Evidence summary

to support

PICO question 17 on PBM implementation:

Effectiveness decision support systems 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

Overview of included studies

We used the evidence form the Cochrane review by Fisher et al. which will be published in 2018[1]: 1 RCT[2] and 1 interrupted time series[3] and 2 retrospective cohort studies[4,5] re-analyzed as interrupted time series.

1. Fisher SA, Docherty AB, Doree C, et al. Computerised decision support systems to promote appropriate use of blood products. Cochrane Database Syst Rev 2017;2017.

2. Rothschild JM, McGurk S, Honour M, et al. Assessment of education and computerized decision support interventions for improving transfusion practice. Transfusion 2007;47:228-39.

3. Kassakian SZ, Yackel TR, Deloughery T, et al. Clinical Decision Support Reduces Overuse of Red Blood Cell Transfusions: Interrupted Time Series Analysis. Am J Med 2016;129:636 e13-20.

4. Adams ES, Longhurst CA, Pageler N, et al. Computerized physician order entry with decision support decreases blood transfusions in children. Pediatrics 2011;127:e1112-9.

5. Goodnough LT, Maggio P, Hadhazy E, et al. Restrictive blood transfusion practices are associated with improved patient outcomes. Transfusion 2014;54:2753-9.

Overview of studies awaiting classification

Choi 2014
Choi JS, Hong CH, Kwack MJ, Lee CK, Cho Y, Park JH. Establishiment of computerized clinical decision support program for improving transfusion practice. Vox Sanguinis 2014;107:21. [DOI: http://dx.doi.org/10.1111/vox.12153]

Chu 2015
Chu FYC, Chang CC, Lee TCl. Computerized provider order entry with clinical decision support reduced unnecessary fresh frozen plasma transfusion. Vox Sanguinis 2015;109:55.

Gross 2009
Gross et al. Reduction in Allogeneic Transfusion: Implementation of a Patient Blood Management Program including Computerized Physician Order Entry for Transfusion (CPOE) System. Not stated 2009:13.

Kolton 2014
Kolton J, Boyd K., Sullivan S, Carr JR. eduction of RBC transfusion in a multi-hospital healthcare system by using a computerized physician order entry to drive a restrictive transfusion strategy. Transfusion 2014;54:241A.

Sroujieh 2016
Sroujieh LS, Monroy D, Warren E. Uing electronic health record (EHR) best practice alert (BPA) to improve RBC transfusion practices and adherence to the guidelines. Chest 2016;150(4 Supplement 1):599A.

Tirado Angles 2013
Tirado Angles G, Rodriguez Chacon L, Santolaria Lopez MA, Garcia-Erce JA. Computerised decision support decreases blood transfusion in critically ill patients. Transfusion Medicine 2013;23:25.

Usmani 2014
Usmani A, Lo A, Hayes C, Ma Y, Shafi H, Mason HM, et al. Effect of computer alerts on non-red blood cell component utilization. Transfusion 2014;54:240-1A.

Overview of ongoing studies

Costermans E; Devos T. Study on patient blood management in haematological patients. clinicaltrials.gov 2017:https://clinicaltrials.gov/ct2/show/NCT03217370.

Overview of excluded studies

Arnold 2011 (reason for exclusion: Not a computerised decision aid)
Arnold DM, Lauzier F, Whittingham H, Zhou Q, Crowther MA, McDonald E, et al. A multifaceted strategy to reduce inappropriate use of frozen plasma transfusions in the intensive care unit. J Crit Care 2011;26(6):636.e7-636.e13.

Baer 2011 (reason for exclusion: Insufficient time points on interrupted time series)
Baer VL, Henry E, Lambert DK, Stoddard RA, Wiedmeier SE, Eggert LD, et al. Implementing a program to improve compliance with neonatal intensive care unit transfusion guidelines was accompanied by a reduction in transfusion rate: a pre-post analysis within a multihospital health care system. Transfusion 2011;51(2):264-9.

Butler 2015 (reason for exclusion: Controlled but single centre)
Butler CE, Noel S, Hibbs SP, Miles D, Staves J, Mohaghegh P, et al. Implementation of a clinical decision support system improves compliance with restrictive transfusion policies in hematology patients. Transfusion 2015;55(8):1964-71.

Chang 2009 (reason for exclusion: Other inappropriate study design)
Lin YC, Chang CS, Yeh CJ, Wu YC. The appropriateness and physician compliance of platelet usage by computerized transfusion decision support system in a medical center in Taiwan. Vox Sanguinis 2009;97:157. [DOI: http://dx.doi.org/10.1111/j.1423-0410.2009.01262.x]

Chang 2011 (reason for exclusion: Other inappropriate study design)
Chang CS, Lin YC, Wu YC, Yeh CJ, Lin YC. The effects of a computerized transfusion decision support system on physician compliance and its appropriateness for fresh frozen plasma use in a medical center. Am J Clin Pathol 2011;135(3):417-22.

