test"[tw] OR "Quick Test"[tw]	322
#18	Search "prothrombin test"[tw] OR "prothrombine time"[tw] OR "protrombin time"[tw]	79
#17	Search pt[tw] OR Thrombotest[tw]	19,741
#16	Search prothrombin[tw] AND time[tw]	14,153
#15	Search "International Sensitivity Index"[tw] OR isi[tw]	2,672
#14	Search "international normalised ratio"[tw]	302
#13	Search "international normalized ratio"[tw] OR inr[tw]	5,087
#12	Search #9 OR #10 OR #11	3,638

#	Query	Results
#11	Search "plasma infusion"[tw] OR "serum transfusion"[tw]	344
#10	Search "plasma transfusion"[tw]	243
#9	Search "fresh frozen plasma"[tw] OR FFP[tw]	3,203
#8	Search #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7	98,504
#7	Search "transfusion blood"[tw] OR "transfusion therapy"[tw]	1,482
#6	Search multitransfusion[tw] OR polytransfusion[tw] OR retransfusion[tw]	478
#5	Search haemotherapy[tw] OR haemotherapy[tw] OR haematotherapy[tw]	67
#4	Search hemotherapy[tw] OR hemotherapy[tw] OR hematotherapy[tw]	513
#3	Search "blood replacement"[tw] OR "blood retransfusion"[tw]	569
#2	Search "blood exchange"[tw] OR "blood infusion"[tw]	485
#1	Search transfus*[tw]	97,701

Table A8.4 CINAHL search conducted 28 June 2009

#	Query	Results
S56	S29 or S36 or S55	137
S55	S9 and S54	83
S54	S45 and S53	93
S53	S46 or S47 or S48 or S49 or S50 or S51 or S52	989
S52	TI ("platelet number" OR "platelet numbers") or AB ("platelet number" OR "platelet numbers")	22
S51	TI ("platelet count" OR "platelet counts") or AB ("platelet count" OR "platelet counts")	662
S50	TI ("thrombocyte counting" OR "platelet counting") or AB ("thrombocyte counting" OR "platelet counting")	5
S49	TI ("thrombocyte number" OR "thrombocyte numbers") or AB ("thrombocyte number" OR "thrombocyte numbers")	0
S48	TI ("thrombocyte counts" OR "thrombocytic counts") or AB ("thrombocyte counts" OR "thrombocytic counts")	5
S47	TI ("thrombocyte count" OR "thrombocytic count") or AB ("thrombocyte count" OR "thrombocytic count")	4
S46	(MH "Platelet Count")	462
S45	S37 or S40 or S41 or S42 or S43 or S44	570
S44	TI ("thrombocyte transfusion" OR "thrombocytic transfusion") or AB ("thrombocyte transfusion" OR "thrombocytic transfusion")	0
S43	TI platelet ^a N3 transfusion ^a or AB platelet ^a N3 transfusion ^a	186
S42	TI ("platelet concentrate" OR "platelet concentrates") or AB ("platelet concentrate" OR "platelet concentrates")	143
S41	TI ("thrombocyte concentrate" OR "thrombocyte concentrates") or AB ("thrombocyte concentrate" OR "thrombocyte concentrates")	1
S40	S38 and S39	86
S39	(MH "Blood Transfusion")	3,490
S38	(MH "Blood Platelets")	1,349

#	Query	Results
S37	(MH "Platelet Transfusion")	320
S36	S9 and S35	19
S35	S31 and S34	41
S34	S32 or S33	1,899
S33	TI (fibrinogen OR "factor 1" OR "factor I") or AB (fibrinogen OR "factor 1" OR "factor I")	1,671
S32	(MH "Fibrinogen")	531
S31	S14 or S30	876
S30	TI (cryoprecipitate OR "cryo precipitate") or AB (cryoprecipitate OR "cryo precipitate")	41
S29	S9 and S28	42
S28	S14 and S27	1,917
S27	S15 or S16 or S17 or S18 or S19 or S20 or S21 or S23 or S24 or S25 or S26	1,917
S26	TI ("partial thromboplastin time" OR ptt OR aptt) or AB ("partial thromboplastin time" OR ptt OR aptt)	355
S25	TI ("Russell Viper Venom Time" OR dRVVT OR RVVT) or AB ("Russell Viper Venom Time" OR dRVVT OR RVVT)	6
S24	TI ("howell test" OR "smith test" OR "Quick Test") or AB ("howell test" OR "smith test" OR "Quick Test")	30
S23	TI ("prothrombin test" OR "prothrombine time" OR "protrombin time") or AB ("prothrombin test" OR "prothrombine time" OR "protrombin time")	1
S22	TI (pt OR Thrombotest) or AB (pt OR Thrombotest)	0
S21	TI prothrombin N1 time or AB prothrombin N1 time	293
S20	TI ("International Sensitivity Index" OR isi) or AB ("International Sensitivity Index" OR isi)	341
S19	TI "international normalised ratio" or AB "international normalised ratio"	31
S18	TI ("international normalized ratio" OR inr) or AB ("international normalized ratio" OR inr)	479
S17	(MH "Partial Thromboplastin Time")	190
S16	(MH "Prothrombin Time")	204
S15	(MH "International Normalized Ratio")	696
S14	S10 or S11 or S12 or S13	864
S13	TI ("plasma infusion" OR "serum transfusion") or AB ("plasma infusion" OR "serum transfusion")	6
S12	TI "plasma transfusion" or AB "plasma transfusion"	27
S11	TI ("fresh frozen plasma" OR FFP) or AB ("fresh frozen plasma" OR FFP)	224
S10	(MH "Plasma")	710
S9	S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8	7,007
S8	TI ("transfusion blood" OR "transfusion therapy") or AB ("transfusion blood" OR "transfusion therapy")	143
S7	TI (multitransfusion OR polytransfusion OR retransfusion) or AB (multitransfusion OR polytransfusion OR retransfusion)	23
S6	TI (haemotherapy OR haemotherapy OR haematotherapy) or AB (haemotherapy OR haemotherapy OR haematotherapy)	0

#	Query	Results
S5	TI (hemotherapy OR hematherapy OR hematotherapy) or AB (hemotherapy OR hematherapy OR hematotherapy)	14
S4	TI ("blood replacement" OR "blood retransfusion") or AB ("blood replacement" OR "blood retransfusion")	18
S3	TI ("blood exchange" OR "blood infusion") or AB ("blood exchange" OR "blood infusion")	16
S2	TI transfus ^a or AB transfus ^a	4,524
S1	(MH "Blood Transfusion+")	5,098

a The search was conducted using EBSCOhost on 30 June 2009

Table A8.5 AMI search conducted 30 June 2009

Set	Search terms	Records
#43	<p>((((((TI = ("platelet number" OR "platelet numbers") OR AB = ("platelet number" OR "platelet numbers")) OR (TI = ("platelet count" OR "platelet counts") OR AB = ("platelet count" OR "platelet counts")) OR (TI = ("thrombocyte counting" OR "platelet counting") OR AB = ("thrombocyte counting" OR "platelet counting")) OR (TI = ("thrombocyte number" OR "thrombocyte numbers") OR AB = ("thrombocyte number" OR "thrombocyte numbers")) OR (TI = ("thrombocyte counts" OR "thrombocytic counts") OR AB = ("thrombocyte counts" OR "thrombocytic counts")) OR (TI = ("thrombocyte count" OR "thrombocytic count") OR AB = ("thrombocyte count" OR "thrombocytic count")) OR ((MH_PHRASE = "Platelet Count")))) AND (((TI = ("thrombocyte transfusion" OR "thrombocytic transfusion") OR AB = ("thrombocyte transfusion" OR "thrombocytic transfusion")) OR (TI = (platelet^a %3 transfusion^a) OR AB = (platelet^a %3 transfusion^a)) OR (TI = ("platelet concentrate" OR "platelet concentrates") OR AB = ("platelet concentrate" OR "platelet concentrates")) OR (TI = ("thrombocyte concentrate" OR "thrombocyte concentrates") OR AB = ("thrombocyte concentrate" OR "thrombocyte concentrates")) OR (((MH_PHRASE = "Blood Transfusion")) AND ((MH_PHRASE = "Blood Platelets")))) OR ((MH_PHRASE = "Platelet Transfusion")))) OR (((((TI = (fibrinogen OR "factor 1" OR "factor I") OR AB = (fibrinogen OR "factor 1" OR "factor I")) OR (MH_PHRASE = "Fibrinogen")) AND (((TI = (cryoprecipitate OR "cryo precipitate") OR AB = (cryoprecipitate OR "cryo precipitate")) OR (((TI = ("plasma infusion" OR "serum transfusion") OR AB = ("plasma infusion" OR "serum transfusion")) OR (TI = ("plasma transfusion") OR AB = ("plasma transfusion")) OR (TI = ("fresh frozen plasma" OR FFP) OR AB = ("fresh frozen plasma" OR FFP)) OR (MH_PHRASE = "Plasma"))))))) OR (((((TI = ("partial thromboplastin time" OR ptt OR aptt) OR AB = ("partial thromboplastin time" OR ptt OR aptt)) OR (TI = ("Russell Viper Venom Time" OR dRVVT OR RVVT) OR AB = ("Russell Viper Venom Time" OR dRVVT OR RVVT)) OR (TI = ("howell test" OR "smith test" OR "Quick Test") OR AB = ("howell test" OR "smith test" OR "Quick Test")) OR (TI = ("prothrombin test" OR "prothrombine time" OR "protrombin time") OR AB = ("prothrombin test" OR "prothrombine time" OR "protrombin time")) OR (TI = ((prothrombin %1 time) OR pt OR Thrombotest) OR AB = ((prothrombin %1 time) OR pt OR Thrombotest)) OR (TI = ("International Sensitivity Index" OR isi) OR AB = ("International Sensitivity Index" OR isi)) OR (TI = ("international normalised ratio" OR AB = ("international normalised ratio")) OR (TI = ("international normalized ratio" OR inr) OR AB = ("international normalized ratio" OR inr)) OR ((MH_PHRASE = "Partial Thromboplastin Time")) OR ((MH_PHRASE = "Prothrombin Time")) OR ((MH_PHRASE = "International Normalized Ratio")))) AND (((TI = ("plasma infusion" OR "serum transfusion") OR AB = ("plasma infusion" OR "serum transfusion")) OR (TI = ("plasma transfusion") OR AB = ("plasma transfusion")) OR (TI = ("fresh frozen plasma" OR FFP) OR AB = ("fresh frozen plasma" OR FFP)) OR (MH_PHRASE = "Plasma")))))))</p>	56

Set	Search terms	Records
#42	(((TI = ("platelet number" OR "platelet numbers") OR AB = ("platelet number" OR "platelet numbers")) OR (TI = ("platelet count" OR "platelet counts") OR AB = ("platelet count" OR "platelet counts")) OR (TI = ("thrombocyte counting" OR "platelet counting") OR AB = ("thrombocyte counting" OR "platelet counting")) OR (TI = ("thrombocyte number" OR "thrombocyte numbers") OR AB = ("thrombocyte number" OR "thrombocyte numbers")) OR (TI = ("thrombocyte counts" OR "thrombocytic counts") OR AB = ("thrombocyte counts" OR "thrombocytic counts")) OR (TI = ("thrombocyte count" OR "thrombocytic count") OR AB = ("thrombocyte count" OR "thrombocytic count")) OR ((MH_PHRASE = "Platelet Count")))) AND (((TI = ("thrombocyte transfusion" OR "thrombocytic transfusion") OR AB = ("thrombocyte transfusion" OR "thrombocytic transfusion")) OR (TI = (platelet ^a %3 transfusion ^a) OR AB = (platelet ^a %3 transfusion ^a)) OR (TI = ("platelet concentrate" OR "platelet concentrates") OR AB = ("platelet concentrate" OR "platelet concentrates")) OR (TI = ("thrombocyte concentrate" OR "thrombocyte concentrates") OR AB = ("thrombocyte concentrate" OR "thrombocyte concentrates")) OR (((MH_PHRASE = "Blood Transfusion")) AND ((MH_PHRASE = "Blood Platelets")))) OR ((MH_PHRASE = "Platelet Transfusion"))))	17
#41	((TI = ("platelet number" OR "platelet numbers") OR AB = ("platelet number" OR "platelet numbers")) OR (TI = ("platelet count" OR "platelet counts") OR AB = ("platelet count" OR "platelet counts")) OR (TI = ("thrombocyte counting" OR "platelet counting") OR AB = ("thrombocyte counting" OR "platelet counting")) OR (TI = ("thrombocyte number" OR "thrombocyte numbers") OR AB = ("thrombocyte number" OR "thrombocyte numbers")) OR (TI = ("thrombocyte counts" OR "thrombocytic counts") OR AB = ("thrombocyte counts" OR "thrombocytic counts")) OR (TI = ("thrombocyte count" OR "thrombocytic count") OR AB = ("thrombocyte count" OR "thrombocytic count")) OR ((MH_PHRASE = "Platelet Count")))	104
#40	TI = ("platelet number" OR "platelet numbers") OR AB = ("platelet number" OR "platelet numbers")	2
#39	TI = ("platelet count" OR "platelet counts") OR AB = ("platelet count" OR "platelet counts")	67
#38	TI = ("thrombocyte counting" OR "platelet counting") OR AB = ("thrombocyte counting" OR "platelet counting")	1
#37	TI = ("thrombocyte number" OR "thrombocyte numbers") OR AB = ("thrombocyte number" OR "thrombocyte numbers")	0
#36	TI = ("thrombocyte counts" OR "thrombocytic counts") OR AB = ("thrombocyte counts" OR "thrombocytic counts")	0
#35	TI = ("thrombocyte count" OR "thrombocytic count") OR AB = ("thrombocyte count" OR "thrombocytic count")	0
#34	(MH_PHRASE = "Platelet Count")	48
#33	((TI = ("thrombocyte transfusion" OR "thrombocytic transfusion") OR AB = ("thrombocyte transfusion" OR "thrombocytic transfusion")) OR (TI = (platelet ^a %3 transfusion ^a) OR AB = (platelet ^a %3 transfusion ^a)) OR (TI = ("platelet concentrate" OR "platelet concentrates") OR AB = ("platelet concentrate" OR "platelet concentrates")) OR (TI = ("thrombocyte concentrate" OR "thrombocyte concentrates") OR AB = ("thrombocyte concentrate" OR "thrombocyte concentrates")) OR (((MH_PHRASE = "Blood Transfusion")) AND ((MH_PHRASE = "Blood Platelets")))) OR ((MH_PHRASE = "Platelet Transfusion")))	34
#32	TI = ("thrombocyte transfusion" OR "thrombocytic transfusion") OR AB = ("thrombocyte transfusion" OR "thrombocytic transfusion")	0
#31	TI = (platelet ^a %3 transfusion ^a) OR AB = (platelet ^a %3 transfusion ^a)	13

Set	Search terms	Records
#30	TI = ("platelet concentrate" OR "platelet concentrates") OR AB = ("platelet concentrate" OR "platelet concentrates")	16
#29	TI = ("thrombocyte concentrate" OR "thrombocyte concentrates") OR AB = ("thrombocyte concentrate" OR "thrombocyte concentrates")	0
#28	((MH_PHRASE = "Blood Transfusion")) AND ((MH_PHRASE = "Blood Platelets"))	1
#27	(MH_PHRASE = "Blood Transfusion")	179
#26	(MH_PHRASE = "Blood Platelets")	40
#25	(MH_PHRASE = "Platelet Transfusion")	9
#24	(((((TI = (fibrinogen OR "factor 1" OR "factor I") OR AB = (fibrinogen OR "factor 1" OR "factor I")) OR (MH_PHRASE = "Fibrinogen")) AND (((TI = (cryoprecipitate OR "cryo precipitate") OR AB = (cryoprecipitate OR "cryo precipitate")) OR (((TI = ("plasma infusion" OR "serum transfusion") OR AB = ("plasma infusion" OR "serum transfusion")) OR (TI = ("plasma transfusion") OR AB = ("plasma transfusion")) OR (TI = ("fresh frozen plasma" OR FFP) OR AB = ("fresh frozen plasma" OR FFP)) OR (MH_PHRASE = "Plasma"))))))))	5
#23	((TI = (fibrinogen OR "factor 1" OR "factor I") OR AB = (fibrinogen OR "factor 1" OR "factor I")) OR (MH_PHRASE = "Fibrinogen"))	206
#22	TI = (fibrinogen OR "factor 1" OR "factor I") OR AB = (fibrinogen OR "factor 1" OR "factor I")	204
#21	MH_PHRASE = "Fibrinogen"	4
#20	((TI = (cryoprecipitate OR "cryo precipitate") OR AB = (cryoprecipitate OR "cryo precipitate")) OR (((TI = ("plasma infusion" OR "serum transfusion") OR AB = ("plasma infusion" OR "serum transfusion")) OR (TI = ("plasma transfusion") OR AB = ("plasma transfusion")) OR (TI = ("fresh frozen plasma" OR FFP) OR AB = ("fresh frozen plasma" OR FFP)) OR (MH_PHRASE = "Plasma"))))	69
#19	TI = (cryoprecipitate OR "cryo precipitate") OR AB = (cryoprecipitate OR "cryo precipitate")	14
#18	(((((TI = ("partial thromboplastin time" OR ptt OR aptt) OR AB = ("partial thromboplastin time" OR ptt OR aptt)) OR (TI = ("Russell Viper Venom Time" OR dRVVT OR RVVT) OR AB = ("Russell Viper Venom Time" OR dRVVT OR RVVT)) OR (TI = ("howell test" OR "smith test" OR "Quick Test") OR AB = ("howell test" OR "smith test" OR "Quick Test")) OR (TI = ("prothrombin test" OR "prothrombine time" OR "protrombin time") OR AB = ("prothrombin test" OR "prothrombine time" OR "protrombin time")) OR (TI = ((prothrombin %1 time) OR pt OR Thrombotest) OR AB = ((prothrombin %1 time) OR pt OR Thrombotest)) OR (TI = ("International Sensitivity Index" OR isi) OR AB = ("International Sensitivity Index" OR isi)) OR (TI = ("international normalised ratio") OR AB = ("international normalised ratio")) OR (TI = ("international normalized ratio" OR inr) OR AB = ("international normalized ratio" OR inr)) OR ((MH_PHRASE = "Partial Thromboplastin Time")) OR ((MH_PHRASE = "Prothrombin Time")) OR ((MH_PHRASE = "International Normalized Ratio")))) AND (((TI = ("plasma infusion" OR "serum transfusion") OR AB = ("plasma infusion" OR "serum transfusion")) OR (TI = ("plasma transfusion") OR AB = ("plasma transfusion")) OR (TI = ("fresh frozen plasma" OR FFP) OR AB = ("fresh frozen plasma" OR FFP)) OR (MH_PHRASE = "Plasma"))))	54

Set	Search terms	Records
#17	((TI = ("partial thromboplastin time" OR ptt OR aptt) OR AB = ("partial thromboplastin time" OR ptt OR aptt)) OR (TI = ("Russell Viper Venom Time" OR dRVVT OR RVVT) OR AB = ("Russell Viper Venom Time" OR dRVVT OR RVVT)) OR (TI = ("howell test" OR "smith test" OR "Quick Test") OR AB = ("howell test" OR "smith test" OR "Quick Test")) OR (TI = ("prothrombin test" OR "prothrombine time" OR "protrombin time") OR AB = ("prothrombin test" OR "prothrombine time" OR "protrombin time")) OR (TI = ((prothrombin %1 time) OR pt OR Thrombotest) OR AB = ((prothrombin %1 time) OR pt OR Thrombotest)) OR (TI = ("International Sensitivity Index" OR isi) OR AB = ("International Sensitivity Index" OR isi)) OR (TI = ("international normalised ratio") OR AB = ("international normalised ratio")) OR (TI = ("international normalized ratio" OR inr) OR AB = ("international normalized ratio" OR inr)) OR ((MH_PHRASE = "Partial Thromboplastin Time")) OR ((MH_PHRASE = "Prothrombin Time")) OR ((MH_PHRASE = "International Normalized Ratio")))	270
#16	TI = ("partial thromboplastin time" OR ptt OR aptt) OR AB = ("partial thromboplastin time" OR ptt OR aptt)	57
#15	TI = ("Russell Viper Venom Time" OR dRVVT OR RVVT) OR AB = ("Russell Viper Venom Time" OR dRVVT OR RVVT)	2
#14	TI = ("howell test" OR "smith test" OR "Quick Test") OR AB = ("howell test" OR "smith test" OR "Quick Test")	5
#13	TI = ("prothrombin test" OR "prothrombine time" OR "protrombin time") OR AB = ("prothrombin test" OR "prothrombine time" OR "protrombin time")	1
#12	TI = ((prothrombin %1 time) OR pt OR Thrombotest) OR AB = ((prothrombin %1 time) OR pt OR Thrombotest)	77
#11	TI = ("International Sensitivity Index" OR isi) OR AB = ("International Sensitivity Index" OR isi)	13
#10	TI = ("international normalised ratio") OR AB = ("international normalised ratio")	23
#9	TI = ("international normalized ratio" OR inr) OR AB = ("international normalized ratio" OR inr)	53
#8	(MH_PHRASE = "Partial Thromboplastin Time")	65
#7	(MH_PHRASE = "Prothrombin Time")	56
#6	(MH_PHRASE = "International Normalized Ratio")	79
#5	((TI = ("plasma infusion" OR "serum transfusion") OR AB = ("plasma infusion" OR "serum transfusion")) OR (TI = ("plasma transfusion") OR AB = ("plasma transfusion")) OR (TI = ("fresh frozen plasma" OR FFP) OR AB = ("fresh frozen plasma" OR FFP)) OR (MH_PHRASE = "Plasma"))	62
#4	TI = ("plasma infusion" OR "serum transfusion") OR AB = ("plasma infusion" OR "serum transfusion")	3
#3	TI = ("plasma transfusion") OR AB = ("plasma transfusion")	0
#2	TI = ("fresh frozen plasma" OR FFP) OR AB = ("fresh frozen plasma" OR FFP)	29
#1	MH_PHRASE = "Plasma"	50

a The search was conducted using Informit online platform on 30 June 2009.

Appendix B Excluded studies

This appendix documents studies that met inclusion criteria determined by PICO, PPO or PRO criteria, but were later excluded. These studies, and their reasons for exclusion, are listed below.

Studies excluded from question 1

Study excluded due to insufficient data: Chiara et al (2006).¹

Studies excluded from question 2

No studies which met the inclusion criteria were excluded from this question.

Studies excluded from generic question 1

No studies which met the inclusion criteria were excluded from this question.

Studies excluded from generic question 2

Studies excluded due to low level evidence:

Dutton et al (2006)²

Munoz et al (2007)³

Rosemurgy et al (1992)⁴

Tran et al (1992).⁵

Studies excluded from generic question 3

No studies which met the inclusion criteria were excluded from this question.

Studies excluded from generic question 4

Studies excluded due to low level evidence:

Harrison et al (2005)⁶

McMorrow et al (2008)⁷

Perkins et al (2007)⁸

Spinella et al (2008).⁹

Studies excluded from generic question 5

No studies which met the inclusion criteria were excluded from this question.

Studies excluded from generic question 6

No studies which met the inclusion criteria were excluded from this question.

