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)

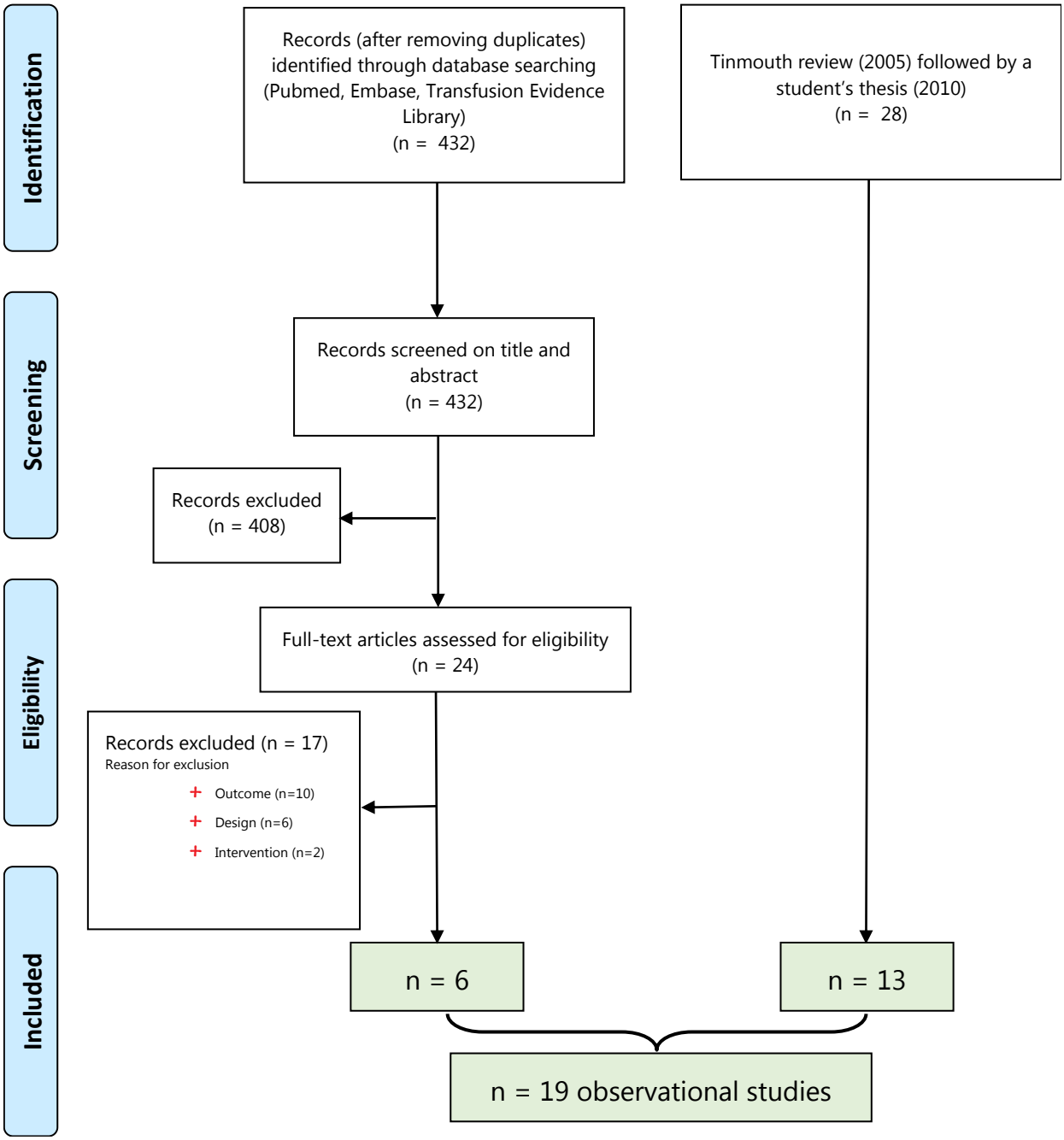
Belgian Red Cross

Belgian Red Cross

Evidence-based by CEBaP

Content

Flow chart


Identification
Screening
Eligibility
Included
Records (after removing duplicates) identified through database searching (Pubmed, Embase, Transfusion Evidence Library)
(n = 432)
Tinmouth review (2005) followed by a student's thesis (2010)
(n = 28)
Records screened on title and abstract
(n = 432)
Records excluded
(n = 408)
Full-text articles assessed for eligibility
(n = 24)
Records excluded (n = 17)
Reason for exclusion
+ Outcome (n=10)
+ Design (n=6)
+ Intervention (n=2)
n = 6
n = 13
n = 19 observational studies

Overview of 19 included studies[1-19]

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.

3. 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.

7. 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 studies[20-49]

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 fresh-frozen 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.

Studies comparing behavioural intervention(s) versus no behavioural interventions

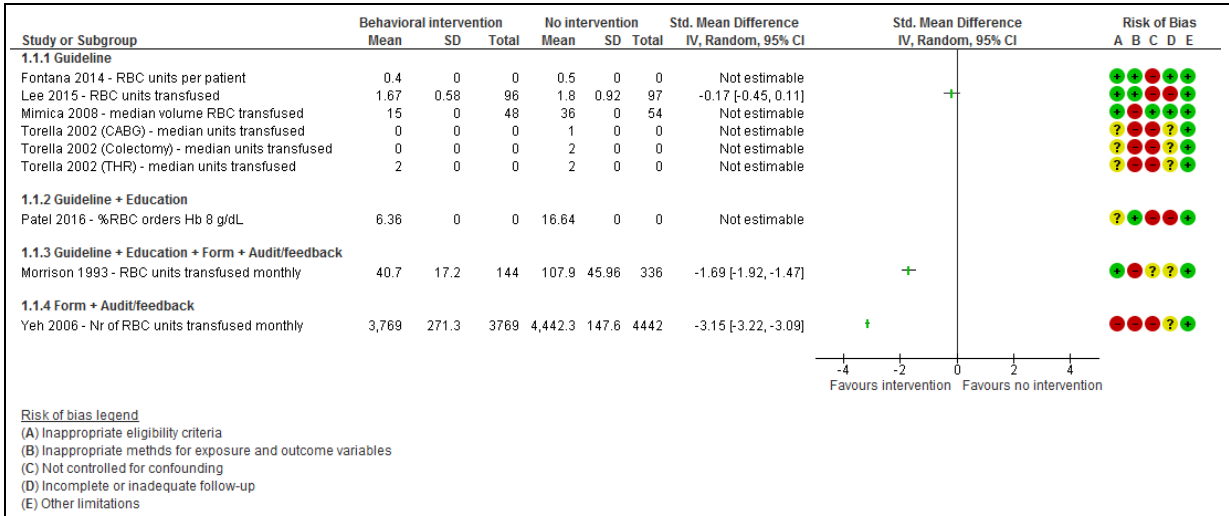
	Intervention(s) to promote blood product ordering					Blood products					Targeted physicians				
	Guideline	Form	Audit-approval	Audit-feedback	Education	RBC	FFP	PLT	Cryoprecipitate	All	Surgeons	Anaesthesiologists	Obstetricians - Gynaecologists	Neontal physicians	All
Abelow, 2017	■			■	■	■									■
Ballantyne, 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 other behavioural interventions

