Draft for Consultation

Transfusion

Blood transfusion

NICE guideline

Appendices A-G

18 May 2015

Draft for consultation

Commissioned by the National Institute for Health and Care Excellence

Royal College of Physicians
The Royal College of Surgeons of England
RCGP Royal College of General Practitioners
Royal College of Nursing
NICE accredited
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Funding
National Institute for Health and Care Excellence

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Appendix A: Scope

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

SCOPE

1 Guideline title

Blood transfusion

1.1 Short title

Transfusion

2 The remit

The Department of Health has asked NICE: 'to develop a cross cutting clinical guideline on the assessment for and management of transfusion'.

3 Clinical need for the guideline

3.1 Epidemiology

a) Blood transfusions are commonly used in clinical practice. In 2011 NHS Blood and Transplant issued 1,829,951 units of red blood cells, 260,278 units of platelets, 248,163 units of fresh frozen plasma and 122,516 units of cryoprecipitate to hospitals in England and North Wales.

b) In 2002 an estimated 430,000 patients received a red blood cell transfusion.

c) Blood transfusion is an essential part of modern healthcare. However, it is also associated with clinical risks. The risk of transfusion-related death was 2.7 per million blood components issued and the risk of transfusion-related major morbidity was 39.9 per million blood components issued. The proportion of adverse incident reports resulting in death or major morbidity has reduced from 34% in 1996/97 to 6.9% in 2011.

Transfusion: Final scope 1 of 12

d) Transfusion of blood to the wrong patient is an avoidable serious hazard of transfusion. It can result from errors made anywhere in the transfusion process, including patient identification, blood sample collection, laboratory testing and handling of samples, retrieval from blood transfusion refrigerators and the bedside check immediately before transfusion. Transfused patients require careful monitoring for any adverse effects.

e) Appropriate decision-making about the use of blood based on clinical findings and laboratory parameters and avoidance of over-transfusion are essential parts of good transfusion practice.

f) Haemovigilance data from the Serious Hazards of Transfusion scheme in the UK indicate that 'incorrect blood component transfused' accounts for the largest proportion of all adverse events, and is the second most frequent cause of mortality and morbidity associated with transfusion.

3.2 Current practice

a) There has been a considerable decline in the use of red blood cell transfusion. A study in the north of England showed a decline in the transfusion rate from 45.5 to 36 units per 100,000 population between 1999 and 2009. In contrast, the use of platelets and fresh frozen plasma has been increasing. However, the use of red blood cells in England remains higher than in some countries such as Canada.

b) The ageing population and new therapies in cancer, transplantation and many other fields of medicine may increase blood use in the future.

c) Between 1999 and 2009 the proportion of red blood cells used in surgical patients declined from 41% to 29%. Over the same period the proportion of red blood cells used in medical patients increased

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from 52% to 64%; use in obstetrics and gynaecology remained stable at 6%.

d) Blood transfusion in the UK is safer now than it has ever been but it is not risk-free. Numerous initiatives over the past 15 years in the UK, primarily involving the education and training of the many staff involved in the transfusion process, have had a considerable effect on improving transfusion safety.

e) A current concern is the high level of inappropriate use of blood components, which is wasting a scarce and costly resource, and putting patients at unnecessary risk. There remains considerable variation between hospitals. Inappropriate use of all blood components is estimated to be 20% or higher from the results of national and large regional audits in the UK.

f) Efforts are needed to promote evidence-based strategies and measures to reduce the inappropriate use of blood components, and increase the use of alternatives to transfusion. These will both improve patient care and reduce hospital costs. New technologies have the potential to improve the safety of the transfusion process, such as using electronic systems for patient identification and to check that the right blood will be transfused. They also have the potential to support the appropriate use of blood by linkage to the electronic patient record to provide 'decision support'. However, as yet, they have not been widely adopted in the NHS.

4 The guideline

The guideline development process is described in detail on the NICE website (see section 6, 'Further information').

This scope defines what the guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on the referral from the Department of Health.