Chang 2012 (reason for exclusion: Other inappropriate study design)
Chang CS, Lin YC, Lin CC, Yeh CJ, Wu YC, Lin YC. The physician compliance of red blood cell transfusion by computerized transfusion decision support system. Kaohsiung J Med Sci 2012;28(6):331-5.
Chang CS, Lin YC, Wu YC, Yeh CJ, Lin YC. The transfusion triggers and physician compliance of red blood cell transfusion by computerized transfusion decision support system in a Medical Center. Vox Sanguinis 2011;101:97. [DOI: http://dx.doi.org/10.1111/j.1423-0410.2011.01498-2.x]

Connor 2017 (reason for exclusion: Not a computerised decision aid)
Connor JP, Cunningham AM, Raife T, Rose WN, Medow JE. Standardization of transfusion practice in organ donors using the Digital Intern, an electronic decision support algorithm. Transfusion 2017;57(6):1369-75.

FernandezPerez 2007 (reason for exclusion: Simple before and after design)
Fernández Pérez ER, Winters JL, Gajic O. The addition of decision support into computerized physician order entry reduces red blood cell transfusion resource utilization in the intensive care unit. Am J Hematol 2007;82(7):631-3.

Hibbs 2014 (reason for exclusion: Simple before and after design)
Hibbs SP, Noel S, Miles D, Staves J, Murphy MF. The impact of electronic decision support and electronic remote blood issue on transfusion practice. Transfus Med 2014;24(5):274-9.

Hicks 2017 (reason for exclusion: Not a computerised decision aid)
Hicks CW, Liu J, Yang WW, DiBrito SR, Johnson DJ, Brito A, et al. A comprehensive choosing wisely quality improvement initiative reduces unnecessary transfusions in an academic dDepartment of surgery. American Journal of Surgery 2017;214(4):571-6.

Jenkins 2017 (reason for exclusion: Simple before and after design)
Jenkins I, Doucet JJ, Clay B, Kopko P, Fipps D, Hemmen E, et al. Transfusing wisely: clinical decision support improves blood transfusion practice. Joint Commission Journal on Quality & Patient Safety 2017;43(8):389-95.

Karkouti 2015 (reason for exclusion: Not a computerised decision aid)
Karkouti K, McCluskey SA, Callum J, Freedman J, Selby R, Timoumi T, et al. Evaluation of a novel transfusion algorithm employing point-of-care coagulation assays in cardiac surgery: a retrospective cohort study with interrupted time-series analysis. Anesthesiology 2015;122(3):560-70.

Kenyon 2017 (reason for exclusion: Not a computerised decision aid)
Kenyon C, Agarwal S, Kerfoot BP, Gagnon DR, McMahon GT, Orlander JD, et al. Transfusion practices at a tertiary cardiac centre and development of real-time electronic clinical decision-making support. Anaesthesia 2017;72(9):84.

Leon Justel 2015 (reason for exclusion: Not a computerised decision aid)
Leon-Justel A, Noval-Padillo JA, Alvarez-Rios AI, Mellado P, Gomez-Bravo MA, Álamo JM, et al. Point-of-care haemostasis monitoring during liver transplantation reduces transfusion requirements and improves patient outcome. Clin Chim Acta 2015;446(June 15):277-83.

Li 2014 (reason for exclusion: Not a computerised decision aid)
Li N, Simonds D, Alva R, Wyatt T, Ramaswamy M. Impact of remote electronic monitoring and tele-intensive care unit based algorithm in monitoring packed red cell transfusion behavior for anemia of critical illness: longitudinal multi-year experience from a single community health system in the United States of America. Intensive Care Medicine 2014;40:S287.

Lin 2010 (reason for exclusion: Other inappropriate study design)
Lin YC, Chang CS, Yeh CJ, Wu YC. The appropriateness and physician compliance of platelet usage by a computerized transfusion decision support system in a medical center. Transfusion 2010;50(12):2565-70.

Littenberg 1995 (reason for exclusion: Not a computerised decision aid)
Littenberg B, Corwin H, Gettinger A, Leichter J, Aubuchon J. A practice guideline and decision aid for blood transfusion. Immunohematology. 1995;11(3):88-94.

Loftus 2016 (reason for exclusion: Simple before and after design)
Loftus TJ, Spratling L, Stone BA, Xiao L, Jacofsky DJ. A patient blood management program in prosthetic joint arthroplasty decreases blood use and improves outcomes. J Arthroplasty 2016;31(1):11-4.

Masear 2017 (reason for exclusion: Not a computerised decision aid)
Masear CG, Frank SM. Best practices for reducing unnecessary preoperative blood orders and associated costs. MLO: Medical Laboratory Observer 2017;49(3):21-2.

McKinney 2015 (reason for exclusion: Not ITS study and unable to derive data from graph, unclear data points)
Gorlin JB, McKinney ZJ, Peters JM, Perry EH. Improved red blood cell orders and utilization with point-of-care clinical decision support. Transfusion 2014;54:58A-59A. [DOI: http://dx.doi.org/10.1111/trf.12845]
McKinney ZJ, Peters JM, Gorlin JB, Perry EH. Improving red blood cell orders, utilization, and management with point-of-care clinical decision support. Transfusion 2015;55(9):2086-94.