	Intervention(s) 1 to promote blood product ordering					Intervention(s) 2 to promote blood product ordering						Blood products					Targeted physicians				
	Guideline	Form	Audit-approval	Audit-feedback	Education	Guideline	Form	Audit-approval	Audit-feedback	Education	CPOE	RBC	FFP	PLT	Cryoprecipitate	All	Surgeons	Anaesthesiologists	Obstetricians - Gynaecologists	Neontal physicians	All
Eindhoven, 2005	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
Patel, 2016	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
Tavares, 2014	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■

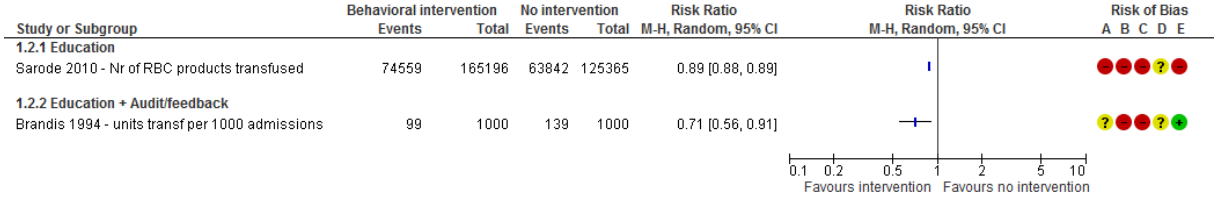
Overview evidence table GRADE software

Certainty assessment							Impact	Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**			
Behavioural intervention(s) versus no intervention: RBC utilization									
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



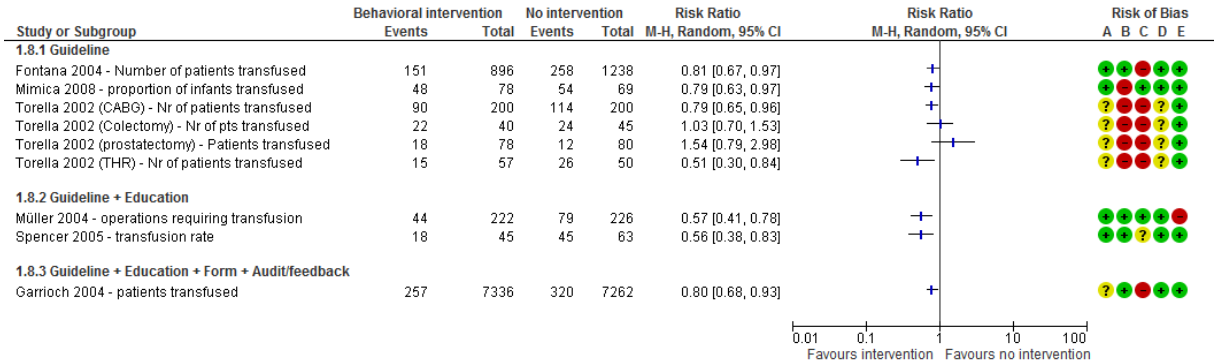
Risk of bias legend
(A) Inappropriate eligibility criteria
(B) Inappropriate methds for exposure and outcome variables
(C) Not controlled for confounding
(D) Incomplete or inadequate follow-up
(E) Other limitations

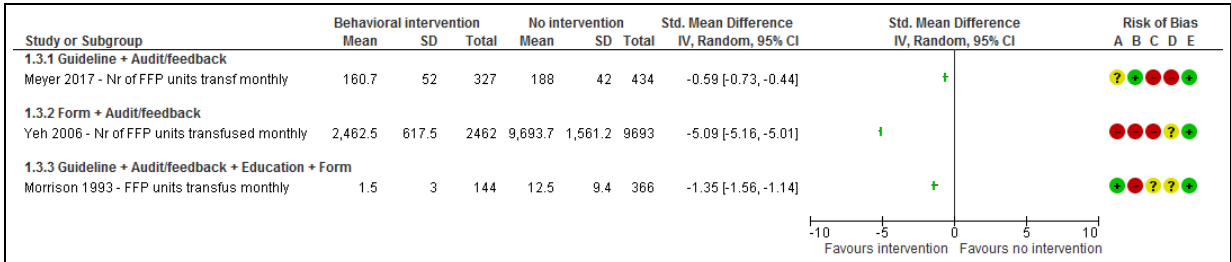
Figure 1: behavioural versus no behavioural intervention: outcome number of RBC units transfused (continuous)



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

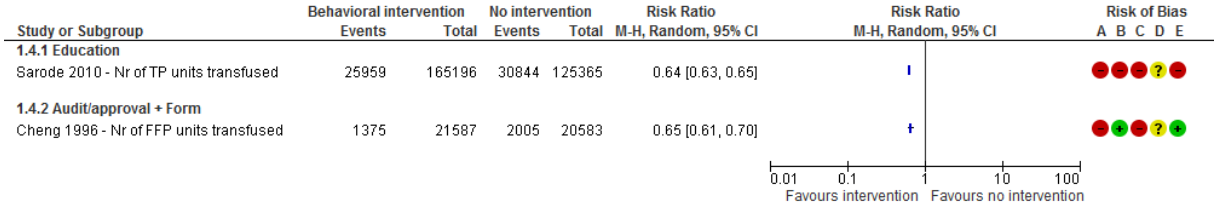
Figure 2: behavioural versus no behavioural intervention: outcome number of RBC units transfused (dichotomous)

