

Evidence summary

to support

PICO question 16 on PBM implementation:

Effectiveness behavioural interventions for blood product ordering

April 2018 (version 1.0) Centre for Evidence-Based Practice (CEBaP) Belgian Red Cross

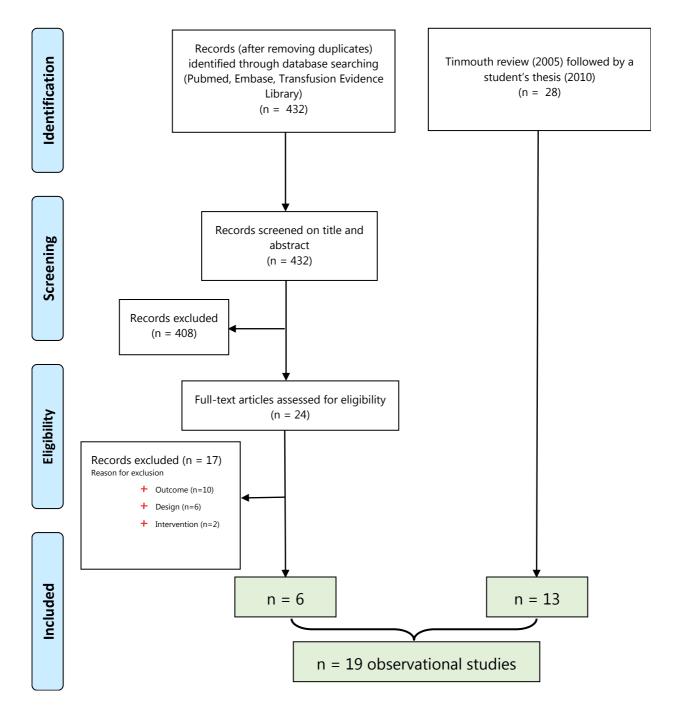




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Flow chart



Overview of 19 included studies¹⁻¹⁹

- 1. Ballantyne A, Walmsley P, Brenkel I. Reduction of blood transfusion rates in unilateral total knee arthroplasty by the introduction of a simple blood transfusion protocol. Knee 2003;10:379-84.
- 2. Brandis K, Richards B, Ghent A, et al. A strategy to reduce inappropriate red blood cell transfusion. Med J Aust 1994;160:721-2.
- Cheng G, Wong HF, Chan A, et al. The effects of a self-educating blood component request form and enforcements of transfusion guidelines on FFP and platelet usage. Queen Mary Hospital, Hong Kong. British Committee for Standards in Hematology (BCSH). Clin Lab Haematol 1996;18:83-7.
- 4. Eindhoven GB, Diercks RL, Richardson FJ, et al. Adjusted transfusion triggers improve transfusion practice in orthopaedic surgery. Transfus Med 2005;15:13-8.
- 5. Fontana S, de la Cuadra C, Muller U, et al. A Simple Guideline Reduces the Need for Red Blood Cell Transfusions in Swiss Hospitals: A Prospective, Multicentre, Before-and-After Study in Elective Hip and Knee Replacement. Transfus Med Hemother 2014;41:182-8.
- 6. Garrioch M, Sandbach J, Pirie E, et al. Reducing red cell transfusion by audit, education and a new guideline in a large teaching hospital. Transfus Med 2004;14:25-31.
- Hui CH, Williams I, Davis K. Clinical audit of the use of fresh-frozen plasma and platelets in a tertiary teaching hospital and the impact of a new transfusion request form. Intern Med J 2005;35:283-8.
- 8. Lee QJ, Mak WP, Yeung ST, et al. Blood management protocol for total knee arthroplasty to reduce blood wastage and unnecessary transfusion. J Orthop Surg (Hong Kong) 2015;23:66-70.
- 9. Meyer MJ, Dzik WH, Levine WC. Reduction in Operating Room Plasma Waste After Evidence-Based Quality Improvement Initiative. Anesth Analg 2017.
- 10. Mimica AF, dos Santos AM, da Cunha DH, et al. A very strict guideline reduces the number of erythrocyte transfusions in preterm infants. Vox Sang 2008;95:106-11.
- 11. Morrison JC, Sumrall DD, Chevalier SP, et al. The effect of provider education on blood utilization practices. Am J Obstet Gynecol 1993;169:1240-5.
- 12. Muller U, Exadaktylos A, Roeder C, et al. Effect of a flow chart on use of blood transfusions in primary total hip and knee replacement: prospective before and after study. BMJ 2004;328:934-8.
- 13. Patel VM, Rains AW, Clark CT. Effectiveness of Provider Education Followed by Computerized Provider Order Entry Alerts in Reducing Inappropriate Red Blood Cell Transfusion. J Blood Transfus 2016;2016:2859720.
- 14. Sarode R, Refaai MA, Matevosyan K, et al. Prospective monitoring of plasma and platelet transfusions in a large teaching hospital results in significant cost reduction. Transfusion 2010;50:487-92.

- 15. Spencer J, Thomas SR, Yardy G, et al. Are we overusing blood transfusing after elective joint replacement?--a simple method to reduce the use of a scarce resource. Ann R Coll Surg Engl 2005;87:28-30.
- 16. Tavares MM, Diquattro PJ, Sweeney JD. Reduction in red blood cell transfusion associated with engagement of the ordering physician. Transfusion 2014;54:2625-30.
- 17. Torella F, Haynes SL, Bennett J, et al. Can hospital transfusion committees change transfusion practice? J R Soc Med 2002;95:450-2.
- 18. Yeh CJ, Wu CF, Hsu WT, et al. Transfusion audit of fresh-frozen plasma in southern Taiwan. Vox Sang 2006;91:270-4.
- 19. Abelow A, Gafter-Gvili A, Tadmor B, et al. Educational interventions encouraging appropriate use of blood transfusions. Vox Sang 2017;112:150-5.

Overview of excluded studies²⁰⁻⁴⁹

Arnold 2011 (Reason for exclusion: inappropriate outcome reporting)

20. Arnold DM, Lauzier F, Whittingham H, et al. A multifaceted strategy to reduce inappropriate use of frozen plasma transfusions in the intensive care unit. J Crit Care 2011;26:636 e7- e13.

Ayoub 1989 (Reason for exclusion: inappropriate study design)

21. Ayoub MM, Clark JA. Reduction of fresh frozen plasma use with a simple education program. Am Surg 1989;55:563-5.

Barty 2015 (Reason for exclusion: inappropriate outcome reporting)

22. Barty RL, Gagliardi K, Owens W, et al. A benchmarking program to reduce red blood cell outdating: implementation, evaluation, and a conceptual framework. Transfusion 2015;55:1621-7.

Westbrook 2010 (Reason for exclusion: inappropriate intervention)

23. Blood Observational Study Investigators of A-CTG, Westbrook A, Pettila V, et al. Transfusion practice and guidelines in Australian and New Zealand intensive care units. Intensive Care Med 2010;36:1138-46.

Bonfante 2016 (Reason for exclusion: inappropriate outcome reporting)

24. Bonfante I. Blood Transfusion Practices in Patients Undergoing Total Joint Replacement: A Research Study. Orthop Nurs 2016;35:183-6.

Damiani 2010 (Reason for exclusion: inappropriate study design)

25. Damiani G, Pinnarelli L, Sommella L, et al. Appropriateness of fresh-frozen plasma usage in hospital settings: a meta-analysis of the impact of organizational interventions. Transfusion 2010;50:139-44.

Debrix 1999 (Reason for exclusion: inappropriate study design)

26. Debrix I, Combeau D, Stephan F, et al. Clinical practice guidelines for the use of albumin: results of a drug use evaluation in a Paris hospital. Tenon Hospital Paris. Pharm World Sci 1999;21:11-6.

Frank 2014 (Reason for exclusion: inappropriate outcome reporting)

27. Frank SM, Oleyar MJ, Ness PM, et al. Reducing unnecessary preoperative blood orders and costs by implementing an updated institution-specific maximum surgical blood order schedule and a remote electronic blood release system. Anesthesiology 2014;121:501-9.

Gallagher-Swann 2011 (Reason for exclusion: inappropriate outcome reporting)

28. Gallagher-Swann M, Ingleby B, Cole C, et al. Improving transfusion practice: ongoing education and audit at two tertiary speciality hospitals in Western Australia. Transfus Med 2011;21:51-6.

Goda 2017 (Reason for exclusion: inappropriate outcome reporting)

29. Goda TS, Sherrod B, Kindell L. An Interdisciplinary Education Initiative to Promote Blood Conservation in Cardiac Surgery. J Healthc Qual 2017;39:e33-e41.

Hameedullah 2000 (Reason for exclusion: inappropriate study design)

30. Hameedullah, Khan FA, Kamal RS. Improvement in intraoperative fresh frozen plasma transfusion practice--impact of medical audits and provider education. J Pak Med Assoc 2000;50:253-6.

Handler 1983 (Reason for exclusion: inappropriate study design)

31. Handler S. Does continuing medical education affect medical care? a study of improved transfusion practices. Minn Med 1983;66:167-80.

Hawkins 1994 (Reason for exclusion: inappropriate study design)

32. Hawkins TE, Carter JM, Hunter PM. Can mandatory pretransfusion approval programmes be improved? Transfus Med 1994;4:45-50.

Kakkar 2004 (Reason for exclusion: inappropriate study design)

33. Kakkar N, Kaur R, Dhanoa J. Improvement in fresh frozen plasma transfusion practice: results of an outcome audit. Transfus Med 2004;14:231-5.

Lam 1997 (Reason for exclusion: inappropriate outcome reporting)

34. Lam HT, Schweitzer SO, Petz L, et al. Effectiveness of a prospective physician self-audit transfusion-monitoring system. Transfusion 1997;37:577-84.

Lam 1996 (Reason for exclusion: inappropriate outcome reporting)

35. Lam HT, Schweitzer SO, Petz L, et al. Are retrospective peer-review transfusion monitoring systems effective in reducing red blood cell utilization? Arch Pathol Lab Med 1996;120:810-6.

Lin 2016 (Reason for exclusion: inappropriate outcome reporting)

36. Lin Y, Cserti-Gazdewich C, Lieberman L, et al. Improving transfusion practice with guidelines and prospective auditing by medical laboratory technologists. Transfusion 2016;56:2903-5.

Luca 1997 (Reason for exclusion: inappropriate study design)

37. Lucas RE, Oberli H. An audit to assess the impact of a strategy to reduce inappropriate red cell transfusions at Honiara Hospital. Trop Doct 1997;27:97-9.

Madrigal 2017 (Reason for exclusion: inappropriate study design)

38. Madrigal E, Prajapati S, Avadhani V, et al. Adequacy of physician documentation and correlation with assessment of transfusion appropriateness: a follow-up study in the setting of prospective audits and patient blood management. Transfusion 2017;57:367-75.

McCullough 1988 (Reason for exclusion: inappropriate study design)

39. McCullough J, Steeper TA, Connelly DP, et al. Platelet utilization in a university hospital. JAMA 1988;259:2414-8.

Mukhtar 2013 (Reason for exclusion: inappropriate study design)

40. Mukhtar SA, Leahy MF, Koay K, et al. Effectiveness of a patient blood management data system in monitoring blood use in Western Australia. Anaesth Intensive Care 2013;41:207-15.