McWilliams 2014 (reason for exclusion: No control period without decision support)
McWilliams B, Triulzi DJ, Waters JH, Alarcon LH, Reddy V, Yazer MH.. Trends in RBC ordering and use after implementing adaptive alerts in the electronic computerized physician order entry system. Am J Clin Pathol. 2014;141(4):534-41.

Michetti 2016 (reason for exclusion: Simple before and after design)
Michetti CP, Prentice HA, Lita E, Wright J, Ng E, Newcomb AB. Reducing transfusions in critically injured patients using a restricted-criteria order set. J Trauma Acute Care Surg 2016;81(5):889-896.

Nakayama 2015 (reason for exclusion: Not a computerised decision aid)
Nakayama Y, Nakajima Y, Tanaka KA, Sessler DI, Maeda S, Iida J, et al. Thromboelastometry-guided intraoperative haemostatic management reduces bleeding and red cell transfusion after paediatric cardiac surgery. The British Journal of Anaesthesia 2015;114(1):91-102.

Pentti 2003 (reason for exclusion: Simple before and after design)
Pentti J, Syrjala M, Pettila V. Computerized quality assurance of decisions to transfuse blood components to critically ill patients. Acta Anaesthesiol Scand 2003;47(8):973-8.

Picton 2017 (reason for exclusion: Simple before and after design)
Picton P, Starr J, Kheterpal S, Thompson AML, Housey M, Sathishkumar S, et al. Promoting a restrictive intraoperative transfusion strategy: the influence of a transfusion guideline and a novel software tool. Anesthesia & Analgesia 2017;15:8.

Rana 2006 (reason for exclusion: Simple before and after design)
Rana R, Afessa B, Keegan MT, Whalen FX Jr, Nuttall GA, Evenson LK, et al. Evidence-based red cell transfusion in the critically ill: quality improvement using computerized physician order entry. Crit Care Med 2006;34(7):1892-7.

Razavi 2014 (reason for exclusion: Simple before and after design)
Razavi SA, Carter AB, Puskas JD, Gregg SR, Aziz IF, Buchman TG. Reduced red blood cell transfusion in cardiothoracic surgery after implementation of a novel clinical decision support tool. J Am Coll Surg 2014;219(5):1028-36.

Rinehart 2016 (reason for exclusion: Not a computerised decision aid)
Rinehart JB, Lee TC, Kaneshiro K, Tran MH, Sun C, Kain ZN. Perioperative blood ordering optimization process using information from an anesthesia information management system. Transfusion 2016;56(4):938-45.

Saag 2017 (reason for exclusion: Assessing effect of an education programme)
Saag HS, Lajam CM, Jones S, Lakomkin N, Bosco JA, Wallack R, et al. Reducing liberal red blood cell transfusions at an academic medical center. Transfusion 2017;57(April 2017):959-64.

Scheurer 2010 (reason for exclusion: Other inappropriate study design)
Scheurer DB, Roy CL, McGurk S, Kachalia A. Effectiveness of computerized physician order entry with decision support to reduce inappropriate blood transfusions. Journal of Clinical Outcomes Management 2010;17(1):17-26.

Shah 2017 (reason for exclusion: Simple before and after design)
Shah N, Baker SA, Spain D, Shieh L, Shepard J, Hadhazy E, et al. Real-time clinical decision support decreases inappropriate plasma transfusion. American journal of clinical pathology 2017;148(2):154-60.

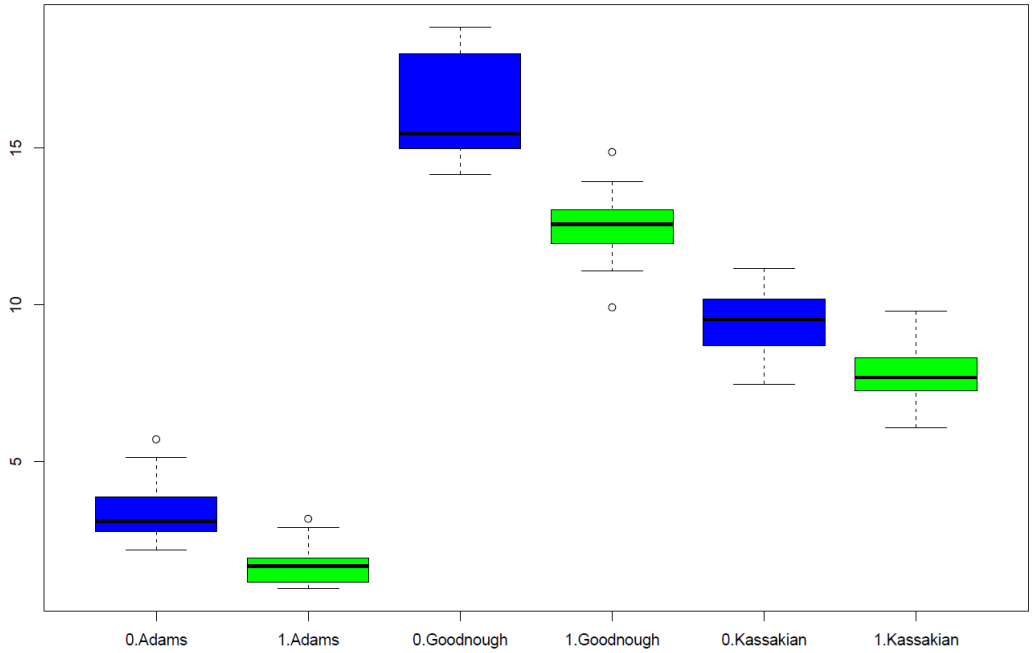
Shore Lesserson 1999 (reason for exclusion: Not a computerised decision aid)
Shore-Lesserson L, Manspeizer HE, DePerio M, Francis S, Vela-Cantos F, Ergin MA.. Thromboelastography-guided transfusion algorithm reduces transfusions in complex cardiac surgery. Anesth Analg 1999;88(2):312-9.