Appendix C Literature search result

C1 Search results – question 1

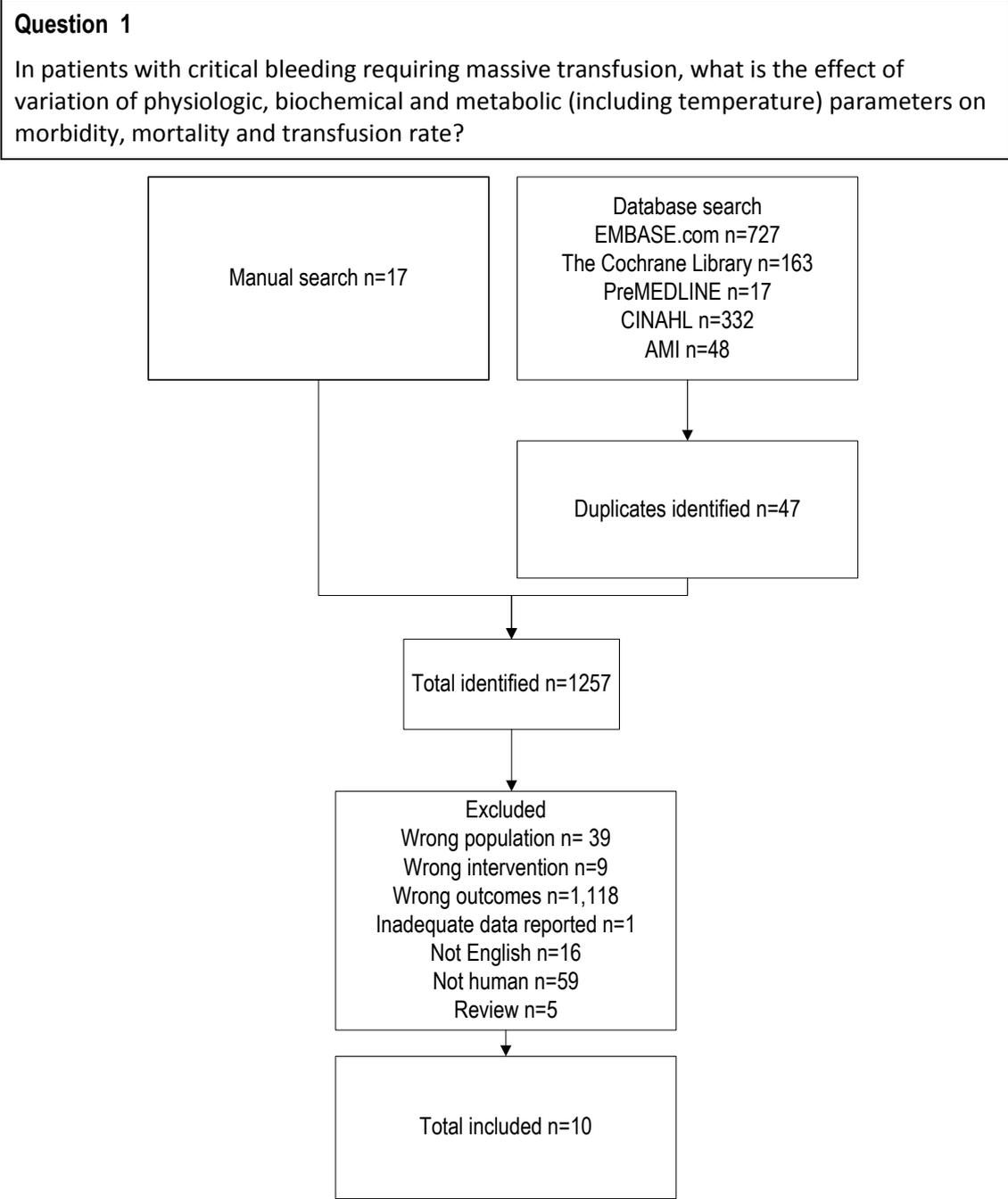


Figure C1 Search results – question 1

C2 Search results – question 2

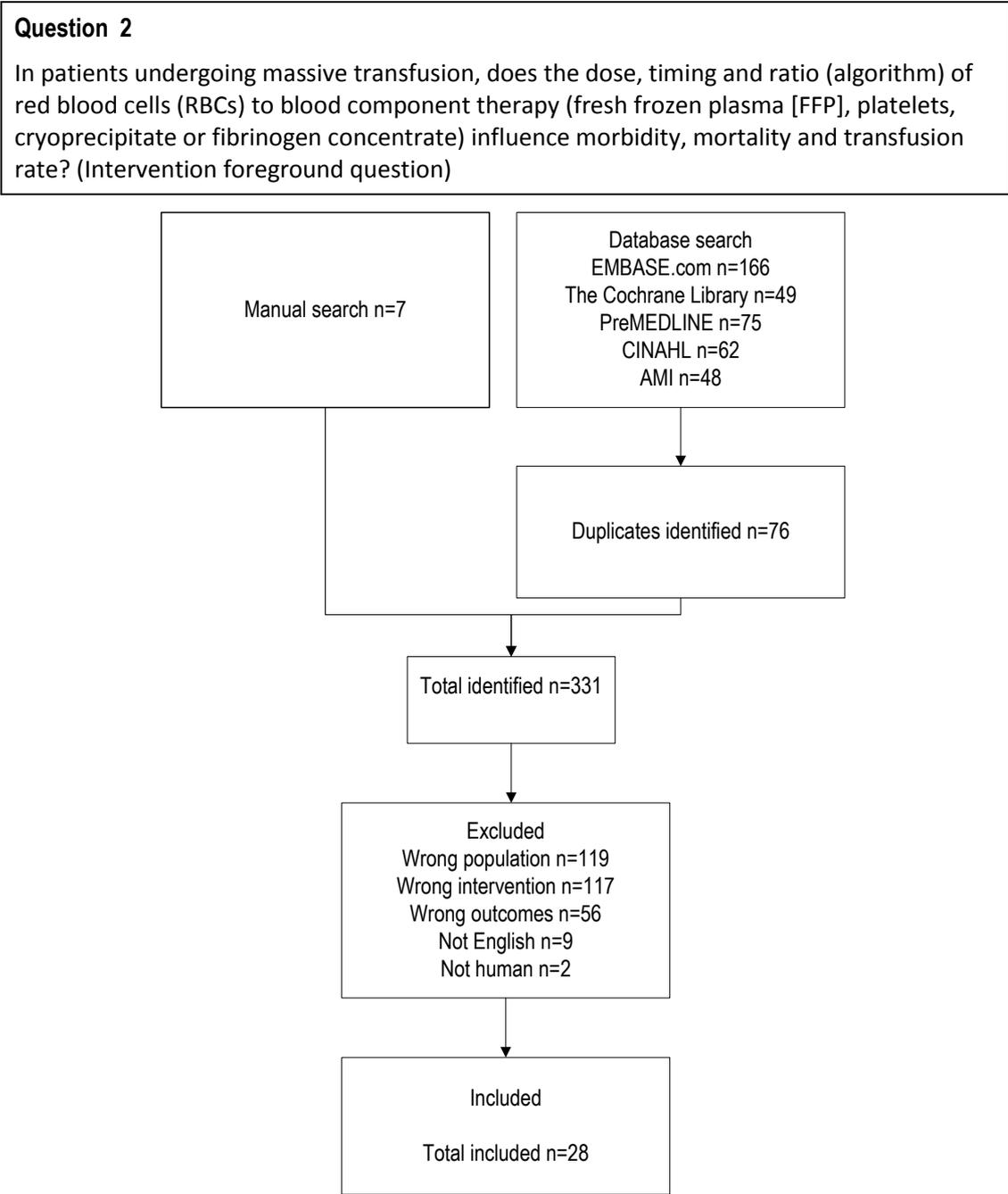


Figure C2 Search results – question 2

C3 Search results – question 3

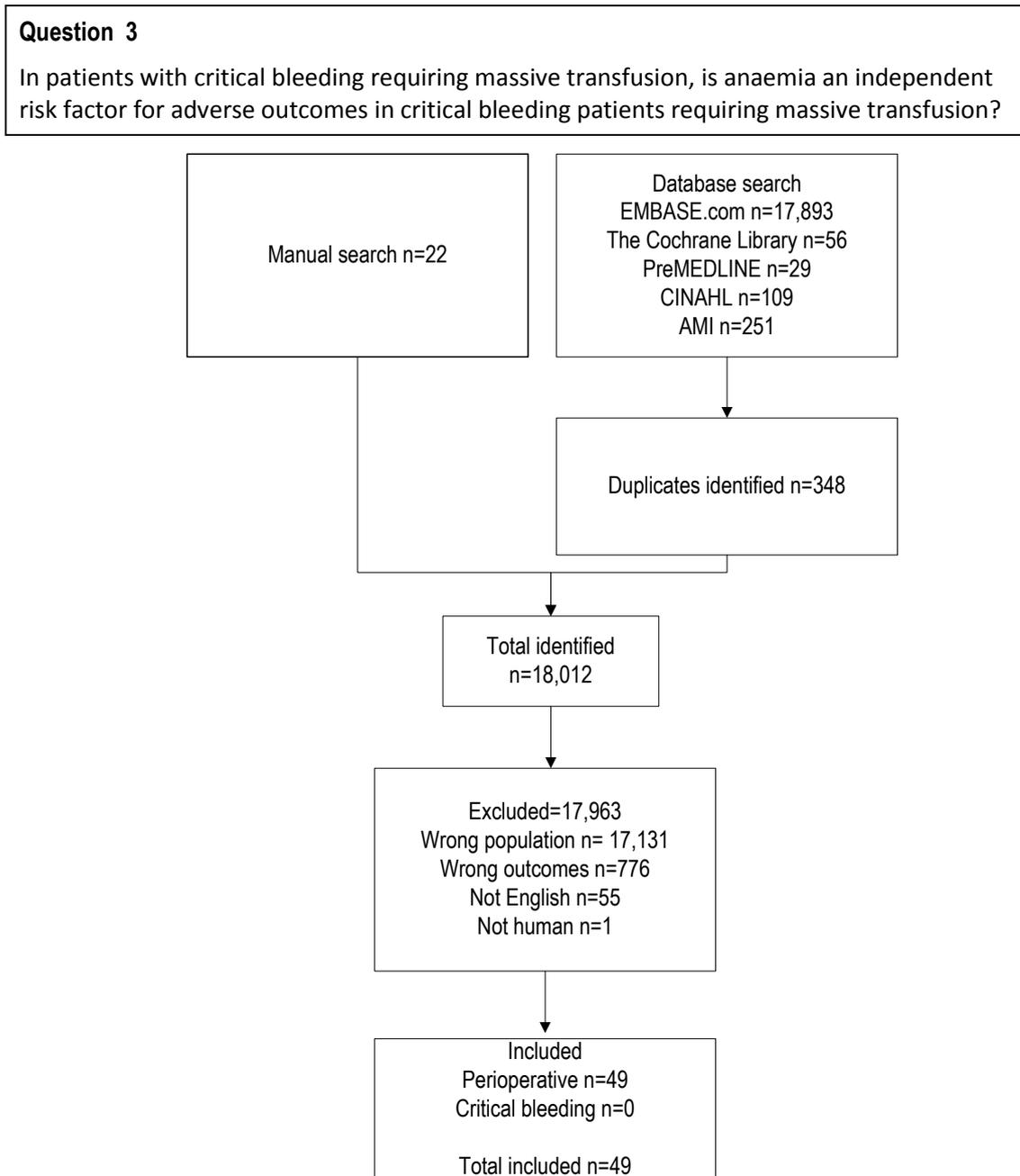


Figure C3 Search results – question 3

C4 Search results – question 4

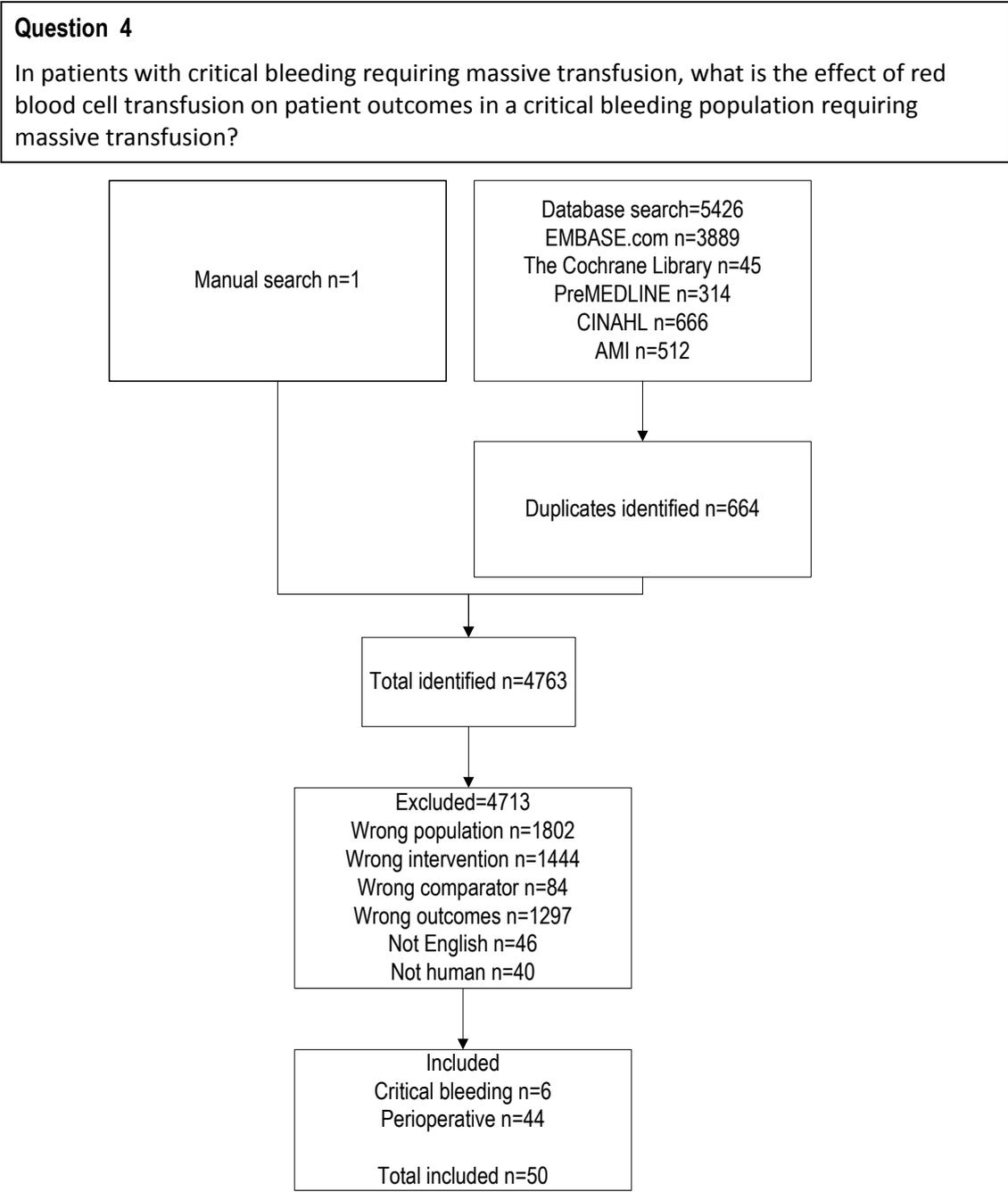


Figure C4 Search results – question 4

C5 Search results – question 5

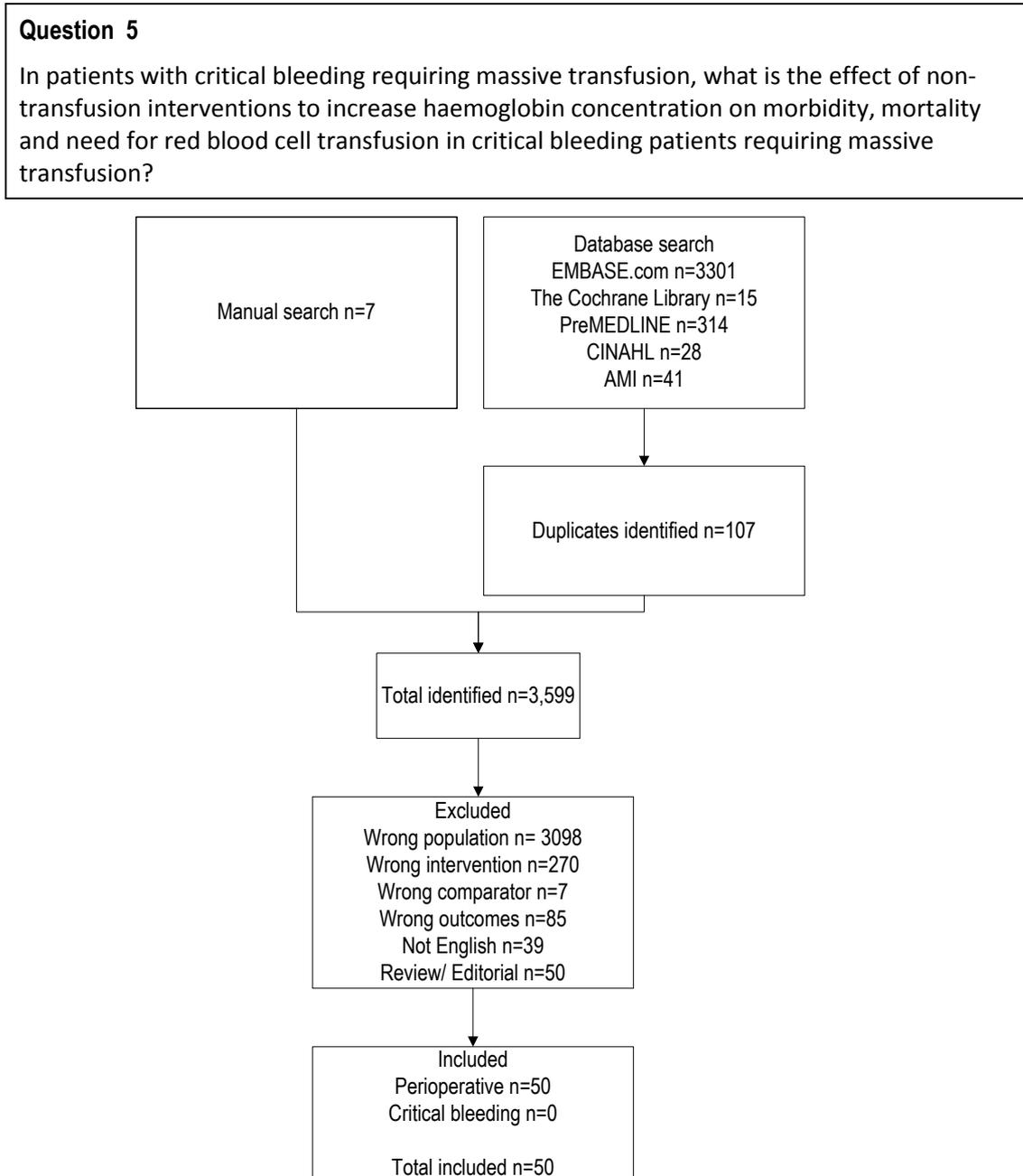


Figure C5 Search results – question 5

C6 Search results – question 6

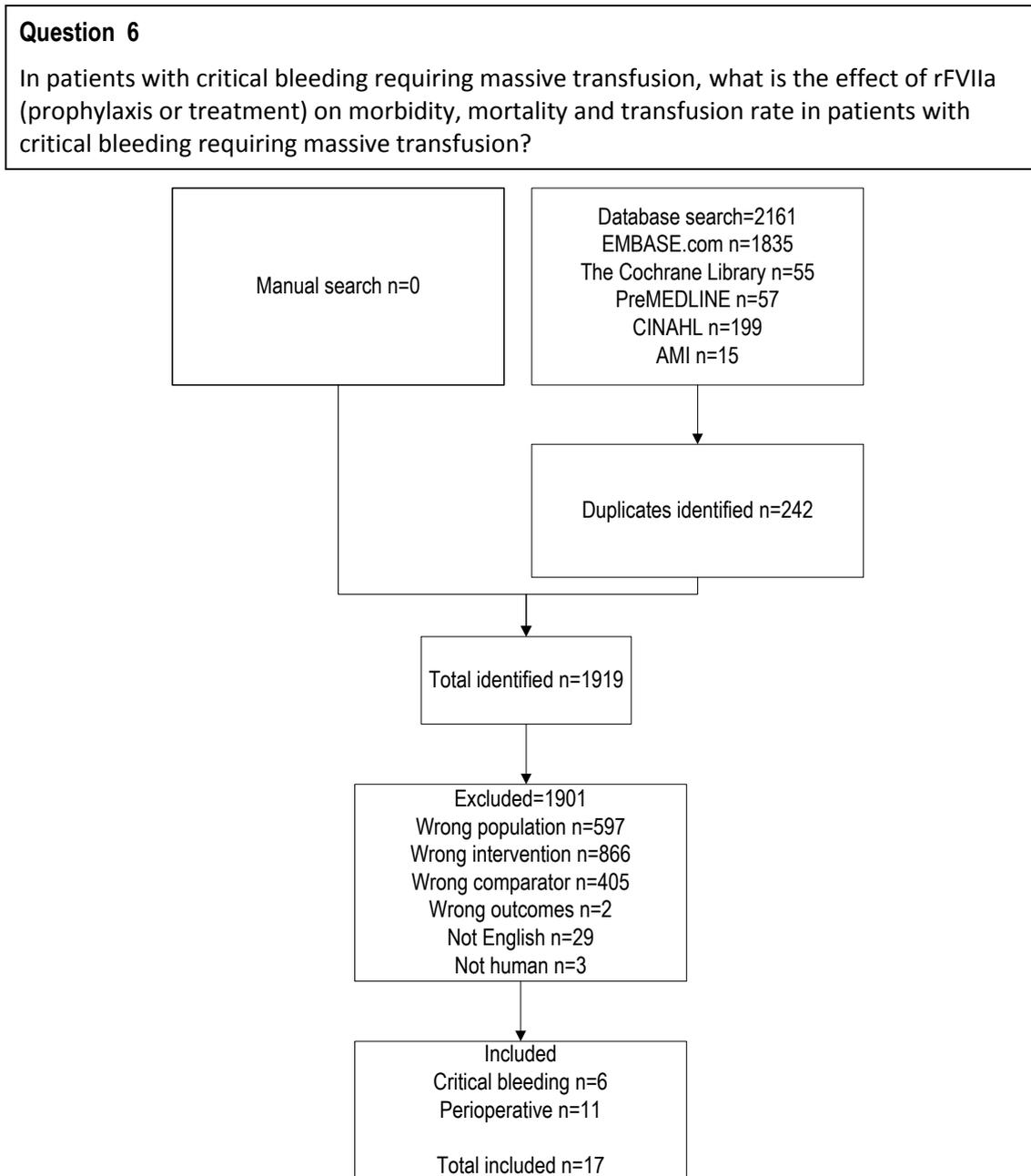


Figure C6 Search results – question 6

C7 Search results – question 7

Question 7

In patients with critical bleeding requiring massive transfusion, what is the effect of fresh frozen plasma, cryoprecipitate, fibrinogen concentrate, and/or platelet transfusion on patient outcomes?

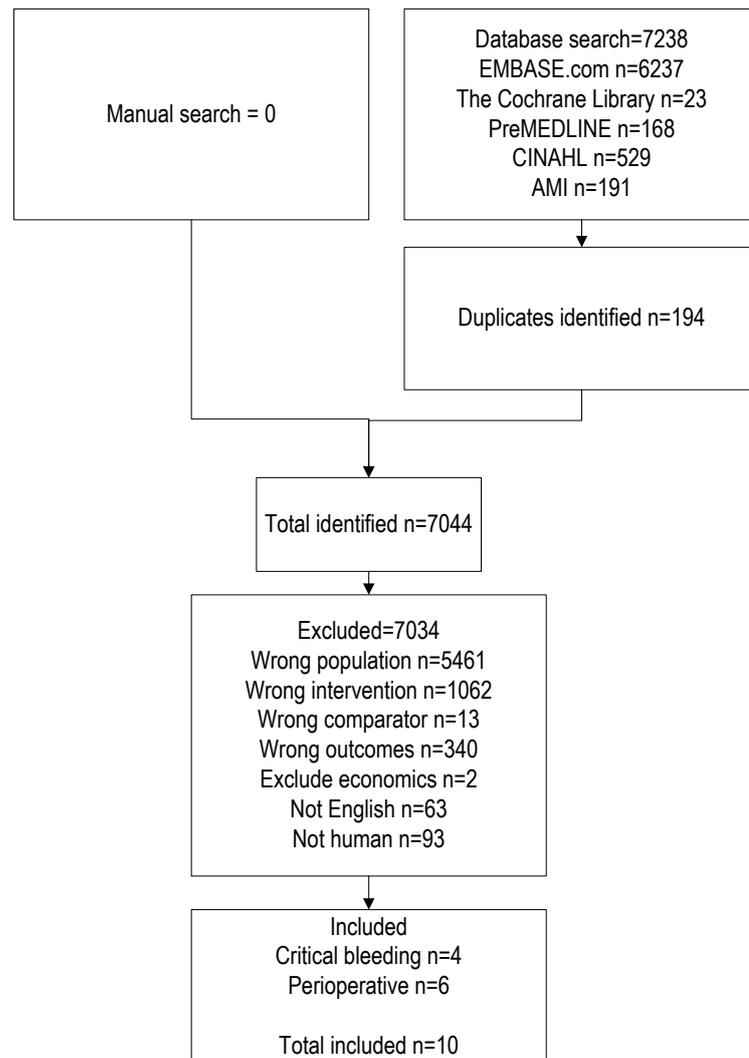
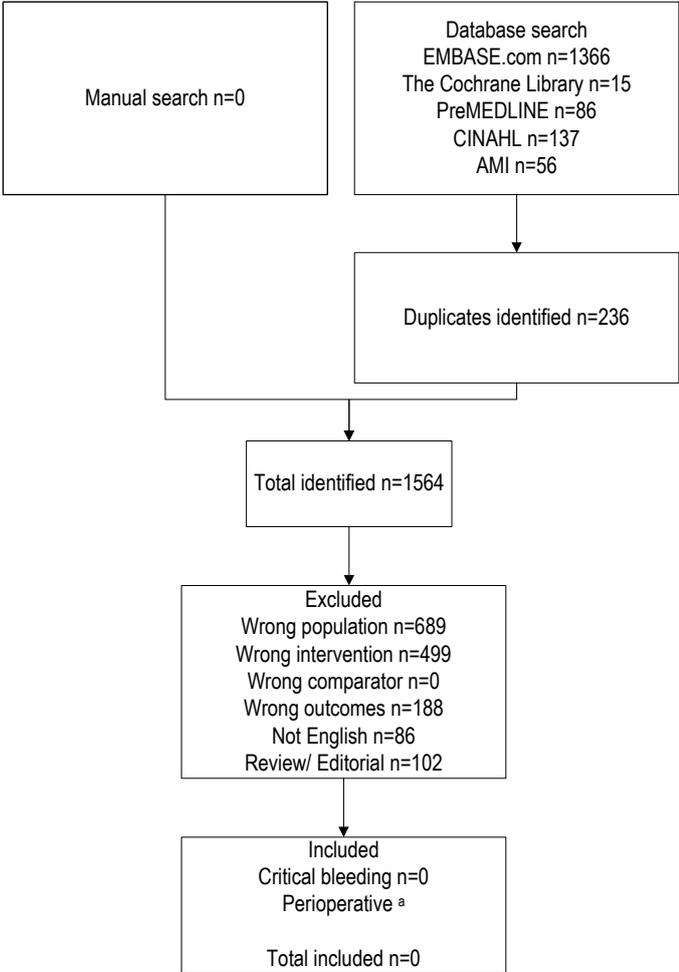


Figure C7 Search results – question 7

C8 Search results – question 8

Question 8
 In patients with critical bleeding requiring massive transfusion, at what INR (or PT/APTT) for fresh frozen plasma, fibrinogen level for cryoprecipitate, platelet count for platelet concentrates should patients be transfused to avoid risks of significant adverse events in patients with critical bleeding requiring massive transfusion?



^a A separate search was run for perioperative generic question 8

Figure C8 Search results – question 8

Appendix D Evidence matrixes

D1 Evidence – question 1

Question 1

In patients with critical bleeding requiring massive transfusion, what is the effect of variation of physiologic, biochemical and metabolic (including temperature) parameters on morbidity, mortality and transfusion rate?