Norgaard 2014 (Reason for exclusion: inappropriate outcome reporting)

41. Norgaard A, De Lichtenberg TH, Nielsen J, et al. Monitoring compliance with transfusion guidelines in hospital departments by electronic data capture. Blood Transfus 2014;12:509-19.

Rehm 1998 (Reason for exclusion: inappropriate study design)

42. Rehm JP, Otto PS, West WW, et al. Hospital-wide educational program decreases red blood cell transfusions. J Surg Res 1998;75:183-6.

Rideau 2010 (Reason for exclusion: inappropriate study design)

43. Rideau C, Gaertner E, Blay M, et al. Successful management of fresh-frozen plasma transfusion therapy based upon clinical symptoms for total knee arthroplasty in a patient with severe factor V deficiency. Haemophilia 2010;16:381-3.

Rinehart 2016 (Reason for exclusion: inappropriate intervention)

44. Rinehart JB, Lee TC, Kaneshiro K, et al. Perioperative blood ordering optimization process using information from an anesthesia information management system. Transfusion 2016;56:938-45.

Rosen 1993 (Reason for exclusion: inappropriate study design)

45. Rosen NR, Bates LH, Herod G. Transfusion therapy: improved patient care and resource utilization. Transfusion 1993;33:341-7.

Sekhar 2016 (Reason for exclusion: inappropriate outcome reporting)

46. Sekhar M, Clark S, Atugonza R, et al. Effective implementation of a patient blood management programme for platelets. Transfus Med 2016;26:422-31.

Shanberge 1987 (Reason for exclusion: inappropriate study design)

47. Shanberge JN. Reduction of fresh-frozen plasma use through a daily survey and education program. Transfusion 1987;27:226-7.

Solomon 1988 (Reason for exclusion: inappropriate study design)

48. Solomon RR, Clifford JS, Gutman SI. The use of laboratory intervention to stem the flow of freshfrozen plasma. Am J Clin Pathol 1988;89:518-21.

Woodrum 2017 (Reason for exclusion: inappropriate study design)

49. Woodrum CL, Wisniewski M, Triulzi DJ, et al. The effects of a data driven maximum surgical blood ordering schedule on preoperative blood ordering practices. Hematology 2017;22:571-7.

Overview tables included studies: behavioural intervention(s) – blood products – targeted physicians.

		ventic od pre					Bloo	d pro	ducts		Tar	gete	d phy	/sicia	ns
	Guideline	Form	Audit-approval	Audit-feedback	Education	RBC	FFP	PLT	Cryoprecipitate	All	Surgeons	Anaesthesiologists	Obstetricians - Gynaecologists	Neontal physicians	All
Abelow, 2017															
Ballantyne, 2004															
Brandis, 1994															
Cheng, 1996															
Fontana, 2014															
Garrioch, 2004															
Hui, 2005															
Lam, 1996															
Lee, 2015															
Meyer, 2017															
Mimica, 2008															
Morrison, 1993															
Müller, 2004															
Sarode, 2010															
Spencer, 2005															
Torella, 2014															
Yeh, 2006															

Studies comparing behavioural intervention(s) versus no behavioural interventions

		nterve omote o		l prod				tion(s) produ				I	31000	l prod	ducts		Та	rgete	d ph	ysicia	ins
	Guideline	Form	Audit-approval	Audit-feedback	Education	Guideline	Form	Audit-approval	Audit-feedback	Education	CPOE	RBC	FFP	РЦ	Cryoprecipitate	All	Surgeons	Anaesthesiologists	Obstetricians - Gynaecologists	Neontal physicians	All
Eindhoven, 2005																					
Patel, 2016																					
Tavares, 2014																					

Overview evidence table GRADE software

			Certainty as	sessment					
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Impact	Certainty	Importance
Behaviour	al intervention(s) v	ersus no in	tervention: RBC utili	ization					
12	observational studies	serious ^a	not serious	not serious	not serious	none	(Statistically significant) reduction in RBC utilization after versus before implementation of different behavioural interventions (Guideline only, Education only, Guideline + Education, Guideline + Education + Form + Audit/feedback, Education + Audit/feedback) (Figure 1-3)	⊕○○○ VERY LOW	CRITICAL

Study or Subgroup 1.1.1 Guideline	Rehavior							
		ral interve			ervention	Std. Mean Difference	Std. Mean Difference	Risk of Bias
	Mean	SD	Total	Mean	SD Tot	al IV, Random, 95% Cl	IV, Random, 95% CI	ABCDE
Fontana 2014 - RBC units per patient	0.4	0	0	0.5	0	0 Not estimable		
Lee 2015 - RBC units transfused	1.67	0.58	96	1.8		-0.17 [-0.45, 0.11]	-+-	
Mimica 2008 - median volume RBC transfused	15	0.50	48	36		54 Not estimable		
Torella 2002 (CABG) - median units transfused	0	Ő	0	1		0 Not estimable		? • • ? •
Torella 2002 (Colectomy) - median units transfused	ŏ	Ő	õ	2		0 Not estimable		20020
Torella 2002 (THR) - median units transfused	2	Ō	Ō	2		0 Not estimable		2 🔴 🖗 ? 🖷
4.4.0 Cuidelles - Education								
1.1.2 Guideline + Education								
Patel 2016 - %RBC orders Hb 8 g/dL	6.36	0	0	16.64	0	0 Not estimable		? • • • •
1.1.3 Guideline + Education + Form + Audit/feedback								
Morrison 1993 - RBC units transfused monthly	40.7	17.2	144	107.9	45.96 33	36 -1.69 [-1.92, -1.47]	+	• • ? ? •
	40.1	11.2		101.0				
1.1.4 Form + Audit/feedback								
Yeh 2006 - Nr of RBC units transfused monthly	3,769	271.3	3769	4,442.3	147.6 444	42 -3.15 [-3.22, -3.09]	+	•••?•
							-4 -2 0 2	4
							Favours intervention Favours no inter	vention
B. 1. (1) 1								
Risk of bias legend								
(A) Inappropriate eligibility criteria	orioblog							
(B) Inappropriate methods for exposure and outcome values (C) Not controlled for confounding.	ariables							
(C) Not controlled for confounding (D) Incomplete or inadequate follow-up								
(E) Other limitations								
(E) Other Infitations								
								``
igure 1: behavioural versus no be	enavio	ural int	terver	ntion:	outcon	ne number of RE	BC units transfused (conti	nuous)
	Behavior	al interve	ntion	No inter	vention	Risk Ratio	Risk Ratio	Risk of Rias
Study or Subaroup		ral interve nts		No inter Events		Risk Ratio M-H. Random, 95% Cl	Risk Ratio M-H. Random, 95% Cl	Risk of Bias A B C D E
Study or Subgroup	Behavior Eve			No inter Events		Risk Ratio M-H, Random, 95% Cl	Risk Ratio M-H, Random, 95% Cl	Risk of Bias A B C D E
1.2.1 Education	Eve	nts	Total	Events	Total	M-H, Random, 95% CI		ABCDE
		nts		Events				
1.2.1 Education Sarode 2010 - Nr of RBC products transfused	Eve	nts	Total	Events	Total	M-H, Random, 95% CI		ABCDE
1.2.1 Education Sarode 2010 - Nr of RBC products transfused 1.2.2 Education + Audit/feedback	Ever 745	nts 559 1	Total 65196	Events 63842	Total 125365	M-H, Random, 95% Cl 0.89 (0.88, 0.89)	M-H, Random, 95% Cl	A B C D E ●●●?●
1.2.1 Education Sarode 2010 - Nr of RBC products transfused	Ever 745	nts	Total	Events	Total 125365	M-H, Random, 95% CI		ABCDE
1.2.1 Education Sarode 2010 - Nr of RBC products transfused 1.2.2 Education + Audit/feedback	Ever 745	nts 559 1	Total 65196	Events 63842	Total 125365	M-H, Random, 95% Cl 0.89 (0.88, 0.89)	M-H, Random, 95% Cl	A B C D E ●●●?● ?●●?●
1.2.1 Education Sarode 2010 - Nr of RBC products transfused 1.2.2 Education + Audit/feedback	Ever 745	nts 559 1	Total 65196	Events 63842	Total 125365	M.H, Random, 95% Cl 0.89 (0.88, 0.89) 0.71 (0.56, 0.91) 0.7	M-H, Random, 95% Cl	<u>ABCDE</u> ●●●?● ?●●?● 10
1.2.1 Education Sarode 2010 - Nr of RBC products transfused 1.2.2 Education + Audit/feedback	Ever 745	nts 559 1	Total 65196	Events 63842	Total 125365	M.H, Random, 95% Cl 0.89 (0.88, 0.89) 0.71 (0.56, 0.91) 0.7	M-H, Random, 95% Cl	<u>ABCDE</u> ●●●?● ?●●?● 10
1.2.1 Education Sarode 2010 - Nr of RBC products transfused 1.2.2 Education + Audit/feedback Brandis 1994 - units transfiper 1000 admissions	Ever 745	nts 559 1	Total 65196	Events 63842	Total 125365	M.H, Random, 95% Cl 0.89 (0.88, 0.89) 0.71 (0.56, 0.91) 0.7	M-H, Random, 95% Cl	<u>ABCDE</u> ●●●?● ?●●?● 10
1.2.1 Education Sarode 2010 - Nr of RBC products transfused 1.2.2 Education + Audit/Teedback Brandis 1994 - units transf per 1000 admissions Risk of bias legend	Ever 745	nts 559 1	Total 65196	Events 63842	Total 125365	M.H, Random, 95% Cl 0.89 (0.88, 0.89) 0.71 (0.56, 0.91) 0.7	M-H, Random, 95% Cl	<u>ABCDE</u> ●●●?● ?●●?● 10
1.2.1 Education Sarode 2010 - Nr of RBC products transfused 1.2.2 Education + Audit/feedback Brandis 1994 - units transf per 1000 admissions Risk of bias legend (A) Inappropriate eligibility criteria	<u>Eve</u> 745	nts 559 1 99	Total 65196	Events 63842	Total 125365	M.H, Random, 95% Cl 0.89 (0.88, 0.89) 0.71 (0.56, 0.91) 0.7	M-H, Random, 95% Cl	<u>ABCDE</u> ●●●?● ?●●?● 10
1.2.1 Education Sarode 2010 - Nr of RBC products transfused 1.2.2 Education + Audit/feedback Brandis 1994 - units transf per 1000 admissions Risk of bias legend (A) Inappropriate eligibility criteria (B) Inappropriate methods for exposure and outcometers	<u>Eve</u> 745	nts 559 1 99	Total 65196	Events 63842	Total 125365	M.H, Random, 95% Cl 0.89 (0.88, 0.89) 0.71 (0.56, 0.91) 0.7	M-H, Random, 95% Cl	<u>ABCDE</u> ●●●?● ?●●?● 10
1.2.1 Education Sarode 2010 - Nr of RBC products transfused 1.2.2 Education + Audit/feedback Brandis 1994 - units transf per 1000 admissions Risk of bias legend (A) Inappropriate eligibility criteria (B) Inappropriate methods for exposure and outcom- (C) Not controlled for confounding	<u>Eve</u> 745	nts 559 1 99	Total 65196	Events 63842	Total 125365	M.H, Random, 95% Cl 0.89 (0.88, 0.89) 0.71 (0.56, 0.91) 0.7	M-H, Random, 95% Cl	<u>ABCDE</u> ●●●?● ?●●?● 10
1.2.1 Education Sarode 2010 - Nr of RBC products transfused 1.2.2 Education + Audit/feedback Brandis 1994 - units transf per 1000 admissions Risk of bias legend (A) Inappropriate eligibility criteria (B) Inappropriate methods for exposure and outcome (C) Not controlled for confounding (D) Incomplete or inadequate follow-up	<u>Eve</u> 745	nts 559 1 99	Total 65196	Events 63842	Total 125365	M.H, Random, 95% Cl 0.89 (0.88, 0.89) 0.71 (0.56, 0.91) 0.7	M-H, Random, 95% Cl	<u>ABCDE</u> ●●●?● ?●●?● 10
1.2.1 Education Sarode 2010 - Nr of RBC products transfused 1.2.2 Education + Audit/Teedback Brandis 1994 - units transf per 1000 admissions Risk of bias legend (A) Inappropriate eligibility criteria (B) Inappropriate methods for exposure and outcom- (C) Not controlled for confounding	<u>Eve</u> 745	nts 559 1 99	Total 65196	Events 63842	Total 125365	M.H, Random, 95% Cl 0.89 (0.88, 0.89) 0.71 (0.56, 0.91) 0.7	M-H, Random, 95% Cl	<u>ABCDE</u>
1.2.1 Education Sarode 2010 - Nr of RBC products transfused 1.2.2 Education + Audit/feedback Brandis 1994 - units transf per 1000 admissions Risk of bias legend (A) Inappropriate eligibility criteria (B) Inappropriate methods for exposure and outcome (C) Not controlled for confounding (D) Incomplete or inadequate follow-up (E) Other limitations	Ever 745 e variables	nts 559 1 99	Total 165196 1000	Events 63842 139	Total 125385 1000	M.H, Random, 95% Cl 0.89 (0.88, 0.89) 0.71 (0.56, 0.91)	M-H, Random, 95% Cl	A B C D E
1.2.1 Education Sarode 2010 - Nr of RBC products transfused 1.2.2 Education + Audit/feedback Brandis 1994 - units transf per 1000 admissions Risk of bias legend (A) Inappropriate eligibility criteria (B) Inappropriate methds for exposure and outcome (C) Not controlled for confounding (D) Incomplete or inadequate follow-up (E) Other limitations	Ever 745 e variables	nts 559 1 99	Total 165196 1000	Events 63842 139	Total 125385 1000	M.H, Random, 95% Cl 0.89 (0.88, 0.89) 0.71 (0.56, 0.91)	M-H, Random, 95% Cl	A B C D E
1.2.1 Education Sarode 2010 - Nr of RBC products transfused 1.2.2 Education + Audit/feedback Brandis 1994 - units transf per 1000 admissions Risk of bias legend (A) Inappropriate eligibility criteria (B) Inappropriate methds for exposure and outcome (C) Not controlled for confounding (D) Incomplete or inadequate follow-up (E) Other limitations	Ever 745 e variables	nts 559 1 99	Total 165196 1000	Events 63842 139	Total 125385 1000	M.H, Random, 95% Cl 0.89 (0.88, 0.89) 0.71 (0.56, 0.91)	M-H, Random, 95% Cl	A B C D E
1.2.1 Education Sarode 2010 - Nr of RBC products transfused 1.2.2 Education + Audit/feedback Brandis 1994 - units transf per 1000 admissions Risk of bias legend (A) Inappropriate eligibility criteria (B) Inappropriate methods for exposure and outcome (C) Not controlled for confounding (D) Incomplete or inadequate follow-up	Ever 745 e variables	nts 559 1 99	Total 165196 1000	Events 63842 139	Total 125385 1000	M.H, Random, 95% Cl 0.89 (0.88, 0.89) 0.71 (0.56, 0.91)	M-H, Random, 95% Cl	A B C D E
1.2.1 Education Sarode 2010 - Nr of RBC products transfused 1.2.2 Education + Audit/feedback Brandis 1994 - units transf per 1000 admissions Risk of bias legend (A) Inappropriate eligibility criteria (B) Inappropriate methds for exposure and outcome (C) Not controlled for confounding (D) Incomplete or inadequate follow-up (E) Other limitations	Ever 745 e variables	nts 559 1 99	Total 165196 1000	Events 63842 139	Total 125385 1000	M.H, Random, 95% Cl 0.89 (0.88, 0.89) 0.71 (0.56, 0.91)	M-H, Random, 95% Cl	A B C D E
1.2.1 Education Sarode 2010 - Nr of RBC products transfused 1.2.2 Education + Audit/feedback Brandis 1994 - units transf per 1000 admissions Risk of bias legend (A) Inappropriate eligibility criteria (B) Inappropriate methds for exposure and outcomm (C) Not controlled for confounding (D) Incomplete or inadequate follow-up (E) Other limitations	Ever 745 e variables	nts 559 1 99	Total 165196 1000	Events 63842 139	Total 125385 1000	M.H, Random, 95% Cl 0.89 (0.88, 0.89) 0.71 (0.56, 0.91)	M-H, Random, 95% Cl	A B C D E