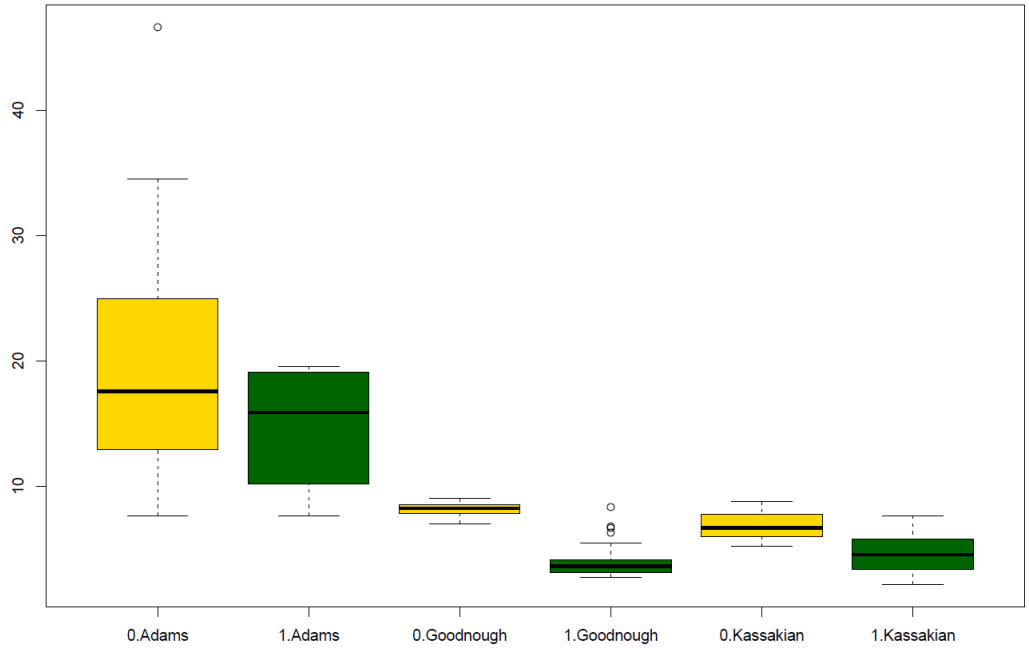
Yazer 2013 (reason for exclusion: Other inappropriate study design)
Yazer MH, Triulzi DJ, Reddy V, Waters JH. Effectiveness of a real-time clinical decision support system for computerized physician order entry of plasma orders. Transfusion 2013;53(12):3120-7.

Zuckerberg 2015 (reason for exclusion: Not ITS study and unable to derive data from graph, unclear data points)
Published and unpublished data
Frank SM, Zuckerberg GS, Pawlik TM, Ness PM, Resar LM. Analysis of blood utilization and cost-savings data using a web based blood management intelligence portal. Transfusion 2014;54:229A. [DOI: http://dx.doi.org/10.1111/trf.12845]
Zuckerberg GS, Scott AV, Wasey JO, Wick EC, Pawlik TM, Ness PM. Efficacy of education followed by computerized provider order entry with clinician decision support to reduce red blood cell utilization. Transfusion 2015;55(7):1628-36.

Overview evidence table GRADE software

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**decision support systems**	**no decision support systems**	**Relative (95% CI)**	**Absolute (95% CI)**		
Appropriate transfusions (follow up: 4 months)												
1	randomised trials	serious [a]	not serious	serious [b]	not serious	none	546/1350 (40.4%)	503/1546 (32.5%)	**RR 1.24** (1.13 to 1.37)	**78 more per 1.000** (from 42 more to 120 more)	⨁⨁◯◯ LOW	CRITICAL
Overall RBC usage (RBC transfusions per 100 inpatient days) (follow up: range 12 months to 42 months)												
3	observational studies	serious [c]	not serious	serious [d]	not serious	none	A statistical significant reduction in overall red cell usage (red cell transfusions per 100 inpatient days) (P < 0.0001) was found in addition to a statistically significant reduction in red cell usage over time (P = 0.01) (see boxplot 1)				⨁◯◯◯ VERY LOW	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**decision support systems**	**no decision support systems**	**Relative (95% CI)**	**Absolute (95% CI)**		
 Box plot 1. Pre-post results – Interrupted time series (3 studies – x-axis). Overall RBC usage: number of RBC transfusion per 100 inpatient days (y-axis). Analysis (meta-regression) from upcoming/unpublished Cochrane review by Fisher et al. (confidential information).											
Inappropriate RBC usage (RBC transfusions per 100 inpatient days) (follow up: range 12 months to 42 months)												
3	observational studies	serious [c]	not serious	serious [d]	not serious	none	A statistically significant reduction in inappropriate red cell usage (red cell transfusions per 100 inpatient days) was found (P < 0.001), in addition to a statistically significant reduction in inappropriate red cell usage over time (P < 0.001) (see boxplot 2)		⊕◯◯◯ VERY LOW		CRITICAL	