Table D1.1 Evidence matrix for question 1

Key question In Patients with Critical Bleeding requiring Massive Transfusion, what is the Effect of Variation of Physiologic, Biochemical and Metabolic (including Temperature) Parameters on Morbidity, Mortality and Transfusion Rate?	Evidence table ref: Borgman et al (2007), ¹⁰ Ferrara et al (1990), ¹¹ Gonzalez et al (2007), ¹² Mitra et al (2007), ¹³ Moore et al (2008), ¹⁴ Stinger et al (2008), ¹⁵ Vaslef et al (2002), ¹⁶ Wilson et al (1992) ¹⁷	
1. Evidence base (<i>quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements</i>)		
8 level IV studies ¹⁰⁻¹⁷ with high risk of bias	A	Excellent (One or more level I studies with a low risk of bias or several level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency (<i>the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence</i>)		
Studies investigating Hypothermia: Consistency in definition of outcome. Similar direction of effect (i.e. hypothermia associated with poor survival), although some inconsistency in statistical significance, with three studies showing similar results and two studies in which temperature was not a significant predictor of mortality. pH : All five studies were consistent with regard to low pH/acidosis being significantly associated with poorer survival. The definition of the outcome and the threshold parameters for pH values were also consistent. Base deficit: Consistency in outcome definition. There was some inconsistency in direction of effect – three studies indicated an association between increased base deficit and poor survival, and two indicated that base deficit was not a significant predictor of mortality. INR: All four studies were consistent with regard to a higher international normalised ratio (INR) being associated with poor survival. The definition of the outcome and the threshold parameters for INR values were also consistent. Prothrombin time: One study included for this outcome. Partial thromboplastin time: Two studies identified were inconsistent with regard to the association between PTT and mortality. Platelet count: Three studies were inconsistent with regard to the association between low platelet count and mortality, primarily because different definitions were used.	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)

3. Clinical impact (<i>the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications</i>)		
<p>Studies investigating</p> <p>Hypothermia: Sample size was sufficiently large (ranged from $n = 45$ to $n = 246$). Three studies showed that reduced core body temperature was associated with increased mortality in patients who had critical bleeding and those who were transfused. Gonzalez et al (2007)¹² and Moore et al (2008)¹⁴ showed that reduced body temperature was not significantly associated with mortality in patients who experienced shock resuscitation or haemorrhagic shock.</p> <p>pH: All five studies showed that reduced pH was associated with increased mortality in patients with critical bleeding and those who were transfused.</p> <p>Base deficit: Sample size was sufficiently large (ranged from $n = 45$ to $n = 252$). Three studies showed that an increase in base deficit was associated with an increased mortality in critically bleeding and transfused patients. Two studies showed base deficit was not significantly associated with mortality in patients who experience shock resuscitation or haemorrhagic shock patients.</p> <p>INR: Sample size was sufficiently large (ranged from $n = 97$ to $n = 247$). All studies^{10,12-14} showed that an increase in INR was associated with an increased mortality in critically bleeding and transfused patients. Gonzalez and colleagues¹² stratified analysis by admission to emergency department and admission to ICU.</p> <p>Prothrombin time: Small sample size ($n = 45$).</p> <p>Partial thromboplastin time: Two studies included are of limited clinical impact, each demonstrating different APTT parameters and statistical significance. Sample size is sufficient ($n = 45$ to $n = 119$).</p> <p>Platelet count: Three studies included; the largest study reporting on this outcome found that non-survivors had lower platelet counts. Sample size is sufficient with the included studies ($n = 45$ to $n = 174$).</p> <p>In all studies consideration of adverse events was not applicable to this recommendation as the outcome is mortality.</p>	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability (<i>how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?</i>)		
<p>Studies investigating</p> <p>Hypothermia: All participants in three studies were trauma patients and one study analysed shock resuscitation patients. All patients were critically bleeding.</p> <p>pH: Participants in four studies were trauma patients; one study analysed patients with haemorrhagic shock</p> <p>Base deficit: Participants in three studies were trauma patients^{10,15-16} one study was on hemorrhagic shock patients¹⁴ and one study on shock resuscitation patients.¹²</p> <p>INR: Participants in two studies were trauma patients^{10,13} one hemorrhagic shock¹⁴ and one study shock resuscitation patients.¹²</p> <p>Prothrombin time: One study included.</p> <p>Partial thromboplastin time: Small sample size and contradictory results for the two studies included.</p> <p>Platelet count: Contradictory results for all three studies included.</p> <p>There were no study design restrictions as all studies were case series; hence, patients were in natural environments when the outcome was measured.</p>	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)

5. Applicability (<i>the extent to which the body of evidence is directly applicable to Australian healthcare context</i>)		
<p>Studies investigating</p> <p>Hypothermia: Three USA based studies and one Australian based study.</p> <p>pH: Four USA based studies and one in Australian based study.</p> <p>Base deficit: Five USA based studies</p> <p>INR: Three USA based studies and one Australian based study</p> <p>Prothrombin time: One USA based study</p> <p>Partial thromboplastin time: One USA based and one Australian based study</p> <p>Platelet count: Two USA based studies and one Australian based study</p> <p>This evidence base is applicable to the Australian setting as there are no organisational or cultural barriers</p>	A	Excellent (directly applicable to Australian healthcare context)
	B	Good (applicable to Australian healthcare context with few caveats)
	C	Satisfactory (probably applicable to Australian healthcare context with some caveats)
	D	Poor (not applicable to Australian healthcare context)
6. Other factors (<i>Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation</i>)		
EVIDENCE STATEMENT		
<i>Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions.</i>		
Component	Rating	Description
Evidence base	D	Poor
Consistency	C	Satisfactory
Clinical impact	C	Satisfactory
Generalisability	B	Good
Applicability	B	Good
<i>Indicate any dissenting opinions</i>		
RECOMMENDATION	GRADE OF RECOMMENDATION (<i>A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B.</i>)	C
<i>What recommendation (s) does the guideline development group draw from this evidence?</i>		
No recommendation made		
UNRESOLVED ISSUES		
<i>If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up</i>		
IMPLEMENTATION OF RECOMMENDATION		
<i>Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline.</i>		
Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organised?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

D2 Evidence – question 2

Question 2

In patients undergoing massive transfusion, does the dose, timing and ratio (algorithm) of red blood cells (RBCs) to blood component therapy (fresh frozen plasma [FFP], platelets, cryoprecipitate or fibrinogen concentrate) influence morbidity, mortality and transfusion rate? (Intervention foreground question)

Table D2.1 Evidence matrix for question 2

Key question (CB2.1) In patients undergoing massive transfusion, does the dose, timing and ratio (algorithm) of red blood cells (RBCs) to blood component therapy (fresh frozen plasma [FFP], platelets, cryoprecipitate or fibrinogen concentrate) influence morbidity, mortality and transfusion rate? (Intervention foreground question)	Evidence table ref: Cotton et al (2009) ¹⁸ Dente et al (2009) ¹⁹	
1. Evidence base (quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)		
One Level III study with a high risk of bias, ¹⁸ one Level III study with a moderate risk of bias ¹⁹	A	Excellent (One or more level I studies with a low risk of bias or several level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency (the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)		
The studies were mostly consistent in their findings and inconsistency may be explained.	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact (the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)		
Studies included predominantly small sample sizes for an assessment of mortality differences, but the clinical impact was significant, with an absolute difference in mortality of approximately 10%	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability (how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)		
Both studies included patients with critical bleeding requiring massive transfusion.	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability (the extent to which the body of evidence is directly applicable to Australian healthcare context)		

Both studies were conducted in US healthcare settings.	A	Excellent (directly applicable to Australian healthcare context)
	B	Good (applicable to Australian healthcare context with few caveats)
	C	Satisfactory (probably applicable to Australian healthcare context with some caveats)
	D	Poor (not applicable to Australian healthcare context)
6. Other factors (Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)		
EVIDENCE STATEMENT		
Component	Rating	Description
Evidence base	D	One Level III study with a high risk of bias, one Level III study with a moderate risk of bias
Consistency	B	Both studies were mostly consistent in their findings and inconsistency may be explained.
Clinical impact	B	Studies included predominantly small sample sizes for an assessment of mortality differences, but the clinical impact was significant with an absolute difference in mortality of approximately 10%
Generalisability	B	Both studies included patients with critical bleeding requiring massive transfusion.
Applicability	C	Both studies were conducted in United States healthcare settings.
<i>Indicate any dissenting opinions</i>		
RECOMMENDATION <i>What recommendation (s) does the guideline development group draw from this evidence?</i>	GRADE OF RECOMMENDATION (A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B).	C
It is recommended that institutions develop an MTP that includes the dose, timing and ratio of blood component therapy for use in trauma patients with, or at risk of, critical bleeding requiring massive transfusion (Grade C) (Grade C). Note: This recommendation is supported by two evidence statements developed for research question CB2 – Evidence statement CB2.1 and CB2.3 Note to readers: The use of the term 'protocol' in this report is not strictly prescriptive and is intended to allow individual clinical discretion		
UNRESOLVED ISSUES <i>If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up</i>		
IMPLEMENTATION OF RECOMMENDATION <i>Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline.</i> Note: For this recommendation, there are no particular implementation issues pertinent to Australia's indigenous population		
<i>Will this recommendation result in changes in usual care?</i> The development and implementation of massive transfusion procedural guidelines in health care services in Australia and NZ.	Yes	No
<i>Are there any resource implications associated with the implementing this recommendation?</i> There are logistic and resource implications	Yes	No
<i>Will the implementation of this recommendation require changes in the way care is currently organized?</i> Yes. Increased collaboration and consultation between health care providers and transfusion and laboratory services.	Yes	No
<i>Is the guideline development group aware of any barriers to the implementation of this recommendation?</i> Political, logistic and resource barriers; awareness, knowledge and uptake	Yes	No

Table D2.2 Evidence matrix for question 2

Key question (CB2.2) In patients undergoing massive transfusion, does the dose, timing and ratio (algorithm) of red blood cells (RBCs) to blood component therapy (fresh frozen plasma [FFP], platelets, cryoprecipitate or fibrinogen concentrate) influence morbidity, mortality and transfusion rate? (Intervention foreground question)	Evidence table ref: Sperry et al (2008) ²⁰ , Zink et al (2009) ²¹
1. Evidence base (quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)	

Both studies were level IV studies.	A	Excellent (One or more level I studies with a low risk of bias or several level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency (the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)		
Both studies were consistent with their findings.	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact (the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)		
More than 400 patients were reviewed in each study.	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability (how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)		
Both studies included patients with critical bleeding requiring massive transfusion. The populations were both civilian.	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability (the extent to which the body of evidence is directly applicable to Australian healthcare context)		
Both studies were conducted in US healthcare setting.	A	Excellent (directly applicable to Australian healthcare context)
	B	Good (applicable to Australian healthcare context with few caveats)
	C	Satisfactory (probably applicable to Australian healthcare context with some caveats)
	D	Poor (not applicable to Australian healthcare context)
6. Other factors (Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)		
EVIDENCE STATEMENT		
Component	Rating	Description
Evidence base	D	Two Level IV studies with a high risk of bias.
Consistency	A	The studies were consistent in their findings.
Clinical impact	C	More than 400 patients were reviewed in each study.
Generalisability	B	Both studies included patients with critical bleeding requiring massive transfusion and the

		populations were civilian.
Applicability	C	Both studies were conducted in United States healthcare setting.
<i>Indicate any dissenting opinions</i>		
RECOMMENDATION <i>What recommendation (s) does the guideline development group draw from this evidence?</i>	GRADE OF RECOMMENDATION <i>(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B).</i>	
None developed		
UNRESOLVED ISSUES <i>If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up</i>		
IMPLEMENTATION OF RECOMMENDATION <i>Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline.</i>		
Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Table D2.3 Evidence matrix for question 2

Key question (CB2.3) In patients undergoing massive transfusion, does the dose, timing and ratio (algorithm) of red blood cells (RBCs) to blood component therapy (fresh frozen plasma [FFP], platelets, cryoprecipitate or fibrinogen concentrate) influence morbidity, mortality and transfusion rate? (Intervention foreground question)	Evidence table ref: Cinat et al (1999) ²² , Dente et al (2009) ¹⁹ , Gunter et al (2008) ²³	
1. Evidence base <i>(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)</i>		
Two Level III studies with a high risk of bias, ²²⁻²³ one Level III study with a moderate risk of bias. ¹⁹ Survivor bias is likely to have affected results.	A	Excellent (One or more level I studies with a low risk of bias or several level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency <i>(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)</i>		
All studies were consistent in their findings.	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact <i>(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)</i>		
Studies included predominantly small sample sizes.	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)

4. Generalisability (<i>how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?</i>)		
All studies included patients with critical bleeding requiring massive transfusion; however, the definition of massive transfusion in Cinat et al (1999) was ≥ 50 units of RBC or whole blood in 48 hours.	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability (<i>the extent to which the body of evidence is directly applicable to Australian healthcare context</i>)		
All studies were conducted in US healthcare settings.	A	Excellent (directly applicable to Australian healthcare context)
	B	Good (applicable to Australian healthcare context with few caveats)
	C	Satisfactory (probably applicable to Australian healthcare context with some caveats)
	D	Poor (not applicable to Australian healthcare context)
6. Other factors (<i>Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation</i>)		
EVIDENCE STATEMENT		
Component	Rating	Description
Evidence base	D	Two Level III studies with a high risk of bias, ²²⁻²³ one Level III study with a moderate risk of bias. ¹⁹ Survivor bias is likely to have affected results.
Consistency	A	All studies were consistent in their findings.
Clinical impact	C	Studies included predominantly small sample sizes.
Generalisability	C	Moderate clinical impact. All studies included patients with critical bleeding requiring massive transfusion; however, the definition of massive transfusion in Cinat et al (1999) ⁶⁹ was ≥ 50 units of RBC or whole blood in 48 hours.
Applicability	C	All studies were conducted in United States healthcare settings.
<i>Indicate any dissenting opinions</i>		
RECOMMENDATION <i>What recommendation (s) does the guideline development group draw from this evidence?</i>	GRADE OF RECOMMENDATION (<i>A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B</i>).	
See recommendation in evidence matrix for key question CB2.1 – Evidence statement CB2.1 and CB2.3 were used to support this recommendation.		
UNRESOLVED ISSUES <i>If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up</i>		
IMPLEMENTATION OF RECOMMENDATION <i>Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline.</i>		
Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

D3 Evidence – question 3

Question 3

In patients with critical bleeding requiring massive transfusion, is anaemia an independent risk factor for adverse outcomes?

No evidence was found relating to anaemia as an independent risk factor for adverse outcomes in critical bleeding patients requiring massive transfusion.

D4 Evidence – question 4

Question 4

In patients with critical bleeding requiring massive transfusion, what is the effect of RBC transfusion on patient outcomes?

Table D4.1 Evidence matrix for question 4

Key question What is the Effect of Red Blood Cell Transfusion on Patient Outcomes in a Critical Bleeding Population Requiring Massive Transfusion? The evidence pertaining to mortality is considered in this evidence statement (GN2.1)	Evidence table ref: Chaiwat et al (2009); ²⁴ Silverboard et al (2005) ²⁵	
1. Evidence base (quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)		
Two Fair quality Level III studies	A	Excellent (One or more level I studies with a low risk of bias or several level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency (the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)		
Results of the 2 studies were consistent, although the different reference group in the studies make comparison unclear	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact (the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)		
The studies are underpowered, with confidence interval values that cross 1.0 (odds ratio); thus, the likely clinical impact is unclear.	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability (how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)		
Some generalisability to the target population.	A	Excellent (directly generalisable to target population)

	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability (the extent to which the body of evidence is directly applicable to Australian healthcare context)		
Both USA based studies	A	Excellent (directly applicable to Australian healthcare context)
	B	Good (applicable to Australian healthcare context with few caveats)
	C	Satisfactory (probably applicable to Australian healthcare context with some caveats)
	D	Poor (not applicable to Australian healthcare context)
6. Other factors (Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)		
EVIDENCE STATEMENT Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account.		
Component	Rating	Description
Evidence base	C	Two Level III studies with a moderate risk of bias.
Consistency	B	Results of the two studies were consistent, although the different reference group in the studies make comparisons not completely clear.
Clinical impact	D	The studies are underpowered, with confidence interval values that cross 1.0 (odds ratio); thus, the likely clinical impact is unclear.
Generalisability	C	Some generalisability to the target population.
Applicability	C	Both studies were completed in the United States.
Indicate any dissenting opinions		
RECOMMENDATION What recommendation (s) does the guideline development group draw from this evidence?	GRADE OF RECOMMENDATION (A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)	
No recommendation developed		
UNRESOLVED ISSUES If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up		
IMPLEMENTATION OF RECOMMENDATION Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline		
Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Table D4.2 Evidence matrix for question 4

Key question What is the Effect of Red Blood Cell Transfusion on Patient Outcomes in a Critical Bleeding Population Requiring Massive Transfusion? The evidence pertaining to the morbidity outcome ARDS is considered in this evidence statement (GN2.2)	Evidence table ref: Chaiwat et al (2009); ²⁴ Silverboard et al (2005) ²⁵
1. Evidence base (quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)	
Two Fair quality Level III studies	A Excellent (One or more level I studies with a low risk of bias or several level II studies with a low risk of

		bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency (the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)		
Results of both studies were consistent, although the different reference group in the studies make comparison unclear	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact (the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)		
Unclear whether the link of RBC transfusion is the cause of ARDS or if the number of transfusions is linked to the severity of the injury/damage before transfusion	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability (how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)		
Hard to determine how much of the results is based on a massive transfusion population. Some generalisability to the target population.	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability (the extent to which the body of evidence is directly applicable to Australian healthcare context)		
Both USA based studies	A	Excellent (directly applicable to Australian healthcare context)
	B	Good (applicable to Australian healthcare context with few caveats)
	C	Satisfactory (probably applicable to Australian healthcare context with some caveats)
	D	Poor (not applicable to Australian healthcare context)
6. Other factors (Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)		
EVIDENCE STATEMENT		
Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions.		
Component	Rating	Description
Evidence base	C	Two Level III studies with a moderate risk of bias.
Consistency	B	Results of the two studies were consistent, although the different reference group in the studies make comparisons not completely clear.
Clinical impact	C	The studies report a moderate clinical impact.

Generalisability	C	Some generalisability to the target population.
Applicability	C	Both studies were completed in the United States.
<i>Indicate any dissenting opinions</i>		
RECOMMENDATION <i>What recommendation (s) does the guideline development group draw from this evidence?</i> No recommendation developed	GRADE OF RECOMMENDATION <i>(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)</i>	
UNRESOLVED ISSUES <i>If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up</i>		
IMPLEMENTATION OF RECOMMENDATION <i>Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline</i>		
Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

D5 Evidence – question 5

Question 5

In patients with critical bleeding requiring massive transfusion, what is the effect of non-transfusion interventions to increase haemoglobin concentration on morbidity, mortality and need for RBC blood transfusion?

There was no evidence relevant for inclusion for this question in the critical bleeding/massive transfusion setting.

D6 Evidence – question 6

Question 6

In patients with critical bleeding requiring massive transfusion, what is the effect of rFVIIa (prophylaxis or treatment) on morbidity, mortality and transfusion rate in patients with critical bleeding requiring massive transfusion?

Table D6.1 Evidence matrix for question 6

Key question What is the Effect of rFVIIa (Prophylaxis or Treatment) on Morbidity, Mortality and Transfusion Rate in Patients with Critical Bleeding Requiring Massive Transfusion? The evidence base pertaining to mortality is considered in this evidence statement (GN4.1)	Evidence table ref: Boffard et al (2005) ²⁶	
1. Evidence base <i>(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)</i>		
One good quality Level II study	A	Excellent (One or more level I studies with a low risk of bias or several level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)

	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency (the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)		
Only one study	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact (the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)		
There is no clinical impact - administration of rFVIIa has no effect on 48 hour or 30 day mortality	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability (how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)		
The studies seem to be generalisable to critical bleeding patients resulting from blunt or penetrating trauma; however, the additional exclusion criteria need to be taken in to consideration before considering the results generalisable to all critically bleeding patients.	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability (the extent to which the body of evidence is directly applicable to Australian healthcare context)		
Study samples from 32 hospitals through Australia, Canada, France, Germany, Israel, Singapore, South Africa and the United Kingdom. Although only one hospital was in Australia, the Canadian and United Kingdom settings are comparable to Australia.	A	Excellent (directly applicable to Australian healthcare context)
	B	Good (applicable to Australian healthcare context with few caveats)
	C	Satisfactory (probably applicable to Australian healthcare context with some caveats)
	D	Poor (not applicable to Australian healthcare context)
6. Other factors (Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)		
EVIDENCE STATEMENT		
Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions		
Component	Rating	Description
Evidence base	B	Good
Consistency	NA	Not applicable
Clinical impact	D	Poor
Generalisability	C	Satisfactory
Applicability	B	Good
Indicate any dissenting opinions		

RECOMMENDATION <i>What recommendation (s) does the guideline development group draw from this evidence?</i>	GRADE OF RECOMMENDATION (<i>A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B</i>)	B, C
The routine use of rFVIIa in trauma patients with critical bleeding requiring massive transfusion is not recommended because of its lack of effect on mortality (Grade B) ²⁶ and variable effect on morbidity (Grade C). ²⁶ Note: This recommendation was developed from the evidence base presented in all evidence matrices in this appendix.		
UNRESOLVED ISSUES <i>If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up</i>		
IMPLEMENTATION OF RECOMMENDATION <i>Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline</i> Note: For this recommendation, there are no particular implementation issues pertinent to Australia's indigenous population		
Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Table D6.2 Evidence matrix for question 6

Key question What is the Effect of rFVIIa (Prophylaxis or Treatment) on Morbidity, Mortality and Transfusion Rate in Patients with Critical Bleeding Requiring Massive Transfusion? The evidence base pertaining to the morbidity outcome, thromboembolism, is considered in this evidence statement (GN4.2)	Evidence table ref: Boffard et al (2005) ²⁶	
1. Evidence base (<i>quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements</i>)		
Evidence based is made from one good quality Level II study (results combined)	A	Excellent (One or more level I studies with a low risk of bias or several level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency (<i>the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence</i>)		
Only one study	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact (<i>the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications</i>)		
The low incidence of the thromboembolic events and consequent lack of statistical power mean that the data are insufficient to draw any conclusions.	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)

	D	Poor (slight or restricted clinical impact)
4. Generalisability (<i>how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?</i>)		
The studies seem to be generalisable to a critically bleeding population resulting from blunt or penetrating trauma; however, the additional exclusion criteria need to be taken into account before considering the results generalisable to all critically bleeding patients.	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability (<i>the extent to which the body of evidence is directly applicable to Australian healthcare context</i>)		
Study samples from 32 hospitals throughout Australia, Canada, France, Germany, Israel, Singapore, South Africa and the United Kingdom. Although only one hospital was in Australia, the Canadian and United Kingdom settings are comparable to Australia.	A	Excellent (directly applicable to Australian healthcare context)
	B	Good (applicable to Australian healthcare context with few caveats)
	C	Satisfactory (probably applicable to Australian healthcare context with some caveats)
	D	Poor (not applicable to Australian healthcare context)
6. Other factors (<i>Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation</i>)		
EVIDENCE STATEMENT <i>Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions</i>		
Component	Rating	Description
Evidence base	B	Good
Consistency	NA	Not applicable
Clinical impact	D	Poor
Generalisability	C	Satisfactory
Applicability	B	Good
<i>Indicate any dissenting opinions</i>		
RECOMMENDATION <i>What recommendation (s) does the guideline development group draw from this evidence?</i>	GRADE OF RECOMMENDATION (<i>A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B</i>)	B, C
The routine use of rFVIIa in trauma patients with critical bleeding requiring massive transfusion is not recommended because of its lack of effect on mortality (Grade B) ²⁶ and variable effect on morbidity (Grade C). ²⁶ Note: This recommendation was developed from the evidence base presented in all evidence matrixes in this appendix. Note: For this recommendation, there are no particular implementation issues pertinent to Australia's indigenous population		
UNRESOLVED ISSUES <i>If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up</i>		
IMPLEMENTATION OF RECOMMENDATION <i>Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline</i>		
Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Table D6.3 Evidence matrix for question 6

<p>Key question What is the Effect of rFVIIa (Prophylaxis or Treatment) on Morbidity, Mortality and Transfusion Rate in Patients with Critical Bleeding Requiring Massive Transfusion? Th evidence base pertaining to the morbidity and transfusion requirements is considered in this evidence statement (GN4.3)</p>	<p>Evidence table ref: Boffard et al (2005)²⁶</p>	
<p>1. Evidence base (quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)</p>		
<p>Evidence based is made from one good quality Level II study (results combined)</p>	A	Excellent (One or more level I studies with a low risk of bias or several level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
<p>2. Consistency (the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)</p>		
<p>Only one study</p>	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
<p>3. Clinical impact (the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)</p>		
<p>In blunt trauma patients administration of rFVIIa is associated with reduced RBC transfusion requirements and the incidence of ARDS. In patients with penetrating trauma administration of rFVIIa has no effect on morbidity.</p>	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
<p>4. Generalisability (how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)</p>		
<p>The studies seem to be generalisable to a critical bleed population resulting from blunt or penetrating trauma; however, the additional exclusion criteria need to be taken in to consideration before considering the results generalisable to all critically bleeding patients.</p>	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
<p>5. Applicability (the extent to which the body of evidence is directly applicable to Australian healthcare context)</p>		
<p>Study samples from 32 hospitals throughout Australia, Canada, France, Germany, Israel, Singapore, South Africa and the United Kingdom. Although only one hospital was in Australia the Canadian and United Kingdom settings are comparable to Australia.</p>	A	Excellent (directly applicable to Australian healthcare context)
	B	Good (applicable to Australian healthcare context with few caveats)
	C	Satisfactory (probably applicable to Australian healthcare context with some caveats)

	D	Poor (not applicable to Australian healthcare context)
6. Other factors (Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)		
EVIDENCE STATEMENT Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions		
Component	Rating	Description
Evidence base	B	Good
Consistency	NA	Not applicable
Clinical impact	C	Satisfactory
Generalisability	C	Satisfactory
Applicability	B	Satisfactory
Indicate any dissenting opinions		
RECOMMENDATION What recommendation (s) does the guideline development group draw from this evidence?	GRADE OF RECOMMENDATION (A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B).	B, C
The routine use of rFVIIa in trauma patients with critical bleeding requiring massive transfusion is not recommended because of its lack of effect on mortality (Grade B) ²⁶ and variable effect on morbidity (Grade C) ²⁶ Note: This recommendation was developed from the evidence base presented in all evidence matrixes in this appendix. Note: For this recommendation, there are no particular implementation issues pertinent to Australia's indigenous population		
UNRESOLVED ISSUES If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up		
IMPLEMENTATION OF RECOMMENDATION Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline.		
Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

D7 Evidence – question 7

Question 7

In patients with critical bleeding requiring massive transfusion, what is the effect of fresh frozen plasma, cryoprecipitate, fibrinogen concentrate, and/or platelet transfusion on patient outcomes?

Table D7.1 Evidence matrix for question 7

Key question In Critically Bleeding Patients Undergoing Massive Transfusion what is the Effect of Fresh Frozen Plasma, cryoprecipitate, fibrinogen concentrate, and/or platelet transfusion on mortality? (GN5.1)	Evidence table ref: Borgman et al (2007) ¹⁰ , Duchesne et al (2008) ²⁷	
1. Evidence base (quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)		
Both studies are level III, with a high risk of bias	A	Excellent (One or more level I studies with a low risk of bias or several level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)

	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency (the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)		
Both studies look at several different outcomes. Where similar outcomes were reported findings were generally consistent	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact (the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)		
One study has $n = 246$, ¹⁰ the other has $n = 135$. ²⁷ A RBC:FFP ratio of $\leq 2:1$ was reported to be associated with reduced mortality, but there is uncertainty about whether this is related to survivor bias or the effect of the intervention.	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability (how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)		
Both studies included patients with critical bleeding who required massive transfusion. One study was conducted in a military war zone setting which is not directly generalisable to a civilian setting.	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability (the extent to which the body of evidence is directly applicable to Australian healthcare context)		
One study was in a United States military hospital and the other was in the United States health-care setting.	A	Excellent (directly applicable to Australian healthcare context)
	B	Good (applicable to Australian healthcare context with few caveats)
	C	Satisfactory (probably applicable to Australian healthcare context with some caveats)
	D	Poor (not applicable to Australian healthcare context)
6. Other factors (Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)		
EVIDENCE STATEMENT		
Component	Rating	Description
Evidence base	D	Two Level III studies with a high risk of bias.
Consistency	B	Both studies looked at several different outcomes. Where similar outcomes were reported findings were generally consistent.
Clinical impact	C	One study has $n = 246$, the other has $n = 135$. A RBC:FFP ratio of $\leq 2:1$ was reported to be associated with reduced mortality, but there is uncertainty about whether this is related to survivor bias or the effect of the intervention.
Generalisability	C	Both studies included patients with critical bleeding who required massive transfusion. One study was conducted in a military war zone setting which is not directly generalisable to a civilian setting.
Applicability	C	One study was in a United States military hospital and the other ⁷⁴ was in the United States

		health-care setting.
<i>Indicate any dissenting opinions</i>		
RECOMMENDATION <i>What recommendation (s) does the guideline development group draw from this evidence?</i>	GRADE OF RECOMMENDATION <i>(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)</i>	
No recommendation developed		
UNRESOLVED ISSUES <i>If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up</i>		
IMPLEMENTATION OF RECOMMENDATION		
<i>Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline</i>		
Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

D8 Evidence – question 8

Question 8

At what INR (or PT/APTT) for fresh frozen plasma, fibrinogen level for cryoprecipitate, platelet count for platelet concentrates should patients be transfused to avoid risks of significant adverse events in patients with critical bleeding requiring massive transfusion?

No evidence was found relating to anaemia as an independent risk factor for adverse outcomes in critical bleeding patients requiring massive transfusion.

Appendix E Quality analyses

E1 Analysis – question 1

Question 1

In patients with critical bleeding requiring massive transfusion, what is the effect of variation of physiologic, biochemical and metabolic (including temperature) parameters on morbidity, mortality and transfusion rate?

Reference quality checklist

Because all included studies for this chapter were case reports, it was not appropriate to complete reference quality checklist tables.