			Certainty as	sessment					
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Impact	Certainty	Importance
Mimica 2008 - Torella 2002 (C Torella 2002 (C Torella 2002 (C Torella 2002 (C 1.8.2 Guideline Müller 2004 - o Spencer 2005 - 1.8.3 Guideline Garrioch 2004 - Risk of bias lec (A) Inappropria (C) Not controll (D) Incomplete (E) Other limita	Number of patients transfused Number of patients transfused CABG) - Nr of patients transfused CABG) - Nr of patients transfused CABG) - Nr of patients transfused Feducation perations requiring transfusion transfusion rate Feducation + Form + Audit/fed patients transfused e telucation transfused definition transfused	Events I 15' 44 d 99 d 22' Ised 11 edback 25' come variables	896 258 123 78 54 6 200 114 20 2 40 24 4 3 78 12 8 5 57 26 5 4 222 79 22 3 45 45 6 7 7336 320 726	9 0,79 [0.63, 0.97] 0 0,79 [0.65, 0.96] 5 1,03 [0.70, 1.53] 0 1.54 [0.79, 2.98] 0 0.51 [0.30, 0.84] 6 0.57 [0.41, 0.78] 3 0.56 [0.38, 0.83] 2 0.80 [0.68, 0.93] 0 0.5 10.00 [0.68, 0.93]	avours intervention Favours				
Behaviour 6	al intervention(s) v observational studies	ersus no in	tervention: FFP utili: not serious	zation not serious	not serious	none	(Statistically significant) reduction in FFP utilization after versus before implementation of different behavioural interventions (Guideline + Audit/feedback , Form + Audit/feedback, Guideline + Audit/feedback + Education + Form, Education only, Audit/approval + Form). In one study (Hui 2005), a statistically significant reduction in inappropriate FFP transfusions could not be demonstrated. (Figure 8-10)	⊕ VERY LOW	CRITICAL

1									
Study or Subgroup	Behaviora Mean	il interventi SD	ion Total	No int Mean	ervention SD 1	Std. Mean E	ifference om. 95% Cl	Std. Mean Differen IV, Random, 95% (
1.3.1 Guideline + Audit/feedback	Mean	30	Total	Mean	30 1	otal IV, Rand	/m, 35 / Ci	IV, Randon, 33/0	
Meyer 2017 - Nr of FFP units transf monthly	160.7	52	327	188	42	434 -0.59 [-).73,-0.44]	+	? • • • •
1.3.2 Form + Audit/feedback Yeh 2006 - Nr of FFP units transfused monthly	2,462.5	617.5	2462 (9,693.7	1,561.2 9)693 -5.09 [-:	5.16, -5.01]	н. — — — — — — — — — — — — — — — — — — —	•••?•
1.3.3 Guideline + Audit/feedback + Education + Fo Morrison 1993 - FFP units transfus monthly	orm 1.5	3	144	12.5	9.4	366 -1.35 [-	.56, -1.14]	+	••??•
								-10 -5 0 Favours intervention Favours	5 10 no intervention
Risk of bias legend (A) Inappropriate eligibility criteria (B) Inappropriate methds for exposure and outcon (C) Not controlled for confounding (D) Incomplete or inadequate follow-up (E) Other limitations	ne variable:	3							
Figure 8: behavioural versus no	behavi	oural ir	nterv	entio	n: outc	ome numt	er of F	FP units transfused (continuous)
B	ehavioral i	nterventic	on No	o interve	ntion	Risk Ratio		Risk Ratio	Risk of Bias
Study or Subgroup	Events	T/	otal E	vents	Total I	M-H, Random, 9	5% CI	M-H, Random, 95% CI	ABCDE
1.4.1 Education									
Sarode 2010 - Nr of TP units transfused	25959	1651	196 3	30844 1	25365	0.64 [0.63,	0.65]	1	
1.4.2 Audit/approval + Form									
Cheng 1996 - Nr of FFP units transfused	1375	21/	587	2005	20583	0.65 [0.61,	0.70]	+	•••?•
							0.0 F	1 0.1 1 avours intervention Favours n	0 100 0 intervention
Risk of bias legend (A) Inappropriate eligibility criteria (B) Inappropriate methds for exposure and out (C) Not controlled for confounding (D) Incomplete or inadequate follow-up (E) Other limitations	tcome varia	ables							

			Certainty as	sessment					
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Impact	Certainty	Importance
Study or Subg	roup	Behavioral int Events		Risk Ratio M-H, Random, 95% Cl	Risk Ratio M-H, Random, 95% C	Risk of Bias I A B C D E			
1.9.1 Audit/app Cheng 1996 - i	oroval + Form inappropriate FFP transfusions	3 293	1375 1424 2005	0.30 [0.27, 0.33]	+	•••?•			
	e + Form + Audit/feedback opropriate FFP transfusions	17	137 10 131	1.63 [0.77, 3.42] 0.01 Fa	0.1 1 vours intervention Favours (• • • ? •			
 (B) Inappropria (C) Not controll (D) Incomplete (E) Other limita 	ite eligibility criteria te methds for exposure and or led for confounding or inadequate follow-up tions behavioural versus i		iral intervention: pro	portion of patients	receiving FFP trans	sfusion			
Behaviour	al intervention(s) v	ersus no in	tervention: PLT utili	zation					
5	observational studies	serious ^c	not serious	not serious	not serious	none	(Statistically significant) reduction in PLT utilization after versus before implementation of different behavioural interventions (Form + Audit/feedback, Education only, Audit/approval + Form, Guideline only). In one study (Hui 2005), a statistically significant reduction in inappropriate PLT transfusions could not be demonstrated. (Figure 11-13)	⊕⊖⊖⊖ VERY LOW	CRITICAL