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	decision support systems	no decision support systems	Relative (95% CI)	Absolute (95% CI)		
												
Box plot 2. Pre-post results – Interrupted time series (3 studies – x-axis). Inappropriate RBC usage: number of RBC transfusion per 100 inpatient days (y-axis). Analysis (meta-regression) from upcoming/unpublished Cochrane review by Fisher et al. (confidential information).												
Mortality (follow up: 42 months)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**decision support systems**	**no decision support systems**	**Relative (95% CI)**	**Absolute (95% CI)**		
1	observational studies	serious [c]	not serious	serious [b]	not serious	none	347/10528 (3.3%)	199/3622 (5.5%)	**RR 0.60** (0.51 to 0.71)	**22 fewer per 1.000** (from 16 fewer to 27 fewer)	⨁◯◯◯ VERY LOW	CRITICAL
30-day readmission (follow up: 42 months)												
1	observational studies	serious [c]	not serious	serious [b]	not serious	none	894/10528 (8.5%)	496/3622 (13.7%)	**RR 0.62** (0.56 to 0.69)	**52 fewer per 1.000** (from 42 fewer to 60 fewer)	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. Reporting bias, selection bias (allocation concealment) unclear, attrition bias unclear; b. 1 single-centre US trial (limited generaliziblity to other settings/countries); c. Inappropriate eligibility criteria and not controlled for confounding; d. 3 single-centre US trials (limited generalizibility to other settings/countries).

Detailed evidence summary

Topic	Patient Blood Management (PBM)
Subtopic	Implementation PBM programs
Intervention	Decision support systems (DSS) to promote appropriate use of blood products
Question (PICO)	Is a specific decision support system [intervention] more effective to improve the appropriate use of blood products or clinical outcomes [outcome] compared to no intervention or another decision support system/behavioural intervention [comparison]?
Search Strategy	We used the evidence from the Cochrane systematic review by Fisher et al. 'Computer decision support systems to promote appropriate use of blood products.', which will be published in 2018.
Search date	23 February 2018 (Fisher et al.)
In/Exclusion criteria	**Population:** *Included:* all people (adults and children) who are considered for transfusion of red blood cells (RBCs), platelets, plasma, cryoprecipitate, or granulocytes in any clinical setting. *Excluded:* people who receive other blood products e.g. intravenous immunoglobulin, factor VIII. **Intervention:** *Included:* Any electronic/computerised DSS that provides clinicians with recommendations on RBC, platelet, plasma, cryoprecipitate, or granulocyte ordering at the time the decision to order a transfusion is being made based on individual patient characteristics. **Comparison:** no DSS **Outcome:** *Included:* - Primary outcomes ➔ Proportion of participants who receive transfusions ➔ Amount of blood product used per participant (number of units in adults and volume in mL in infants and children) ➔ Serious adverse event (1) transfusion-related, transfusion-transmitted infection, transfusion-associated circulatory overload, transfusion-associated dyspnea, acute transfusion reactions, 2) bleeding (including WHO grade 3 or 4, or equivalent or bleeding that requires an operation), 3) infection, 4) arterial or venous thromboembolism (including deep vein thrombosis, pulmonary embolism, stroke, myocardial infarction). - Secondary outcomes ➔ Number of transfusions compliant with institutional transfusion guidelines ➔ Blood count or coagulation parameter (e.g. haematocrit, haemoglobin, prothrombin time, partial thromboplastin time, or platelet count) preceding and after the transfusion. ➔ Length of participant stay (in-hospital) ➔ Length of participant stay (ICU) ➔ All-cause mortality ➔ Clinician workflow (additional time per intervention implemented)