Certainty assessment							Impact	Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**			
 Figure 3: behavioural versus no behavioural intervention: proportion of patients receiving RBC transfusion (dichotomous)									
Behavioural intervention(s) versus no intervention: FFP utilization									
6	observational studies	serious [b]	not serious	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



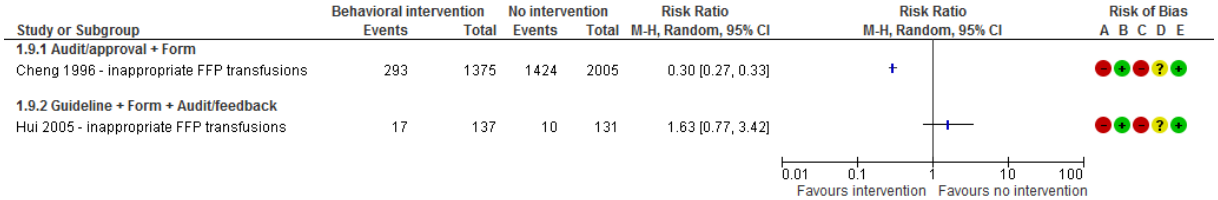
Risk of bias legend
(A) Inappropriate eligibility criteria
(B) Inappropriate methds for exposure and outcome variables
(C) Not controlled for confounding
(D) Incomplete or inadequate follow-up
(E) Other limitations

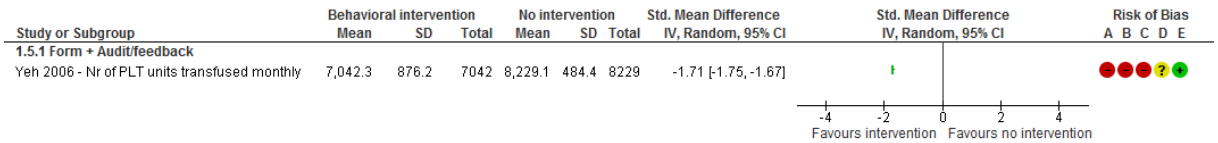
Figure 8: behavioural versus no behavioural intervention: outcome number of FFP units transfused (continuous)



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

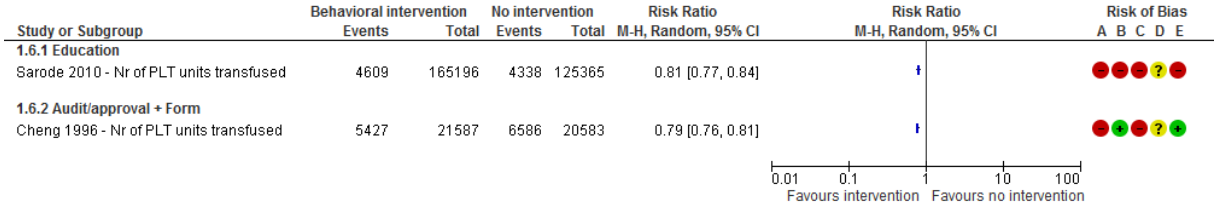
Figure 9: behavioural versus no behavioural intervention: outcome number of FFP units transfused (dichotomous)

Certainty assessment							Impact	Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**			
 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 10: behavioural versus no behavioural intervention: proportion of patients receiving FFP transfusion (dichotomous)									
Behavioural intervention(s) versus no intervention: PLT utilization									
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



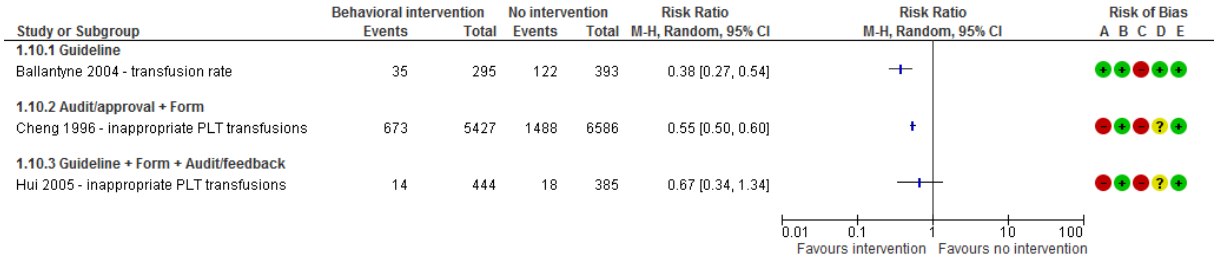
Risk of bias legend
(A) Inappropriate eligibility criteria
(B) Inappropriate methds for exposure and outcome variables
(C) Not controlled for confounding
(D) Incomplete or inadequate follow-up
(E) Other limitations

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



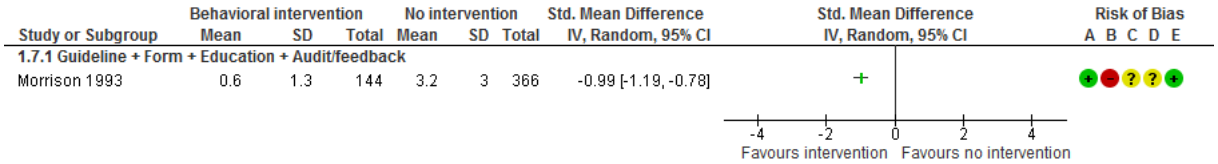
Risk of bias legend
(A) Inappropriate eligibility criteria
(B) Inappropriate methds for exposure and outcome variables
(C) Not controlled for confounding
(D) Incomplete or inadequate follow-up
(E) Other limitations