E2 Analysis – question 2

Question 2

In patients undergoing massive transfusion, does the dose, timing and ratio (algorithm) of red blood cells (RBCs) to blood component therapy (fresh frozen plasma [FFP], platelets, cryoprecipitate or fibrinogen concentrate) influence morbidity, mortality and transfusion rate? (Intervention foreground question)

Good All or all but one criterion met

Fair 2 or 3 criteria not met

Poor ≥ 4 criteria not met

Table E2.1 Level III cohort studies for question 2

Citation	Cinat et al (1999) ²²
	A. How were subjects selected for the 'new' intervention?
	B. How were subjects selected for the comparison or control group?
	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
<input checked="" type="checkbox"/>	E. Was follow-up long enough for outcomes to occur?
<input type="checkbox"/>	F. Was follow-up complete and were there exclusions from analysis?
Overall assessment	Poor

Citation	Cotton et al (2009) ¹⁸
<input type="checkbox"/>	A. How were subjects selected for the 'new' intervention?
<input type="checkbox"/>	B. How were subjects selected for the comparison or control group?
<input checked="" type="checkbox"/>	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
<input type="checkbox"/>	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
<input checked="" type="checkbox"/>	E. Was follow-up long enough for outcomes to occur?
<input type="checkbox"/>	F. Was follow-up complete and were there exclusions from analysis?
Overall assessment	Poor

Citation	Dente et al (2009) ¹⁹
<input type="checkbox"/>	A. How were subjects selected for the 'new' intervention?
<input type="checkbox"/>	B. How were subjects selected for the comparison or control group?
<input checked="" type="checkbox"/>	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
<input type="checkbox"/>	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
<input checked="" type="checkbox"/>	E. Was follow-up long enough for outcomes to occur?
<input type="checkbox"/>	F. Was follow-up complete and were there exclusions from analysis?
Overall assessment	Poor

Citation	Gunter et al (2008) ²³
<input type="checkbox"/>	A. How were subjects selected for the 'new' intervention?
<input type="checkbox"/>	B. How were subjects selected for the comparison or control group?
<input checked="" type="checkbox"/>	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
<input type="checkbox"/>	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
<input checked="" type="checkbox"/>	E. Was follow-up long enough for outcomes to occur?
<input type="checkbox"/>	F. Was follow-up complete and were there exclusions from analysis?
Overall assessment	Poor

Citation	McLaughlin et al (2008) ²⁸
<input type="checkbox"/>	A. How were subjects selected for the 'new' intervention?
<input type="checkbox"/>	B. How were subjects selected for the comparison or control group?
<input checked="" type="checkbox"/>	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
<input type="checkbox"/>	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
<input checked="" type="checkbox"/>	E. Was follow-up long enough for outcomes to occur?
<input type="checkbox"/>	F. Was follow-up complete and were there exclusions from analysis?
Overall assessment	Poor

Citation	Schreiber et al (2007) ²⁹
<input type="checkbox"/>	A. How were subjects selected for the 'new' intervention?
<input type="checkbox"/>	B. How were subjects selected for the comparison or control group?
<input checked="" type="checkbox"/>	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
<input type="checkbox"/>	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
<input checked="" type="checkbox"/>	E. Was follow-up long enough for outcomes to occur?
<input type="checkbox"/>	F. Was follow-up complete and were there exclusions from analysis?
Overall assessment	Poor

E3 Analysis – question 3

Generic question 3

In patients with critical bleeding requiring massive transfusion, is anaemia an independent risk factor for adverse outcomes?

No evidence was found relating to anaemia as an independent risk factor for adverse outcomes in critical bleeding patients requiring massive transfusion.

E4 Analysis – question 4

Question 4

In patients with critical bleeding requiring massive transfusion, what is the effect of RBC transfusion on patient outcomes?

Good All or all but one criterion met

Fair 2 or 3 criteria not met

Poor ≥ 4 criteria not met

Table E4.1 Level I studies for question 4

Citation	Hill et al (2002) ³⁰
<input checked="" type="checkbox"/>	A. Was a clinical question clearly defined?
<input checked="" type="checkbox"/>	B. Was an adequate search strategy used?
<input checked="" type="checkbox"/>	C. Were the inclusion criteria appropriate and applied in an unbiased way?
<input checked="" type="checkbox"/>	D. Was a quality assessment of included studies undertaken?
<input checked="" type="checkbox"/>	E. Were the characteristics and results of the individual studies appropriately summarised?
<input checked="" type="checkbox"/>	F. Were the methods for pooling the data appropriate?
Overall assessment	Good

Table E4.2 Level I studies for question 4

Citation	Chaiwat et al (2009) ²⁴
<input type="checkbox"/>	A. How were subjects selected for the 'new' intervention?
<input type="checkbox"/>	B. How were subjects selected for the comparison or control group?
<input checked="" type="checkbox"/>	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
<input checked="" type="checkbox"/>	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
<input checked="" type="checkbox"/>	E. Was follow-up long enough for outcomes to occur?
<input checked="" type="checkbox"/>	F. Was follow-up complete and were there exclusions from analysis?
Overall assessment	Fair

Table E4.3 Level I studies for question 4

Citation	Silverboard et al (2005) ²⁵
<input type="checkbox"/>	A. How were subjects selected for the 'new' intervention?
<input type="checkbox"/>	B. How were subjects selected for the comparison or control group?
<input checked="" type="checkbox"/>	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
<input checked="" type="checkbox"/>	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
<input checked="" type="checkbox"/>	E. Was follow-up long enough for outcomes to occur?
<input checked="" type="checkbox"/>	F. Was follow-up complete and were there exclusions from analysis?
Overall assessment	Fair

E5 Analysis – question 5

Question 5

In patients with critical bleeding requiring massive transfusion, what is the effect of non-transfusion interventions to increase haemoglobin concentration on morbidity, mortality and need for RBC blood transfusion?

There was no evidence relevant to this question for inclusion in the critical bleeding/massive transfusion setting.

E6 Analysis – question 6

Question 6

In patients with critical bleeding requiring massive transfusion, what is the effect of rFVIIa (prophylaxis or treatment) on morbidity, mortality and transfusion rate?

Table E6.1 Systematic review for question 6

Citation	Nishijima et al (2009) ³¹
<input checked="" type="checkbox"/>	A. Was a clinical question clearly defined?
<input checked="" type="checkbox"/>	B. Was an adequate search strategy used?
NR	C. Were the inclusion criteria appropriate and applied in an unbiased way?
<input checked="" type="checkbox"/>	D. Was a quality assessment of included studies undertaken?
<input checked="" type="checkbox"/>	E. Were the characteristics and results of the individual studies appropriately summarised?
NA	Were the methods for pooling the data appropriate?
NA	Were the sources of heterogeneity explored?
Overall assessment	Good

Table E6.2 Randomised-controlled trial for question 6

Citation	Boffard et al (2005) ²⁶
<input checked="" type="checkbox"/>	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
<input checked="" type="checkbox"/>	B. Was the study double-blinded?
<input checked="" type="checkbox"/>	C. Were patient characteristics and demographics similar between treatment arms at baseline?
<input type="checkbox"/>	D. Were all randomised patients included in the analysis?
<input checked="" type="checkbox"/>	E. Were the statistical methods appropriate?
NA	F. Were any subgroup analyses carried out?
Overall assessment	Good

E7 Analysis – question 7

Question 7

In patients with critical bleeding requiring massive transfusion, what is the effect of FFP, cryoprecipitate, fibrinogen concentrate, and/or platelet transfusion on patient outcome?

Table E7.1 Level III studies for question 7

Citation	Bochicchio et al (2008) ³²
<input type="checkbox"/>	A. How were subjects selected for the 'new' intervention?
<input type="checkbox"/>	B. How were subjects selected for the comparison or control group?
<input checked="" type="checkbox"/>	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
<input checked="" type="checkbox"/>	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
<input checked="" type="checkbox"/>	E. Was follow-up long enough for outcomes to occur?
<input checked="" type="checkbox"/>	F. Was follow-up complete and were there exclusions from analysis?
Overall assessment	Fair

Table E7.2 Level III studies for question 7

Citation	Borgman et al (2007) ¹⁰
<input type="checkbox"/>	A. How were subjects selected for the 'new' intervention?
<input type="checkbox"/>	B. How were subjects selected for the comparison or control group?
<input checked="" type="checkbox"/>	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
<input type="checkbox"/>	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
<input checked="" type="checkbox"/>	E. Was follow-up long enough for outcomes to occur?
<input checked="" type="checkbox"/>	F. Was follow-up complete and were there exclusions from analysis?
Overall assessment	Fair

Table E7.3 Cohort studies for question 7

Citation	Dente et al (2009) ¹⁹
<input type="checkbox"/>	A. How were subjects selected for the 'new' intervention?
<input type="checkbox"/>	B. How were subjects selected for the comparison or control group?
<input checked="" type="checkbox"/>	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
<input type="checkbox"/>	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
<input checked="" type="checkbox"/>	E. Was follow-up long enough for outcomes to occur?
<input type="checkbox"/>	F. Was follow-up complete and were there exclusions from analysis?
Overall assessment	Poor

Table E7.4 Cohort studies for question 7

Citation	Duchesne et al (2008) ²⁷
<input type="checkbox"/>	A. How were subjects selected for the 'new' intervention?
<input type="checkbox"/>	B. How were subjects selected for the comparison or control group?
<input checked="" type="checkbox"/>	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
<input type="checkbox"/>	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
<input checked="" type="checkbox"/>	E. Was follow-up long enough for outcomes to occur?
<input checked="" type="checkbox"/>	F. Was follow-up complete and were there exclusions from analysis?
Overall assessment	Poor

E8 Analysis – question 8

Question 8

In patients with critical bleeding requiring massive transfusion, at what INR (or PT/APTT) for fresh frozen plasma, fibrinogen level for cryoprecipitate, platelet count for platelets concentrates should patients be transfused to avoid risks of significant adverse events?

There was no evidence relevant to this question for inclusion in the critical bleeding/massive transfusion setting.

Appendix F Evidence summaries

F1 Evidence summaries – question 1

Question 1

In patients with critical bleeding requiring massive transfusion, what is the effect of variation of physiologic, biochemical and metabolic (including temperature) parameters on morbidity, mortality and transfusion rate?

Table F1.1 Summaries for question 1

STUDY DETAILS			
Reference Borgman et al (2007) ¹⁰			
Affiliation/ source of funds Brooke Army Medical Centre, Fort Sam Houston, Texas/ NR			
Study design Case series	Level of evidence IV		Location/ setting USA/ hospital
Intervention: N/A (predictor study)	Comparator(s): N/A		
Sample size: N/A	Sample size: N/A		
Population characteristics: Retrospective chart review of trauma patients admitted to a combat support hospital who received massive blood transfusion (≥ 10 U RBC within 24 hours of admission) during a 22 month period (November 2003–September 2005). N = 246			
Length of follow up: 22 months	Outcome(s) measured: Mortality		
Internal validity: Poor			
Results			
Mortality	Survivors N = NR (range)	Non survivors N = NR (range)	p-value
Temperature ($n = 195$)	96.1 (94.4–97.7)	94.9 (93.2–97.3)	$p = 0.049$
BD ($n = 201$)	7 (3–12)	13 (8–18)	$p < 0.001$
INR ($n = 212$)	1.5 (1.2–1.8)	2.1 (1.6–3.4)	$p < 0.001$
Platelet count ($\times 10^3$) ($n = 174$)	222 (152–278)	175 (118–234)	$p = 0.015$
	OR of mortality	95%CI	p-value
BD	0.89	(0.84, 0.95)	$p < 0.001$
External validity			
Generalisability Trauma patients critically bleeding with no study restrictions as all patients were in their natural environment (ie; trauma centre or hospital setting). Large study population and long term study period			
Applicability This evidence base is applicable to the Australian setting because there are no organisational or cultural barriers			

STUDY DETAILS			
Reference Cosgriff et al (1997) ³³			
Affiliation/ source of funds Department of surgery and pathology, Denver Health medical centre and the University of Colorado Health Sciences Centre, Denver, Colorado/ National Institutes of Health grants			
Study design Case series		Level of evidence IV	Location/ setting: USA/ hospital
Intervention: N/A (predictor study) Sample size: N/A		Comparator(s): N/A Sample size: N/A	
Population characteristics Retrospective chart review of injured patients > 15 years of age and received a massive transfusion (≥ 10 U RBC within 24 hours of admission) during a 24 month period (1993–1995) N = 57			
Length of follow up: 24 months		Outcome(s) measured: Coagulopathy	
Internal validity: Poor			
Results			
Coagulopathy	No coagulopathy N = 31	Coagulopathy N = 27	p-value
pH	7.15 \pm 0.02	7.02 \pm 0.03	$p = 0.0004$
% patients acidosis, pH < 7.1	32	78	$p = 0.0014$
Temperature	34.6 \pm 0.2	33.8 \pm 0.3	$p = 0.05$
% patients hypothermia, temp < 34°C	23	59	$p = 0.01$
	OR of coagulopathy	95%CI	p-value
Acidosis, pH < 7.1	12.3	(2.4, 64.0)	$p = 0.0003$
Hypothermia, temp < 34°C	8.7	(1.8, 41.8)	$p = 0.007$
External validity			
Generalisability Injured patients critically bleeding requiring massive transfusion. No study restrictions as all patients were in their natural environment (ie; trauma centre or hospital setting). Long term study period and a medium size study population ($n = 57$)			
Applicability This evidence base is applicable to the Australian setting because there are no organisational or cultural barriers			

STUDY DETAILS			
Reference Ferrara et al (1990) ¹¹			
Affiliation/ source of funds Departments of Surgery, Bridgeport Hospital and West Haven VA Medical centre, Yale University, West Haven, Connecticut/ NR			
Study design Case series	Level of evidence Level IV	Location/ setting: USA/ hospital	
Intervention: N/A (Predictor study) Sample size: N/A		Comparator(s): N/A Sample size: N/A	
Population characteristics Retrospective records review of all patients with major trauma requiring massive transfusion (≥ 12 U RBC in the first 24 hours of admission) over a 7 year period (January 1981–August 1988). N = 45			
Length of follow up: 7 years		Outcome(s) measured: Mortality	
Internal validity: Poor			
Results			
Mortality	Survivors N = 30	Non survivors N = 15	p-value
Minimum pH	7.18 \pm 0.02	7.04 \pm 0.04	$p < 0.05$
Minimum temp ($^{\circ}$ C)	34 \pm 0.5	31 \pm 1	$p < 0.05$
Minimum PLTcount ($\times 10^3$)	59 \pm 6	58 \pm 7	NS
Maximum PT (sec)	21 \pm 5	31 \pm 9	$p < 0.05$
Maximum APTT (sec)	47 \pm 5	58 \pm 11	NS
Coagulopathy (%)	24	74	NR
Hypothermia (%)	36	80	NR
Hypothermia, acidosis and coagulopathy (%)	23	90	NR
External validity			
Generalisability Trauma patients critically bleeding requiring a massive transfusion. No study restrictions as all patients were in their natural environment (ie; trauma centre or hospital setting). Large study population and long term study period			
Applicability This evidence base is applicable to the Australian setting because there are no organisational or cultural barriers			

STUDY DETAILS			
Reference Gonzalez et al (2007) ¹²			
Affiliation/ source of funds Department of surgery, University of Texas Houston Medical School; US army institute of surgical research, Fort Sam, Houston Texas/ NIGMS grants			
Study design Case series	Level of evidence IV		Location/ setting USA/ hospital
Intervention: N/A (Predictor study) Sample size: N/A		Comparator(s): N/A Sample size: N/A	
Population Characteristics Retrospective data review from trauma research database of shock resuscitation patients who received massive transfusion (≥ 10 U RBC within 24 hours of admission) during a 51 month period ending January 2003 N = 97			
Length of follow up: 51 months		Outcome(s) measured: Mortality	
Internal validity: Poor			
Results			
Mortality	Survivors N = 68	Non survivors N = 29	p-value
ED INR	1.9 \pm 0.2	1.5 \pm 0.1	NS
ED BD (mEq/L)	10 \pm 1	11 \pm 1	NS
ICU* admit INR	1.5 \pm 0.1	1.7 \pm 0.1	$p < 0.05$
ICU* admit BD (mEq/L)	6 \pm 1	8 \pm 0.2	NS
ICU* admit temperature (°C)	35.4 \pm 0.2	35.3 \pm 0.2	NS
	OR of mortality	95%CI	p-value
ED INR	0.74	NR	$p = 0.38$
ED BD (mEq/L)	1.07	NR	$p = 0.18$
ICU* admit INR	9.25	NR	$p = 0.02$
ICU* admit BD (mEq/L)	1.14	NR	$p = 0.04$
External validity			
Generalisability Shock resuscitation patients critically bleeding requiring a massive transfusion. No study restrictions as all patients were in their natural environment (ie; trauma centre or hospital setting). Large study population ($n = 97$) and long term study period (51 months)			
Applicability This evidence base is applicable to the Australian setting because there are no organisational or cultural barriers			

STUDY DETAILS			
Reference Mitra et al (2007) ¹³			
Affiliation/ source of funds Emergency and Trauma Centre, The Alfred hospital, Melbourne Australia; Department of epidemiology and preventative medicine, Monash University, Australia; National Trauma Research Institute, The Alfred Hospital, Melbourne Australia/ Educational grant from NovoNordisk			
Study design Case series	Level of evidence IV	Location/ setting Australia/hospital	
Intervention: N/A (Predictor study) Sample size: N/A		Comparator(s): N/A Sample size: N/A	
Population characteristics Retrospective records review of all trauma patients admitted to The Alfred Hospital who received blood transfusion (≥ 5 U RBC within 4 hours of presentation) during a 26 month period (July 2002–September 2004) N = 119			
Length of follow up: 26 months		Outcome(s) measured: Mortality, thrombocytopenia, acidosis	
Internal validity: Poor			
Results			
Mortality	Patient baseline characteristics	OR of mortality (95%CI)	p-value
pH	7.2 \pm 0.1	0.01(0, 0.29)	$p = 0.01$
Temperature ($^{\circ}$ C)	34.4 \pm 1.4	0.72 (0.56, 0.92)	$p = 0.01$
Mean PLT count (k/mm ³)	211.5 \pm 70.6	0.99(0.98, 1)	$p < 0.01$
Maximum APTT (sec)	79.5 \pm 58.4	1.01 (1.01, 1.02)	$p < 0.01$
INR	2.2 \pm 1.1	1.62 (1.18, 2.24)	$p < 0.01$
Base excess	8.7 \pm 4.4	NR	NR
Bicarbonate	18.8 \pm 3.3	0.86 (0.77, 0.96)	$p = 0.01$
Fibrinogen	1.5 \pm 0.6	0.52(0.28, 0.99)	$p = 0.05$
Acidosis	No acidosis N (%)	Acidosis N (%)	p-value
pH < 7.2	79 (66.4)	40 (33.6)	NR
Thrombocytopenia	No thrombocytopenia N (%)	Thrombocytopenia N (%)	p-value
Platelet count < 100x10 ⁹	107 (89.9)	12 (10.1)	NR
INR > 2.5	94 (79)	25 (21)	NR
APTT > 60 sec	83 (69.8)	36 (30.2)	NR
External validity			
Generalisability Trauma patients critically bleeding requiring a massive transfusion. No study restrictions as all patients were in their natural environment (ie; trauma centre or hospital setting). Large study population ($n = 119$) and long term study period (26 months)			
Applicability This evidence base is applicable to the Australian setting because there are no organisational or cultural barriers and the study is based in Australia			

STUDY DETAILS			
Reference Moore et al (2008) ¹⁴			
Affiliation/ source of funds Hutchinson Technology Inc Hutchinson, Minnesota; Department of surgery, University of Colorado Denver, Colorado; Department of surgery, University of Toronto Ontario Canada; Department of Surgery , University of Southern California, Los Angeles, California; Department of surgery , University of Pittsburgh, Pittsburgh, Pennsylvania; Department of surgery, University of Minnesota, Minneapolis, Minnesota; Department of surgery, University of Texas Health science centre San Antonio, San Antonio and Technomics Research, Minnesota/ Hutchinson Technology Inc Hutchinson			
Study design Case series	Level of evidence IV	Location/ setting USA/ hospital	
Intervention: N/A (Predictor study) Sample size: N/A		Comparator(s): N/A Sample size: N/A	
Population characteristics Prospective, multi centre, observational non-randomised analysis from a database of patients presenting with haemorrhagic shock during a 16 month period ending February 2006. N = 114			
Length of follow up: 16 months		Outcome(s) measured: Mortality	
Internal validity: Poor			
Results			
Mortality 1 hour post admission model	Survivors (Good outcome) N = 56	Non survivors (Poor outcome) N = 57	p-value
Minimum pH	7.1 ± 0.1	7.1 ± 0.2	p = 0.0094
Minimum temperature (°C)	35.3 ± 1.6	34.9 ± 2.2	p = 0.5224
Minimum platelet count (k/mm ³)	217 ± 106	193 ± 89	p = 0.2702
Maximum BD	11.1 ± 5.7	12.7 ± 6.4	p = 0.2113
Maximum INR	1.4 ± 0.4	1.9 ± 1.9	p = 0.1915
Mortality 3 hour post admission model	Survivors (Good outcome) N = 56	Non survivors (Poor outcome) N = 57	p-value
Minimum pH	7.2 ± 0.1	7.1 ± 0.2	p = 0.0003
Minimum temperature (°C)	34.9 ± 1.6	34.5 ± 1.9	p = 0.3823
Minimum platelet count (x10 ³)	178 ± 117	141 ± 96	p = 0.1308
Maximum BD	12.1 ± 5.6	13.7 ± 7.2	p = 0.1096
Maximum INR	1.6 ± 0.6	2.9 ± 2.7	p = 0.0016
External validity			
Generalisability Haemorrhagic shock patients critically bleeding, no indication if patients required a massive transfusion hence generalisability may be lower in this study. No study restrictions as all patients were in their natural environment (ie; trauma centre or hospital setting). Large study population (n = 114) and medium term study period (16 months)			
Applicability This evidence base is applicable to the Australian setting because there are no organisational or cultural barriers			

STUDY DETAILS			
Reference Stinger et al (2008) ¹⁵			
Affiliation/ source of funds Brooke Army Medical Centre, U.S. Army Institute of Surgical Research, San Antonio/ United States Army Institute of surgical research and the National Centre for Research Resources			
Study design Case series	Level of evidence IV		Location/ setting USA/ hospital
Intervention: N/A (predictor study) Sample size: N/A		Comparator(s): N/A Sample size: N/A	
Population Characteristics Retrospective chart review of combat trauma patients at a US Army combat support hospital who received massive transfusion (≥ 10 U RBC within 24 hours of admission) during a 22 month period (January 2004–October 2005). N = 252			
Length of follow up: 22 months		Outcome(s) measured: Mortality	
Internal validity: Poor			
Results			
Mortality	OR of mortality	95%CI	p-value
BD	1.075	1.02, 1.129	0.003
External validity			
Generalisability Combat trauma patients critically bleeding requiring a massive transfusion. No study restrictions as all patients were in their natural environment (ie; trauma centre or hospital setting). Large study population ($n = 252$) and long term study period (22 months)			
Applicability This evidence base is applicable to the Australian setting because there are no organisational or cultural barriers			

STUDY DETAILS			
Reference Vaslef et al (2002) ¹⁶			
Affiliation/ source of funds Department of Surgery and Anaesthesiology, Duke University Medical Centre, Durham, North Carolina/ NR			
Study design Case series	Level of evidence IV		Location/ setting USA/ NR
Intervention: N/A (predictor study) Sample size: N/A		Comparator(s): N/A Sample size: N/A	
Population characteristics Retrospective chart and registry data review of trauma patients who received a massive transfusion (> 50 U blood products within 24 hours of admission) during a 5 year period (July 1995–June 2000). N = 44			
Length of follow up: 5 years		Outcome(s) measured: Mortality	
Internal validity: Poor			
Results			
Mortality	Survivors N = NR	Non survivors N = NR	p-value
Arterial pH	7.14 ± 0.13	7.02 ± 0.15	p = 0.01
% patients acidosis, pH < 7.1	31.6	68	p = 0.017
BD (mmol/L)	12.7 ± 5	17 ± 5	p = 0.008
% patients BD (mmol/L) > 12	42.1	80	p = 0.01
External validity			
Generalisability Trauma patients critically bleeding requiring a massive transfusion (> 50 units of blood within 24 hours of admission). No study restrictions as all patients were in their natural environment (ie; trauma centre or hospital setting). Small to medium size study population (n = 44) and long term study period (5 years)			
Applicability This evidence base is applicable to the Australian setting because there are no organisational or cultural barriers			

STUDY DETAILS			
Reference Vivien et al (2005) ³⁴			
Affiliation/ source of funds Department of Anaesthesiology and Critical Care; Department of Emergency Biology,; Department of Emergency Medicine and Surgery; Centre Hospitalo-universitaire; Universite Pierre et Marie Curie; SAMU de Paris/ NR			
Study design Case series	Level of evidence IV	Location/ setting France/NR	
Intervention: N/A (predictor study) Sample size: N/A		Comparator(s): N/A Sample size: N/A	
Population Characteristics Prospective review of consecutive trauma patients (ISS = 34) resuscitated in the pre-hospital phase with fluid loading, during a 1 year period (2002). N = 212			
Length of follow up: 1 year		Outcome(s) measured: Hypocalcemia	
Internal validity: Poor			
Results			
Hypocalcemia	Normocalcaemia N = 56	Severe hypocalcaemia N = 21	p-value
Arterial pH	7.37 ± 0.05	7.05 ± 0.18	<i>p</i> < 0.05
pH < 7.2, <i>n</i> (%)	0 (0)	17 (81)	<i>p</i> < 0.05
Total calcium	2.16 ± 0.16	1.55 ± 0.23	NS
Hb	12.7 ± 1.9	7.6 ± 2.9	<i>p</i> < 0.05
Platelet count (G/L)	224 ± 62	119 ± 69	<i>p</i> < 0.05
Fibrinogen	2.7 ± 0.9	0.7 ± 0.6	<i>p</i> < 0.05
Maximum PT (% of control)	79 ± 16	24 ± 14	<i>p</i> < 0.05
Maximum APTT (sec)	35 ± 10	116 ± 59	<i>p</i> < 0.05
Bicarbonates (mmol/L)	25.8 ± 3.3	14 ± 3.9	<i>p</i> < 0.05
Lactates (mmol/L)	1.5 ± 0.7	9.4 ± 5.2	<i>p</i> < 0.05
External validity			
Generalisability Trauma patients critically bleeding requiring a fluid loading. Fluid loading was not described in detail in the study; hence its generalisability to the overall guidelines for massively transfused patients may be reduced. No study restrictions as all patients were in their natural environment (ie; trauma centre or hospital setting). Large study population (<i>n</i> = 212) and medium term study period (1 year)			
Applicability This evidence base is applicable to the Australian setting because there are no organisational or cultural barriers			

STUDY DETAILS			
Reference Wilson et al (1992) ¹⁷			
Affiliation/ source of funds Department of Surgery, Detroit Receiving Hospital and Wayne State University School of Medicine, Detroit, Michigan/ NR			
Study design Case series	Level of evidence IV		Location/ setting USA/ hospital
Intervention: N/A (predictor study) Sample size: N/A		Comparator(s): N/A Sample size: N/A	
Population Characteristics Retrospective record review of patients receiving ≥ 10 U blood within 24 hours of admission during an 11-year period (1980–1991). N = 471			
Length of follow up: 11 years		Outcome(s) measured: Mortality	
Internal validity: Poor			
Results			
Mortality	Survivors N = 180	Non survivors N = 159	p-value
pH	7.21 \pm 0.15	7.08 \pm 0.15	$p < 0.001$
Magnesium (mmHg)	1.9 \pm 0.5	2.3 \pm 0.7	NS
External validity			
Generalisability Trauma patients critically bleeding requiring a massive transfusion. No study restrictions as all patients were in their natural environment (ie; trauma centre or hospital setting). Large study population ($n = 471$) and long term study period (11 years)			
Applicability This evidence base is applicable to the Australian setting because there are no organisational or cultural barriers			

F2 Evidence summaries – question 2

Question 2

In patients undergoing massive transfusion, does the dose, timing and ratio (algorithm) of red blood cells (RBCs) to blood component therapy (fresh frozen plasma [FFP], platelets, cryoprecipitate or fibrinogen concentrate) influence morbidity, mortality and transfusion rate? (Intervention foreground question)