Characteristics of included studies

Author, year, Country	Study design	Population	Comparison	Concurrent interventions
Adams, 2011, USA	Observational: interrupted time series (retrospective cohort study)	Children (medical, surgical, ICU) after (3492 discharges, 7.18±6.2 years, 51.5% males)	Comparison: after DSS implementation versus before DSS implementation Details of DSS:	None

		versus before implementation (3293 discharges, 7.16±6.1 years, 54.3%) of a DSS intervention Study centre: single centre, tertiary hospital	CPOE (Cerner), alerts were created according to the current best-practice recommendations. The CPOE alert was designed to analyse the patient record and hemodynamic status Variables in the alert algorithm included the patient's age, diagnosis, most recent serum haemoglobin level and blood pressure. The alert window along with a hyperlink to the supporting evidence was provided if a RBCT order was written in case appropriate age range (1 month – 18 years), normal blood pressure, and a haemoglobin level >7 g/dL. Overriding the alert was an option if the clinician determined that it was in the patient's best interest to order the RBCT. Blood ordering products: RBC only Follow-up period before implementation: 12 months Follow-up period after implementation: 12 months	
Goodnough, 2014, USA	Observational: interrupted time series (retrospective cohort study)	177020 adult inpatient discharges (ED, medical, surgical, obstetrics, and ICU): 10528 (mean age 59.8±17.4, 49.8% males) after versus 3622 (mean age 59.7±17.0 years, 45.7% males) before implementation DSS available	Comparison: after DSS implementation versus before DSS implementation Details of DSS: CPOE (Epic systems) Orders for RBC units triggered an interruptive alert in patients with the most recent (within 24 hr) Hb level of higher than 7 g/dL (8 g/dL in patients with acute coronary syndrome or post–cardiothoracic surgery).	Education about the consensus transfusion guidelines was disseminated to providers in various different clinical services via in-person meetings and electronic communication for almost 1

		Additional analysis on clinical outcomes in a cohort of stable adult medical and surgical (postoperative) patients who received blood transfusions: 10528 patients after (59.8±17 years, 49.8% males) versus 3622 patients before implementation DSS intervention (59.7±17.4 years, 46.7% males) Study centre: single centre, tertiary hospital	The alert contained the consensus guidelines, a link to relevant literature, and an "acknowledgment" reason for transfusion if the provider chose to continue with the RBC order. Blood ordering products: RBC only Follow-up period before implementation: 30 months Follow-up period after implementation: 42 months	year (prior to the implementation of DSS intervention)
Kassakian, 2016, USA	Observational: interrupted time series (retrospective)	All adult patients admitted to all services except obstetrics: 71258 admissions (mean age 54.3 years, 53.1% males) after DSS implementation versus 71621 admissions (mean age 53.1 years, 52.4% males) before DSS implementation Study centre: single centre, tertiary hospital	Comparison: after DSS implementation versus before DSS implementation Details of DSS: Htc ≥21% and order for RBC transfusion is followed by an interruptive alert which also allows the user to turn off the alert with common reasons for RBC transfusion in patients with Htc ≥21% such as tachycardia, hypotension, active bleeding, acute coronary syndrome, instability, and imminent surgery. Blood ordering products: RBC only Follow-up period before implementation: 36 months Follow-up period after implementation: 36 months	Ad hoc education related to appropriate transfusion (6 departmental talks given over a 2-year period)
Rothschild, 2007, USA	Experimental: randomized controlled trial	453 Junior Housestaff (1st, 2nd and 3rd year	Comparison: DSS (CPOE system) versus no DSS	Educational intervention (prior to RCT):

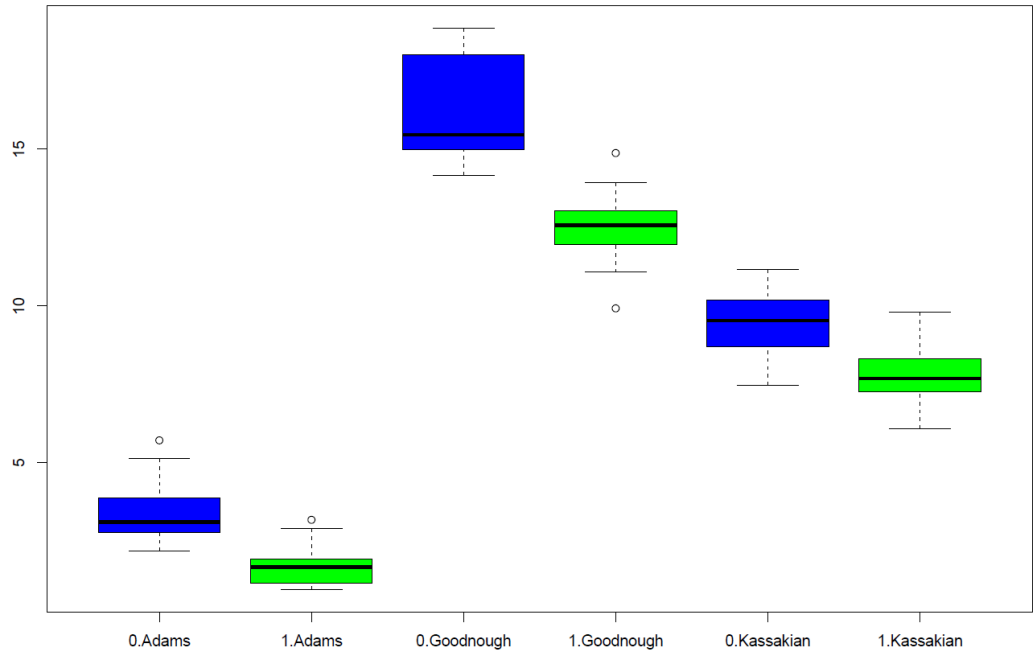
		residents; medical, surgical, obstetrics, ICU) randomized into the intervention group (DSS) (n=227) and a control group (no DSS) (n=226) Study centre: single centre, tertiary hospital	Details of DSS: Hct level for RBC, Plt count for Plt, PT/INR or APIT for plasma. DS-recommended doses were calibrated to patient characteristics and the preceding "trigger" laboratory results for component blood orders The DS logic recommended a dose (number of units) of product based on the most recent laboratory values, the patient's characteristics, and the expected therapeutic result of the product. Blood ordering products: RBC, plasma, Plt only Follow-up period: 4 months	broad dissemination of institutional transfusion guidelines through direct mailings with pocket cards to all physicians, didactic lectures, housestaff meetings, newletters, and inclusion in an Intranet-based reference handbook.