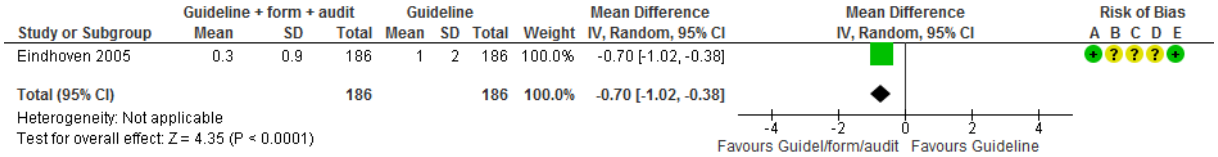
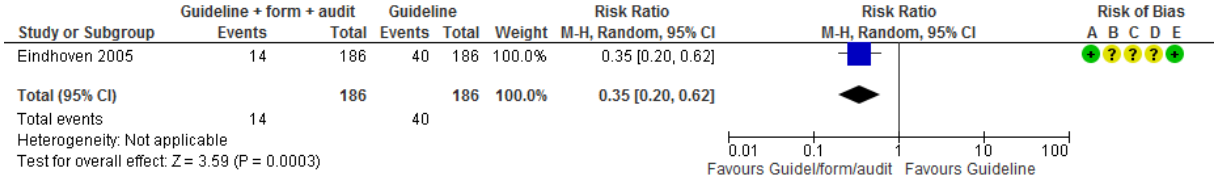
Figure 12: behavioural versus no behavioural intervention: outcome number of PLT units transfused (dichotomous)



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

Certainty assessment							Impact	Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**			
Behavioural intervention(s) versus no intervention: Cryoprecipitate									
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
 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 14: behavioural versus no behavioural intervention: outcome number of cryoprecipitate units transfused (continuous)									
Guideline + Form + Audit versus Guideline: RBC utilization									
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 assessment							Impact	Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**			
 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 4: Guideline + Form + Audit versus Guideline: number of RBC units transfused per patient.									
 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 5: Guideline + Form + Audit versus Guideline: proportion of patients receiving RBC transfusions.									
Computerized decision support (CPOE) versus Guideline + Educaton: RBC utilization									

Certainty assessment							Impact	Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**			
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 OUTCOMES			
Estimated annual savings on FFP and PLT	After vs before implementation of intervention	Saving of 2500 units FFP and 5000 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		227.80 SFr	Muller, 2004
Estimated annual saving expenditure for blood transfusions		52.280 SFr	Muller, 2004
RBC product acquisition cost savings		$ 130.000	Patel, 2016

Detailed evidence summary

Topic	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 **The Cochrane Library** (systematic reviews and controlled trials) using the following search strategy: 1. "Patient Blood Management":ti,ab,kw 2. [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 translation:ti,ab,kw OR transfer:ti,ab,kw OR uptake:ti,ab,kw OR sustainab*:ti,ab,kw OR institutionali*:ti,ab,kw OR routin*:ti,ab,kw OR maintenance:ti,ab,kw OR capacity:ti,ab,kw OR integration:ti,ab,kw 3. 1 AND 2 (#hits on July 14: 29) **MEDLINE** (via PubMed interface) using the following search strategy: 1. "Patient Blood Management"[TIAB] 2. 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 improv*[TIAB] OR "organizational innovation"[Mesh] OR change*[TIAB] OR program*[TIAB] OR practice*[TIAB] OR scal*[TIAB] OR diffusion[TIAB] OR incorporation[TIAB] OR adherence[TIAB] OR transformation[TIAB] OR translation[TIAB] OR transfer[TIAB] OR uptake[TIAB] OR sustainab*[TIAB] OR institutionali*[TIAB] OR routin*[TIAB] OR maintenance[TIAB] OR capacity[TIAB] OR integration[TIAB] 3. 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: 1. Patient blood management (#hits on July 18: 307) 2. 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) 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	30th of January 2018
In/Exclusion criteria	**Population:** *Included:* patients who might need transfusion (surgical and non-surgical patients/ acute and chronic disease patients/ adults and children). **Intervention:** *Included:* 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. *Excluded:* 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:** Include: 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

Characteristics of included studies

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

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

Hui, 2005, Australia	Observational: Non-concurrent cohort study	Targeted physicians: all	Comparison: after versus before implementation intervention Intervention(s): - Guidelines - Form - Audit/feedback Blood products: FFP, platelets, cryoprecipitate	From thesis (2010)
Lee, 2015, Hong Kong	Observational: Non-concurrent cohort study	Targeted physicians: surgeons	Comparison: after versus before implementation intervention Intervention(s): - Guideline Blood products: RBC	Update 2010-2018
Meyer, 2017, USA	Observational: Non-concurrent cohort study	Targeted physicians: anaesthesiologists	Comparison: after versus before implementation intervention Intervention(s): - Guideline - Audit/feedback Blood products: FFP	Update 2010-2018
Mimica, 2008, Brazil	Observational: Non-concurrent cohort study	Targeted physicians: neonatal	Comparison: after versus before implementation intervention Intervention(s): - Guideline Blood products: RBC	From thesis (2010)
Morrison, 1993, USA	Observational: Non-concurrent cohort study	Targeted physicians: obstetricians/gynaecologists	Comparison: after versus before implementation intervention Intervention(s): - Audit/feedback - Education - Guideline - Form Blood products: RBC	From Tinmouth review (2005)
Muller, 2004, Switzerland	Observational: Non-concurrent cohort study (prospective)	Targeted physicians: surgeons	Comparison: after versus before implementation intervention Intervention(s): - Education - Guideline Blood products: RBC	From Tinmouth review (2005)
Patel, 2016, USA	Observational: Non-concurrent cohort study	Targeted physicians: all	Comparison: after versus before implementation intervention	Update 2010-2018

			Intervention(s) 1 : - Guideline - Education Intervention(s) 2 (followed after intervention 1): - CPOE Blood products: RBC	
Sarode, 2010, USA	Observational: Non-concurrent cohort study	Targeted physicians: all	Comparison: after versus before implementation intervention Intervention(s): - Education Blood products: RBC, FFP, PLT	From thesis (2010)
Spencer, 2005, UK	Observational: Non-concurrent cohort study	Targeted physicians: surgeons	Comparison: after versus before implementation intervention Intervention(s): - Education - Guideline Blood products: all	From thesis (2010)
Tavares, 2014, USA	Observational: Non-concurrent cohort study	Targeted physicians: all	Comparison: after versus before implementation intervention Intervention(s) 1 : - Guideline - Education Intervention(s) 2 (followed after intervention 1): - CPOE Blood products: RBC	Update 2010-2018
Torella, 2002, UK	Observational: Non-concurrent cohort study (retrospective)	Targeted physicians: surgeons	Comparison: after versus before implementation intervention Intervention(s): - Guideline Blood products: RBC	From Tinmouth review (2005)
Yeh, 2006, Taiwan	Observational: Non-concurrent cohort study	Targeted physicians: all	Comparison: after versus before implementation intervention Intervention(s): - Form - Audit/feedback Blood products: FFP	From thesis (2010)