Table F2.1 Summaries for question 2

STUDY DETAILS				
Reference Borgman et al (2007) ¹⁰				
Affiliation/Source of funds Brooke Army Medical Center/NR				
Study design Case-series or cross sectional study/retrospective chart review		Level of evidence IV		Location/setting Iraq/Military
Intervention FFP:RBC ratio Low ratio group, 1 U FFP+FWB:8 U RBC+FWB (0:12–1:5), sample size $n = 31$ Medium ratio group, 1 U FFP+FWB:2.5 U of RBC+FWB (1:3.0–1:2.3), sample size $n = 53$ High ratio group, 1 U FFP+FWB:1.4 U RBC+FWB (1:1.7–1:1.2), sample size $n = 162$				Comparator No comparator
Population characteristics Intervention group—All patients who received ≥ 10 units RBC or FWB in 24 hours. The study population was split into three groups for comparison based on the ratio of FFP:RBC received over 24 hours as described above. No significant differences between the baseline characteristics of the groups were observed except for the following: Severe thoracic injury scores were significantly more common in the low ratio group ($p < 0.05$); and haemoglobin levels were significantly lower in the low ratio group ($p < 0.05$)				
Length of follow-up NA		Outcomes measured Morbidity/mortality		
INTERNAL VALIDITY				
Allocation	Comparison of study groups	Blinding analysis	Treatment measurement bias	Follow-up (ITT)
Not applicable	See above	Not blinded	Groups were treated and measured the same	Not applicable
Overall quality assessment (descriptive): Despite not being an RCT, the study is of good quality				

RESULTS					
Outcome	Intervention group	Control group		Measure of effect/effect size (95%CI)	Benefits (NNT) (95%CI)
Mortality/morbidity	FFP:RBC	Not applicable		See below	See below
		FFP:RBC ratio			p-value
		High ratio: 1:1.4 (n = 162)	Medium ratio: 1:2.5 (n = 53)	Low ratio: 1:8 (n = 31)	
Mortality at 30 days	FFP:RBC	19	34	65	p < 0.001
Excluding rFVIIa treatment (%)	FFP:RBC	15	38	69	p < 0.05
Excluding whole blood (%)	FFP:RBC	19	27	66	p < 0.05
Excluding thoracic trauma (%)	FFP:RBC	19	29	57	p < 0.05
Excluding neurotrauma (%)	FFP:RBC	15	36	62	p < 0.05
Mortality associated with haemorrhage (%)	FFP:RBC	37	78	92.5	p < 0.001 (high vs low) p < 0.05 (high vs medium)
Median time to death (h)	FFP:RBC	38	4	2	NR
Overall survival associated with FFP:RBC ratio		OR		95%CI	p-value
		8.6		2.1-35	p = 0.003
<p>Any other adverse events Patients who received high FFP:RBC ratios had a higher incidence of death from sepsis and MOF versus haemorrhage as a result of surviving long enough to develop these complications. This is supported by the median time to death of the low and median ratio groups to the high ratio group. Because of the retrospective nature of the study, it is not possible to rule out the possibility that the increased use of FFP, aPLT and cryoprecipitate in the study contributed to these results</p>					
			Clinical importance: 2	Clinical relevance: 1	
EXTERNAL VALIDITY					
<p>Generalisability The patients in the study are from a military population. This may affect their generalisability from a civilian population, the target of the blood management guidelines as they are able to use fresh whole blood in their treatment regime and the pattern of injury may differ significantly from the civilian population. For example, patients in military trials presenting with critical bleed often present with more severe penetrating trauma and less blunt trauma. However, massive transfusion is also likely to be observed more frequently within a military population, improving the ability to research new treatment regimes</p>					
<p>Applicability Due to the nature of critical bleeding and the inherent difficulty in performing a controlled, randomised trial, the potential benefits of the outcomes of the research in this trial outweigh the potential harms for the treatment of civilian patients with critical bleeding</p>					
<p>Comments The outcomes of this study have important implications for patients with critical bleeding as they suggest that in a military population, patients with critical bleeding respond better to high ratios of FFP:RBC. This finding needs to be interpreted cautiously as the trial is not prospective, randomised, nor controlled, but may be directly applicable to the civilian population. Given the inherent difficulties of conducting RCTs in critically bleeding patients, the outcomes of all studies performed need to be taken into account</p>					

STUDY DETAILS				
Reference Cinat et al (1999) ²²				
Affiliation/Source of funds: University of California Irvine Medical Center				
Study design Cohort study / retrospective		Level of evidence III-2		Location/setting USA / Hospital
Intervention FFP:RBC, late cohort (1993–1997) sample size $n = 20$			Comparator FFP:RBC, early cohort (1988–1992) sample size $n = 25$	
<p>Population characteristics Intervention group—All patients who received > 50 units RBC or whole blood in the 48 hours following admission to the emergency department between 1993 and 1997</p> <p>Comparator group—All patients who received > 50 units RBC or whole blood in the 48 hours following admission to the emergency department between 1993 and 1997</p> <p>Demographics in the two cohorts were similar. However, patients in the Intervention group were significantly older. The difference was independent of a 79 year old survivor in the Intervention group</p>				
Length of follow-up Not applicable		Outcomes measured Morbidity/mortality, dose/type of transfusion		
INTERNAL VALIDITY				
Allocation	Comparison of Study groups	Blinding analysis	Treatment / measurement bias	Follow-up (ITT)
By year period	See above	Not blinded	The groups were treated and measured the same—the only difference was that due to time	Not applicable
Overall quality assessment (descriptive) The overall quality of the trial was good for a non-randomised, non-controlled study. The number of patients in the study was low. Results should be interpreted with caution				
RESULTS				
Ratio of blood products and survival	Measure	Ratio, mean \pm SEM		Statistical significance
		Survivors (N = 13)	Non-survivors (N = 32)	
	FFP:RBC	1:1.8 \pm 0.3	1:2.5 \pm 0.9	$p = 0.06$
PLT:RBC	1:7.7 \pm 1.9	1:11.9 \pm 4.9	$p = 0.03$	
Mean RBC units transfused	Measure	MT	No MT	Statistical significance
	Mean RBC units, 48 hours \pm SEM (N)	63.1 \pm 13.4 (45)	NR	NR
Other reported adverse events		Clinical importance: 3		Clinical relevance:1
EXTERNAL VALIDITY				
Generalisability The study is small, but focuses on patients requiring massive transfusion, which is equivalent to the study population. In addition, this study focuses on patients requiring > 50 units RBC in 24 hours, suggesting patients in this study are severely injured. The population studied is generalisable to the target protocol population				
Applicability The study has a small population, highlights differences in transfusion practice over time and shows that patients being treated more aggressively with PLT and FFP have increased survival. These results are applicable to the target audience, but due to the size of the study, need to be treated with caution				
Comments This study is applicable to the target population, but due to it's design and low sample size, should be treated with caution				

STUDY DETAILS					
Reference Cosgriff et al (1997) ³³					
Affiliation/Source of funds Denver Health Medical Center, University of Colorado Health Sciences Center/NIH grants: P50GM49222 and T32GU08315					
Study design Case-series or cross sectional study / retrospective chart review			Level of evidence IV		Location/setting USA / Hospital
Intervention RBC, FFP, PLT, cryoprecipitate; sample size $n = 58$			Comparator No comparator		
Population characteristics Intervention group—All patients > 15 years of age who received a massive transfusion (> 10 units RBC in 24 hours) Patients with massive head injuries were excluded as well as those with pre-existing disease. The mean age of the group was 34.5 years, injury severity score was 30.6 and RBC transfused was 24.2 units in 24 hours					
Length of follow-up NA		Outcomes measured Morbidity/mortality, dose/type of transfusion			
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding analysis	Treatment / Measurement bias	Follow-up (ITT)	
Not applicable	Not applicable	Not blinded	Not applicable	Not applicable	
Overall quality assessment (descriptive) The overall design of the study is adequate for a non-randomised, non controlled, case review study					
RESULTS					
Volume of product transfused over 48 hours (mean \pm SD)					
Author	Blood component	Survivor ($n = 33$)	Non-survivors ($n = 25$)	Total	p-value
Cosgriff et al (1997) ³³	PLT	18.8 \pm 12.9	12.6 \pm 2.6	NR	NR
Cosgriff et al (1997) ³³	RBC	22.8 \pm 1.8	26.0 \pm 2.9	NR	NR
Mean transfusion volume, first 24 hours (Mean \pm SD)					
Author	Blood component	Units	p-value		
Cosgriff et al (1997) ³³	RBC	24.2 \pm 1.6	NR		
Cosgriff et al (1997) ³³	FFP	14.0 \pm 1.2	NR		
Cosgriff et al (1997) ³³	PLT	16.1 \pm 2.0	NR		
Cosgriff et al (1997) ³³	Cryopreceptitate	11.4 \pm 1.2	NR		
Mortality rate associated with RBC transfusion					
Author	Time period	Units (mean)	Mortality (%)	p-value	
Cosgriff et al (1997) ³³	24 hours	24	43	NR	

Average ratio of blood components transfused over 48 hours				
Author	Blood component ratio	Survivors (<i>n</i> = 33)	Non-survivors (<i>n</i> = 25)	p-value
Cosgriff et al (1997) ³³	PLT:RBC	0.79 ± 0.09	0.48 ± 0.09	<i>p</i> = 0.001
Other adverse events: NR				
		Clinical importance 2	Clinical relevance 1	
EXTERNAL VALIDITY				
Generalisability The study looked at patients requiring massive transfusion > 15 years old, excluding those with massive head injuries and pre-existing disease. This population would represent the population aimed for by the guidelines				
Applicability The potential benefit that may be offered by this research will outweigh the potential harms				

STUDY DETAILS				
Reference Cotton et al (2009) ¹⁸				
Affiliation/Source of funds Vanderbilt University Medicine Center, Tennessee Valley VA Medical Centre. Source of funding not reported				
Study design Cohort study. The exsanguination protocol (TEP) involves the immediate delivery of products in a 3:2 ratio	Level of evidence III-2		Location/setting USA / Hospital	
Intervention TEP, underwent transfusion according to MTP, sample size $n = 125$		Comparator Pre-TEP, underwent transfusion prior to MTP, sample size $n = 141$		
Population characteristics The baseline characteristics of the two groups were significantly different for the mechanism of penetrating trauma and injury scores, with the pre-TEP group significantly lower for each characteristic				
Length of follow-up NA		Outcomes measured Mortality/morbidity		
INTERNAL VALIDITY				
Allocation	Comparison of study groups:	Blinding analysis	Treatment / measurement bias	Follow-up (ITT)
Not reported	EP group patients were more severely injured (ISS 33.3 vs 28.0, $p = 0.006$) and demonstrated a higher physiological severity on arrival (3.48 vs 4.29, $p = 0.006$)	Not blinded	Not reported	Not reported
Overall quality assessment (descriptive) The study was well designed for a non-randomised cohort trial. Univariate and multivariate analysis were performed accounting for confounding factors. The population being studied was appropriate to the guideline population				
RESULTS				
Mortality				
Author	Measure	MTP	No MTP	Statistical significance
Cotton et al (2009) ¹⁸	Overall mortality, at 24 hours, % of patients (N)	31 (125)	39 (141)	$p = 0.185$ (NS)
Cotton et al (2009) ¹⁸	Mortality at 30 days, % of patients (N)	43.2 (125)	62.4 (141)	$p = 0.001$

Units of blood components transfused				
Author	Measure	MTP	No MTP	Statistical significance
Cotton et al (2009) ¹⁸	Crystalloid, mean L given intra-operatively (N)	4.8 (125)	7.0 (141)	$p < 0.001$
<i>Total average units transfused postoperatively</i>				
Cotton et al (2009) ¹⁸	RBC, mean units postoperatively at 24 hours (N)	31.2 (125)	38.7 (141)	$p = 0.05$
<i>Total average units transfused up to 6 hours</i>				
Cotton et al (2009) ¹⁸	RBC, mean units intra-operatively (N)	14.7 (125)	11.0 (141)	$p = 0.001$
	Clinical importance 2		Clinical relevance 1	
Any other adverse events There was no difference between groups with regard to the development of systemic inflammatory response syndrome, ventilator dependent respiratory failure or need for renal replacement therapy. However, severe sepsis or septic shock and ventilator-associated pneumonia were both lower in the TEP group (10% vs 20%, $p = 0.019$ and 27% vs 39% $p = 0.041$ respectively). Simple logistic regression found TEP associated with a 58% reduction in severe sepsis or septic shock (OR 0.428, $p = 0.022$, 95%CI: [0.207, 0.884]) and a 51% odds reduction in ventilator assisted pneumonia (OR 0.491, $p = 0.005$, 95%CI: [0.299, 0.807])				
EXTERNAL VALIDITY				
Generalisability This study was performed in a population receiving ≥ 10 units RBC in 24 hours and assessed the differences associated with using a massive transfusion protocol against not using a massive transfusion protocol. There were no significant differences in the population that would preclude the findings of this study being transferred to the guideline population				
Applicability The potential benefits outlined in the study outweigh the potential harms in the guideline population				
Comments The outcomes of this study show that a massive transfusion protocol improves the outcomes (morbidity and mortality) for patients undergoing a massive transfusion. Due to the size of the population studied and the retrospective nature of the study, these results should be interpreted with caution, but are applicable to the population that the guideline will target				

STUDY DETAILS					
Reference Dann et al (2008) ³⁵					
Affiliation/Source of funds Rambam Health Care Campus, Haifa Israel and Israel University of Technology. Source of funding not reported					
Study design Case-series or cross sectional study ,The experience of 33 days of warfare at a level 1 trauma centre, a retrospective chart review			Level of evidence IV		Location/setting Israel/Military
Intervention > 10 units RBC, sample size $n = 21$			Comparator No comparator		
Population characteristics Median age was 24 (range 20–58), 20 of the patients were soldiers; 4 had concomitant hypothermia					
Length of follow-up NA			Outcomes measured Dose/type of transfusion		
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding analysis	Treatment / measurement bias	Follow-up (ITT)	
Not applicable	Not applicable	Not blinded	Not applicable	Not applicable	
Overall quality assessment (descriptive) The study design is fairly poor, with a low patient population					
RESULTS					
Median and Mean units of blood components administered at different time points					
Author	Blood component ratio	Total	First 6 hours	First 12 hours	First 24 hours
Dann et al (2008) ³⁵	Crystalloids (median)	3000 mL	NR	NR	NR
Dann et al (2008) ³⁵	RBC, units (mean \pm SD)	14 (13 \pm 7)	NR	NR	NR
Dann et al (2008) ³⁵	FFP, units (mean \pm SD)	10 (11.1 \pm 8.9)	NR	NR	NR
Dann et al (2008) ³⁵	Cryoprecipitate (mean \pm SD)	10 u (11.2 \pm 10.5)	NR	NR	NR
Dann et al (2008) ³⁵	PLT, units (mean \pm SD)	6u (8.6 \pm 6.5)	NR	NR	NR
Other adverse events reported Three of 20 survivors developed alloantibodies to RBC antigens. Two patients had anti-Kell and 2 had anti-D after a transfusion of Rh+ RDPs					
Clinical importance 3			Clinical relevance 2		
EXTERNAL VALIDITY					
Generalisability The study has low patient numbers in a military setting which may not be generalisable to a civilian patient population. Patients were provided with random donor platelets which are not available in a civilian population. Thus, results of this study should be treated with caution					
Applicability The potential benefits identified in this study outweigh the potential harms					

STUDY DETAILS					
Reference Dente et al. (2009) ¹⁹					
Affiliation/Source of funds Grady memorial Hospital and Emory University School of Medicine/NR					
Study design Cohort study, retrospective		Level of evidence III-2	Location/setting USA / Hospital		
Intervention MTP group, sample size: $n = 73$		Comparator Non-MTP group, sample size: $n = 84$			
Population characteristics Both groups had comparable demographics and injury severity scores Intervention group—MTP, received ≥ 10 units RBC following MTP designed to reach a blood product ratio RBC:FFP:PLT = 1:1:1 Comparator group—pre-MTP, received ≥ 10 units RBC in the first 24 hours of hospitalisation before instituting MTP					
Length of follow-up NA		Outcomes measured Morbidity/mortality, dose/type of transfusion, transfusion frequency			
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding analysis	Treatment / measurement bias	Follow-up (ITT)	
Not allocated	MTP group received significantly more RBC and FFP transfusions than the pre-MTP group ($p < 0.001$) and significantly less crystalloid ($p = 0.006$)	Not blinded	Patients were treated equally other than the institution of an MTP protocol	Not applicable	
Overall quality assessment (descriptive) The study was of good quality					
RESULTS					
Mortality by ratio of blood product to RBC					
Mortality at 24 hours					
Author	Measure	Ratio			Statistical significance
		High, 1:1–2:1 (N)	Medium, 2:1–3:1 (N)	Low, > 3:1 (N)	
Dente et al (2009) ¹⁹	RBC:FFP, % of patients	14 (50)	19 (16)	57 (7)	$p < 0.001$
Dente et al (2009) ¹⁹	RBC:PLT, % of patients	10 (50)	18 (11)	50 (12)	$p < 0.001$
Hospital mortality					
Author	Measure	Ratio			Statistical significance
		High, 1:1–2:1 (N)	Medium, 2:1–3:1 (N)	Low, > 3:1 (N)	
Dente et al (2009) ¹⁹	RBC:FFP, % of patients	31 (50)	36 (16)	57 (7)	$p < 0.001$
Dente et al (2009) ¹⁹	RBC:PLT, % of patients	36 (50)	27 (11)	50 (12)	NS

Mortality				
Author	Measure	MTP	No MTP	Statistical significance
Dente et al (2009) ¹⁹	Overall mortality, at 24 hours, % of patients (N)	17 (72)	36 (84)	$p = 0.008$
Dente et al (2009) ¹⁹	Mortality at 30 days, % of patients (N)	34 (72)	55 (84)	$p = 0.04$
Dente et al (2009) ¹⁹	Mortality due to blunt trauma prior to discharge, % of patients (N)	34 (72)	55 (84)	$p = 0.042$
Units of blood components transfused				
Author	Measure	MTP	No MTP	Statistical significance
Dente et al (2009) ¹⁹	RBC, mean units (N)	23.7 (72)	22.8 (84)	$p = 0.67$ (NS)
Dente et al (2009) ¹⁹	FFP, mean units (N)	15.6 (72)	7.6 (84)	$p < 0.001$
Dente et al (2009) ¹⁹	Crystalloid, mean L (N)	6.9 (72)	9.4 (84)	$p = 0.006$
<i>Total average units transfused up to 6 hours</i>				
Dente et al (2009) ¹⁹	RBC, mean units up to 6 hours (N)	22 (72)	19.4 (84)	NS
Dente et al (2009) ¹⁹	FFP, mean units up to 6 hours (N)	13.7 (72)	5.5 (84)	$p < 0.05$
Dente et al (2009) ¹⁹	PLT, mean units up to 6 hours (N)	14.1 (72)	9.2 (84)	$p < 0.05$
Dente et al (2009) ¹⁹	Cryoprecipitate, mean units up to 6 hours (N)	11.6 (72)	7.6 (84)	$p < 0.05$
<i>Total average units transfused postoperatively</i>				
Dente (2009) ¹⁹	RBC, mean additional units (N)	1.7 (72)	3.4 (84)	NS
Blood component ratios				
Author	Measure	MTP	No MTP	Statistical significance
Dente et al (2009) ¹⁹	RBC:FFP ratio, mean (N)	1.9:1 (72)	NR	NR
Dente et al (2009) ¹⁹	RBC:PLT ratio, mean (N)	1.48:1 (72)	NR	NR
Any other adverse events NR				
	Clinical importance 2		Clinical relevance 1	
EXTERNAL VALIDITY				
Generalisability The population reviewed in the study is equivalent to the population targeted in the guidelines and therefore, the results of the study are generalisable to the guideline population				
Applicability The potential benefits from the finding of this study outweigh the potential harms				
Comments The results of this study need to be interpreted with caution due to the small patient numbers and retrospective study design. However the results are generalisable and applicable to the critical bleed population the guideline is targeting and therefore, the results may be applied to this population				

STUDY DETAILS				
Reference Duchesne et al (2008) ²⁷				
Affiliation/Source of funds: NR				
Study design Case-series of cross sectional study/retrospective chart review	Level of evidence IV		Location/setting USA / Hospital	
Intervention > 10 units RBC/FFP in 24 hours, sample size $n = 135$	Comparator < 10 units RBC/FFP in 24 hours, sample size $n = 626$			
Population characteristics Intervention group—All patients admitted to the trauma centre who received > 10 units RBC in 24 hours Comparator group—Patients receiving < 10 units RBC				
Length of follow-up NR		Outcomes measured Morbidity/mortality		
INTERNAL VALIDITY				
Allocation	Comparison of study groups	Blinding analysis	Treatment /measurement bias	Follow-up (ITT)
Not allocated	No significant difference in baseline results, except patients receiving > 10 units blood, compared to those receiving < 10 units blood had: higher ISS ($p = 0.001$), fewer penetrating traumas ($p = 0.008$) and lower SBP ($p = 0.008$).	Not blinded	Not reported	Not reported
Overall quality assessment (descriptive) Quality retrospective case series review that performed univariate and multivariate analysis to deal with confounding factors				
RESULTS				
Mortality				
Overall mortality stratified by FFP:RBC ratio (%)				
Author	Ratio of blood products	FFP: RBC ratio		p-value
		High ratio: 1:1 ($n = 19$)	Low ratio: 1:4 ($n = 56$)	
Duchesne et al (2008) ²⁷	FFP:RBC	26	87.5	$p = 0.001$
Mortality associated with haemorrhage stratified by ratio of FFP to RBC (%)				
Author	Ratio of FFP: RBC			p-value
	High ratio: 1:1 ($n = 19$)	Low ratio: 1:4 ($n = 56$)		
Duchesne et al (2008) ²⁷	15.7	19.6		NR

Relative risk of mortality associated with a high vs low FFP:RBC ratio				
Author	Ratio definition (<i>n</i>)	RR	95%CI	p-value
Duchesne et al (2008) ²⁷	High ratio: 1:4 (<i>n</i> = 19) vs low ratio: 1:1 (<i>n</i> = 56)	18.88	(6.32, 56.36)	<i>p</i> = 0.001
	Clinical importance: 2	Clinical relevance: 1		
Any other adverse events There were no significant differences between the groups for adverse events				
EXTERNAL VALIDITY				
Generalisability The population studied were adults requiring massive transfusion vs adults who were not requiring massive transfusion. This is not significantly different from the population targeted by the guidelines				
Applicability The potential outcome benefits outweigh potential harms				

STUDY DETAILS					
Reference Gonzalez et al (2007) ¹²					
Affiliation/Source of funds University of Texas Houston Medical School, US Army Institute of Medical Research/Supported by NIGMS grants P50-GM38529 and T32-GM008792					
Study design Case-series or cross sectional study /patients who were admitted to the Shock Trauma ICU		Level of evidence IV		Location/setting USA/Hospital	
Intervention Crystalloids, sample size $n = 97$; FFP, sample size $n = 97$				Comparator No comparator	
Population characteristics Patients receiving MT (≥ 10 units RBC within 24 hours of admission). Median age = 39, ISS = 29					
Length of follow-up NA		Outcomes measured Morbidity/mortality, dose/type of transfusion, transfusion frequency			
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding analysis	Treatment / measurement bias	Follow-up (ITT)	
Not applicable	Not applicable	Not blinded	Not applicable	Not applicable	
Overall quality assessment (descriptive) A case series review study that aimed to evaluate the value of implementing a massive transfusion protocol. However, the study does not have a control group, so it is difficult to evaluate if there is an advantage to the implementation of such a protocol. Indeed, the study aimed more at evaluating if patients treated using the protocol, met the protocol criteria, As such, there is limited value to this study					
RESULTS					
Volume of product transfused over 48 hours (mean \pm SD)					
Author	Blood component	Survivors ($n = 68$)	Non-survivors ($n = 29$)	Total ($n = 97$)	p-value
Gonzalez et al (2007) ¹²	FFP	6 ± 1	4 ± 0.4	5 ± 0.4	NR
Gonzalez et al (2007) ¹²	Crystalloids	8 ± 1	11 ± 3	9 ± 1	NR
Gonzalez et al (2007) ¹²	RBC	11 ± 1	13 ± 2	12 ± 1	NR
Transfusion frequency					
Author	Blood component	First 12 hours	Second 12 hours	p-value	
Gonzalez et al (2007) ¹²	Platelets (volume)	3 ± 0.4 (6 pk) ($n/N = 48/50$)	3 ± 1 (6 pk) ($n/N = 29/30$)	NR	
Gonzalez et al (2007) ¹²	Cryoprecipitate (volume)	2 ± 0.4 (10 pk) ($n/N = 19/20$)	2 ± 1 (10 pk) ($n/N = 4/4$)	NR	
Gonzalez et al (2007) ¹²	FFP (volume)	8 ± 1 unit ($n/N = 78/80$)	5 ± 1 unit ($n/N = 43/44$)	NR	
Clinical importance 3			Clinical relevance 3		

EXTERNAL VALIDITY
Generalisability The study examines the same target population as the proposed guidelines. However, the study examined efficacy of an existing MTP. This may reduce the generalisability of the results because a control group was not used, rendering it difficult to quantify results gained
Applicability The benefits outweigh the harms for a critically bleeding population
Comments Due to its retrospective and non-comparative nature, and given that this study aimed to justify MTP use, results should be treated with caution when applied to a critically bleeding population. The absence of a comparator makes interpreting any clinical advantage of implementing and meeting the protocol difficult

STUDY DETAILS					
Reference Gunter et al (2008) ²³					
Affiliation/Source of funds Vanderbilt University School of Medicine, Tennessee Valley VA Medical Center. The source of funding was not reported					
Study design Cohort study/retrospective		Level of evidence III-2		Location/setting USA / Hospital	
Intervention TEP activation group, sample size: $n = 118$. Patients were further compared according to who received: an FFP and RBC transfusion ratio of $> 2:3$ to $< 2:3$, sample size $n = 64$ vs $n = 195$; platelet and RBC transfusion ratio of $> 1:5$ vs $< 1:5$, sample size $n = 63$ vs $n = 196$			Comparator Pre-TEP group, sample size: $n = 140$		
Population characteristics Demographic comparisons were made between patients who did/did not receive TEP. The following were significantly different between the two groups: Penetrating injuries (%)—higher in the pre-TEP group; median TRISS—higher in the pre-TEP group					
Length of follow-up 30 days			Outcomes measured Morbidity/mortality		
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding analysis	Treatment / measurement bias	Follow-up (ITT)	
Not reported	30 day survival was higher in the TEP group ($p = 0.02$)	No blinding	Not an RCT	30 days	
Overall quality assessment (descriptive) Retrospective nature of the study and lack of true comparison means that overall the study will always be considered lower level limiting the conclusions that can be drawn. However due to the critical patients involved studies are limited to how they can be met by patient need in a trauma setting					
RESULTS					
30 day mortality (FFP:RBC)					
Author	Ratio				Statistical significance
	FFP:RBC $< 1:1$, % of patients (N)	FFP:RBC $\geq 1:1$, % of patients (N)	FFP:RBC $< 2:3$, % of patients (N)	FFP:RBC $\geq 2:3$, % of patients (N)	
Gunter et al (2008) ²³	NR	NR	62 (195)	41 (64)	$p = 0.008$
Gunter et al (2008) ²³	57 (214)	49 (45)	NR	NR	$p = 0.32$
<i>Ratio of FFP:RBC as an independent predictor of mortality</i>					