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The areas that will be addressed by the guideline are described in the following sections.

4.1 Population

4.1.1 Groups that will be covered

a) Adults.

b) Children and young people.

c) Specific consideration will be given to the needs of:

- Elderly population
- Religious groups

4.1.2 Groups that will not be covered

a) Neonates and infants up to 1 year of age (except for patient safety issues listed in section 4.5.5).

b) Foetuses.

4.2 Healthcare setting

a) All healthcare settings.

4.3 Clinical management

4.3.1 Key clinical issues that will be covered

a) Appropriate use of red blood cell transfusion:

- indications for starting transfusion, based on clinical considerations, medical comorbidities such as myocardial infarction and haemoglobin (Hb) concentration thresholds
- dose of red blood cells (number of units of red blood cells)
- target Hb levels.

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b) Appropriate use of platelet transfusion:

- indications for starting transfusion, based on clinical considerations including the presence or absence of bleeding and platelet count thresholds
- dose of platelets
- target platelet counts.

c) Appropriate use of fresh frozen plasma (FFP), cryoprecipitate andprothrombin complex concentrate (PCC) transfusion:

- indications for starting transfusion, based on clinical considerations including the presence or absence of bleeding and abnormalities of tests of haemostasis
- dose of FFP, cryoprecipitate and PCC
- target results of haemostasis tests.

d) Alternative treatments to blood transfusion in surgical patients:

- oral iron
- intravenous (IV) iron
- recombinant erythropoietin
- tranexamic acid as an adjunct to minimise transfusion. Note that guideline recommendations will normally fall within licensed indications; exceptionally, and only if clearly supported by evidence, use outside a licensed indication may be recommended. The guideline will assume that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients
- cell salvage therapy.

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e) Patient safety:

- monitoring of signs and symptoms of acute transfusion reaction
- electronic patient identification systems to ensure patient safety during blood transfusions.

f) Electronic decision support at the time of blood ordering for the appropriate use of blood

g) Patient information and support specific to blood transfusion.

4.3.2 Clinical issues that will not be covered

a) Investigations and treatment of anaemia in medical patients

b) Use and administration of blood products, including:

- immunoglobulin.

c) Coagulation factor concentrates

d) Recombinant activated factor VII

e) Albumin

f) Fibrinogen

g) Identification and testing for anaemia

h) Treatment of anaemia in medical patients

i) Laboratory procedures relating to the quality and safety of blood products (content, characteristics, storage and residual risks of infection) including:

- handling of samples
- documentation
- ABO and RhD blood grouping

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- antibody screening and identification
- selection and issue of red blood cells
- procedures after blood components have been issued.

j) Near patient testing of haemoglobin and haemostasis

k) Human leucocyte antigen (HLA) sensitisation with transplantation.

l) This is a cross cutting guideline focussing on the general principles of transfusion and the appropriate use of blood. No specific clinical condition will be excluded, but the detailed management of specific clinical conditions (such as haemoglobinopathy, minor coagulopathy, obstetrics) will not be considered. The following specialist areas will not be included in the guidance as they are covered by other related NICE guidance:

- anaemia in chronic kidney disease
- upper gastrointestinal bleeding
- trauma or massive haemorrhage.

4.4 Main outcomes

a) Mortality

b) Quality of life

c) Length of stay (hospitalisation)

d) Infections (for example, pneumonia)

e) Number of patients needing transfusions

f) Number of units transfused

g) Bleeding

h) Serious adverse events.

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4.5 Review questions

4.5.1 Red blood cell transfusion

a) What is the clinical and cost effectiveness of red blood cell transfusion at different haemoglobin concentrations?

b) What is the clinical and cost effectiveness of red blood cell transfusion based on clinical considerations including medical comorbidities?

c) What is the clinical and cost effectiveness of different doses of red blood cell transfusion?

d) What is the clinical and cost effectiveness of different target levels of post-transfusion haemoglobin concentrations for red blood cell transfusion?