Synthesis of findings

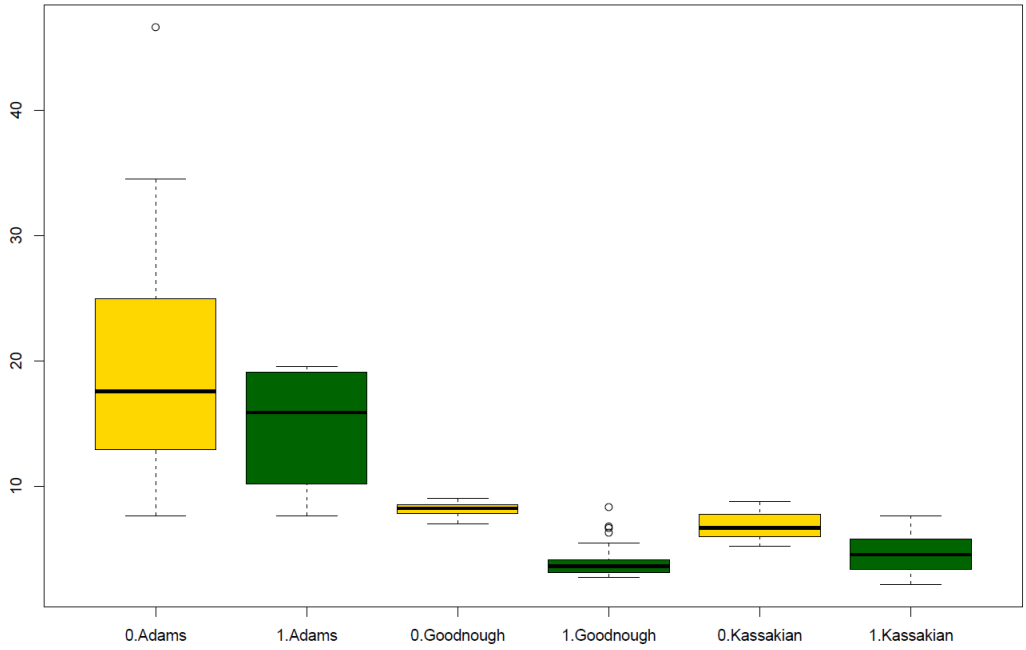
Outcome	Comparison/Risk factor	Effect Size	#studies, # participants	Reference
Appropriate transfusions	DSS versus no DSS	Statistically significant: 546/1350 vs 503/1546 RR: 1.24, 95%CI [1.13;1.37] (p<0.0001) In favour of DSS	1, 1350 vs 1546	Rothschild, 2007
Overall RBC usage (RBC transfusions per 100 inpatient days)		Statistically significant: 3/100 versus 2/100 λ (see boxplot 1) (p<0.0001) *In favour of DSS*	1, 3492 versus 3294 (discharges)	Adams, 2011
		Statistically significant: 9.5/100 versus 7.5/100 λ (see boxplot 1) (p<0.0001) *In favour of DSS*	1, 353439 versus 361686 (in-patient days)	Kassakian, 2016
		Statistically significant: 15.5/100 versus 12.5/100 λ (see boxplot 1) (p<0.0001) *In favour of DSS*	1, no raw data available	Goodnough, 2014
Inappropriate RBC usage (RBC transfusions per 100 inpatient days)		Statistically significant: 18.5/100 versus 16.5/100 λ (see boxplot 2) (p<0.001) *In favour of DSS*	1, 3492 versus 3294 (discharges)	Adams, 2011
		Statistically significant: 8/100 versus 6.5/100 λ (see boxplot 2) (p<0.001) *In favour of DSS*	1, 353439 versus 361686 (in-patient days)	Kassakian, 2016

		Statistically significant: 8.5/100 versus 3.5/100 λ (see boxplot 2) (p<0.001) *In favour of DSS*	1, no raw data available	Goodnough, 2014
Mortality		Statistically significant: 347/10528 versus 199/3622 RR: 0.60, 95%CI [0.51;0.71] (p<0.00001) *In favour of DSS*	1, 10528 versus 3622	Goodnough, 2014
30-day readmission		Statistically significant: 894/10528 versus 496/3622 RR: 0.62, 95%CI [0.56;0.69] (p<0.00001) *In favour of DSS*		Goodnough, 2014

λ data extracted from graph



Box plot 1. Pre-post results – Interrupted time series (3 studies – x-axis). Overall RBC usage: number of RBC transfusion per 100 inpatient days (y-axis). Analysis (meta-regression) from upcoming/unpublished Cochrane review by Fisher et al. (confidential information).