Author	Measure	Ratio	Mortality, % of patients	Statistical significance
Gunter et al (2008) ²³	Ratio of FFP:RBC with the lowest mortality at 30 days	1:1.5–1:1.01	36	$p < 0.001$
Gunter et al (2008) ²³	Independent predictor of mortality at 30 days	NA	NA	OR = 1.78 (95%CI: [1.01, 3.14])
30 day mortality (PLT:RBC)				
Author	PLT:RBC < 1:5, % of patients (N)	PLT:RBC ≥ 1:5, % of patients (N)	Statistical significance	
Gunter et al (2008) ²³	61 (196)	38 (63)	$p = 0.001$	
Blood component ratios				
Author	Measure	MTP	No MTP	Statistical significance
Gunter et al (2008) ²³	PLT:RBC, intra-operative, median (IQR)	0.12 (0.03–0.25)	0.0 (0–0.11)	$p < 0.01$
Gunter et al (2008) ²³	PLT:RBC, 24 h, median (IQR)	0.14 (0.06–0.25)	0.25 (0.04–0.50)	$p < 0.01$
Gunter et al (2008) ²³	% Reaching a PLT:RBC ratio of 1:5 intra-operatively (N)	63 (119)	42 (140)	$p < 0.01$
Gunter et al (2008) ²³	% Reaching a PLT:RBC ratio of ≥ 1:5 at 24 h (N)	58 (119)	37 (140)	$p < 0.01$
Any other adverse events: NR				
		Clinical importance 2	Clinical relevance 1	
EXTERNAL VALIDITY				
Generalisability Generally, the study is concerned with trauma patients who require transfusion practices, and so are very similar to the demographic to which these guidelines pertain				
Applicability Because these patients were mainly critical trauma patients, it is likely that most would die without some form of intervention, so benefits would nearly always outweigh the potential harms				

STUDY DETAILS					
Reference Holcomb et al (2008) ³⁶					
Affiliation/Source of funds United States Army Institute of Surgical Research, Department of Epidemiology and Biostatistics at the University of Texas Health Science Center/Source of funding not reported					
Study design Case-series or cross sectional study/retrospective chart review		Level of evidence IV		Location/setting USA / Hospital	
Intervention ≥ 10 units RBC, 24 hours, sample size $n = 466$				Comparator No comparator	
<p>Population characteristics All patients given ≥ 10 units RBC in > 24 hours. The baseline characteristics varied by treatment centre (there were 16 treatment centres in total). The differences in demographic information between centres were not reported</p> <p>Patients were analysed in 4 different groups:</p> <p>High plasma:high platelets ($n = 151$)</p> <p>High plasma:low platelets ($n = 101$)</p> <p>Low plasma:high platelets ($n = 83$)</p> <p>Low plasma:low platelets ($n = 131$)</p>					
Length of follow-up NA		Outcomes measured Morbidity/mortality, dose/type of transfusion			
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding analysis	Treatment/ measurement bias		Follow-up (ITT)
Not applicable	Baseline recordings for the four comparison groups were significantly different for the following: Admission blood pressure, base deficit and GCS	Not blinded	Patients were treated very differently in each centre, depending on the centre's method of treating massive transfusion patients		Not applicable
<p>Overall quality assessment (descriptive) The differences in treatment at different centres may result in treatment bias. Some patients were treated with a massive transfusion protocol, others were not. Patients treated in different centres baseline results and post treatment results were pooled</p>					
RESULTS					
Overall mortality stratified by FFP and PLT:RBC ratio (%)					
Author	FFP & PLT: RBC ratio				p-value
	1) High FFP: ≥ 1:2 & high PLT: ≥ 1:2 ($n = 151$)	2) High FFP: ≥ 1:2 & low: < 1:2 PLT ($n = 101$)	3) Low FFP: < 1:2 & high PLT: ≥ 1:2 ($n = 83$)	4) Low FFP: < 1:2 & low PLT: < 1:2 ($n = 131$)	
Holcomb et al (2008) ³⁶	29	48	38	59	$p < 0.001$
Mortality at 6 hours					
Mortality at 6 hours stratified by FFP:RBC ratio (%)					

Author	FFP:RBC ratio				p-value
	1) High FFP: \geq 1:2 & high PLT: \geq 1:2 (n = 151)	2) High FFP: \geq 1:2 & low: < 1:2 PLT (n = 101)	3) Low FFP: < 1:2 & high PLT: \geq 1:2 (n = 83)	4) Low FFP: < 1:2 & low PLT: < 1:2 (n = 131)	
Holcomb et al (2008) ³⁶	2	14	17	42	$p < 0.001$
Mortality at 24 hours					
Mortality at 24 hours stratified by FFP:RBC ratio (%)					
Author	1) High FFP: \geq 1:2 & high PLT: \geq 1:2 (n = 151)	2) High FFP: \geq 1:2 & low: < 1:2 PLT (n = 101)	3) Low FFP: < 1:2 & high PLT: \geq 1:2 (n = 83)	4) Low FFP: < 1:2 & low PLT: < 1:2 (n = 131)	p-value
Holcomb et al (2008) ³⁶	13	25	23	50	$p < 0.001$
Mortality at 30 days					
Mortality at 30 days stratified by PLT:RBC ratio (%)					
Author	PLT:RBC ratio				p-value
	High: \geq 1:2 (n = 234)		Low: < 1:2 (n = 232)		
Holcomb et al (2008) ³⁶	59.9		40.1		$p < 0.01$
Mortality at 30 days stratified by FFP & PLT: RBC ratio (%)					
Author	FFP & PLT: RBC ratio				p-value
	1) High FFP: \geq 1:2 & high PLT: \geq 1:2 (n = 151)	2) High FFP: \geq 1:2 & low: < 1:2 PLT (n = 101)	3) Low FFP: < 1:2 & high PLT: \geq 1:2 (n = 83)	4) Low FFP: < 1:2 & low PLT: < 1:2 (n = 131)	
Holcomb et al (2008) ³⁶	27	46	33	57	$p < 0.001$
Mortality associated with haemorrhage stratified by ratio of FFP & PLT to RBC (%)					
Author	Ratio of FFP & PLT: RBC				p-value
	1) High FFP: \geq 1:2 & high PLT: \geq 1:2 (n = 151)	2) High FFP: \geq 1:2 & low: < 1:2 PLT (n = 101)	3) Low FFP: < 1:2 & high PLT: \geq 1:2 (n = 83)	4) Low FFP: < 1:2 & low PLT: < 1:2 (n = 131)	
Holcomb et al (2008) ³⁶	10	25	22	44	$p < 0.001$

Median time to death stratified by product component ratio (h)					
Author	FFP & PLT: RBC ratio				p-value
	1) High FFP: ≥ 1:2 & high PLT: ≥ 1:2 (n = 151)	2) High FFP: ≥ 1:2 & low: < 1:2 PLT (n = 101)	3) Low FFP: < 1:2 & high PLT: ≥ 1:2 (n = 83)	4) Low FFP: < 1:2 & low PLT: < 1:2 (n = 131)	
Holcomb et al (2008) ³⁶	35	18	6	4	p < 0.001
Transfusion requirements by plasma and platelet ratios (mean units ± SD)					
Author	FFP & PLT:RBC ratio				p-value
	1) High FFP: ≥ 1:2 & high PLT: ≥ 1:2 (n = 151)	2) High FFP: ≥ 1:2 & low: < 1:2 PLT (n = 101)	3) Low FFP: < 1:2 & high PLT: ≥ 1:2 (n = 83)	4) Low FFP: < 1:2 & low PLT: < 1:2 (n = 131)	
FFP					
Holcomb et al (2008) ³⁶	17 ± 12	16 ± 10	7 ± 5	6 ± 6	p < 0.001
PLT					
Holcomb et al (2008) ³⁶	20 ± 16	5 ± 6	18 ± 10	4 ± 6	p < 0.001
RBC					
Holcomb et al (2008) ³⁶	22 ± 17	21 ± 12	21 ± 11	21 ± 12	NS
Crystalloid					
Holcomb et al (2008) ³⁶	14 ± 10	13 ± 7	17 ± 12	11 ± 10	p < 0.001
FFP:RBC ratio					
Holcomb et al (2008) ³⁶	0.8 ± 0.3	0.8 ± 0.3	0.3 ± 0.1	0.2 ± 0.1	p < 0.001
PLT:RBC ratio					
Holcomb et al (2008) ³⁶	0.9 ± 0.4	0.2 ± 0.2	0.9 ± 0.4	0.1 ± 0.2	p < 0.001
Crystalloid: RBC ratio					
Holcomb et al (2008) ³⁶	0.8 ± 0.5	0.8 ± 0.6	0.9 ± 0.6	0.6 ± 0.5	p < 0.001
	Clinical importance 2		Clinical relevance 1		
Other adverse events reported Hospital free days were reported to be significantly lower for patients receiving a low platelet ratio, but any level of FFP (p < 0.001), Significantly lower numbers of ICU-free days (p < 0.001) and significantly fewer ventilator-free days (p < 0.001). The least number of ventilator-free days was recorded for the high plasma, low platelet ratio group					

EXTERNAL VALIDITY
Generalisability The patient population studied was equivalent to the patient population that will be targeted by the guideline for critical bleeding management
Applicability The benefits gained from the research will outweigh the harms and thus, for the critical bleed population, provide potential advancement in treatment regimens

STUDY DETAILS					
Reference Kashuk et al (2008) ³⁷					
Affiliation/Source of funds Denver Health Medical Center, Denver Health Sciences Center/Not reported					
Study design Case-series or cross sectional study/retrospective chart review			Level of evidence IV		Location/setting USA / Hospital
Intervention ≥ 10 units RBC in < 6 hours, sample size <i>n</i> = 133			Comparator No comparator		
<p>Population characteristics All patients who had received ≥ 10 units RBC in < 6 hours were eligible for entry into the study. Comparison groups were formed on the basis of FFP:RBC ratios received by each patient. Five comparison groups were formed: 1:1, 1:2, 1:3, 1:4 and 1:5</p> <p>Baseline characteristics across the different groups were compared, with differences noted in pH, temperature, INR at 6 hours, FFP and PLT transfusion at 6 and 24 hours, RBC, FFP and PLT administered from 7 to 24 hours, crystalloids administered at 24 hours and survival in hours. These differences became less apparent when the ratios 1:1 to 1:3 are compared with 1:4 and greater</p>					
Length of follow-up NA		Outcomes measured Morbidity/mortality, dose/type of transfusion, transfusion frequency			
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding analysis	Treatment / measurement bias	Follow-up (ITT)	
Not applicable	See above	Not blinded	Patients were treated the same	Not applicable	
Overall quality assessment (descriptive) Quality study that has some limitations due to its retrospective nature and lack of control groups. The inherent difficulties of performing prospective controlled trials in critical bleeding; however, make the findings of this study relevant to the broader critical bleed population					
RESULTS					
Odds ratio associated with volume of RBC transfused at 6 hours					
Author	Blood component	6 hours	OR	p-value	
Kashuk et al (2008) ³⁷	RBC	1.038–1.505	1.248	NR	
Median ratio for survival, median (UQ-LQ)					
Author	Blood component ratio	Survivors (<i>n</i> = NR)	Non-survivors (<i>n</i> = NR)	p-value	
Kashuk et al (2008) ³⁷	FFP:RBC	1:2 (1:2-1:3)	1:4 (1:2-1:5)	NR	
% of units of PRBC given at different time periods					
Author	First 6 hours	First 12 hours	First 24 hours	Next 24 hours	> 48 hours
Kashuk et al (2008) ³⁷	> 80%	NR	NR	NR	NR

Median and mean units of blood components administered at different time points					
Author	Blood component ratio	Total	First 6 hours	First 12 hours	First 24 hours
Kashuk et al (2008) ³⁷	RBC median (range) (n = 133)	NR	18 (14–25)	NR	21 (15–30)
Kashuk et al (2008) ³⁷	FFP median (range) (n = 133)	NR	6 (4–10)	NR	8 (4–14)
Kashuk et al (2008) ³⁷	PLT median (range) (n = 133)	NR	1 (0–2)	NR	1 (1–3)
Kashuk et al (2008) ³⁷	Crystalloids median (range) (n = 133)	NR	NR	NR	14,000 (7,000–19,500)
Kashuk et al (2008) ³⁷	FFP:RBC ratio (n = 133)	NR	3 (2-5)	NR	14 (2–21)
Units transfused by ratio of FFP:RBC at different times (median)					
Author	Ratio of FFP:RBC				
	1:1 (n = 11)	1:2 (n = 48)	1:3 (n = 27)	1:4 (n = 12)	> 1:5 (n = 35)
RBC units transfused to 6 hours (median)					
Kashuk et al (2008) ³⁷	18	17	20	23.5	18
RBC units transfused between 7 and 24 hours (median)					
Kashuk et al (2008) ³⁷	5	0	0	0	0
RBC units transfused to 24 hours (median)					
Kashuk et al (2008) ³⁷	23	21.5	20	24	18
FFP units transfused to 6 hours (median)					
Kashuk et al (2008) ³⁷	15	8	6	6	2
FFP units transfused between 7 and 24 hours (median)					
Kashuk et al (2008) ³⁷	7	0	0	0	0
FFP units transfused to 24 hours (median)					
Kashuk et al (2008) ³⁷	22	12	8	6	2
PLT units transferred to 6 hours (median)					
Kashuk et al (2008) ³⁷	2	1.6	1	1	0

PLT units transfused between 7 and 24 hours (median)					
Kashuk et al (2008) ³⁷	1	0	0	0	0
Crystalloid units transfused to 24 hours (median)					
Kashuk et al (2008) ³⁷	14,250	16,000	16,750	12,000	8,000
Survival at 24 hours (%)					
Kashuk et al (2008) ³⁷	72	6.9	10	1.5	1.8
Other adverse events reported: NR					
	Clinical importance: 2			Clinical relevance: 1	
EXTERNAL VALIDITY					
Generalisability The population studied was civilian and all patients requiring a massive transfusion. This is equivalent to the patient population targeted by the blood management guidelines					
Applicability The benefits afforded by this study far outweigh any harms					

STUDY DETAILS				
Reference Maegele et al (2008) ³⁸				
Affiliation/Source of funds NR				
Study design Case-series or cross sectional study/retrospective chart review		Level of evidence IV	Location/setting Germany/ Hospital	
Intervention ≥ 10 units RBC in 24 hours, sample size <i>n</i> = 713			Comparator No comparator	
Population characteristics The patient population was stratified by the ratio of RBC/ FFP transfusion received into three groups: RBC:FFP > 1:1 (<i>n</i> = 484) RBC:FFP 0.9–1:1 (<i>n</i> = 114) RBC:FFP < 0.9 (<i>n</i> = 115) No significant differences between the baseline characteristics of patients in the different groups were observed				
Length of follow-up NA			Outcomes measured Morbidity/mortality	
INTERNAL VALIDITY				
Allocation	Study group comparison:	Blinding analysis	Treatment/ measurement bias	Follow-up (ITT)
Not applicable	See above	Not blinded	Patients were treated the same	Not applicable
Overall quality assessment (descriptive) A retrospective analysis comparing the results of a large pool of patients across three stratified patient pools. The quality of the study was reasonable				
RESULTS				
Mortality at 6 hours				
Mortality at 6 hours stratified by FFP:RBC ratio (%)				
Author	High ratio: > 1:1 (<i>n</i> = 484)	Medium ratio: 0.9-1.1 (<i>n</i> = 114)	Low ratio: < 0.9 (<i>n</i> = 115)	p-value
Maegele et al (2008) ³⁸	24.6	9.6	3.5	<i>p</i> < 0.0001
Mortality at 24 hours				
Mortality at 24 hours stratified by FFP:RBC ratio (%)				
Author	High ratio: > 1:1 (<i>n</i> = 484)	Medium ratio: 0.9-1.1 (<i>n</i> = 114)	Low ratio: < 0.9 (<i>n</i> = 115)	p-value
Maegele et al (2008) ³⁸	32.6	16.7	11.3	<i>p</i> < 0.005
In hospital mortality				
In hospital mortality stratified by FFP:RBC ratio (%)				
Author	High ratio: > 1:1 (<i>n</i> = 484)	Medium ratio: 0.9-1.1 (<i>n</i> = 114)	Low ratio: < 0.9 (<i>n</i> = 115)	p-value
Maegele et al (2008) ³⁸	45.9	36	30.4	<i>p</i> < 0.005

<i>Mortality at 30 days stratified by FFP: RBC ratio (%)</i>					
Author	Product ratio	RBC:FFP ratio			p-value
		High ratio: > 1:1 (n = 484)	Medium ratio: 0.9-1.1 (n = 114)	Low ratio: < 0.9 (n = 115)	
Maegele et al (2008) ³⁸	RBC:FFP	45.5	35.1	24.3	p < 0.005
Transfusion requirements by RBC and FFP ratios					
Author	Blood component	Ratio RBC:FFP			p-value
		High ratio: > 1:1 (n = 484)	Medium ratio: 0.9-1.1 (n = 114)	Low ratio: < 0.9 (n = 115)	
Maegele et al (2008) ³⁸	RBC (mean units [SD])	20.3 (11.8)	17.9 (10.9)	17.3 (10.7)	p < 0.05
Maegele et al (2008) ³⁸	FFP (units) (mean units [SD])	10.7 (8.3)	17.7 (10.4)	26 (14.9)	p < 0.005
Other adverse events reported: The frequency for septic complications and organ failure was higher in the RBC:FFP 0.9–1:1 group, ventilator days and length of stay for the intensive care unit and overall in hospital were highest in the RBC:FFP ratio group < 0.9 (p < 0.0005)					
		Clinical importance 2		Clinical relevance 1	
EXTERNAL VALIDITY					
Generalisability The study population is comparable to the target population of the blood management guidelines- all adults in the civilian population who require a massive transfusion					
Applicability The benefits of massive transfusion using a ratio of FFP:RBC 1:1 outweigh the risks associated with the higher ratio					

STUDY DETAILS				
Reference McLaughlin et al (2008) ²⁸				
Affiliation/Source of funds United States Institute of Surgical Research, Walter Reed Army Institute of Research, Walter Reed Army Medical Center. Source of funds not reported				
Study design Cohort study/retrospective cohort study		Level of evidence III-3		Location/setting USA / Military
Intervention MT ≥ 10 units, 24 hours, sample size $n = 80$			Comparator No MT < 10 units, 24 hours, sample size $n = 222$	
Population characteristics The MT group had higher ISS ($p < 0.001$), and in-hospital mortality ($p < 0.001$) compared with the non-MT patients				
Length of follow-up NA			Outcomes measured Morbidity/mortality, dose/type of transfusion	
INTERNAL VALIDITY				
Allocation	Comparison of study group	Blinding analysis	Treatment measurement bias	Follow-up (ITT)
No applicable	See above	Not blinded	Both groups of patients were treated equally	Not reported.
Overall quality assessment (descriptive) The study was well designed for a non-randomised, non-controlled study. However limited patient numbers and its retrospective nature limit the value of its findings				
RESULTS				
Mortality				
Author	Outcome	Survivors	Non-survivors	p-value
McLaughlin et al (2008) ²⁸	Mortality in hospital, % of patients (N)	29 (80)	7 (222)	$p < 0.001$
Other adverse events: NR				
			Clinical importance 2	Clinical relevance 1
EXTERNAL VALIDITY				
Generalisability The study focussed on patients requiring a massive transfusion, which is the same as the group targeted by the guideline				
Applicability The potential benefits of the results of the study will outweigh potential harms				

STUDY DETAILS				
Reference Perkins et al (2009) ³⁹				
Affiliation/Source of funds Walter Reed/ Source of funds not reported				
Study design Case-series or cross sectional study /retrospective chart review	Level of evidence IV		Location/setting Iraq / Military	
Comparator ≥ 10 units RBC in 24 hours, sample size: see population characteristics below.			Comparator No comparator	
<p>Population characteristics All patients receiving ≥ 10 units RBC but not fresh whole blood were included in the study population. The group was divided into subgroups defined by the source of platelets:</p> <ol style="list-style-type: none"> 1. patients who received an aPLT:RBC ratio of < 1:16 (low) <i>n</i> = 214 2. patients who received an aPLT:RBC ratio 1:16 - < 1:8 (medium) <i>n</i> = 154 3. patients who received an aPLT:RBC ratio ≥ 1:8 (high) <i>n</i> = 96 				
Length of follow-up 30 days		Outcomes measured Morbidity/mortality, dose/type of transfusion		
INTERNAL VALIDITY				
Allocation	Results measurement bias	Blinding analysis	Treatment/ measurement bias	Follow-up (ITT)
Not applicable	No significant differences in the population demographics were found between comparison groups	Not blinded	Patients were treated equally	Not applicable
<p>Overall quality assessment (descriptive) The study was of reasonable quality given that it was retrospective and non-comparative. Results should be interpreted with caution. However, univariate and multivariate analysis was performed to remove confounding factors, improving certainty in the results</p>				
RESULTS				
Univariate regression of variables associated with mortality at 24 hours				
Author	Component	OR	95%CI	p-value
Perkins et al (2009) ³⁹	Stored RBC	1.04	(1.02, 1.07)	<i>p</i> < 0.001
Perkins et al (2009) ³⁹	Cryoprecipitate	0.96	(0.93, 0.99)	<i>p</i> = 0.01
Multivariate regression of variables associated with mortality at 24 hours				
Author	Blood component	HR	95%CI	p-value
Perkins et al (2009) ³⁹	Cryoprecipitate	0.93	(0.87, 0.997)	<i>p</i> = 0.04
Perkins et al (2009) ³⁹	Stored RBC	1.08	(1.004, 1.16)	<i>p</i> = 0.04

Univariate regression of variables associated with mortality at 30 days				
Author	Blood component	OR	95%CI	p-value
Perkins et al (2009) ³⁹	Stored RBC	1.02	(1.01, 1.04)	$p = 0.001$
Perkins et al (2009) ³⁹	Cryoprecipitate	0.97	(0.95, 0.996)	$p = 0.02$
Multivariate regression of variables associated with mortality at 30 days				
Author	Component or ratio	HR	95%CI	p-value
Perkins et al (2009) ³⁹	Cryoprecipitate	0.97	(0.94, 1.003)	$p = 0.07$
Perkins et al (2009) ³⁹	Stored RBC	1.03	(0.996, 1.07)	$p = 0.08$
Mortality At 24 hours stratified by aPLT:RBC ratio (%)				
Author	High ratio: $\geq 1:8$ ($n = 96$)	Medium ratio: 1:16– < 1:8 ($n = 154$)	Low ratio: < 1:16 ($n = 214$)	p-value
Perkins et al (2009) ³⁹	5	13	36	$p = 0.04$ (medium vs high) and $p < 0.001$ (low vs medium vs high)
Univariate regression of variables associated with survival at 24 hours				
Author	Component	OR	95%CI	p-value
Perkins et al (2009) ³⁹	FFP:RBC	0.95	(0.94, 0.96)	$p < 0.001$
Perkins et al (2009) ³⁹	aPLT:RBC (%)	0.88	(0.84, 0.92)	$p < 0.001$
Multivariate regression—Mortality at 24 hours				
24 hours	Component or ratio	OR	95%CI	p-value
Perkins et al (2009) ³⁹	PLT:RBC (%)	0.94	(0.91, 0.96)	$p < 0.001$
Perkins et al (2009) ³⁹	aPLT:RBC (%)	0.82	(0.72, 0.93)	$p = 0.002$
Mortality at 30 days stratified by aPLT: RBC ratio (%)				
Author	High: $\geq 1:8$ ($N = 96$)	Medium: 1:16– < 1:8 ($N = 154$)	Low: < 1:16 ($n = 214$)	p-value
Perkins et al (2009) ³⁹	22	40	57	$p < 0.001$ (medium vs high) and $p < 0.001$ (low vs medium vs high)

Univariate regression of variables associated with mortality at 30 days					
Author	Component	OR	95%CI	p-value	
Perkins et al (2009) ³⁹	FFP:RBC (%)	0.97	(0.97, 0.98)	$p < 0.001$	
Perkins et al (2009) ³⁹	aPLT:RBC (%)	1.01	(0.98, 1.03)	$p < 0.001$	
Multivariate regression of variables associated with mortality at 30 days					
Author	Component or ratio	HR	95%CI	p-value	
Perkins et al (2009) ³⁹	FFP:RBC (%)	0.98	(0.97, 0.99)	$p = 0.01$	
Perkins et al (2009) ³⁹	aPLT:RBC (%)	0.91	(0.86, 0.95)	$p < 0.001$	
Cause of death: haemorrhage stratified by ratio of aPLT to RBC (%)					
Author	Ratio of aPLT: RBC			p-value	
	High ratio: $\geq 1:8$ ($n = 96$)	Medium ratio: $1:16 - < 1:8$ ($n = 154$)	Low ratio: $< 1:16$ ($n = 214$)		
Perkins et al (2009) ³⁹	2.1	8.6	28.6	$p = 0.04$ (medium vs high) and $p < 0.001$ (low vs medium vs high)	
Median time to death stratified by product component ratio (h)					
Author	Blood component ratio	aPLT:RBC ratio			p-value
		High: $\geq 1:8$ ($N = 96$)	Medium: $1:16 - < 1:8$ ($N = 154$)	Low: $< 1:16$ ($n = 214$)	
Perkins et al (2009) ³⁹	aPLT:RBC	80.2	7.6	2.3	$p < 0.001$
Transfusion requirements by RBC and FFP ratios					
Author	Blood product	Ratio of aPLT:RBC			p-value
		High ratio: $\geq 1:8$ ($n = 96$)	Medium ratio: $1:16 - < 1:8$ ($n = 154$)	Low ratio: $< 1:16$ ($n = 214$)	
Perkins et al (2009) ³⁹	RBC (median units (range))	20 (10–54)	17 (10–58)	14 (10–56)	$p < 0.001$
Perkins et al (2009) ³⁹	aPLT (median units (range))	3 (2–9)	2 (1–6)	0 (0–3)	$p < 0.001$

Perkins et al (2009) ³⁹	FFP (median units [range])	14 (4–42)	12 (4–32)	7 (0–37)	$p < 0.001$
Perkins et al (2009) ³⁹	Cryoprecipitate (median units [range])	10 (0–50)	10 (0–52)	0 (0–38)	$p < 0.001$
Perkins et al (2009) ³⁹	Plasma ratio (%±SD)	74 (±22)	71±24	49 ± 32	$p < 0.001$
Other adverse events reported Adverse events were similar between study groups					
	Clinical importance 2		Clinical relevance 1		
EXTERNAL VALIDITY					
Generalisability Patients studied were similar to the target population of the critical bleeding blood management guideline, all adults requiring a massive transfusion					
Applicability The benefits reported of using a ratio of 1:8 aPLT:RBC in massive transfusion far outweigh the risks					

STUDY DETAILS				
Reference Phillips et al (1987) ⁴⁰				
Affiliation/Source of funds Detroit Receiving Hospital/ Source of funding not reported				
Study design Case-series or cross sectional study/ retrospective chart review		Level of evidence IV		Location/setting USA/Hospital
Intervention > 21 units RBC in 24 hours, sample size $n = 56$				Comparator No comparator
Population characteristics All patients transfused with > 21 units RBC in 24 hours. Most patients had sustained penetrating trauma				
Length of follow-up NR			Outcomes measured Morbidity/mortality	
INTERNAL VALIDITY				
Allocation	Comparison of study groups	Blinding analysis	Treatment / measurement bias	Follow-up (ITT)
Not applicable	Not applicable	Not blinded	Patients were treated equally	Not applicable
Overall quality assessment (descriptive) The study examined a very small patient population, and therefore, must be treated with caution				
RESULTS				
Mortality rate associated with RBC transfusion				
Phillips et al (1987) ⁴⁰	Time period	Units (mean)	Mortality (%)	p-value
	Hospitalisation	33	61	NR
Other adverse events				
			Clinical importance: 3	Clinical relevance: 2
EXTERNAL VALIDITY				
Generalisability The population studied was equivalent to the population targeted by the critical bleed patient management guidelines				
Applicability The study focussed on perioperative outcomes as well as massive transfusion. The benefits identified in the study outweigh the harms				
Comments This study contributes little to the development of guidelines				