	Debautant		No inter-				Dials of D're-
Study or Subgroup	Behavioral inte Mean	ervention SD Total	No inter Mean	SD Total	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% Cl	Risk of Bias A B C D E
1.5.1 Form + Audit/feedback							
Yeh 2006 - Nr of PLT units transfused monthly	7,042.3 876	5.2 7042	8,229.1 4	84.4 8229	-1.71 [-1.75, -1.67]	+ -4 -2 0 2 Favours intervention Favours no inter	●●● ? ● 4 vention
Risk of bias legend (A) Inappropriate eligibility criteria (B) Inappropriate methds for exposure and outco (C) Not controlled for confounding (D) Incomplete or inadequate follow-up (E) Other limitations	ome variables						
Figure 11: behavioural versus n	no behaviou	ural inte	rventior	n: outco	ome number of	PLT units transfused (cont	tinuous)
Study or Subgroup	Behavioral inter Events	vention I Total	No interven Events		Risk Ratio I, Random, 95% Cl	Risk Ratio M-H, Random, 95% Cl	Risk of Bias A B C D E
1.6.1 Education Sarode 2010 - Nr of PLT units transfused	4609	165196	4338 12	5365	0.81 [0.77, 0.84]	+	•••?•
1.6.2 Audit/approval + Form Cheng 1996 - Nr of PLT units transfused	5427	21587	6586 2	0583	0.79 [0.76, 0.81]		•••?•
					<u>اب</u> 0.0 ۴	1 0.1 1 10 Favours intervention Favours no intervention	100 ention
Risk of bias leagend (A) Inappropriate eligibility criteria (B) Inappropriate methds for exposure and or (C) Not controlled for confounding (D) Incomplete or inadequate follow-up (E) Other limitations	utcome variables	3					
Figure 12: behavioural versus n	no behaviou	ural inte	rventior	n: outco	ome number of	PLT units transfused (dich	otomous)
Study or Subgroup	Behavioral in Events	tervention Total	No interv Events		Risk Ratio I-H, Random, 95% Cl	Risk Ratio M-H, Random, 95% Cl	Risk of Bias ABCDE
1.10.1 Guideline Ballantyne 2004 - transfusion rate	35	295	i 122	393	0.38 [0.27, 0.54]	+	
1.10.2 Audit/approval + Form Cheng 1996 - inappropriate PLT transfusions	673	5427	1488	6586	0.55 [0.50, 0.60]	+	•••?•
1.10.3 Guideline + Form + Audit/feedback Hui 2005 - inappropriate PLT transfusions	14	444	18	385	0.67 [0.34, 1.34]	-+	•••?•
					L O	01 0.1 1 10 Favours intervention Favours no interv	100 rention
Risk of bias legend (A) Inappropriate eligibility criteria (B) Inappropriate methds for exposure and ou (C) Not controlled for confounding (D) Incomplete or inadequate follow-up (E) Other limitations	tcome variables						
Figure 13: behavioural versus n (dichotomous)	io behaviou	ural inte	rventior	n: propo	ortion of patien	ts receiving PLT transfusic	'n

			Certainty as	sessment					
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Impact	Certainty	Importance
Behaviour	al intervention(s) v	versus no in	tervention: Cryopre	cipitate				•	
1	observational studies	serious ^d	not serious	not serious	serious ^e	none	(Statistically significant) reduction in cryoprecipitate utilization after versus before implementation of a behavioural intervention (Guideline + Form + Education + Audit/feedback) (Figure 14)	⊕⊖⊖⊖ VERY LOW	IMPORTANT
Study or Sul 1.7.1 Guideli Morrison 199	ne + Form + Education + A	D Total Mea udit/feedback	an SD Total IV, Rand	Difference Jom, 95% CI -1.19, -0.78] -4 Favours in	Std. Mean Difference IV, Random, 95% CI + -2 0 2 ntervention Favours no in	Risk of Bias A B C D E ● ● ? ? ● 4 ntervention			
(B) Inapprop (C) Not contr (D) Incomple (E) Other lim	riate eligibility criteria riate methds for exposure a olled for confounding te or inadequate follow-up itations behavioural versus		iables iral intervention: out	come number of cr	yoprecipitate units	s transfused			
Guideline	+ Form + Audit ve	ersus Guide	line: RBC utilization					I	I
1	observational studies	serious ^f	not serious	not serious	serious ^e	none	(Statistically significant) reduction in RBC utilization after implementation of a guideline + form + audit versus a guideline only. (Figure 4-5)	⊕⊖⊖⊖ VERY LOW	CRITICAL

			Certainty ass	sessment					
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Impact	Certainty	Importance
<u>Risk of bias lee</u> (A) Inappropria (B) Inappropria (C) Not controll (D) Incomplete (E) Other limita	05 0.3 0.9 Not applicable Leffect: Z = 4.35 (P < 0.0001 <u>gend</u> ate eligibility criteria ate methds for exposure an led for confounding Lef for confounding or inadequate follow-up ations	Total Mean 186 1 186) d outcome variabl	<u>SD Total Weight IV, Ra</u> 2 186 100.0% -0.70 186 100.0% -0.70 les Guideline: number o	I [-1.02, -0.38] [-1.02, -0.38] -4 Favours Guid	Mean Difference IV, Random, 95% Cl	Risk of Bias A B C D E			
Test for overall <u>Risk of bias le</u> (A) Inappropria (B) Inappropria (C) Not control (D) Incomplete (E) Other limita Figure 5: Gu	14 14 Not applicable I effect: Z = 3.59 (P = 0.000 aend ate eligibility criteria ate methds for exposure ar lied for confounding e or inadequate follow-up ations	186 40 186 40 3) nd outcome varial	186 100.0% 0.35)	[0.20, 0.62] [0.20, 0.62] 0.01 0 Favours Guide	Worm/audit Favours Guid				

	Certainty assessment								
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Impact	Certainty	Importance
2	observational studies	serious ^g	not serious	not serious	serious ^e	none	(Statistically significant) reduction in number of RBC transfusions per 1000 discharges (Tavares 2014) after implementation of CPOE in addition to a guideline + education. However, a statistically significant difference in % RBC orders with a pretransfusion Hb level >8 g/dL could not be demonstrated. (Patel 2016)	⊕⊖⊖⊖ VERY LOW	CRITICAL

CI: Confidence interval

a. see "Risk of bias" items in forest plots (figure 1-3); b. see "Risk of bias" items in forest plots (figure 8-10); c. see "Risk of bias" items in forest plots (figure 11-13); d. see "Risk of bias" items in forest plot (figure 14); e. Limited sample size; f. see "Risk of bias" items in forest plots (figure 4-5); g. see "Risk of bias" items in forest plots (figure 6-7)

GRADE domain: resource costs

FINANCIAL OUTCOME	S		
Estimated annual		Saving of 2500 units FFP and 5000	
savings on FFP and PLT		units PLT at HK\$200 ~£ 16 each: > HK\$ 1 000 000 ~ £ 80 000	Cheng 1996
Cost savings		\$ 145 156 savings comparing both study periods	Morrison, 1993
Average saving per operation	After vs before implementation of	227.80 SFr	Muller, 2004
Estimated annual saving expenditure for blood transfusions	intervention	52.280 SFr	Muller, 2004
RBC product acquisition cost savings		\$ 130.000	Patel, 2016

Detailed evidence summary

Торіс	Patient Blood Management (PBM)
Subtopic	Implementation
Intervention	Behavioural interventions to promote/support the implementation of blood
	product ordering
Question (PICO)	Is a specific behavioural intervention to promote the implementation of blood product ordering [intervention] more effective to improve clinical and economic outcomes [outcomes] compared to no/another behavioural intervention [comparison]?
Search Strategy	Databases
Search Strategy	 Databases The Cochrane Library (systematic reviews and controlled trials) using the following search strategy: "Patient Blood Management":ti,ab,kw [mh Education] OR educat*:ti,ab,kw OR implement*:ti,ab,kw OR monitor*:ti,ab,kw OR [mh "information dissemination"] OR disseminat*:ti,ab,kw OR adopt*:ti,ab,kw OR [mh "quality improvement"] OR improv*:ti,ab,kw OR [mh "organizational innovation"] OR change*:ti,ab,kw OR program*:ti,ab,kw OR practice*:ti,ab,kw OR scal*:ti,ab,kw OR diffusion:ti,ab,kw OR incorporation:ti,ab,kw OR adherence:ti,ab,kw OR transformation:ti,ab,kw OR transformation:ti,ab,kw OR sustainab*:ti,ab,kw OR adherence:ti,ab,kw OR noutin*:ti,ab,kw OR sustainab*:ti,ab,kw OR capacity:ti,ab,kw OR integration:ti,ab,kw OR maintenance:ti,ab,kw OR capacity:ti,ab,kw OR integration:ti,ab,kw MEDLINE (via PubMed interface) using the following search strategy: "Patient Blood Management"[TIAB] Education[Mesh] OR educat*[TIAB] OR implement*[TIAB] OR monitor*[TIAB] OR "information dissemination"[Mesh] OR disseminat*[TIAB] OR adopt*[TIAB] OR "quality improvement"[Mesh] OR incorporation[TIAB] OR program*[TIAB] OR reactice*[TIAB] OR sustainab*[TIAB] OR change*[TIAB] OR program*[TIAB] OR practice*[TIAB] OR transformation[TIAB] OR ransfer[TIAB] OR uptake[TIAB] OR diffusion[TIAB] OR transfer[TIAB] OR ransfer[TIAB] OR uptake[TIAB] OR sustainab*[TIAB] OR institutionali*[TIAB] OR ransfer[TIAB] OR uptake[TIAB] OR capacity[TIAB] OR institutionali*[TIAB] OR ransfer[TIAB] OR uptake[TIAB] OR capacity[TIAB] OR institutionali*[TIAB] OR ransfer[TIAB] OR maintenance[TIAB] OR maintenance[TIAB] OR capacity[TIAB] OR institutionali*[TIAB] OR maintenance[TIAB] OR capacity[TIAB] OR integration[TIAB] 1 AND 2 (#hits on July 18: 210)
	 Embase (via Embase.com interface) using the following search strategy: 1. 'Patient Blood Management':ab,ti 2. Education/exp OR educat*:ab,ti OR implement*:ab,ti OR monitor*:ab,ti OR 'information dissemination'/exp OR disseminat*:ab,ti OR adopt*:ab,ti OR 'total quality management'/exp OR improv*:ab,ti OR change*:ab,ti OR program*:ab,ti OR practice*:ab,ti OR scal*:ab,ti OR diffusion:ab,ti OR incorporation:ab,ti OR adherence:ab,ti OR transformation:ab,ti OR translation:ab,ti OR transfer:ab,ti OR uptake:ab,ti OR sustainab*:ab,ti OR institutionali*:ab,ti OR routin*:ab,ti OR maintenance:ab,ti OR capacity:ab,ti OR integration:ab,ti 3. 1 AND 2 (#hits on July 18: 507) Transfusion Evidence Library using the following search strategy:
	 Patient blood management (#hits on July 18: 307) educat* OR implement* OR monitor* OR disseminat* OR adopt* OR improv* OR "organizational innovation" OR change* OR program* OR practice* OR