Synthesis of findings

Outcome	Comparison/Risk factor	Effect Size	#studies, # participants	Reference

The number of units transfused				
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) *Median [Range]*	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	Statistically significant: 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)	1, 200 vs 200	Torella, 2002
		Total hip replacement Statistically significant: 0 (0-1.5) vs 2 (0-3) (p=0.003) *in favour of after implementation of guideline*	1, 57 vs 50	
		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	Statistically significant: 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 intervention	Statistically significant: 0.4 vs 0.5 MD: -0.1, 95% CI [-0.08; -0.2] (p=0.014)* *In favour of after implementation behavioural intervention*	1, 896 vs 1238	Fontana, 2014
RBC units transfused	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
Number of RBC transfusions per 1000 discharges	After (CPOE followed after education) versus after education (only)	Statistically significant: 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)				
Number of FFP units transfused (relative to the total number of admissions)	Form vs Audit/approval	Statistically significant: 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
Number of FFP units 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
Number of TP units transfused (Units) (relative to the total number of admissions)	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
Number of FFP units 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): 2462.5 vs 9693.7 q (number of months analysed): 7 vs 4 §	Yeh 2006
PLT (Figure 11-13)				
Number of PLT units transfused (relative to the total number of admissions)	Form vs Audit/approval	Statistically significant: 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
Number of PLT units transfused (Units) (relative to the total	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 admissions)		(p<0.0001) * *In favour of education*	n (transfusions): not reported m (Units transfused): 4609 vs 4338	
Number of PLT units used per month	Computerized feedback + Weekly audit/feedback vs No intervention or Education	Statistically significant: 7042.3±876.2 vs 8229.1±484.4 MD: -1186.8, 95% CI [-1991.0; -382.7] (p=0.004) * *In favour of Computerized feedback + Weekly audit/feedback*	1 study, N (patients): not reported n (transfusion requests): not reported m (Units transfused): 7042.3 vs 8229.1 q (number of months analysed): 7 vs 4 §	Yeh 2006
Cryoprecipitate (Figure 14)				
Units per month transfused	after versus before implementation of intervention	Statistically significant: 0.6±1.3 vs 3.2±3.0 MD: -2.60, 95%CI [-2.98;-2.22] (p<0.00001) * *In favour of implementation of intervention* (Mean±SD calculated in Excel)	1, 144 vs 366	Morrison, 1993
Proportion of patients who received transfusions				
RBC (Figure 1-7)				
Patients transfused	Guideline (after 1 year) vs standard customs	Statistically significant: 14/186 vs 40/186 § RR: 0.35, 95%CI [0.20;0.62] (p=0.0003) * *In favour of guidelines (after 1 year)*	1, 186 vs 186	Eindhoven, 2005
Patients transfused	After vs before implementation of intervention	Statistically significant: 257/7336 vs 320/7262 RR: 0.80, 95%CI [0.68;0.93] (p=0.0052)* *in favour of after implementation of intervention*	1, 7336 vs 7262	Garrioch, 2004
Proportion of infants transfused	Very strict guideline vs Strict guideline	Statistically significant: 48/78 vs 54/69 § RR: 0.79, 95% CI [0.63;0.97] (p=0.03) * *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
Operations requiring transfusion	After vs before implementation of intervention	Statistically significant: 44/222 vs 79/226 aOR: 0.20, 95%CI [0.10;0.39] (p<0.05) *in favour of after implementation of intervention*	1, 222 operations (in 217 patients) vs 226 operations (in 208 patients)	Muller, 2004
% RBC orders with a pretransfusion Hb level >8 g/dL	After versus before implementation behavioural intervention	Statistically significant: 6.36% vs 16.64% (p<0.001) *in favour of after implementation of intervention*	1, not reported	Patel, 2016
	CPOE + education versus education	Not statistically significant: 6.1% vs 6.3% (p>0.05)	1, not reported	Patel, 2016
Transfusion rate	1 year after vs before implementation of guideline	Statistically significant: 18/45 vs 45/63 § RR: 0.56, 95%CI [0.38;0.83] (p=0.004)* *In favour of 1 year after implementation of guideline*	1, 45 vs 63	Spencer, 2005
Number of patients transfused	After vs before implementation of guideline	*Coronary artery bypass graft* Statistically significant: 90/200 vs 114/200	1, 200 vs 200	Torella, 2002

		RR: 0.79, 95%CI [0.65;0.96] (p=0.0174)* *in favour of after implementation of guideline*		
		Total hip replacement Statistically significant: 15/57 vs 26/50 RR: 0.51, 95%CI [0.30;0.84] (p=0.0088)* *in favour of after implementation of guideline*	1, 57 vs 50	
		Colectomy Not statistically significant: 22/40 vs 24/45 RR: 1.03, 95%CI [0.70;1.53] (p=0.88)*	1, 40 vs 45	
		Transurethral prostatectomy Not statistically significant: 18/78 vs 12/80 RR: 1.54, 95%CI [0.79;2.98] (p=0.20)*	1, 78 vs 80	
Number of patients transfused	After vs before implementation of guideline	Statistically significant: 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	Statistically significant: 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
FINANCIAL OUTCOMES				

Estimated annual savings on FFP and PLT	After vs before implementation of intervention	Saving of 2500 units FFP and 5000 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		227.80 SFr	Muller, 2004
Estimated annual saving expenditure for blood transfusions		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
£ 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