STUDY DETAILS				
Reference Rose et al (2009) ⁴¹				
Affiliation/Source of funds St James's University Hospital/NR				
Study design Case-series or cross sectional study/retrospective chart review		Level of evidence IV	Location/setting UK/Hospital	
Intervention ≥ 8 units RBC in 24 hours, sample size $n = 204$			Comparator No comparator	
Population characteristics No significant difference, except when comparing those who died with survivors. These populations varied in age (died: 65, survived: 58, $p < 0.02$) and lower creatinine levels ($p < 0.001$)				
Length of follow-up NA		Outcomes measured Morbidity/mortality, dose/type of transfusion		
INTERNAL VALIDITY				
Allocation	Comparison of study groups	Blinding analysis	Treatment/ measurement bias	Follow-up (ITT)
Not applicable	Not applicable	Not blinded	Not applicable	Not applicable
Overall quality assessment (descriptive) The population studied was quite large. A lower transfusion threshold of 8 units in 24 hours was used; however, the study was included. The study is a retrospective case series review so findings must be treated with caution				
RESULTS				
Median blood components used per massive transfusion				
Author	Blood component	Survivors ($n = 134$)	Non-survivors ($n = 70$)	p-value
Rose et al (2009) ⁴¹	RBC units (median, IQR, range)	10, 8–13, 8–42	12, 10–20, 8–61	NR
Rose et al (2009) ⁴¹	FFP units (median, IQR, range)	7, 4–11, 0–36	8, 6–12, 0–40	NR
Rose et al (2009) ⁴¹	PLT units (median, IQR, range)	1, 0–2, 0–8	2, 1–4, 0–12	NR
Rose et al (2009) ⁴¹	Cryoprecipitate units (median, IQR, range)	0, 0–5, 0–30	0, 0–10, 0–40	NR
Factors associated with in-hospital survival				
Author	Component or ratio	OR	95%CI	p-value
Rose et al (2009) ⁴¹	FFP:RBC ratio > 1.1	7.22	(1.95, 26.68)	$p = 0.0031$
Factors associated with in-hospital mortality				
Author	Component or ratio	OR	95%CI	p-value
Rose et al (2009) ⁴¹	Units of platelets	0.69	(0.57, 0.83)	$p = 0.0001$
Ratios of blood components used per massive transfusion				
Author		Survivors ($n = 134$)	Non-survivors ($n = 70$)	p-value
Rose et al (2009) ⁴¹	FFP:RBC units (median, IQR, range)	0.54, 0.40–0.89, 0.00–1.80	0.62, 0.44–0.87, 0.00–1.78	NR
Rose et al (2009) ⁴¹	PLT:RBC units (median, IQR, range)	0.41, 0.00–0.80, 0.00–2.66	0.53, 0.35–0.99, 0.00–2.40	NR

Rose et al (2009) ⁴¹	Cryoprecipitate:RBC units (median, IQR, range)	0.00, 0.00–0.48, 0.00–2.31	0.00, 0.00–0.56, 0.00–2.05	NR
Other adverse events NR				
		Clinical importance 2	Clinical relevance 1	
EXTERNAL VALIDITY				
Generalisability The population studied was equivalent to the population targeted by the patient blood management guidelines. The patient population was large and the products used are all available in the Australian setting. The study was performed in the UK				
Applicability The benefits associated with increasing the ratio of FFP:RBC in patients requiring massive transfusion were found to outweigh the risks				

STUDY DETAILS				
Reference Scalea et al (2008) ⁴²				
Affiliation/Source of funds: University of Maryland School of Medicine. Partially funded by NIH grant 1T32GM075767				
Study design Case-series or cross sectional study/retrospective chart review			Level of evidence IV	Location/setting USA / Hospital
Intervention ≥ 10 units RBC in 24 hours, sample size $n = 81$ (massive transfusion subgroup analysis)			Comparator No comparator	
Population characteristics 81 patients were identified who required ≥ 10 units RBC and FFP within 24 hours				
Length of follow-up NR			Outcomes measured Morbidity/mortality	
INTERNAL VALIDITY				
Allocation	Results measurement bias	Blinding analysis	Treatment / measurement bias	Follow-up (ITT)
Not reported	Not applicable	Not blinded	Not applicable	Not applicable
Overall quality assessment (descriptive) Only a small amount of data was reported on patients who received a massive transfusion. A regression analysis was performed on the group to show individual factors affecting morbidity and mortality. Thus, the quality of the study was fairly poor for the massively transfused population				
RESULTS				
Factors associated with in-hospital survival				
Author	Component or ratio	OR	95%CI	p-value
Scalea et al (2008) ⁴²	FFP:RBC—1:1 (continuous variable)	1.49	(0.63, 3.53)	NS
Scalea et al (2008) ⁴²	FFP:RBC—1:1 (binary variable)	0.60	(0.21, 1.75)	NS
Other adverse events: No significant relationship was reported for FFP:RBC ratio of 1:1 and length of hospital or ICU stay				
Clinical importance: 2			Clinical relevance: 2	
EXTERNAL VALIDITY				
Generalisability The population studied was comparable to the study population targeted by the blood management guidelines. Little information was provided on the baseline characteristics of those patients receiving a massive transfusion				
Applicability No significant effect on mortality with an FFP:RBC ratio of 1:1 was found. However, no harms were associated with the same ratio				
Comments This study shows no significant harms or benefits associated with a higher ratio of FFP:RBC. However, some bias may have been introduced because the study examined only patients who survived long enough to get to the ICU and excluded all others				

STUDY DETAILS				
Reference Schreiber et al (2007) ²⁹				
Affiliation/Source of funds Oregon Health and Science University, Walter Reed Army Medical Center, United States Army Institute of Surgical Research/Not reported				
Study design Cohort study/retrospective		Level of evidence III-3		Location/setting Iraq/Military
Intervention MT, > 10 units blood 24 hours, sample size $n = 247$		Comparator No MT, < 10 units of blood 24 hours, sample size $n = 311$		
Population characteristics Both study groups differed significantly at baseline regarding: Trauma due to a blunt mechanism was significantly higher in the no MT group ($p < 0.001$), INR was significantly lower in the no MT group ($p < 0.001$), prothrombin and prothrombin time were significantly higher in the MT population, HgB was significantly higher in the no MT group ($p < 0.001$) and platelet levels were significantly higher in the no MT group ($p < 0.001$)				
Length of follow-up NA		Outcomes measured Morbidity/mortality, dose/type of transfusion		
INTERNAL VALIDITY				
Allocation	Comparison of study groups	Blinding analysis	Treatment / Measurement bias	Follow-up (ITT)
Not applicable	See above	Not blinded	Both groups were treated the same	Not applicable
Overall quality assessment (descriptive) The study has several limitations—it is a retrospective analysis that was limited by the data available in a combat setting. The study design was good for a non-randomised, non-controlled trial. Some confounding factors were accounted for in univariate and multivariate analysis				
RESULTS				
Author	Measure	MT	No MT	Statistical significance
Mean RBC units transfused				
Schreiber et al (2007) ²⁹	Mean RBC units (N)	17.9 (247)	1.1 (311)	$p < 0.001$
Mortality				
Schreiber et al (2007) ²⁹	Survival to discharge, % (N)	61 (247)	99	$p = 0.001$
Average units of blood components transfused				
Schreiber et al (2007) ²⁹	RBC (units), % of patients (N)	17.9 (247)	1.1 (311)	$p < 0.001$
Blood component ratios				
Schreiber et al (2007) ²⁹	RBC:FFP (N)	3:2 (247)	NR	NR
Schreiber et al (2007) ²⁹	RBC:PLT (N)	6:1 (247)	NR	NR
Schreiber et al (2007) ²⁹	RBC:Cryo (N)	2:1 (247)	NR	NR
Clinical importance: 2			Clinical relevance: 1	

EXTERNAL VALIDITY
Generalisability The study was conducted in a military setting, and hence, the patient population could differ greatly from critically bleeding civilian patients in the pattern, cause and severity of injury. However, given the difficulty in studying critical bleed patients who require massive transfusion, the data are valid
Applicability The potential benefits of the outcomes of the study outweigh the potential harms

STUDY DETAILS				
Reference Schwab et al (1986) ⁴³				
Affiliation/Source of funds Robert Wood Johnson Medical School, Staunton Medical Center/NR				
Study design		Level of evidence	Location/setting	
Case-series or cross sectional study/retrospective chart review		IV	USA/ Hospital	
Intervention		Comparator		
Massive transfusion (≥ 10 units RBC in 24 hours), sample size $n = 40$		No massive transfusion, sample size: $n = 44$		
Population characteristics Population characteristics were similar between groups with no significant differences observed				
Length of follow-up Not applicable			Outcomes measured Morbidity/mortality	
INTERNAL VALIDITY				
Allocation	Study group comparison	Blinding analysis	Treatment/ measurement bias	Follow-up (ITT)
Not applicable	See above	Not blinded	Not applicable	Not applicable
Overall quality assessment (descriptive) Patients were similar to those targeted by the guidelines and there were no difference between patient demographics of those receiving massive transfusion vs no massive transfusion. However, little data was provided for the massive transfusion vs no massive transfusion comparison				
RESULTS				
The overall mortality for the MT group was 28%. The massive transfusion group used almost twice the RBC quantity as the non-MT group				
Adverse events reported: Not reported				
		Clinical importance: 3	Clinical relevance: 2	
EXTERNAL VALIDITY				
Generalisability Patients were equivalent to those targeted for development of the guidelines. However, insufficient data were presented on the outcomes of these patients compared to the overall study				
Applicability There were no real harms or benefits reported in the study in terms of massive transfusion vs no massive transfusion				
Comments This study is of very limited value				

STUDY DETAILS					
Reference Snyder et al (2009) ⁴⁴					
Affiliation/Source of funds University of Alabama-Birmingham/ funding not reported					
Study design		Level of evidence		Location/setting	
Case-series or cross sectional study / retrospective chart review		IV		USA/Hospital	
Intervention			Comparator		
≥ 10 units RBC in 24 hours, sample size $n = 134$			No comparator		
Population characteristics Mean age (of survivors) = 36.8 (64.2% male); mean age (of non-survivors) = 41.6 (77.6% male) Patients were compared between groups: High FFP:RBC ratio (> 1:2) Low FFP:RBC ratio (< 1:2)					
Length of follow-up NR			Outcomes measured Morbidity/mortality		
INTERNAL VALIDITY					
Allocation	Study group comparison	Blinding analysis	Treatment /measurement bias	Follow-up (ITT)	
Not applicable	Not reported	Not blinded	Groups treated equally	Not applicable	
Overall quality assessment (descriptive) The study is a retrospective chart review limiting the value of its findings. However, univariate and multivariate regressions were performed to account for some confounding factors, improving the validity of the study finding. Any conclusions could not be substantially supported					
RESULTS					
Median blood components used per massive transfusion					
Author	Blood component	Survivors ($n = 67$)	Non-survivors ($n = 67$)	p-value	
Snyder et al (2009) ⁴⁴	RBC (median)	15.0	18.5	NR	
Snyder et al (2009) ⁴⁴	FFP (median)	10.0	7.5	NR	
Snyder et al (2009) ⁴⁴	PLT (median)	2	2	NR	
Snyder et al (2009) ⁴⁴	Received cryoprecipitate (%)	56	33	NR	
% of units RBC given at different time periods					
Author	First 6 hours	First 12 hours	First 24 hours	Next 24 hours	> 48 hours
Snyder et al (2009) ⁴⁴	68%	92%	NR	NR	NR
Time to transfusion of first blood component (median minutes, range)					
Author	Blood component	Time median (range)		p-value	
Snyder et al (2009) ⁴⁴	RBC	18 (1–348)		NR	

Snyder et al (2009) ⁴⁴	FFP	93 (24–350)	NR	
Mortality				
Overall mortality stratified by FFP:RBC ratio (%)				
Author	FFP:RBC ratio		p-value	
	High ratio: $\geq 1:2$ ($n = 60$)	Low ratio: $< 1:2$ ($n = 74$)		
Snyder et al (2009) ⁴⁴ (24 hour cumulative)	40	58	$p < 0.001$	
Relative risk of mortality associated with a high vs low FFP:RBC ratio				
Author	Ratio definition (n)	RR	95%CI	p-value
Snyder et al (2009) ⁴⁴	High ratio: $\geq 1:2$ ($n = \text{NR}$) vs Low ratio: $< 1:2$ ($n = \text{NR}$)	0.84	0.47, 1.50	NR
Transfusion requirement based on ratio of FFP:RBC and timing—12 hours				
Author	Blood component ratio	High ratio: $N = 60$	Low ratio: $N = 74$	p-value
Snyder et al (2009) ⁴⁴	FFP:RBC (mean ratio \pm SD)	0.76 (1:1.3) ± 0.28	0.27 (1:3.7) ± 0.76	NR
Other adverse events: Not reported				
		Clinical importance: 2	Clinical relevance: 1	
EXTERNAL VALIDITY				
Generalisability Patients studied are equivalent to the population of patients targeted by the critical bleeding guidelines. The patient population is relatively small and there is no direct comparison, so the outcomes of the study must be interpreted with caution				
Applicability The benefits identified by the study outweigh the harms. The study questions the validity of higher ratios of FFP:RBC effect on mortality due to confounding factors associated with patient survival. Patients apparently surviving longer due to receiving a higher ratio of FFP: RBC may simply have survived long enough to receive more of these products compared to someone who died earlier, appearing that they have not received as high a ratio of FFP:RBC. The study accounts for the survival advantage and fails to find a survival advantage associated with a high ratio of FFP:RBC				
Comments The study questions the validity of existing studies due to the inherent survival bias allowed to affect the outcomes of retrospective chart review studies. Thus, the results of this study and many other retrospective studies need to be treated with caution				

STUDY DETAILS					
Reference Sperry et al (2008) ²⁰					
Affiliation/Source of funds University of Pittsburgh Medical Centre, University of Texas Southwestern Medical Center, Harbourview Medical Centre, University of Washington Seattle, Denver Health Medical Centre, University of Colorado Health Sciences Centre/Not reported					
Study design Case-series or cross sectional study/ retrospective chart review			Level of evidence IV	Location/setting USA /Hospital	
Intervention				Comparator	
≥ 8 units transfused in the first 12 hours of admission. Group was stratified into low vs high FFP:RBC groups, sample size $n = 415$				No comparator	
Population characteristics Demographics for the different low vs high FFP:RBC ratio groups was similar					
Length of follow-up NR		Outcomes measured Morbidity/mortality, dose/type of transfusion, transfusion frequency			
INTERNAL VALIDITY					
Allocation	Study group comparison	Blinding analysis	Treatment / Measurement bias	Follow-up (ITT)	
Not applicable	See above	Not blinded	Not applicable	Not applicable	
Overall quality assessment (descriptive) The study is limited by its design. As a retrospective, chart review, the results obtained in the study must be interpreted cautiously					
RESULTS					
Median and mean units of blood components administered at different time points					
Author	Blood component ratio	Total	First 6 hours	First 12 hours	First 24 hours
Sperry et al (2008) ²⁰	RBC (median units)	NR	NR	14	NR
Mortality at 24 hours					
Mortality at 24 hours stratified by FFP:RBC ratio (%)					
Author	High ratio ≥ 1:1.5 ($n = 102$)		Low ratio < 1:1.5 ($n = 313$)		p-value
Sperry et al (2008) ²⁰	3.9		12.8		$p = 0.0012$
Transfusion requirement based on ratio of FFP:RBC and timing—12 hours					
Author	Blood component (units)	Ratio of FFP:RBC		p-value	
		High ratio ≥ 1:1.5 ($n = 102$)	Low ratio < 1:1.5 ($n = 313$)		
Sperry et al (2008) ²⁰	RBC	14.3±7	20.5 ±15	$p = 0.001$	
Sperry et al (2008) ²⁰	FFP	14.0±7	6.8±7	$p = 0.001$	
Sperry et al (2008) ²⁰	Cryoprecipitate	3.2±4	2.0±4	$p = 0.006$	

Transfusion requirement based on ratio of FFP: RBC and timing—24 hours				
Author	Blood component (units)	Ratio of FFP:RBC		p-value
		High ratio \geq 1:1.5 (<i>n</i> = 102)	Low ratio < 1:1.5 (<i>n</i> = 313)	
Sperry et al (2008) ²⁰	RBC	16.0 \pm 9	22.0 \pm 17	<i>p</i> = 0.001
Sperry et al (2008) ²⁰	FFP	15.2 \pm 9	7.6 \pm 9	<i>p</i> = 0.001
Sperry et al (2008) ²⁰	Cryoprecipitate	3.3 \pm 4	2.3 \pm 4	<i>p</i> = 0.030
Adverse events reported A high FFP:RBC ratio was not associated with a higher risk of organ failure or nosocomial infection, however, was associated with an almost twofold higher risk of acute respiratory distress syndrome, after controlling for important confounders				
		Clinical importance: 2		Clinical relevance: 1
EXTERNAL VALIDITY				
Generalisability The group studied is equivalent to the patient population targeted by the guidelines. The study is focussed on patients with blunt trauma				
Applicability The benefits identified by the study far outweigh the harms in a critical bleeding population requiring massive transfusion				

STUDY DETAILS				
Reference Spinella et al (2008) ⁹				
Affiliation/Source of funds US Army Institute of Surgical Research, Connecticut Children's Medical Center, Brooke Army Medical Center, Madigan Army Medical Center. Source of funding not reported				
Study design Case-series or cross sectional study/retrospective		Level of evidence IV	Location/setting Iraq / Military	
Intervention ≥ 10 units RBC transfused in < 24 hours, sample size: <i>n</i> = 124			Comparator No comparator	
Population characteristics Most patients had penetrating wounds. Baseline characteristics were not reported				
Length of follow-up NA		Outcomes measured Dose/type of transfusion		
INTERNAL VALIDITY				
Allocation	Study group comparison	Blinding analysis	Treatment / measurement bias	Follow-up (ITT)
Not applicable	Not reported	Not blinded	All patients treated equally	Not applicable
Overall quality assessment (descriptive) The study assessed a small patient group and included the use of rFVIIa. Only results were reported which did not include rFVIIa, but this was difficult given the lack of reporting				
RESULTS				
Median total blood component usage at 24 hours, median (range)				
Author	Blood component	Survivor (<i>n</i> = 71)	Non-survivors (<i>n</i> = 19)	p-value
Spinella et al (2008) ⁹	Crystalloids (L)	11.6 (8.3–14)	9.8(7.6–12.1)	NS
Spinella et al (2008) ⁹	RBC (u)	16 (12–21)	14 (11–20)	NS
Spinella et al (2008) ⁹	FFP (u)	10 (7–13)	8 (5–11)	NS
Spinella et al (2008) ⁹	aPLT (u)	0 (0–1)	0 (0–1)	NS
Spinella et al (2008) ⁹	Crystalloids (u)	9 (0–17)	9 (0–10)	NS
Adverse events reported: The incidence of adverse events was similar for all patients studied				
		Clinical importance: 2		Clinical relevance: 1
EXTERNAL VALIDITY				
Generalisability The population studied was a military population which may show significant differences to the critical bleeding population in a civilian setting. However, given the inherent difficulties in performing quality studies in massively bleeding patients, the results of this study could still be applied successfully to a civilian population, similar to the population targeted by the guidelines				
Applicability The benefits identified by the study outweigh the harms				
Comments Despite being a military population, the findings of this study given the difficulties in performing controlled studies in critically bleeding patients, could be successfully applied to a civilian population similar to that targeted in the guidelines				

STUDY DETAILS				
Reference Stinger et al (2008) ¹⁵				
Affiliation/Source of funds Brooke Army Medical Centre, University of Texas Health Science Centre, Walter Reed Army Medical Centre, University of Maryland School of Medicine, Madigan Army Medical Centre/ Sponsored by the National Centre for Research resources grant M01-RR-01346				
Study design Case-series or cross sectional study/retrospective chart review		Level of evidence IV		Location/setting USA / Military
Intervention ≥ 10 units RBC in < 24 hours, sample size $n = 252$				Comparator No comparator
Population characteristics The group was stratified by the ratio of fibrinogen:RBC received: Low ratio = < 0.2 g/unit, ($n = 52$) High ratio = ≥ 0.2 g/unit, ($n = 200$)				
Length of follow-up NA		Outcomes measured Morbidity/mortality, dose/type of transfusion		
INTERNAL VALIDITY				
Allocation	Study group comparison	Blinding analysis	Treatment / measurement bias	Follow-up (ITT)
Not applicable	Not reported	Not blinded	Groups treated the same	Not applicable
Overall quality assessment (descriptive) A small patient population was examined in this retrospective chart review limiting the value of findings from this study				
RESULTS				
Overall mortality stratified by fibrinogen:RBC ratio (%)				
Author	Fibrinogen:RBC ratio		p-value	
	High ratio: ≥ 0.2 g/unit ($n = 200$)	Low ratio: < 0.2 g/unit ($n = 48$)		
Stinger et al (2008) ¹⁵	24	52	$p < 0.001$	
Mortality associated with haemorrhage stratified by ratio of fibrinogen to RBC (%)				
Author	Ratio of fibrinogen:RBC		p-value	
	High ratio: ≥ 0.2 g/unit ($n = 48$)	Low ratio: < 0.2 g/unit ($n = 27$)		
Stinger et al (2008) ¹⁵	44	85	$p < 0.001$	
Odds ratio of mortality associated with a high vs low fibrinogen:RBC ratio				
Author	Ratio definition (n)	OR	95%CI	p-value
Stinger et al (2008) ¹⁵	High ratio: ≥ 0.2 g/unit ($n = 48$) vs Low ratio: < 0.2 g/unit ($n = 27$)	0.37	(0.171, 0.812)	$p = 0.013$

Transfusion requirement by fibrinogen:RBC ratio				
Author	Blood component	Ratio of fibrinogen:RBC		p-value
		High ratio: > 0.2 g/unit (n = 200)	Low ratio: < 0.2 g/unit (n = 52)	
Stinger et al (2008) ¹⁵	Fibrinogen:RBC ratio transfused (mean ± SD)	0.48 g/unit ± 0.2	0.1 g/unit ± 0.06	p < 0.001
Stinger et al (2008) ¹⁵	FFP units (mean ± SD)	11.2 ± 7.4	3.5 ± 2.9	p < 0.001
Stinger et al (2008) ¹⁵	PLT units (mean ± SD)	0.72 ± 1.4	0.0 ± 0.0	p < 0.001
Stinger et al (2008) ¹⁵	Cryoprecipitate units (mean ± SD)	9.33 ± 10.9	0.77 ± 2.6	p < 0.001
Other adverse events reported: NR				
	Clinical importance: 2		Clinical relevance: 1	
EXTERNAL VALIDITY				
Generalisability The population studied consisted of a mixture of military and civilian patients. This is not directly applicable to the population targeted by the blood management guidelines, but given the difficulty of performing studies in critical bleeding, it is assumed that the results of the study could be successfully applied to the target population				
Applicability The results of the study indicate that a higher ratio of fibrinogen:RBC was associated with increased survival. This finding far outweighs the harms associated with increasing the ratio of fibrinogen to RBC				
Comments Despite being a mixed population, the outcomes of this study may still impact on the target population for the guidelines, thus, the results of this study must be considered, although with some caution				

STUDY DETAILS					
References Teixeira et al (2009) ⁴⁵					
Affiliation/Source of funds University of Southern California, Cedars-Sinai Medical Center, University of Texas Medical Branch-Brackenridge Hospital, University of Arizona./NR					
Study design Case-series or cross sectional study/ retrospective case review			Level of evidence IV		Location/setting USA/ Hospital
Intervention ≥ 10 units RBC in < 24 hours, sample size <i>n</i> = 484			Comparator No comparator		
Population characteristics Population was stratified by FFP:RBC ratio received as follows: High ratio group: > 1:3 and ≤1:2 Medium ratio group: > 1:8–≤1:3 Low ratio group: ≤1:8 The differences in baseline characteristics for each group were not reported					
Length of follow-up NA			Outcomes measured Morbidity/mortality		
INTERNAL VALIDITY					
Allocation	Study group comparison	Blinding analysis	Treatment / Measurement bias	Follow-up (ITT)	
Not applicable	Not reported	Not blinded	All patients treated equally	Not applicable	
Overall quality assessment (descriptive) The study was a retrospective, small population study so the results should be interpreted with caution					
RESULTS					
Mortality					
Overall mortality stratified by FFP:RBC ratio (%)					
	Highest ratio: > 1:2 (<i>n</i> = 115)	High ratio: > 1:3 and ≤1:2 (<i>n</i> = 111)	Medium ratio > 1:8 and ≤ 1:3 (<i>n</i> = 95)	Low ratio ≤ 1:8 (<i>n</i> = 62)	
Teixeira et al (2009) ⁴⁵	26	25	49	90	<i>p</i> < 0.01 (low vs medium vs high)
Relative risk of mortality associated with a high vs low FFP:RBC ratio					
Author	Ratio definition (<i>n</i>)	RR	95%CI	p-value	
Teixeira et al (2009) ⁴⁵	High ratio: > 1:3 & ≤1:2 (<i>n</i> = 111) vs highest ratio: > 1:2 (<i>n</i> = 115)	0.97	NR	NS	
Teixeira et al (2009) ⁴⁵	Medium ratio: > 1:8 (<i>n</i> = 95) & ≤ 1:2 vs highest ratio: > 1:2 (<i>n</i> = 115)	1.90	NR	<i>p</i> < 0.01	
Teixeira et al (2009) ⁴⁵	Low ratio: < 1:8 (<i>n</i> = 62) vs highest ratio: > 1:2 (<i>n</i> = 115)	3.46	NR	<i>p</i> < 0.01	

Mean FFP:RBC ratio—survivors vs non-survivors				
Author	Blood component ratio	Survivors (n = 218)	Non-survivors (n = 165)	
Teixeira et al (2009) ⁴⁵	FFP:RBC ratio	1:2.1	1:3.7	p < 0.001
Adverse events reported: NR				
	Clinical importance: 2		Clinical relevance:1	
EXTERNAL VALIDITY				
Generalisability The population examined in this review is equivalent to the population targeted in the blood management guidelines—trauma patients requiring a massive transfusion				
Applicability The benefits identified in the study of a higher FFP:RBC ratio far outweigh the harms				

STUDY DETAILS					
Reference Vaslef et al (2002) ¹⁶					
Affiliation/Source of funds Duke University Medical Center/Not reported					
Study design Case-series or cross sectional study/retrospective		Level of evidence IV		Location/setting USA / Hospital	
Intervention ≥ 50 units transfused in < 24 hours, sample size: <i>n</i> = 44				Comparator No comparator	
Population characteristics The population of patients was stratified by the total number of RBC units received in 24 hours into the following groups: 51–75 units RBC, sample size <i>n</i> = 28 76–100 units RBC, sample size <i>n</i> = 10 > 100 units RBC, sample size <i>n</i> = 6					
Length of follow-up NA			Outcomes measured Dose/type of transfusion		
INTERNAL VALIDITY					
Allocation	Study group comparison	Blinding analysis	Treatment / measurement bias	Follow-up (ITT)	
Not applicable	Significant differences occurred in survivors vs non-survivors for the following: ISS -29.4 ± 13.9 ; 42.5 ± 20.9 , <i>p</i> = 0.023, % base deficit > 12 -42.1 :80.0, <i>p</i> = 0.010, % arterial pH < 7.1 -31.6 :68.0, <i>p</i> = 0.017	Not blinded	All patients treated equally	Not applicable	
Overall quality assessment (descriptive) The patient numbers were very small and the study design was a retrospective chart review. This reduces the validity of the results observed					
RESULTS					
Mean total blood and component transfusion requirements in massive transfusion survivors and non-survivors (Mean ± SD)					
Author	Blood components	Survivors (<i>n</i> = 19)	Non-survivors (<i>n</i> = 25)	Total (<i>n</i> = 44)	<i>p</i> -value
Vaslef et al (2002) ¹⁶	Total blood products (units)	71 ± 17	79 ± 26	75 ± 22	<i>p</i> = 0.263
Vaslef et al (2002) ¹⁶	% transfused > 75 units	31.6	40.0	36.4	<i>p</i> = 0.565
Vaslef et al (2002) ¹⁶	RBC (units)	26 ± 9	38 ± 16	33 ± 14	<i>p</i> = 0.005
Vaslef et al (2002) ¹⁶	% transfused > 25 units RBC	47.4	76.0	63.6	<i>p</i> = 0.051
Vaslef et al (2002) ¹⁶	FFP (units)	10 ± 6	9 ± 5	9 ± 5	<i>p</i> = 0.469