	scal* OR diffusion OR incorporation OR adherence OR transformation OR
	translation OR transfer OR uptake OR sustainab* OR institutionali* OR routin* OR maintenance OR capacity OR integration
	3. 1 AND 2 (#hits on July 18: 141)
	$3. \mathbf{I} \text{ AND } 2 (\text{"Ints on Sury 10. If I})$
	After removing duplicates, 674 papers were screened on title and abstract
	In addition to the current search strategies, the first 20 related citations of all
	included papers were screened and included (if appropriate).
Search date	30 th of January 2018
In/Exclusion	Population: <i>Included</i> : patients who might need transfusion (surgical and non-
criteria	surgical patients/ acute and chronic disease patients/ adults and children).
	Intervention: <i>Included:</i> the following behavioural interventions to promote the
	implementation of a PBM program:
	- Behavioral interventions intended to promote appropriate blood usage.
	➔ Guidelines
	 Educational sessions (group or individual)
	➔ A reminder system (computer aids or transfusion forms containing
	reminders of appropriate criteria for transfusion)
	Audit with feedback (retrospective audits with feedback given to
	individuals or groups after the transfusion)
	Audit with approval (audit with approval needed before transfusion
	of products).
	If guidelines were disseminated or accompanied by educational
	sessions, then the study interventions were classified as guidelines and
	education.
	Comparison: another or no intervention
	Outcome: Included: Tinmouth systematic review (effectiveness behavioural
	interventions to reduce blood product utilization): the number of units transfused
	and the proportion of patients who received transfusions. Additional outcome:
	financial outcomes. <i>Excluded</i> : papers that only narratively/descriptively reported on
	blood product utilization outcomes (i.e. no raw data and/or effect estimated, only
	p-values, percentages).
	Study design: <u>Include</u> : 1) we used the systematic review by Tinmouth et al (2005),
	the thesis that performed an update of the Tinmouth review until 2010 and we
	performed an update of the Tinmouth review between 2010 and 2017. Included
	individual studies involve both an intervention group and a control group. Controlled
	clinical trials that mandated adherence to a specific transfusion trigger or protocol
	were excluded.
	Language: English, French and German

Author, year,	Study design	Population	Comparison	Remark		
Country						
Abelow, 2017, Israel	Observational: Non-concurrent cohort study	Targeted physicians: all	Comparison: after versus before implementation intervention	Update 2010-2018		
			Intervention(s): - Guideline - Education - Audit/feedback			

Characteristics of included studies

Ballantyne, 2004, UK	Observational: Non-concurrent cohort study	Targeted physicians: surgeons	Blood products: RBC Comparison: after versus before implementation intervention	From thesis (2010)
			Intervention(s): - Guideline	
			Blood products: all	
Brandis, 1994, South Africa	Observational: Non-concurrent cohort study	Targeted physicians: all	Comparison: after versus before implementation intervention	From Tinmouth review (2005)
	(prospective)		Intervention(s): - Audit/feedback - Education	
			Blood products: RBC	
Cheng, 1996, Hong Kong	Observational: Non-concurrent cohort study	Targeted physicians: all	Comparison: after versus before implementation intervention	From Tinmouth review (2005)
	(prospective, retrospective)		Intervention(s): - Audit/approval - Form	
			Blood products: FFP, platelets	
Eindhoven, 2005, The Netherlands	Observational: controlled before- after study	Targeted physicians: surgeons	Comparison: Intervention 1 versus intervention 2	From thesis (2010)
			Intervention 1: - Guideline	
			Intervention 2: - Guideline - Form - Audit	
			Blood products: RBC	
Fontana, 2014, Switzerland	Observational: Non-concurrent cohort study (prospective)	Targeted physicians: all	Comparison: after versus before implementation intervention	Update 2010-2018
			Intervention(s): - Guideline	
			Blood products: RBC	
Garrioch, 2004, UK	Observational: Non-concurrent cohort study	Targeted physicians: all	Comparison: after versus before implementation intervention	From thesis (2010)
			Intervention(s): - Guideline - Education - Form	
			- Audit/feedback	
			Blood products: RBC	

Switzerland	Non-concurrent cohort study (prospective)	surgeons	before implementation intervention Intervention(s): - Education - Guideline	review (2005)
Muller, 2004,	Observational:	Targeted physicians:	Intervention(s): - Audit/feedback - Education - Guideline - Form Blood products: RBC Comparison: after versus before implementation	From Tinmouth
Morrison, 1993, USA	Observational: Non-concurrent cohort study	Targeted physicians: obstetricians/gynaecologists	Blood products: RBC Comparison: after versus before implementation intervention	From Tinmouth review (2005)
	cohort study		intervention Intervention(s): - Guideline	
Mimica, 2008, Brazil	Observational: Non-concurrent	Targeted physicians: neonatal	Blood products: FFP Comparison: after versus before implementation	From thesis (2010)
			Intervention(s): - Guideline - Audit/feedback	
Meyer, 2017, USA	Observational: Non-concurrent cohort study	Targeted physicians: anaesthesiologists	Blood products: RBC Comparison: after versus before implementation intervention	Update 2010-2018
			Intervention(s): - Guideline	
Lee, 2015, Hong Kong	Observational: Non-concurrent cohort study	Targeted physicians: surgeons	Comparison: after versus before implementation intervention	Update 2010-2018
			Blood products: FFP, platelets, cryoprecipitate	
			Intervention(s): - Guidelines - Form - Audit/feedback	
Hui, 2005, Australia	Observational: Non-concurrent cohort study	Targeted physicians: all	Comparison: after versus before implementation intervention	From thesis (2010)

	•		1	
			Intervention(s) 1 :	
			- Guideline	
			- Education	
			Intervention(s) 2 (followed	
			after intervention 1):	
			- CPOE	
			Blood products: RBC	
Sarode, 2010, USA	Observational:	Targeted physicians: all	Comparison: after versus	From thesis (2010)
	Non-concurrent		before implementation	
	cohort study		intervention	
	,			
			Intervention(s):	
			- Education	
			Blood products: RBC, FFP,	
			PLT	
Spencer, 2005, UK	Observational:	Targeted physicians:	Comparison: after versus	From thesis (2010)
	Non-concurrent	surgeons	before implementation	
	cohort study	surgeons	intervention	
	conore study			
			Intervention(s):	
			- Education	
			- Guideline	
			Guideinie	
			Blood products: all	
Tavares, 2014,	Observational:	Targeted physicians: all	Comparison: after versus	Update 2010-2018
USA	Non-concurrent	Targetea physicians. an	before implementation	000000 2010 2010
034	cohort study		intervention	
	conort study		intervention	
			Intervention(s) 1 :	
			- Guideline	
			- Education	
			- Education	
			Intervention(s) 2 (followed	
			after intervention 1):	
			- CPOE	
			Blood products: RBC	
Torella, 2002, UK	Observational:	Targeted physicians:	Comparison: after versus	From Tinmouth
	Non-concurrent	surgeons	before implementation	review (2005)
	cohort study	Surgeons	intervention	10000
	(retrospective)			
	(renospective)		Intervention(s):	
			- Guideline	
			Guideinie	
			Blood products: RBC	
Yeh, 2006, Taiwan	Observational:	Targeted physicians: all	Comparison: after versus	From thesis (2010)
	Non-concurrent		before implementation	. 10111 (10313 (2010)
	cohort study		intervention	
	conore study			
			Intervention(s):	
			- Form	
			- Audit/feedback	
			Addiviceuback	
			Blood products: FFP	
	L	I	bioou products. Hr	1

Synthesis of findings						
	Comparison/Risk factor	Effect Size	#studies, # participants	Reference		
	lactor					

The number of units to	ransfused			
RBC (Figure 1-7) Number of RBC transfused >8 g/dL	After vs before implementation of intervention	Statistically significant: 2334 vs 3114 MD: -780 (p<0.05) in favour of behavioural intervention	1, not reported	Abelow, 2017
Units transfused per 1000 hospital admissions	After vs before implementation of intervention	Statistically significant: 99/1000 vs 139/1000 RR: 0.71, 95%CI [0.56;0.91] (p=0.006)* in favour of behavioural intervention	1, 2769 vs 2458	Brandis, 1994
PRC/patient	Guideline (after 1 year) vs standard customs	Statistically significant: 0.3±0.9 vs 1.0±2.0 MD: -0.7, 95%CI [-1.02;-0.38] (p<0.0001) * In favour of guideline	1, 186 vs 186 §	Eindhoven, 2005
Volume of RBC transfused (ml/kg) <i>Median [Range]</i>	Very strict guideline vs Strict guideline	Statistically significant: 15 [0-137] vs 36 [0-290] Median difference: -21 £† (p=0.001) In favour of Very strict guideline	1 study, N (patients): 78 vs 69 § n (transfusions): 48 vs 54 m (Units transfused): not reported	Mimica 2008
Units per month transfused	after versus before implementation of intervention	Statistically significant: 40.7±17.2 vs 107.9±45.96 MD: -67.20, 95%CI [-72.86;-61.54] (p<0.00001) * In favour of after implementation of intervention	1, 144 vs 336	Morrison, 1993
RBC orders with a pretransfusion Hb level >8 g/dL	After education versus before implementation of intervention			
Number of RBC products transfused (Units) (relative to the total number of admissions)	Education vs No education	<u>Statistically significant</u> : 74559/165196 vs 63842/125365 RR: 0.89, 95% CI [0.88;0.89] (p<0.0001) * In favour of Education	1 study, N (patients): 165196 vs 125365 n (transfusions): not reported m (Units transfused): 74559 vs 63842	Sarode 2010
Units transfused (median (IQR))	After vs before implementation of guideline	Coronary artery bypass graft Not statistically significant: 0 (0-2) vs 1 (0-2) (p=0.12) Total hip replacement Statistically significant: 0 (0-1.5) vs 2 (0-3) (p=0.003) in favour of after implementation of quideline	1, 200 vs 200	Torella, 2002
		Colectomy Not statistically significant: 2 (0-5) vs 2 (0-5) (p=0.94)	1, 40 vs 45	
Number of RBC units used per month	Computerized feedback + Weekly audit/feedback vs No intervention or Education	<u>Statistically significant</u> : 3769.0±271.3 vs 4442.3±147.6 MD: -673.3, 95% CI [-920.9; -425.7] (p<0.0001) * In favour of Computerized feedback + Weekly audit/feedback	1 study, N (patients): not reported n (transfusion requests): not reported m (Units transfused): 3769.0 vs 4442.3 q (number of months analysed): 7 vs 4 §	Yeh 2006