4.5.2 Platelet transfusion

a) What is the clinical and cost effectiveness of platelet transfusion at different platelet count thresholds?

b) What is the clinical and cost effectiveness of platelet transfusion based on clinical considerations including the presence of or absence of bleeding?

c) What is the clinical and cost effectiveness of different doses of platelet transfusion?

d) What is the clinical and cost effectiveness of different target levels of post-transfusion platelet counts?

4.5.3 Fresh frozen plasma (FFP), cryoprecipitate and prothrombin complex concentrate (PCC) transfusion

a) What is the clinical and cost effectiveness of FFP, cryoprecipitate and PCC transfusion at different levels of abnormal haemostasis?

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b) What is the clinical and cost effectiveness of FFP, cryoprecipitate and PCC transfusion based on clinical considerations including the presence or absence of bleeding?

c) What is the clinical and cost effectiveness of different doses of FFP, cryoprecipitate and PCC?

d) What is the clinical and cost effectiveness of different target levels of post-transfusion haemostasis tests?

4.5.4 Alternative treatments to blood transfusion in surgical patients

a) What is the clinical and cost effectiveness of oral iron and IV iron in reducing blood transfusion requirements in surgical patients?

b) What is the clinical and cost effectiveness of recombinant erythropoietin in reducing blood transfusion requirements in surgical patients?

c) What is the clinical and cost effectiveness of tranexamic acid in reducing blood transfusion requirements in surgical patients?

d) What is the clinical and cost effectiveness of cell salvage therapy in reducing blood transfusion requirements in surgical patients?

4.5.5 Patient safety

a) What is the clinical and cost effectiveness of monitoring for acute reactions at different times in relation to the transfusion?

b) What are the clinical and cost effectiveness of electronic patient identification systems such as patient identification bands, bar codes or radiofrequency identification to ensure patient safety during blood transfusions?

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4.5.6 Electronic decision support blood order systems

a) What are the clinical and cost effectiveness of electronic decision support blood order systems to reduce inappropriate blood transfusions?

4.5.7 Patient information and support specific to blood transfusion

a) What is the clinical and cost effectiveness of providing information to people receiving blood transfusion and their family members or carers?

4.6 Economic aspects

Developers will take into account both clinical and cost effectiveness when making recommendations involving a choice between alternative interventions. A review of the economic evidence will be conducted and analyses will be carried out as appropriate. The preferred unit of effectiveness is the quality-adjusted life year (QALY), and the costs considered will usually be only from an NHS and personal social services (PSS) perspective. Further detail on the methods can be found in 'The guidelines manual' (see 'Further information').

4.7 Status

4.7.1 Scope

This is the final scope.

4.7.2 Timing

The development of the guideline recommendations will begin in June 2013.

5 Related NICE guidance

5.1 Published guidance

- Acute upper gastrointestinal bleeding. NICE clinical guideline 141 (2012).
- Caesarean section. NICE clinical guideline 132 (2011).

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- Anaemia management in people with chronic kidney disease. NICE clinical guideline 114 (2011).
- Neonatal jaundice. NICE clinical guideline 98 (2010).
- Intraoperative blood cell salvage during radical prostatectomy or radical cystectomy. NICE interventional procedure guidance 258 (2008).
- Intraoperative blood cell salvage in obstetrics. NICE interventional procedure guidance 144 (2005).
- Preoperative tests. NICE clinical guideline 3 (2003).

5.2 Guidance under development

NICE is currently developing the following related guidance (details available from the NICE website):

- Intravenous fluid therapy in adults. NICE clinical guideline. Publication expected November 2013.
- Intravenous fluids therapy in children. NICE clinical guideline. Publication expected November 2015.
- Ulcerative colitis. NICE clinical guideline. Publication expected June 2013.
- Erythropoiesis-stimulating agents (epoetin and darbepoetin) for the treatment of cancer-treatment induced anaemia (including review of TA142). NICE technology appraisal. Publication expected August 2014.
- Intrapartum care. NICE clinical guideline. Publication expected October 2014.
- Major trauma. NICE clinical guideline. Publication expected June 2015.
- Trauma services. NICE clinical guideline. Publication expected October 2015.
- Intrapartum care for high risk women. NICE clinical guideline. Publication date to be confirmed.
- Anaemia management in chronic kidney disease (update). NICE clinical guideline. Publication date to be confirmed.