Vaslef et al (2002) ¹⁶	Cryoprecipitate (units)	26 ± 10	24 ± 14	25 ± 12	p = 0.615
Vaslef et al (2002) ¹⁶	PLT(units)	8 ± 5	7 ± 6	8 ± 6	p = 0.554
Total blood and component therapy stratified by the number of transfusions received in the first day (Mean ± SD)					
Author	Blood component	Total blood products transfused in 24 hours			p-value
		> 100 units (n = 6)	76-100 units (n = 10)	51-75 units (n = 28)	
Vaslef et al (2002) ¹⁶	Total blood products	120±14	88±7	61±8	NR
Vaslef et al (2002) ¹⁶	RBC (units)	53±13	40±10	26±10	NR
Vaslef et al (2002) ¹⁶	FFP (units)	15±7	12±5	8±4	NR
Vaslef et al (2002) ¹⁶	Cryoprecipitate (units)	38±4	27±13	22±11	NR
Vaslef et al (2002) ¹⁶	PLT(units)	14±6	9±5	6±5	NR
Adverse events reported Survivors had significantly more hospital days and ICU days than non-survivors. Within the different groups, patients receiving > 100 units had less hospital days, less ICU days but a higher mortality rate than those in the other groups					
		Clinical importance 2		Clinical relevance 1	
EXTERNAL VALIDITY					
Generalisability The higher levels of blood transfusions required by all patients in this study suggest they are the more severely injured than patients other studies have examined. These patients would fall into the most severe category of the patients targeted by the blood management guidelines. The numbers of patients studied does not confer confidence in the results of this study					
Applicability The benefits identified in this study outweigh the harms. However, the results of the study are limited by the small patient numbers, severity of patient injury and the retrospective nature of the study					
Comments The results of this study should be interpreted cautiously. The overriding message from the study is that massive transfusions are beneficial and should continue					

STUDY DETAILS						
Reference Velmahos et al (1998) ⁴⁶						
Affiliation/Source of funds University of Southern California Medical School/NR						
Study design Case-series or cross sectional study/retrospective		Level of evidence IV		Location/setting USA/Hospital		
Intervention Massive transfusion, > 20 units RBC during pre-operative and intra-operative resuscitation, sample size $n = 141$				Comparator No comparator		
Population characteristics The group was divided into subgroups based on the number of units RBC received as follows: 20–29 units; 30–39 units; 40–49 units; and 50–68 units. There were no significant differences in the baseline characteristics of survivors vs non-survivors, except age (26 for survivors vs 32 for non-survivors, $p = 0.006$)						
Length of follow-up NA		Outcomes measured Morbidity/mortality, dose/type of transfusion				
INTERNAL VALIDITY						
Allocation	Results measurement bias	Blinding analysis	Treatment /measurement bias	Follow-up (ITT)		
Not applicable	Not applicable	Not blinded	All patients treated equally	Not applicable		
Overall quality assessment (descriptive) Small patient numbers, retrospective case chart review study and no real comparison means the results from this study need to be interpreted with caution						
RESULTS						
Mean total blood and component transfusion requirements in massive transfusion survivors and non-survivors (mean \pm SD)						
Author	Blood components	Survivors ($n = NR$)	Non-survivors ($n =$)	Total ($n =$)	p-value	
Velmahos et al (1998) ⁴⁶	RBC (units)	31 \pm 11	32 \pm 10	NR	$p = 0.52$	
Survival based on numbers of RBC units transfused (%)						
Author	Total number of RBC units transfused					p-value
	20–29 units ($n = 70$)	30–39 units ($n = 45$)	40–49 units ($n = 15$)	50–69 units ($n = 11$)	Total ($n = 141$)	
Velmahos et al (1998) ⁴⁶	33	29	27	27	30	0.94
Mortality rate associated with RBC transfusion						
	Time period	Units (mean)	Mortality (%)	p-value		
Velmahos et al (1998) ⁴⁶	NR	32	69.5	NR		
Adverse events reported NR						
	Clinical importance 1		Clinical relevance 1			

EXTERNAL VALIDITY
Generalisability The population studied was equivalent to the target population—patients undergoing massive transfusion. Patients were at the severe end of the transfusion spectrum, requiring more than 20 units RBC in 24 hours but the result may still be applied to the general, civilian population
Applicability The results of this study show that the benefits of massive transfusion far outweigh the harms with significant survival rates shown regardless of the number of RBC units transfused
Comments Patients were at the severe end of the transfusion and injury spectrum, requiring 20 units RBC in 24 hours. Multivariate and univariate analysis was performed to reduce confounding factors. However, the patient numbers enrolled in the study and the retrospective study design limit the validity of the results and encourage caution when interpreting the results

STUDY DETAILS					
Reference Wudel et al (1991) ⁴⁷					
Affiliation/Source of funds NR					
Study design Case-series or cross sectional study/ retrospective			Level of evidence IV		Location/setting USA/Hospital
Intervention MT > 20 units during hospitalisation period, sample size $n = 92$				Comparator No comparator	
Population characteristics NR					
Length of follow-up 25 years			Outcomes measured Morbidity/mortality, dose/type of transfusion		
INTERNAL VALIDITY					
Allocation	Study group comparison		Blinding analysis	Treatment / measurement bias	Follow-up (ITT)
Not applicable	Not reported		Not blinded	All patients treated equally	Not applicable
Overall quality assessment (descriptive) Retrospective, small patient population case-study report. Limited value is able to be placed on the results of this study					
RESULTS					
Mortality rate associated with RBC transfusion					
Author	Time period	Units (mean)		Mortality (%)	p-value
Wudel et al (1991) ⁴⁷	Hospitalisation	33		48	NR
% of units RBC given at different time periods					
Author	First 6 hours	First 12 hours	First 24 hours	Next 24 hours	> 48 hours
Wudel et al (1991) ⁴⁷	NR	NR	82%	5.5%	12.5%
Adverse events reported NR					
			Clinical importance 2		Clinical relevance 1
EXTERNAL VALIDITY					
Generalisability Patients included in the study were equivalent to the target population of the guidelines – all patients requiring a massive transfusion. Patients included in this study represent more severe patients due to the requirement for > 20 units RBC in 24 hours, however, the outcomes of the study could be applied across the entire guideline target population					
Applicability The benefits identified by the study outweigh the harms					

STUDY DETAILS					
Reference Zink et al (2009) ²¹					
Affiliation/Source of funds Oregon Health and Science University/NR					
Study design Case-series or cross sectional study/ retrospective		Level of evidence IV		Location/setting USA / Hospital	
Intervention ≥ 10 units RBC in < 24 hours, sample size <i>n</i> = 452			Comparator No comparator		
Population characteristics Population stratified by the ratio of FFP:RBC received as follows: Low ratio: < 1:4 Medium ratio: 1:4–1:1 or High ratio: ≥ 1:1 Average age < 1:4 was 36, 72.5% were males; 1:4–1:1 was 36, 76.3% were male; ≥ 1:1 was 28.3, 88.2% were male					
Length of follow-up NA		Outcomes measured Morbidity/mortality, transfusion frequency			
INTERNAL VALIDITY					
Allocation	Study group compared	Blinding analysis	Treatment/ measurement bias	Follow-up (ITT)	
Not applicable	No significant differences between groups other than INR (<i>p</i> = 0.03)	Not blinded	All patients treated equally	Not applicable	
Overall quality assessment (descriptive) A retrospective case chart review, with small patient numbers means this study needs to be interpreted with caution					
RESULTS					
Mortality at 6 hours					
Mortality at 6 hours stratified by FFP:RBC ratio (%)					
Author	High (≥ 1:1) (<i>n</i> = 51)	Medium (1:4–1:1) (<i>n</i> = 299)	Low (< 1:4) (<i>n</i> = 102)	p-value	
Zink et al (2009) ²¹	2.0	15.2	37.3	<i>p</i> < 0.001	
Mortality at 6 hours stratified by PLT:RBC ratio (%)					
Author	Blood product ratio	High (≥ 1:1) (<i>n</i> = 51)	Medium (1:4-1:1) (<i>n</i> = 299)	Low (< 1:4) (<i>n</i> = 102)	p-value
Zink et al (2009) ²¹	PLT:RBC	3.2	19	22.8	<i>p</i> < 0.002
In hospital mortality					
In hospital mortality stratified by FFP:RBC ratio (%)					
Author	High (≥ 1:1) (<i>n</i> = 51)	Medium (1:4-1:1) (<i>n</i> = 299)	Low (< 1:4) (<i>n</i> = 102)	p-value	
Zink et al (2009) ²¹	25.5	41.4	54.9	<i>p</i> < 0.04	
In hospital mortality stratified by PLT:RBC ratio (%)					
Author	High (≥ 1:1) (<i>n</i> = 51)	Medium (1:4-1:1) (<i>n</i> = 299)	Low (< 1:4) (<i>n</i> = 102)	p-value	

Zink et al (2009) ²¹	27.4	46.8	43.7	$p < 0.04$
Median FFP:RBC ratio at 6 hours affect on median blood product requirements at 24 hours				
		Ratio at 6 hours		
Author	Blood component ratio	High ratio: $\geq 1:1$ ($n = 62$)	Low ratio: $< 1:1$ ($n = 390$)	p-value
Median RBC units at 24 hours				
Zink et al (2009) ²¹	FFP:RBC	13	18	$p < 0.001$
Zink et al (2009) ²¹	PLT:RBC	13	17.5	$P = 0.008$
Adverse events reported There was no difference seen in the respiratory outcomes based on ratio of FFP:RBC. For ratios of PLT:RBC, respiratory outcomes improved with higher ratios				
	Clinical importance: 2		Clinical relevance: 1	
EXTERNAL VALIDITY				
Generalisability The population studied represents a similar population to that targeted by the blood management guidelines—patients requiring a massive transfusion				
Applicability The benefits of using a higher ratio of FFP:RBC and PLT:RBC far outweighed the harms in this study				
Comments Overall, the results of this study are in favour of using a higher ratio of FFP:RBC and PLT:RBC, but due to limitations in study design, the results need to be treated with caution				

F3 Evidence summary – question 3

Question 3

In patients with critical bleeding requiring massive transfusion, is anaemia an independent risk factor for adverse outcomes?

No evidence was found relating to anaemia as an independent risk factor for adverse outcomes in critical bleeding patients who require massive transfusion.

F4 Evidence summaries – question 4

Question 4

In patients with critical bleeding requiring massive transfusion, what is the effect of RBC transfusion on patient outcomes?

Table F4.1 Summaries for question 4

STUDY DETAILS				
Reference Chaiwat et al (2009) ²⁴				
Affiliation/Source of funds Grant from National Centre for Injury Prevention; Grant from National Centre for Injury Prevention and Control of the Centres for Disease Control and Prevention				
Study design Prospective cohort		Level of evidence III		Location/setting USA
Intervention RBC transfusion in first 24 hours, sample size = 2934		Comparator(s) IV fluid/standard of care/no transfusion, sample size = 11,136		
Population characteristics Patients aged 18-84 years with at least one injury, AIS score > 3				
Length of follow-up NA		Outcome(s) measured Development of ARDS, in-hospital mortality		
Internal Validity				
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)
Patients selected on basis of sampling scheme	Logistic regression	Study was not blinded	Not all eligible patients were included.	All patients were followed up
Overall quality assessment (descriptive) Fair				
Results				
Patients transfused with 6–10 units (OR 2.48) and > 10 units (OR 2.62) of RBC showed higher risk of ARDS than those with no transfusion; In-hospital mortality was not significantly different between groups.				
Outcome [19] ARDS	Intervention group 6-10 units 75/534 > 10 units 116/501	Control group 189/11,136	Measure of effect/effect size 95%CI OR 6-10 units: 2.24 (1.06, 4.73) > 10 units: 2.18 (0.93, 5.11)	Benefits (NNT) 95%CI
	Clinical Importance 2		Relevance 2	
Any other adverse effects NA				
External Validity				
Generalisability				
This study was performed in injured trauma patients undergoing transfusion which is generalisable to the relevant patients population				

Applicability

This study was carried out in the US which is generally applicable to the Australian healthcare setting, but has some differences

STUDY DETAILS				
Reference Silverboard et al (2005) ²⁵				
Affiliation/Source of funds Emory University School of Medicine				
Study design Prospective cohort		Level of evidence III		Location/setting USA
Intervention RBC transfusion within the first 24 hours 6–10 units, sample size = 32 and > 10 units, sample size = 28			Comparator(s) RBC transfusion within 24 hours 0–5 units, sample size = 42	
Population Patients with severe trauma defined as an ISS \geq 16 and who also require endotracheal intubation				
Length of follow-up NA			Outcome(s) measured Development of ARDS, mortality	
Internal validity				
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)
NR	Multivariable logistic regression analysis	Unblinded study	Groups were measured and treated the same	All patients were followed up for their entire hospital course
Overall quality assessment (descriptive) Fair				
Results > 6 units was related to ARDS (OR 1.04) when compared to 0–5 units as was in-hospital mortality				
Any other adverse effects: NA				
External Validity				
Generalisability: Study population considered similar to guideline target population				
Applicability Reduced – study performed in the USA, which has some difference to Australian clinical practice				

F5 Evidence summary – question 5

Question 5

In patients with critical bleeding requiring massive transfusion, what is the effect of non-transfusion interventions to increase haemoglobin concentration on morbidity, mortality and need for RBC blood transfusion?

No evidence was found relating to this question.

F6 Evidence summary – question 6

Question 6

In patients with critical bleeding requiring massive transfusion, what is the effect of rFVIIa (prophylaxis or treatment) on morbidity, mortality and transfusion rate?

Table F6.1 Summaries for question 6

STUDY DETAILS						
Reference Boffard et al (2005) ²⁶						
Affiliation/Source of funds fNovo Nordisk A/S						
Study design RCT	Level of evidence II		Location/setting South Africa/Australia/Canada/France/Germany/Israel/Singapore/UK			
Intervention rFactor VIIa, sample size = 139			Comparator(s) Adjunctive therapy, sample size = 138			
Population characteristics: Patients aged 16–65 years, with severe blunt and/or penetrating trauma						
Length of follow-up 30 days			Outcome(s) measured Number of RBC units used, use of other transfusion products, in-hospital mortality, days on ventilator, days in ICU			
Internal Validity						
Allocation	Comparison of study groups		Blinding:	Treatment/measurem ent bias	Follow-up	
Randomised	Blinded		Double blinded	None	30 days	
Overall quality assessment (descriptive) Good						
Results						
Total RBC Transfusion during 48hours after first dose of trial drug						
	Placebo		rFVIIa		Estimated RBC reduction with 90% CI	<i>p</i>
	N	Median (range)	N	Median (range)		
Blunt	–	N = 74	–	N = 69	–	–
Alive at 48h	59	7.5 (0–35)	52	7.0 (0–29)	2.6 [0.7;4.6]	0.02
All patients	72	7.2 (0–35)	64	7.8 (0–18)	2.0 [0.0;4.6]	0.07
Penetrating	–	N = 64	–	N = 70	–	–
Alive at 48 h	52	4.2 (0–41)	57	3.9 (0–30)	1.0 [0.0;2.6]	0.10
All patients	61	4.8 (0–41)	69	4.0 (0–37)	0.2 [–0.9;2.4]	0.24
Mortality						
	Blunt trauma			Penetrating trauma		
	Placebo (N = 74)	rFVIIa (N = 69)	<i>p</i>	Placebo (N = 64)	rFVIIa (N = 70)	<i>p</i>
48 h mortality	13 (18%)	13 (19%)	<i>p</i> = 1.00	10 (16%)	12 (17%)	<i>p</i> = 1.00
30 day mortality	22 (30%)	17 (25%)	<i>p</i> = 0.58	18 (28%)	17 (24%)	<i>p</i> = 0.69

Any other adverse effects Multiple organ failure, ARDS
External Validity
Generalisability Patient population considered similar to guideline target population
Applicability Applicable—study performed in several countries that have healthcare systems similar to Australia

F7 Evidence summary – question 7

Question 7

In patients with critical bleeding requiring massive transfusion, what is the effect of FFP, cryoprecipitate, fibrinogen concentrate, and/or platelet transfusion on patient outcomes?

Table F7.1 Summaries for question 7

STUDY DETAILS				
Reference Bochichio et al (2008) ³²				
Affiliation/Source of funds The authors of this study were affiliated to the R. Adams Cowley Shock Trauma Center and the Department of Epidemiology at the University of Maryland School of Medicine, Baltimore USA. The funding source of this study was not disclosed				
Study design Prospective observational study		Level of evidence III-2	Location/setting USA/Hospital	
Intervention Blood transfusion (packed red blood cell, frozen fresh plasma, platelets), sample size = 786		Comparator No blood transfusion, sample size = 386		
Population characteristics Consecutive trauma patients admitted to the ICU for longer than 48 hours at the trauma center over a 2 year period				
Length of follow-up Length of hospital stay		Outcomes measured Mortality, infection rate, ICU and hospital length of stay		
INTERNAL VALIDITY				
Allocation	Results/measurement bias	Blinding analysis	Treatment /measurement bias	Follow-up (ITT)
Blood transfusion was determined by trauma or ICU team based on clinical need. No formal transfusion protocol was used	Transfusion (any type) was associated with greater rates of mortality (19% vs. 8.3; $p < 0.001$) and infection (34% vs. 9.4%; $p < 0.001$) longer hospital and ICU LoS (18.6 vs. 9 days; $p < 0.001$ and 13.7 vs. 7.4 days; $p < 0.001$ respectively) The risk analysis adjusted for age, ISS and Glasgow Coma Index Score revealed that the odds of mortality increased by 3.5% (95%CI: [2, 5%]) for every unit of FFP transfused This study provided evidence that patients transfused with FFP have greater odds of developing an infection after transfusion was, and would have increased chance of longer ICU and hospital stays	Due to study design and basis for allocation of interventions, blinding was not carried out in this study	Outcomes were collected by a single individual throughout the study	Outcomes from all 1172 patients were obtained

RESULTS	
Outcome	Measure of effect/effect size (95%CI) (Intervention vs Control)
Mortality (FFP)	Adjusted OR = 1.03 (1.02, 1.05)
Mortality (platelet)	Adjusted OR = 1.03 (1.02, 1.04)
Infection (FFP)	Adjusted OR = 1.02 (1.01, 1.04)
Infection (platelet)	Adjusted OR = 0.94 (0.96, 1.0)
ICU LoS (FFP)	Adjusted OR = 1.25 (1.2, 1.31)
ICU LoS (platelet)	Adjusted OR = -0.08 (-0.14, 0.01)
Hospital LoS (FFP)	Adjusted OR = 1.3 (1.3,1.41)
Hospital LoS (platelet)	Adjusted OR = -0.15 (-0.023, 0.07)
EXTERNAL VALIDITY	
Generalisability There were more men than women in this study (74% vs.26%).However; more women were provided blood transfusion than men. ($p < 0.001$)There was also a significant difference in injury severity scores between transfused and non transfused patients. ($p < 0.001$). The difference in injury scores was appropriately controlled for in the risk analysis	
Applicability This study was not conducted in Australia	
Comments This study also reported the impact of RBC transfusion. These outcomes were not extracted	

STUDY DETAILS				
Reference Borgman et al (2007) ¹⁰				
Affiliation/Source of funds Brooke Army Medical Centre, Fort Sam, Houston Texas, USA				
Study design Retrospective analysis of Trauma Registry	Level of evidence III-2		Location/setting US Army Combat support Hospital in Baghdad, Iraq	
Intervention High plasma to RBC ratio = 1:1.4 (Range = 1:2 to 1:0.6) Sample size: <i>n</i> = 162			Comparator Medium plasma to RBC ratio = 1:2.5 (Range = 1:3.9 to 1:2.1) Sample size: <i>n</i> = 53 Low plasma to RBC ratio = 1:8 (Range 0:22 to 1:4) Sample size: <i>n</i> = 31	
Population characteristics Massively transfused patients who received > 10 units of RBC within 24 hours of admission at a US Army Combat Support Hospital in Iraq between November 2003 and September 2005				
Length of follow-up Mortality was tracked differently for US military and non-US military patients. Mortality in US military patients was tracked through all levels of care in US. Mortality of non-US military patients was followed-up until discharge from the Combat Support Hospital in Baghdad			Outcomes measured ISS, AIS, mortality, laboratory and vital scores at admission and blood product use within 24 hours of admission	
INTERNAL VALIDITY				
Allocation	Results measurement bias	Blinding analysis	Treatment /measurement bias	Follow-up (ITT)
Not reported	Results suggest that the mortality rate decreases as the ratio of plasma to RBC transfused increases. The proportions of patients who died were 65%, 34% and 19% in the low, medium and high ratio groups respectively (<i>p</i> < 0.001). Purported that plasma to RBC ratios independently associated with overall survival (OR = 8.6; 95%CI: 2.1, 35.2)	No blinding	One investigator reviewed all charts and records to calculate ISS and AIS	Not reported
RESULTS				
Outcome	Intervention group	Control group	Measure of effect/effect size (95%CI)	
Mortality (all cause)	High = 19%	Medium = 34%; low = 65%	<i>p</i> < 0.001	

Mortality (haemorrhage)	High = 11.5/31 (37%)	Medium = 14/18 (77.8%) Low = 18/20 (92.5%)	High vs. low group: Absolute reduction = 55%; Relative reduction = 60%; $p < 0.001$ High vs. medium group ($p < 0.05$)
EXTERNAL VALIDITY			
Generalisability There were only 2 female patients in this cohort. The study population is confined to patients with war injuries with a high proportion of patients with penetrating trauma			
Applicability This study was not undertaken in Australia or in a greater civilian population. There are differences in the health care system			

STUDY DETAILS				
Reference Duchesne et al (2008) ²⁷				
Affiliation/Source of funds Tulane University School of Medicine New Orleans Louisiana, Louisiana State University School of Medicine, New Orleans, Louisiana				
Study design Retrospective		Level of evidence III-2		Location/setting Level I Trauma centre, New Orleans, Louisiana
Intervention Ratio of FFP: RBC of 1:1 Transfusion of FFP and RBC were provided at a ratio of approximately 1:1 (transfusion of < 2 RBC units for every 1 unit FFB was included in this group) Sample size: <i>n</i> = 118			Comparator Ratio of FFP: RBC of 1:4 Transfusion of FFP and RBC were provided at a ratio of approximately 1:4. (Transfusion of > 2 RBC units for every 1 unit FFB was included in this group) Sample size: <i>n</i> = 132	
Population characteristics Trauma patients who underwent emergency surgery and were transfused with > 10 units FFP:RBC within 24 hours of admission to the emergency department (during and after their initial surgical intervention). <i>N</i> = 135				
Length of follow-up NR			Outcomes measured Mortality	
INTERNAL VALIDITY				
Allocation	Results measurement bias	Blinding analysis	Treatment measurement bias	Follow-up (ITT)
No protocol—based on clinical judgement	None	None	None, aside from experimental treatment	NR
RESULTS				
Outcome	Intervention group	Control group	Measure of effect/effect size (95%CI)	
Mortality (proportions)	19/71 (26%)	56/64 (87.5%)	<i>p</i> = 0.0001	
Mortality (RR)			RR = 18.88 (6.32, 56.36); <i>p</i> = 0.001	
EXTERNAL VALIDITY				
Generalisability The population investigated involved civilian trauma patients in an urban setting, with approximately similar proportions of blunt and penetrating trauma patients				
Applicability This study was not conducted in Australia. There are differences in the health care system				
Comments Outcomes of patients transfused with ≤10 units of RBC were not extracted for the purpose of this review (wrong population)				

STUDY DETAILS				
Reference Dente et al (2009) ¹⁹				
Affiliation/Source of funds Grady Memorial Hospital and Emory University School of Medicine Atlanta Georgia USA				
Study design Prospective observational study comparing the use of a massive transfusion protocol (MTP) compared against a historical control group before the initiation of the protocol		Level of evidence III-3		Location/setting Atlanta Georgia USA/ Hospital (Urban level I trauma center)
Intervention MTP Transfusion according to a massive transfusion protocol designed to achieve a RBC: frozen fresh plasma: platelet ratio of 1:1:1 Sample size: $n = 73$			Comparator Pre-MTP No use of massive transfusion protocol (historical control, pre-implementation of protocol) Sample size: $n = 84$	
Population characteristics Intervention group: MTP Prospective trauma patients requiring massive transfusion (more than 10 units RBC within any 24 hour period during hospitalisation) who were transfused using the MTP ratio of blood products Comparator group: Pre-MTP A cohort of historical trauma patients who required massive transfusion (more than 10 units RBC within any 24 hour period during hospitalisation) who were matched for age, gender, percentage blunt trauma, ISS and initial base deficit values				
Length of follow-up Until discharge or 30 days from admission			Outcomes measured Mortality, coagulation parameters, transfusion of blood products	
INTERNAL VALIDITY				
Allocation	Results measurement bias	Blinding analysis	Treatment/ measurement bias	Follow-up (ITT)
Massive transfusion protocol was implemented on all eligible patients during study period	None	None	None	Of the 73 patients in the MTP group, 23 received transfusions with ratios of RBC: FFP or RBC: platelet higher than 2:1 and were considered a protocol failure
RESULTS				
Outcome	Intervention group	Control group	Measure of effect/effect size (95%CI)	
Mortality (24 hours)	17%	36%	$p = 0.008$	
Mortality (30 days)	34%	55%	$p = 0.04$	
Survival at discharge (blunt trauma)	66%	45%	$p = 0.042$	

Survival at discharge (penetrating trauma)	24%	34%	$p = 0.38$ (non-significant difference)
Early deaths from coagulopathic bleeding	4/13 (31%)	21/31 (68%)	$p = 0.023$
Mean RBC use	23.7 units	22.8 units	$p = 0.67$
Mean FFP use	15.6 units	7.6 units	$p < 0.001$
Mean early crystalloid use	6.9 L	7.6 L	$p = 0.006$
Prothrombin time on arrival at ICU	15.1 ± 0.26	17.5 ± 1.1	$p = 0.04$
INR on arrival at ICU	1.31 ± 0.29	1.72 ± 0.17	$p = 0.04$
Fibrinogen values on arrival at ICU	324 ± 19	225 ± 19	$p = 0.01$
Partial thromplastin time on arrival at ICU	$32.2 + 1.3$	$48.8 + 7.7$	$p = 0.04$
EXTERNAL VALIDITY			
Generalisability The population investigated involved civilian trauma patients in an urban setting			
Applicability This study was not conducted in Australia			
Comments No specific transfusion trigger or resuscitation algorithm was used. Blood transfusion and resuscitation was provided according to clinical need as judged by clinicians			

F8 Evidence summary – question 8

Question 8

In patients with critical bleeding requiring massive transfusion, at what INR (or PT/APTT) for fresh frozen plasma, fibrinogen level for cryoprecipitate, platelet count for platelets concentrates should patients be transfused to avoid risks of significant adverse events?

There was no relevant evidence in the critical bleeding/massive transfusion setting for this question.

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