Box plot 2. Pre-post results – Interrupted time series (3 studies – x-axis). Inappropriate RBC usage: number of RBC transfusion per 100 inpatient days (y-axis). Analysis (meta-regression) from upcoming/unpublished Cochrane review by Fisher et al. (confidential information).

Quality of evidence
Experimental studies

Author, Year	Random sequence generation and allocation concealment (selection bias)	Blinding of personnel and participants (performance bias) and blinding of outcome assessors (detection bias)	Missing data or incomplete outcome data (attrition bias)	Selection of reported results or selective reporting (reporting bias)	Other limitations
Rothschild, 2007	Randomization Low risk of bias A computerized program generated the randomization scheme for each block (according to clinical specialty and year of training) Allocation concealment: Unclear	Participants: Low risk of bias Junior housestaff were not told which group they were assigned. Outcome assessors: Low risk of bias Abstractors were blinded to the physician randomization. A sample of 50 charts was reviewed by all three chart abstractors to assess inter-rater reliability	Unclear No report of drop-out of physicians or whether intervention and control groups ordered similar amounts of products.	High risk of bias Only one outcome reported by study arm. No trial registration or protocol	Concurrent intervention (education) prior to the randomization

Observational studies

Author, Year	Inappropriate eligibility criteria	Inappropriate methods for exposure and outcome variables	Not controlled for confounding	Incomplete or inadequate follow-up	Other limitations
Adams, 2011	Yes No time-matched controls	No Objective outcomes	Yes Controlled for severity of illness (Case-Mix	No Data from specified time	No data reported on the frequency of the alert

	(historical control group) 'There was a significant difference in patients admitted for diseases of the circulatory system (207 vs 168; P.009), ear, nose, mouth, and throat (473 vs 424; P.006), respiratory system (288 vs 412; P .0001), and endocrine, nutritional, and metabolic disorders (135 vs 217; P .0001) in the control versus study cohort.'	retrieved from hospital CPOE	index = metric derived from all patient-refined, diagnosis-related groups and is used by the Centers for Medicare & Medicaid Services to measure the relative level of "resource intensity" within a hospital. Resource intensity and utilization serve as surrogate indicators for severity of illness.) No other potential confounding factors were taken in to account	periods in CPOE	
Goodnough, 2014	Yes No statistical analysis in demographic variables between 2 cohorts (after versus before DSS), cohort that received DSS seems to be older, more males and increased patient discharge volumes,	No Primary data collected from the laboratory data repository (Rhodes) and Midas (a proprietary clinical database). Microsoft Access was used to merge these data.	Yes Not controlled for confounding variables but unsure if these differences affect the effect estimate.	Yes Hb data from Rhodes were analyzed only after July 2009 as the data integration and validation for the Rhodes database occurred after this time point; clinical outcomes data from Midas continued to be available	One limitation of our study is that within our own EMR, CDS and BPA could not be designed so that the option chosen by the user at the alert ("accept"/"cancel") automatically triggered a downstream action such as canceling or continuing the original RBC product order. Thus, measuring

	patient-days-at-risk, case-mix complexity, volumes of selected surgeries, and solid organ and stem cell transplant procedures.			before this point.	only the rate of accept versus cancel as success in an override can be a misrepresentation of the end-user action.
Kassakian, 2016	No Similar amount of admissions and inpatient days in both groups, demographic characteristic (age/gender) were different	No Transfusion data, lab values, and patient characteristics were extracted from the clinical database using Structured Query Language. No significant changes in either the laboratory or blood banking systems or methods in which those were recorded Secondary use of operational electronic health record data has potential limitations and pitfalls.	Yes Rates of platelet transfusion served as a control variable (from November 2008-July 2013) at which time a separate CDS tool for inappropriate platelet transfusion was implemented + wash-in period of 1 month (+ sensitivity analysis using a 2-month wash-in period) However, significant differences in groups from pre/post intervention on age and sex and did not adjust for confounders and may affect internal validity	No Less than 1% (836 of 84,518) of the transfused units of red blood cells had missing haematocrit value in the 24 hours prior to transfusion administration. The sensitivity analysis showed a negligible (<1%) difference in the point estimates and CI of the results between the 2 analyses.	DSS intervention was implemented +/- 2 years later in the general surgery and bone marrow transplant unit (August 2013) compared to the implementation in the other units (October 2011)

Certainty of the body of evidence: see GRADE Evidence tables

Conclusion	See Evidence-to-Decision template
Reference(s)	See overview list included studies
Evidence used for	Guideline
Project	ICC-PBM 2018
Reviewer(s)	Hans Van Remoortel