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6 Further information

Information on the guideline development process is provided in the following documents, available from the NICE website:

- How NICE clinical guidelines are developed: an overview for stakeholders the public and the NHS
- The guidelines manual.

Information on the progress of the guideline will also be available from the NICE website.

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Appendix B: Declarations of interest

B.1 Shubha Allard

GDG meeting	Declaration of interest	Classification	Action taken
Recruitment	None	None	No action needed.
GDG 1 20 June 2013	A member of several transfusion related guideline development groups.	Personal non-pecuniary	Declared and participated
GDG 2 29 July 2013	GDG member declared that she is a member on several transfusion related guideline development groups.	Personal non-pecuniary	Declared and participated.
GDG 3 3 September 2013	No change to existing declarations.	None	Not applicable
GDG 4 22 October 2013	Chair of the BCSH transfusion task force and has co-authored various guidelines include, Acute Transfusion reactions and Use of Red Cells in Critical Care and has also steered the development of many other guidelines.	Personal non-pecuniary	Declared and participated
GDG 5 20 November 2013	No change to existing declarations.	None	Not applicable
GDG 6 22 January 2014	No change to existing declarations.	None	Not applicable
GDG 7 2 April 2014	No change to existing declarations.	None	Not applicable
GDG 8 7 May 2014	No change to existing declarations.	None	Not applicable
GDG 9 12 June 2014	No change to existing declarations.	None	Not applicable
GDG 10 24 July 2014	No change to existing declarations.	None	Not applicable
GDG 11 17 September 2014	Project lead for a national comparative audit looking at patient information and consent who are soon to publish a report.	Personal non-pecuniary	Declared and participated
GDG 12 4 November 2014	No change to existing declarations.	None	Not applicable
GDG 13 10 December 2014	No change to existing declarations.	None	Not applicable
GDG 14 3 February 2015	No change to existing declarations.	None	Not applicable
GDG 15 29 July 2015			

B.2 David Blackwell

GDG meeting	Declaration of interest	Classification	Action taken
Recruitment	None	None	Not applicable
GDG 1 20 June 2013	No change to existing declarations.	None	Not applicable
GDG 2 29 July 2013	No change to existing declarations.	None	Not applicable
GDG 3 3 September 2013	No change to existing declarations.	None	Not applicable
GDG 4 22 October 2013	No change to existing declarations.	None	Not applicable
GDG 5 20 November 2013	No change to existing declarations.	None	Not applicable
GDG 6 22 January 2014	No change to existing declarations.	None	Not applicable
GDG 7 2 April 2014	No change to existing declarations.	None	Not applicable
GDG 8 7 May 2014	No change to existing declarations.	None	Not applicable
GDG 9 12 June 2014	No change to existing declarations.	None	Not applicable
GDG 10 24 July 2014	No change to existing declarations.	None	Not applicable
GDG 11 17 September 2014	No change to existing declarations.	None	Not applicable
GDG 12 4 November 2014	No change to existing declarations.	None	Not applicable
GDG 13 10 December 2014	No change to existing declarations.	None	Not applicable
GDG 14 3 February 2015	No change to existing declarations.	None	Not applicable
GDG 15 29 July 2015			

B.3 Graham Donald

GDG meeting	Declaration of interest	Classification	Action taken
Recruitment	None	None	Not applicable
GDG 1 20 June 2013	No change to existing declarations.	None	Not applicable
GDG 2 29 July 2013	No change to existing declarations.	None	Not applicable
GDG 3 3 September 2013	No change to existing declarations.	None	Not applicable
GDG 4 22 October 2013	No change to existing declarations.	None	Not applicable
GDG 5	No change to existing declarations.	None	Not applicable