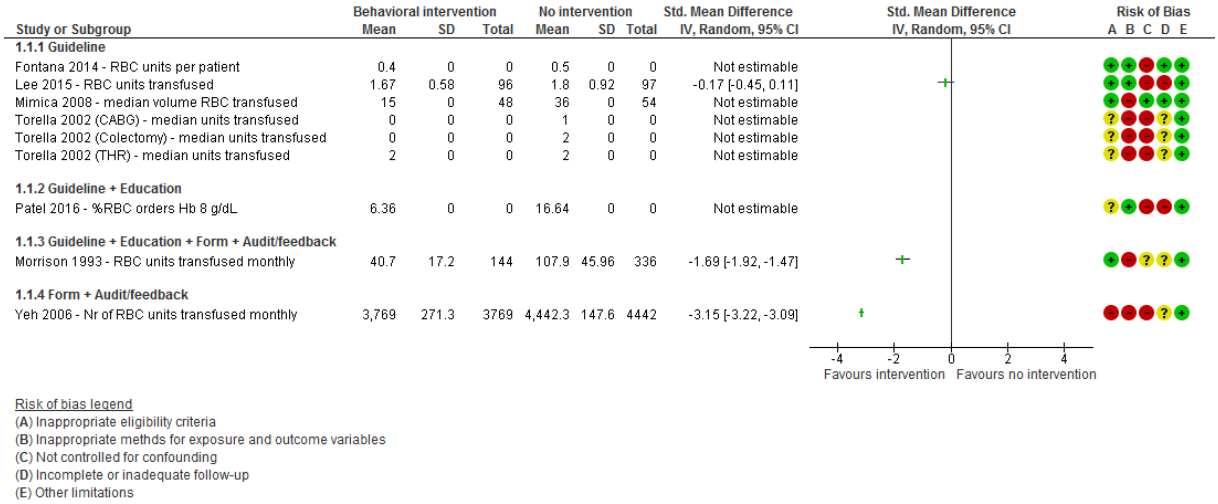


Figure 1: behavioural versus no behavioural intervention: outcome number of RBC units transfused (continuous)

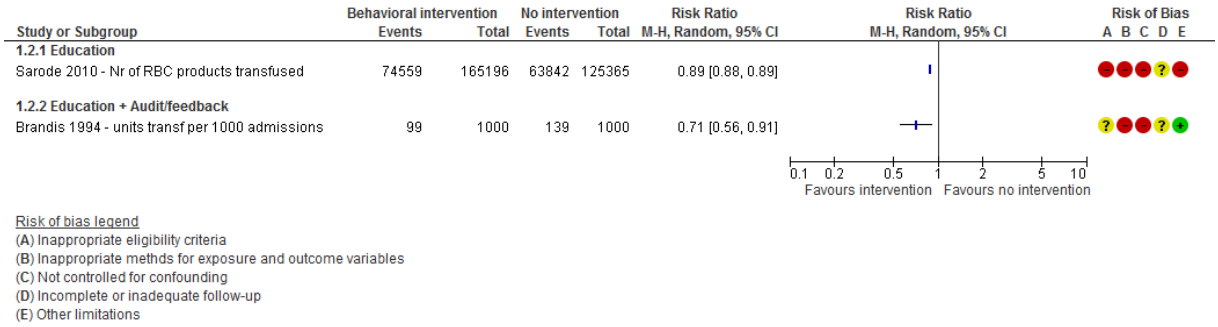


Figure 2: behavioural versus no behavioural intervention: outcome number of RBC units transfused (dichotomous)

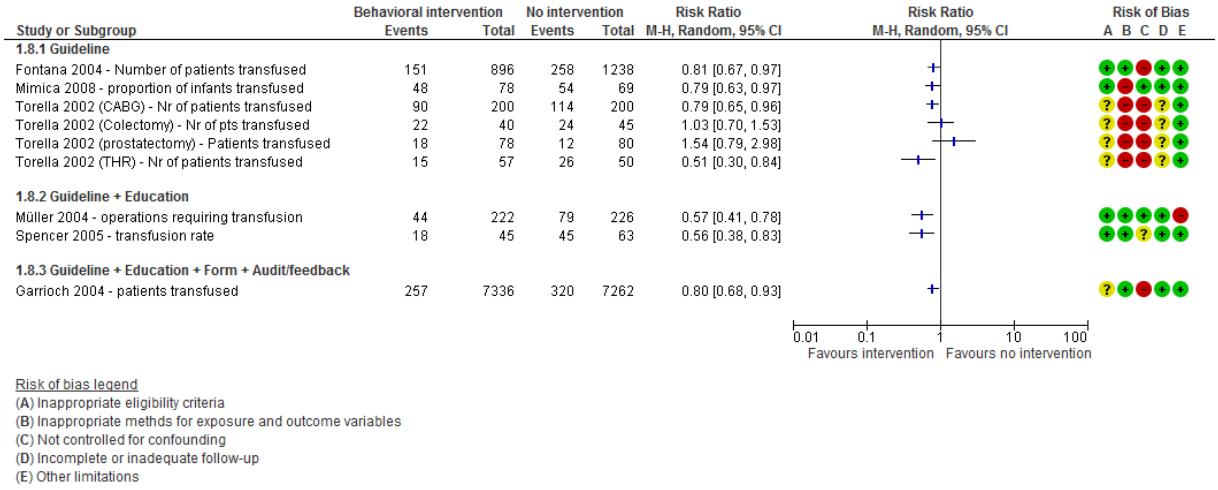


Figure 3: behavioural versus no behavioural intervention: proportion of patients receiving RBC transfusion (dichotomous)

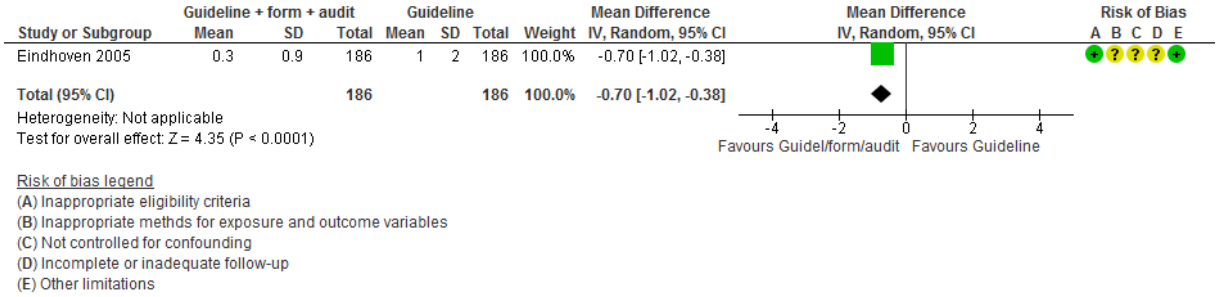


Figure 4: Guideline + Form + Audit versus Guideline: number of RBC units transfused per patient.