RBC units per patient	after versus before implementation of	<u>Statistically significant</u> : 0.4 vs 0.5	1, 896 vs 1238	Fontana, 2014
	intervention	MD: -0.1, 95% CI [-0.08; -0.2] (p=0.014)* In favour of after implementation behavioural intervention		
	after versus before implementation of intervention	Not statistically significant: 1.67±0.58 vs 1.8±0.92 MD: -0.13, 95% CI [-0.35;0.09] (p=0.24)*	1, 96 vs 97	Lee, 2015
transfusions per 1000	After (CPOE followed after education) versus after education (only)	<u>Statistically significant:</u> 394/1000 vs 512/1000 RR: 0.77, 95% CI [0.70;0.85] (p<0.00001)* In favour of after implementation behavioural intervention	1, 1000 vs 1000	Tavares, 2014
FFP (Figure 8-10)	1			
Number of FFP units transfused (relative to the total number of admissions)	Form vs Audit/approval	<u>Statistically significant</u> : 1375/21587 vs 2005/20583 RR: 0.65, 95% CI [0.61;0.70] (p<0.0001) * In favour of Form	1 study, N (patients): 21587 vs 20583 n (transfusion requests): FFP = 359 vs 390 m (Units transfused) = FFP = 1375 vs 2005	Cheng 1996
transfused per month	after versus before implementation of intervention	Not statistically significant 160.7±52 vs 188.4±42 MD: -27.7, 95%CI [-27.0;84] (p>0.05) *	1, 327.3 FFP units per month requested versus 434.9	Meyer, 2017
Units per month transfused	after versus before implementation of intervention	Statistically significant: 1.5±3.0 vs 12.5±9.4 MD: -11.0, 95%CI [-12.12;-9.88] (p<0.00001) * In favour of implementation of intervention (Mean±SD calculated in Excel)	1, 144 vs 366	Morrison, 1993
	Education vs No education	Statistically significant: 25959/165196 vs 30844/125365 RR: 0.64, 95% CI [0.63;0.65] (p<0.0001) * In favour of Education	1 study, N (patients): 165196 vs 125365 n (transfusions): not reported m (Units transfused): 25959 vs 30844	Sarode 2010
used per month	Computerized feedback + Weekly audit/feedback vs No intervention or Education	Statistically significant: 2462.5±617.5 vs 9693.7±1561.2 MD: -7231.2, 95% CI [-8828.1; -5634.3] (p<0.0001) * In favour of Computerized feedback + Weekly audit/feedback	1 study, N (patients): not reported n (transfusion requests): 724 vs 2062 m (Units transfused):	Yeh 2006
PLT (Figure 11-13) Number of PLT units transfused (relative to the total number of admissions)	Form vs Audit/approval	<u>Statistically significant</u> : 5427/21587 vs 6586/20583 RR: 0.79, 95% CI [0.76;0.81] (p<0.0001) * In favour of Form	1 study, N (patients): 21587 vs 20583 n (transfusion requests): PLT = 997 vs 999 m (Units transfused) = PLT = 5427 vs 6586	Cheng 1996
	Education vs No education	Statistically significant: 4609/165196 vs 4338/125365 RR: 0.81, 95% CI [0.77,0.84]	1 study, N (patients): 165196 vs 125365	Sarode 2010

number of		(p<0.0001) *	n (transfusions): not	
admissions)		In favour of education	reported	
			m (Units transfused): 4609	
			vs 4338	
Number of PLT units	Computerized feedback		1 study,	Yeh 2006
used per month	+ Weekly	7042.3±876.2 vs 8229.1±484.4	N (patients): not reported	
	audit/feedback vs No intervention or	MD: -1186.8, 95% CI	n (transfusion requests):	
	Education	[-1991.0; -382.7] (p=0.004) *	not reported m (Units transfused):	
	Luucation	(p=0.004) In favour of Computerized feedback +		
		Weekly audit/feedback	q (number of months	
			analysed): 7 vs 4 §	
Cryoprecipitate (Figure 14)				
Units per month	after versus before	Statistically significant:	1, 144 vs 366	Morrison,
transfused	implementation of	0.6±1.3 vs 3.2±3.0		1993
	intervention	MD: -2.60, 95%CI [-2.98;-2.22]		
		(p<0.00001) *		
		In favour of implementation of		
		intervention		
Proportion of patients	s who received transfusior	(Mean±SD calculated in Excel)		
RBC (Figure 1-7)		13		
Patients transfused	Guideline (after 1 year)	Statistically significant:	1, 186 vs 186	Eindhoven,
	-	14/186 vs 40/186 §		2005
		RR: 0.35, 95%CI [0.20;0.62]		
		(p=0.0003) *		
		In favour of guidelines (after 1 year)		
Patients transfused	After vs before	Statistically significant:	1, 7336 vs 7262	Garrioch, 2004
	implementation of	257/7336 vs 320/7262		
	intervention	RR: 0.80, 95%CI [0.68;0.93]		
		(p=0.0052)*		
		in favour of after implementation of intervention		
Proportion of infants	Very strict guideline vs	Statistically significant:	1 study,	Mimica 2008
transfused	Strict guideline	48/78 vs 54/69 §	N (patients): 78 vs 69	
	5	RR: 0.79, 95% CI [0.63;0.97]	n (transfusions): 48 vs 54	
		(p=0.03) *	m (Units transfused): not	
		In favour of Very strict guideline	reported	
Operations requiring	After vs before	Statistically significant:	1, 222 operations	Muller, 2004
transfusion	implementation of	44/222 vs 79/226	(in 217 patients)	
	intervention	aOR: 0.20, 95%CI [0.10;0.39]	vs 226 operations	
		(p<0.05)	(in 208 patients)	
		in favour of after implementation of intervention		
% RBC orders with a	After versus before	Statistically significant:	1, not reported	Patel, 2016
pretransfusion Hb		6.36% vs 16.64%		1 4101, 2010
level >8 g/dL	behavioural intervention			
,		in favour of after implementation of		
		intervention		
	CPOE + education	Not statistically significant:	1, not reported	Patel, 2016
	versus education	6.1% vs 6.3%		
		(p>0.05)		
Transfusion rate	-	Statistically significant:	1, 45 vs 63	Spencer, 2005
	implementation of	18/45 vs 45/63 §		
	guideline	RR: 0.56, 95%CI [0.38;0.83]		
		(p=0.004)*		
		he for any of 1 ft		
		In favour of 1 year after		
Number of patients	After vs hefore	implementation of guideline	1 200 vs 200	Torella 2002
Number of patients transfused	After vs before implementation of		1, 200 vs 200	Torella, 2002

		RR: 0.79, 95%CI [0.65;0.96] (p=0.0174)* <i>in favour of after implementation of</i> <i>guideline</i> <i>Total hip replacement</i> <u>Statistically significant:</u> 15/57 vs 26/50 RR: 0.51, 95%CI [0.30;0.84] (p=0.0088)* <i>in favour of after implementation of</i> <i>guideline</i> <i>Colectomy</i>	1, 57 vs 50 1, 40 vs 45	-
		Not statistically significant: 22/40 vs 24/45 RR: 1.03, 95%CI [0.70;1.53] (p=0.88)* <i>Transurethral prostatectomy</i> Not statistically significant: 18/78 vs 12/80 RR: 1.54, 95%CI [0.79;2.98] (n=0.20)*	1, 78 vs 80	
Number of patients transfused	After vs before implementation of guideline	(p=0.20)* <u>Statistically significant:</u> 151/896 vs 258/1238 RR: 0.81, 95%CI [0.67;0.97] (p=0.02)* in favour of after implementation of guideline	1, 896 vs 1238	Fontana, 2014
FFP (Figure 8-10) Proportion inappropriate FFP transfusions	Form vs Audit/approval	Statistically significant: 293/1375 vs 1424/2005 RR: 0.30, 95% CI [0.27;0.33] (p<0.0001) * In favour of Form	1 study, N (patients): 21587 vs 20583 n (transfusion requests): FFP = 359 vs 390 m (Units transfused) = FFP = 1375 vs 2005	Cheng 1996
	Form vs No form	Not statistically significant: 17/137 vs 10/131 § RR: 1.63, 95% CI [0.77;3.42] ¥ (p=0.20) *	1 study, N (patients): 95 vs 105 n (transfusion episodes): 137 vs 131 m (Units transfused): 397 vs 396	Hui 2005
PLT (Figure 11-13) Proportion inappropriate PLT transfusions	Form vs Audit/approval	<u>Statistically significant</u> : 673/5427 vs 1488/6586 RR: 0.55, 95% CI [0.50;0.60] (p<0.0001) * In favour of Form	1 study, N (patients): 21587 vs 20583 n (transfusion requests): PLT = 997 vs 999 m (Units transfused) = PLT = 5427 vs 6586	Cheng 1996
	Form vs No form	Not statistically significant: 14/444 vs 18/385 § RR: 0.67, 95% CI [0.34;1.34] ¥ (p=0.26) *	1 study, N (patients): 106 vs 115 n (transfusion episodes): 444 vs 385 m (doses transfused): 529 vs 485	Hui 2005
Transfusion rate	After transfusion protocol vs before transfusion protocol	Statistically significant: 35/295 vs 122/393 § RR: 0.38, 95%CI [0.27;0.54] (p<0.00001)* In favour of transfusion protocol	1, 295 vs 393	Ballantyne, 2004

Estimated annual savings on FFP and		Saving of 2500 units FFP and 5000 units PLT at HK\$200 ~£ 16 each:	Cheng 1996
PLT		> HK\$ 1 000 000 ~ £ 80 000	Cheng 1990
Cost savings		\$ 145 156 savings comparing both study periods	Morrison, 1993
Average saving per operation	After vs before implementation of	227.80 SFr	Muller, 2004
Estimated annual saving expenditure for blood transfusions	intervention	52.280 SFr	Muller, 2004
RBC product acquisition cost savings		\$ 130.000	Patel, 2016

Mean ± SD (unless otherwise indicated)

* Calculations done by the reviewer(s) using Review Manager software

 ${\tt \pounds}$ No means with SDs available, effect size and CI cannot be calculated.

¥ Imprecision (large variability of results)

+ Imprecision (lack of data)

§ Imprecision (limited sample size or low number of events)

Forest plots

	Behavior	al interve	ntion	No int	erventi	on	Std. Mean Difference	Std. Mean Difference	Risk of Bias
udy or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Random, 95% CI	IV, Random, 95% CI	ABCDE
1.1 Guideline									
ontana 2014 - RBC units per patient	0.4	0	0	0.5	0	0	Not estimable		
e 2015 - RBC units transfused	1.67	0.58	96	1.8	0.92	97	-0.17 [-0.45, 0.11]	-+-	
mica 2008 - median volume RBC transfused	15	0	48	36	0	54	Not estimable		
orella 2002 (CABG) - median units transfused	0	0	0	1	0	0	Not estimable		? 🔴 🔁 ? 🛨
orella 2002 (Colectomy) - median units transfused	0	0	0	2	0	0	Not estimable		? 🔴 🔁 ? 😑
orella 2002 (THR) - median units transfused	2	0	0	2	0	0	Not estimable		? 🔴 🔴 ? 😑
1.2 Guideline + Education									
atel 2016 - %RBC orders Hb 8 g/dL	6.36	0	0	16.64	0	0	Not estimable		? 🛛 🖨 🕒 🕄
1.3 Guideline + Education + Form + Audit/feedback									
orrison 1993 - RBC units transfused monthly	40.7	17.2	144	107.9	45.96	336	-1.69 [-1.92, -1.47]	+	•••??•
1.4 Form + Audit/feedback									
eh 2006 - Nr of RBC units transfused monthly	3,769	271.3	3769	4,442.3	147.6	4442	-3.15 [-3.22, -3.09]	+	•••?•
								-4 -2 0 2 4 Favours intervention Favours no interven	

(C) Inappropriate methods for exposure and outcome variables (C) Not controlled for confounding (D) Incomplete or inadequate follow-up

(E) Other limitations

Figure 1: behavioural versus no behavioural intervention: outcome number of RBC units transfused (continuous)

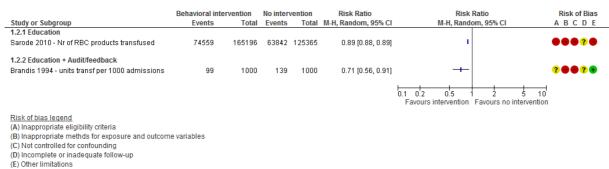


Figure 2: behavioural versus no behavioural intervention: outcome number of RBC units transfused (dichotomous)

	Behavioral interv	ention	No interv	ention	Risk Ratio	Risk Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	M-H, Random, 95% CI	M-H, Random, 95% Cl	ABCDE
1.8.1 Guideline							
Fontana 2004 - Number of patients transfused	151	896	258	1238	0.81 [0.67, 0.97]	+	
Mimica 2008 - proportion of infants transfused	48	78	54	69	0.79 [0.63, 0.97]	+	
Torella 2002 (CABG) - Nr of patients transfused	90	200	114	200	0.79 [0.65, 0.96]	+	? 🔴 🖨 ? 🛨
Torella 2002 (Colectomy) - Nr of pts transfused	22	40	24	45	1.03 [0.70, 1.53]	+	? 🔴 🖨 ? 🕒
Torella 2002 (prostatectomy) - Patients transfused	18	78	12	80	1.54 [0.79, 2.98]	++	? 🔴 🔁 ? 🕒
Torella 2002 (THR) - Nr of patients transfused	15	57	26	50	0.51 [0.30, 0.84]	-+-	? 🔴 🔁 ? 🕒
1.8.2 Guideline + Education							
Müller 2004 - operations requiring transfusion	44	222	79	226	0.57 [0.41, 0.78]	+	
Spencer 2005 - transfusion rate	18	45	45	63	0.56 [0.38, 0.83]	-+-	••?••
1.8.3 Guideline + Education + Form + Audit/feedback	τ						
Garrioch 2004 - patients transfused	257	7336	320	7262	0.80 [0.68, 0.93]	+	? • • • •
						0.01 0.1 1 10 10 Favours intervention Favours no interventi	-

Risk of bias legend (A) Inappropriate eligibility criteria (B) Inappropriate methods for exposure and outcome variables (C) Not controlled for confounding

(D) Incomplete or inadequate follow-up

(E) Other limitations

Figure 3: behavioural versus no behavioural intervention: proportion of patients receiving RBC transfusion (dichotomous)

	Guideline +	form +	audit	Gui	delin	е		Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl	ABCDE
Eindhoven 2005	0.3	0.9	186	1	2	186	100.0%	-0.70 [-1.02, -0.38]		🛨 ? ? ? 🕈
Total (95% CI)			186			186	100.0%	-0.70 [-1.02, -0.38]	◆	
Heterogeneity: Not ap	plicable									_
Test for overall effect:	Z= 4.35 (P <	0.0001)						Fa	-4 -2 U 2 4 avours Guidel/form/audit Favours Guideline	
Risk of bias legend										
(A) Inappropriate eligi	bility criteria									
(B) Inappropriate met	hds for expos	ure and	outcome	variabl	es					
(C) Not controlled for a	confounding									
(D) Incomplete or inac	dequate follov	v-up								
(E) Other limitations										

Figure 4: Guideline + Form + Audit versus Guideline: number of RBC units transfused per patient.

ABCDE
•???+

Figure 5: Guideline + Form + Audit versus Guideline: proportion of patients receiving RBC transfusions.

Study or Subgroup	CPOE + Edu Events	cation Total	Educat Events		Weight	Risk Ratio M-H, Random, 95% C	Risk Ratio M-H, Random, 95% Cl	Risk of Bias ABCDE
Tavares 2014 - Nr RBC transf per 1000 discharges	394	1000	512	1000	100.0%	0.77 [0.70, 0.85	1	? • • • •
Total (95% CI)		1000		1000	100.0%	0.77 [0.70, 0.85	ı 🔸	
Total events Heterogeneity: Not applicable Test for overall effect: Z = 5.25 (P ≺ 0.00001)	394		512			1	0.01 0.1 1 10 10 Favours CPOE+education Favours education	T _D
Risk of blas legend (A) Inappropriate eligibility criteria (B) Inappropriate methds for exposure and outcome v (C) Not controlled for confounding (D) Incomplete or inadequate follow-up (E) Other limitations	ariables							

Figure 6: Education + CPOE versus Education: number of RBC transfusions per 1000 discharges.

	CPOE -	+ Educa	tion	Edu	catio	n		Mean Difference	Mean Diffe	erence	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% C	I IV, Random,	, 95% CI	ABCDE
Patel 2016 - %RBC orders Hb 8 g/dL	6.1	0	0	6.3	0	0		Not estimable	9		? • • • •
Total (95% CI)			0			0		Not estimable	è.		
Heterogeneity: Not applicable									-100 -50 0	50 100	
Test for overall effect: Not applicable									Favours [experimental] F		
Risk of bias legend											
(A) Inappropriate eligibility criteria											
(B) Inappropriate methds for exposure	and outco	ome vari	iables								
(C) Not controlled for confounding											
(D) Incomplete or inadequate follow-up											

(E) Other limitations

Figure 7: Education + CPOE versus Education: % RBC orders with pretransfusion Hb level >8 g/dL.

	Behavior	al interve	ntion	No in	iterventio	n	Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Random, 95% CI	IV, Random, 95% CI	ABCDE
1.3.1 Guideline + Audit/feedback									
Meyer 2017 - Nr of FFP units transf monthly	160.7	52	327	188	42	434	-0.59 [-0.73, -0.44]	+	? 🗨 🗬 🗣
1.3.2 Form + Audit/feedback Yeh 2006 - Nr of FFP units transfused monthly	2,462.5	617.5	2462	9,693.7	1,561.2	9693	-5.09 [-5.16, -5.01]	4	•••?•
1.3.3 Guideline + Audit/feedback + Education +	Form								
Morrison 1993 - FFP units transfus monthly	1.5	3	144	12.5	9.4	366	-1.35 [-1.56, -1.14]	÷	••??•
								-10 -5 0 5	10
								Favours intervention Favours no interven	ntion
Risk of bias legend									

 Risk of bias legend

 (A) Inappropriate eligibility criteria

 (B) Inappropriate methds for exposure and outcome variables

 (C) Not controlled for confounding

 (D) Incomplete or inadequate follow-up

 (E) Other limitations

Figure 8: behavioural versus no behavioural intervention: outcome number of FFP units transfused (continuous)

	Behavioral inter	vention	No inter	vention	Risk Ratio	Risk Rat	io Risk of Bias
Study or Subgroup	Events	Total	Events	Total	M-H, Random, 95% Cl	M-H, Random,	95% CI A B C D E
1.4.1 Education							
Sarode 2010 - Nr of TP units transfused	25959	165196	30844	125365	0.64 [0.63, 0.65]		
1.4.2 Audit/approval + Form							
Cheng 1996 - Nr of FFP units transfused	1375	21587	2005	20583	0.65 [0.61, 0.70]	+	••••
						L	
						0.01 0.1 1	10 100
						Favours intervention Far	vours no intervention
Risk of bias legend							
 (A) Inappropriate eligibility criteria 							
(B) Inappropriate methods for exposure and	d outcome variable:	5					
(C) Not controlled for confounding							

(D) Incomplete or inadequate follow-up (E) Other limitations

Figure 9: behavioural versus no behavioural intervention: outcome number of FFP units transfused (dichotomous)

	Behavioral inter	vention	No interve	ention	Risk Ratio	Risk	Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	M-H, Random, 95% Cl	M-H, Rand	om, 95% Cl	ABCDE
1.9.1 Audit/approval + Form								
Cheng 1996 - inappropriate FFP transfusions	293	1375	1424	2005	0.30 [0.27, 0.33]	+		
1.9.2 Guideline + Form + Audit/feedback								
Hui 2005 - inappropriate FFP transfusions	17	137	10	131	1.63 [0.77, 3.42]	-	 	••••
						teres and the second se		
						0.01 0.1	1 10	100
						Favours intervention	Favours no inter	rvention
Risk of bias legend								
(A) Inappropriate eligibility criteria								
(B) Inannronriate methos for exposure and out	come variables							

me variables

(C) Not controlled for confounding (D) Incomplete or inadequate follow-up (E) Other limitations

Figure 10: behavioural versus no behavioural intervention: proportion of patients receiving FFP transfusion (dichotomous)

	Behavior	al interve	ntion	No int	erventi	on	Std. Mean Difference	Std. Mean	Difference		Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	IV, Random, 95% CI	IV, Rando	om, 95% Cl		ABCDE
1.5.1 Form + Audit/feedback											
Yeh 2006 - Nr of PLT units transfused monthly	7,042.3	876.2	7042	8,229.1	484.4	8229	-1.71 [-1.75, -1.67]	E. F.			•••?•
								-4 -2	ó ż	4	
								Favours intervention	Favours no inte	rvention	ı
Risk of bias legend											

(A) Inappropriate eligibility criteria (B) Inappropriate methds for exposure and outcome variables (C) Not controlled for confounding (D) Incomplete or inadequate follow-up (E) Other limitations

Figure 11: behavioural versus no behavioural intervention: outcome number of PLT units transfused (continuous)

	Behavioral inte	rvention	No inter	vention	Risk Ratio	Risk	Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	M-H, Random, 95% Cl	M-H, Rando	om, 95% CI	ABCDE
1.6.1 Education								
Sarode 2010 - Nr of PLT units transfused	4609	165196	4338	125365	0.81 [0.77, 0.84]	+		•••?•
1.6.2 Audit/approval + Form								
Cheng 1996 - Nr of PLT units transfused	5427	21587	6586	20583	0.79 [0.76, 0.81]	F		•••
						0.01 0.1 1 Favours intervention	10 100 Favours no intervention	
<u>Risk of bias legend</u> (A) Inappropriate eligibility criteria								

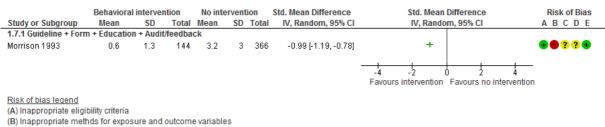
(B) Inappropriate methds for exposure and outcome variables (C) Not controlled for confounding