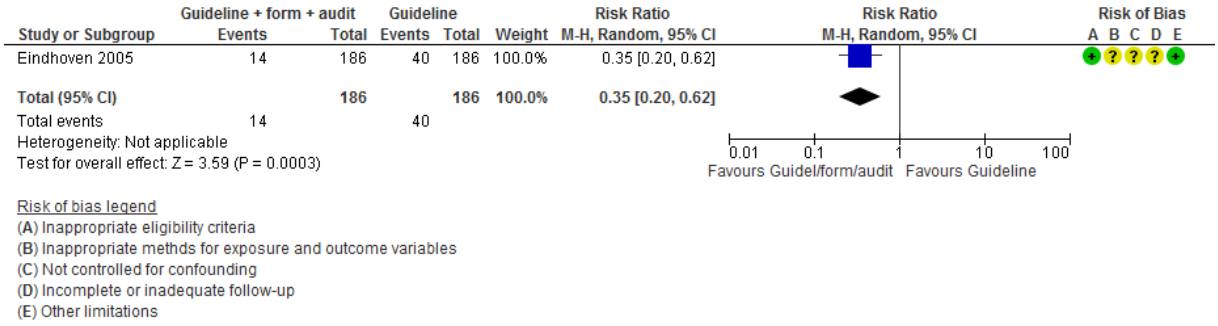


Figure 5: Guideline + Form + Audit versus Guideline: proportion of patients receiving RBC transfusions.

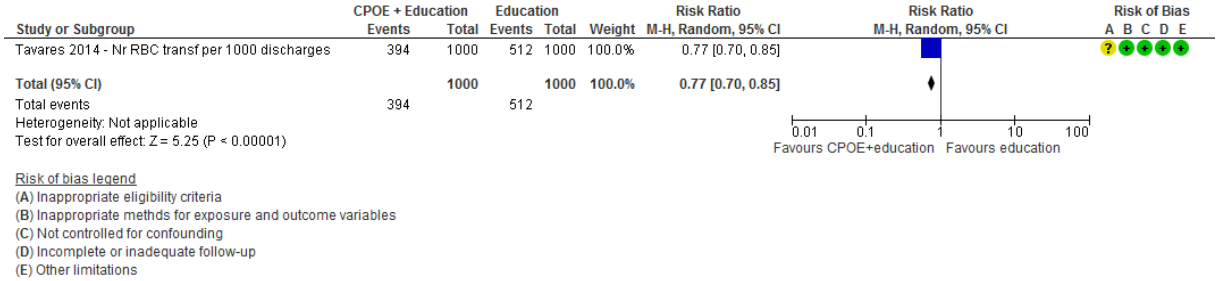


Figure 6: Education + CPOE versus Education: number of RBC transfusions per 1000 discharges.

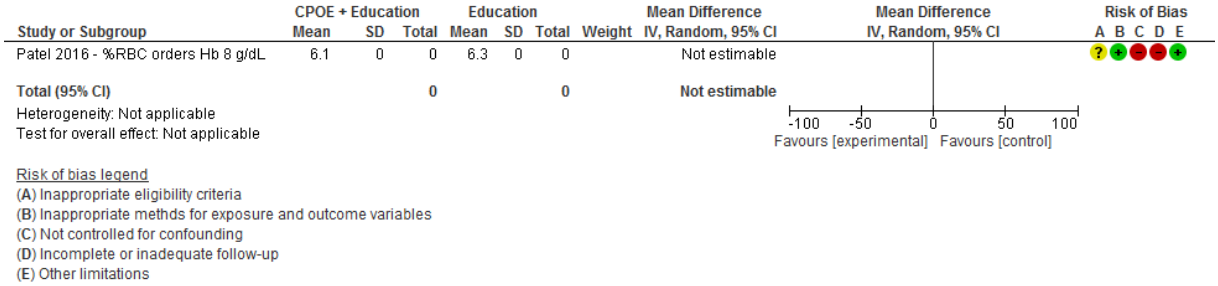
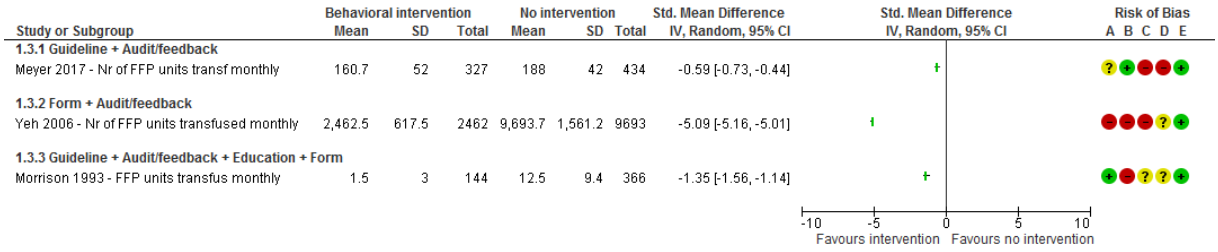
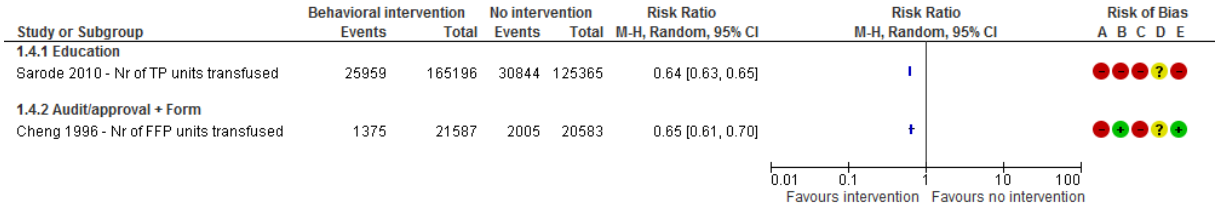


Figure 7: Education + CPOE versus Education: % RBC orders with pretransfusion Hb level >8 g/dL.