(D) Incomplete or inadequate follow-up (E) Other limitations

Figure 12: behavioural versus no behavioural intervention: outcome number of PLT units transfused (dichotomous)

	Behavioral inter	vention	No interv	ention	Risk Ratio	Risk	Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	M-H, Random, 95% CI	M-H, Rando	om, 95% Cl	ABCDE
1.10.1 Guideline								
Ballantyne 2004 - transfusion rate	35	295	122	393	0.38 [0.27, 0.54]	+		
1.10.2 Audit/approval + Form								
Cheng 1996 - inappropriate PLT transfusions	673	5427	1488	6586	0.55 [0.50, 0.60]	+		•••
1.10.3 Guideline + Form + Audit/feedback								
Hui 2005 - inappropriate PLT transfusions	14	444	18	385	0.67 [0.34, 1.34]	-+-	_	•••
						L		
						0.01 0.1 Favours intervention	i 10 100 Favours no intervention	
Risk of bias legend								
(A) Inappropriate eligibility criteria								
(B) Inappropriate methds for exposure and outc	ome variables							
(C) Not controlled for confounding								
(D) Incomplete or inadequate follow-up								
(E) Other limitations								

Figure 13: behavioural versus no behavioural intervention: proportion of patients receiving PLT transfusion (dichotomous)



(C) Not controlled for confounding (D) Incomplete or inadequate follow-up

(E) Other limitations

Figure 14: behavioural versus no behavioural intervention: outcome number of cryoprecipitate units transfused (continuous)

Quality of evi Author, Year	Inappropriate eligibility criteria	Inappropriate methods for exposure and outcome variables	Not controlled for confounding	Incomplete or inadequate follow-up	Other limitations
Abelow, 2017	Unclear, there is no information on the (demographic) characteristics	No, similar methods for exposure and outcome variables in 2 groups	Yes, not controlled for confounding factors for the outcomes of interest.	No, follow-up period of 1 year before and 1 year after the implementation of the intervention.	No
Ballantyne, 2004	No, patients from same hospital who underwent same type of surgery. Patients were comparable for age, male: female ratio, BMI, preoperative haemoglobin and preoperative knee score. Operative details were also similar.	No, an audit nurse was employed to collect data, the same 6 consultants at the same institution carried out all operations.	Yes, not controlled for confounding factors for the outcomes of interest.	No, all patients were followed up prospectively at 6 and 12 months	Different type of knee prosthesis used in both groups (other instruments were the same)
Brandis, 1994	Unclear, there is no information on the (demographic) characteristics of both groups of patients, e.g. age, comorbidities, reason for hospital admission.	Yes, the authors did not include a retrospective evaluation of the inappropriate transfusion fraction. Although they mention that (in)formal monitoring was used, it is not clear whether the medical staff adhered to the new transfusion policy. Moreover, the laboratory was not computerised at the time of the study.	Yes, not controlled for any potential confounder. For example: the hospital may have admitted less surgery or trauma patients after the implementation compared to before. The authors themselves state that their sample includes patients with malignancies and renal failure, as well as surgery, trauma and self-limited anaemia, but that the data did not allow for separation of these categories.	Unclear, no information on potential loss to follow-up.	
Cheng 1996	High risk: Recruitment at the blood requesting phase. If compliance with a guideline is investigated, it is interesting to	Low risk: All requests for blood products were recorded and reviewed for appropriatenes s using	High risk: Not controlled for any potential confounding factor	Unclear risk: No information on potential loss to follow-up reported	Low risk: None identified

	verify how many	unambiguous			
	patients who did	laboratory			
	not receive blood	criteria during			
	products were	the same time			
	treated	of year			
	(in)appropriately as well				
Eindhoven, 2005	as well No, patients underwent same type of surgery in both hospitals. No significant differences in number of patients, sex, age and preoperative Hb between both hospitals.	Unclear, data collected in 2 different hospitals, so probably collected by different persons. Not clear if for example standardized forms were used in both hospitals	Unclear, not mentioned if controlled for confounding factors (probably not)	Unclear, not mentioned how long patients were followed up	
Fontana, 2014	No Selection criteria were similar across different centers, patient characteristics were similar (age, gender, type of surgery)	No Similar methods for interventions and outcome variables across the 10 hospitals	Yes, not controlled for any potential confounder.	No Period phase 1 (before guideline implementation): 7 months Period phase 2 (after guideline implementation): 6 months	No Potential Hawthorne effect was avoided by restricting the information about the project to the single responsible persons in the hospitals and the staffs were informed only at the moment of the training and implementation of the guideline.
Garrioch, 2004	Unclear, there is no information on the (demographic) characteristics of both groups of patients, e.g. age, comorbidities, reason for hospital admission	No, the audit periods before and after implementation both lasted 3 months and were both performed from February until March (2001 and 2002, respectively). Hospital activity (including the number of patients transfused) was monitored with the help of the medical records department and the Hospital Health Care Information	Yes, not controlled for any potential confounder. For example: the hospital may have admitted less surgery or trauma patients after the implementation compared to before.	No, no unaccounted loss of follow-up. The authors report that the data from 64 haematology and oncology patients were excluded from analysis as the haematology department's transfusion workload reduced by 56% between the two audits.	
Hui 2005	High risk:	system (HCIS). Low risk:	High risk:	Unclear risk:	Low risk:
	-		-		
	Recruitment at	All requests for	Not controlled	No information	None identified

Lee 2015	requesting phase. If compliance with a guideline is investigated, it is interesting to verify how many patients who did not receive blood products were treated (in)appropriately as well No Similar demographic variables between 2	were recorded and reviewed for appropriatenes s using unambiguous laboratory criteria during the same time of year No Same surgical approach (for TKAs) in 2 groups	confounding factor Yes Not controlled for any potential confounding factor	to follow-up reported Yes Period before implementation: 2 years versus period after	No
Meyer 2017	groups. Unclear, there is no information	No, same methods for	Yes Not controlled	implementation: 4 months Yes Period before	No
	on the (demographic) characteristics	exposure (intervention) and outcome variables in both groups.	for any potential confounding factor	implementation: 1 year versus period after implementation: 1 year	
Mimica 2008	Low risk: All premature patients meeting unambiguous selection criteria were eligible	High risk: Data from both cohorts were not collected during the same time of year, which might influence clinical factors (e.g. annually returning peaks in disease prevalence) Only proportion of transfused patients reported, not verified how many of these were (in)appropriate according to the guidelines	Low risk: Potential confounders were accounted for in a multivariate analysis	Low risk: No unaccounted loss to follow up present	Low risk: A clinically meaningful difference between both test groups is apparent (cohort 1: lower birth weight, higher incidence of respiratory distress syndrome, higher incidence of clinical sepsis, higher proportion of retinopathy, increased length of mechanical ventilation, higher amount of blood loss & increased hospital death), however seems to be appropriately corrected for in multivariate analysis
Morrison, 1993	No, computed based search for controls in similar period before GL was implemented. Demographic features of the patients were not altered during either study period.	Yes, personnel was educated and had to fill out a blood transfusion form, control group was collected by computer search and data might have been collected	Unclear if controlled for confounding factors	Unclear, not mentioned how long patients were followed up after transfusion	No

		in a different			
Muller, 2004	No, all patients being considered for primary total hip or knee replacements were eligible. Characteristics of included patients and operations are compared, and differences are adjusted for in the multivariable logistic regression.	wayNo, the auditperiods beforeand afterimplementationboth lasted 12months andwere bothperformed fromOctober toSeptember(1998 to 1999)and 1999 to2000,respectively).For the entireduration of thestudy, alloperativeandperioperativeprocedures,includingsurgicaltechniquesand types ofimplants,remainedidentical. Itseems asthough themedical staffadhered to thenew algorithm,since theproportion ofinappropriateallogeneic redbloodtransfusionsdecreased from43.8 to 15.9%.	No, multivariable logistic regression was used for the analyses on the proportion of transfusions, correcting for 10 prespecified, potentially confounding factors: age, sex, presence of risk factors, preoperative haemoglobin concentrations, type of surgery, bilateral operation, type of anaesthesia, duration of operation, estimated intraoperative haemoglobin concentrations.	No, all 421 patients undergoing 448 elective primary total hip or knee replacement operations between 1 October 1998 and 30 September 2000 were included.	The number of operations included in the study (intervention period: n=222, control period: n=226) was lower than the sample size indicated by the power-analysis (n=230 per period).
Patel, 2016	Unclear, there is no information on the (demographic) characteristics	No, similar methods for exposure and outcome variables for both groups were used	Yes Not controlled for any potential confounding factor	Yes, discrepancy between follow- up educational program (12 months) and CPOE (4 months)	No
Sarode 2010	High risk: Recruitment at the blood requesting phase. If compliance with a guideline is investigated, it is interesting to verify how many patients who did not receive blood products were	High risk: Inappropriate orders were not approved, but were not taken into account in the analyses either, it seems	High risk: Not controlled for any potential confounding factor	Unclear risk: No information on potential loss to follow-up reported	High risk: Inappropriate statistical analyses performed for use of RBC, TP, PLT

	treated (in)appropriately as well				
Spencer, 2005	No, patients in different groups underwent same type of surgeries	No, data was recorded by same 2 consultant surgeons.	Unclear, no confounding factors mentioned	No, patients were followed over a 5 or 6 month period.	No
Tavares, 2014	Unclear, there is no information on the (demographic) characteristics	No, blood bank and hospital records were reviewed for a 15-year period (between 1998 and 2012) + use of a case mix index.	No, controlled for changes in surgeons, surgical techniques, patient volume, patient complexity, or general awareness by physicians regarding the lack of efficacy of RBC transfusion.	No, 15-year follow-up period (3 years education followed by 9- year period CPOE)	No
Torella, 2002	Unclear, there is no information on the (demographic) characteristics of both groups of patients	Yes, the authors did not look at inappropriate transfusion fraction. Moreover, they did not assess whether the medical staff adhered to the new transfusion guideline.	Yes, not controlled for any potential confounder. "Although other factors cannot be excluded, we suggest that the reductions in red- cell transfusion were in large part attributable to the new transfusion policy."	Unclear, no information on potential loss to follow-up.	The authors did not report the median number of units transfused for the transurethral prostatectomy surgeries. It is unclear whether they have left these data out on purpose or by mistake.
Yeh 2006	High risk: Recruitment at the blood requesting phase. If compliance with a guideline is investigated, it is interesting to verify how many patients who did not receive blood products were treated (in)appropriately as well	High risk: Data from both cohorts were not collected during the same time of year, which might influence clinical factors (e.g. annually returning peaks in disease prevalence) Only the number of transfused patients reported, not verified how many of these were (in)appropriate according to the guidelines	High risk: Not controlled for any potential confounding factor	Unclear risk: No information on potential loss to follow-up reported	Low risk: None identified

Certainty of the body of evidence : see GRADE evidence tables

Conclusion	See Evidence-to-Decision template
Reference(s)	see reference list included studies
Evidence used for	Guideline
Project	PBM consensus meeting
Reviewer(s)	Hans Van Remoortel, Vere Borra, Jorien Laermans, Bert Avau