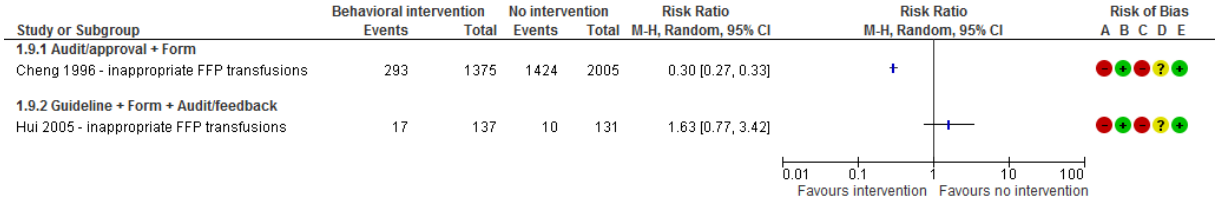
Risk of bias legend
(A) Inappropriate eligibility criteria
(B) Inappropriate methds for exposure and outcome variables
(C) Not controlled for confounding
(D) Incomplete or inadequate follow-up
(E) Other limitations

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



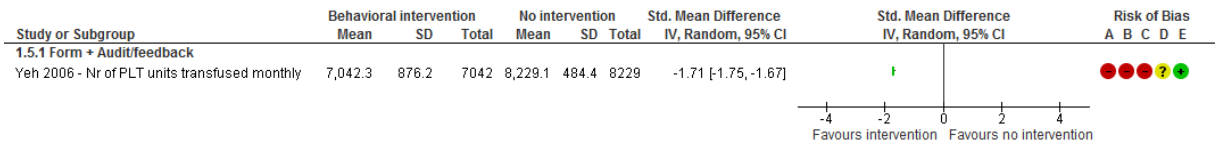
Risk of bias legend
(A) Inappropriate eligibility criteria
(B) Inappropriate methds for exposure and outcome variables
(C) Not controlled for confounding
(D) Incomplete or inadequate follow-up
(E) Other limitations

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



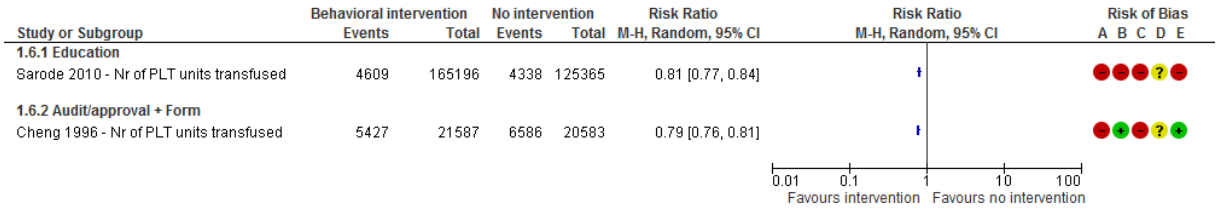
Risk of bias legend
(A) Inappropriate eligibility criteria
(B) Inappropriate methds for exposure and outcome variables
(C) Not controlled for confounding
(D) Incomplete or inadequate follow-up
(E) Other limitations

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



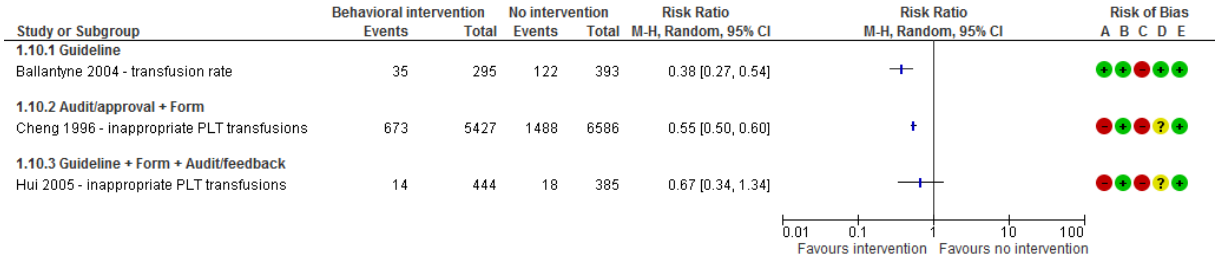
Risk of bias legend
(A) Inappropriate eligibility criteria
(B) Inappropriate methds for exposure and outcome variables
(C) Not controlled for confounding
(D) Incomplete or inadequate follow-up
(E) Other limitations

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



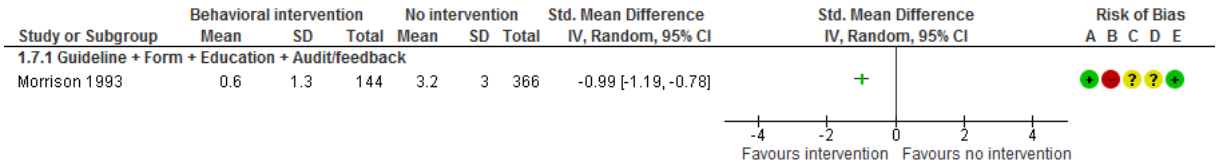
Risk of bias legend
(A) Inappropriate eligibility criteria
(B) Inappropriate methds for exposure and outcome variables
(C) Not controlled for confounding
(D) Incomplete or inadequate follow-up
(E) Other limitations

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



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



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

Quality of evidence

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 patients who did not receive blood products were treated (in)appropriately as well	unambiguous laboratory criteria during the same time of year			
Eindhoven, 2005	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 system (HCIS).	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: Recruitment at the blood	Low risk: All requests for blood products	High risk: Not controlled for any potential	Unclear risk: No information on potential loss	Low risk: None identified

	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	were recorded and reviewed for appropriatenes s using unambiguous laboratory criteria during the same time of year	confounding factor	to follow-up reported	
Lee 2015	No Similar demographic variables between 2 groups.	No Same surgical approach (for TKAs) in 2 groups	Yes Not controlled for any potential confounding factor	Yes Period before implementation: 2 years versus period after implementation: 4 months	No
Meyer 2017	Unclear, there is no information on the (demographic) characteristics	No, same methods for exposure (intervention) and outcome variables in both groups.	Yes Not controlled for any potential confounding factor	Yes Period before implementation: 1 year versus period after implementation: 1 year	No
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 way			
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.	No, the audit periods before and after implementation both lasted 12 months and were both performed from October to September (1998 to 1999 and 1999 to 2000, respectively). For the entire duration of the study, all operative and perioperative procedures, including surgical techniques and types of implants, remained identical. It seems as though the medical staff adhered to the new algorithm, since the proportion of inappropriate allogeneic red blood transfusions decreased from 43.8 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 blood loss, and postoperative 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