GDG meeting	Declaration of interest	Classification	Action taken
20 November 2013			
GDG 6 22 January 2014	No change to existing declarations.	None	Not applicable
GDG 7 2 April 2014	No change to existing declarations.	None	Not applicable
GDG 8 7 May 2014	No change to existing declarations.	None	Not applicable
GDG 9 12 June 2014	No change to existing declarations.	None	Not applicable
GDG 10 24 July 2014	No change to existing declarations.	None	Not applicable
GDG 11 17 September 2014	GDG member declared that he is part of a team that has drafted patient referral leaflets, but no funds have been received for this work.	Personal non-pecuniary	Declared and participated
GDG 12 4 November 2014	No change to existing declarations.	None	Not applicable
GDG 13 10 December 2014	No change to existing declarations.	None	Not applicable
GDG 14 3 February 2015	No change to existing declarations.	None	Not applicable
GDG 15 29 July 2015			

B.4 Kenneth Halligan

GDG meeting	Declaration of interest	Classification	Action taken
Recruitment	None	None	Not applicable
GDG 1 20 June 2013	No change to existing declarations.	None	Not applicable
GDG 2 29 July 2013	No change to existing declarations.	None	Not applicable
GDG 3 3 September 2013	No change to existing declarations.	None	Not applicable
GDG 4 22 October 2013	No change to existing declarations.	None	Not applicable
GDG 5 20 November 2013	No change to existing declarations.	None	Not applicable
GDG 6 22 January 2014	No change to existing declarations.	None	Not applicable
GDG 7 2 April 2014	No change to existing declarations.	None	Not applicable
GDG 8 7 May 2014	No change to existing declarations.	None	Not applicable
GDG 9 12 June 2014	No change to existing declarations.	None	Not applicable
GDG 10	No change to existing declarations.	None	Not applicable

GDG meeting	Declaration of interest	Classification	Action taken
24 July 2014			
GDG 11 17 September 2014	No change to existing declarations.	None	Not applicable
GDG 12 4 November 2014	No change to existing declarations.	None	Not applicable
GDG 13 10 December 2014	No change to existing declarations.	None	Not applicable
GDG 14 3 February 2015	No change to existing declarations.	None	Not applicable
GDG 15 29 July 2015			

B.5 Karen Madgwick

GDG meeting	Declaration of interest	Classification	Action taken
Recruitment	None	None	Not applicable
GDG 1 20 June 2013	No change to existing declarations.	None	Not applicable
GDG 2 29 July 2013	No change to existing declarations.	None	Not applicable
GDG 3 3 September 2013	No change to existing declarations.	None	Not applicable
GDG 4 22 October 2013	No change to existing declarations.	None	Not applicable
GDG 5 20 November 2013	No change to existing declarations.	None	Not applicable
GDG 6 22 January 2014	No change to existing declarations.	None	Not applicable
GDG 7 2 April 2014	No change to existing declarations.	None	Not applicable
GDG 8 7 May 2014	No change to existing declarations.	None	Not applicable
GDG 9 12 June 2014	No change to existing declarations.	None	Not applicable
GDG 10 24 July 2014	No change to existing declarations.	None	Not applicable
GDG 11 17 September 2014	No change to existing declarations.	None	Not applicable
GDG 12 4 November 2014	No change to existing declarations.	None	Not applicable
GDG 13 10 December 2014	No change to existing declarations.	None	Not applicable
GDG 14 3 February 2015	No change to existing declarations.	None	Not applicable
GDG 15 29 July 2015			

B.6 Mary Marsden

GDG meeting	Declaration of interest	Classification	Action taken
Recruitment	None	None	Not applicable
GDG 1 20 June 2013	No change to existing declarations.	None	Not applicable
GDG 2 29 July 2013	No change to existing declarations.	None	Not applicable
GDG 3 3 September 2013	No change to existing declarations.	None	Not applicable
GDG 4 22 October 2013	No change to existing declarations.	None	Not applicable
GDG 5 20 November 2013	No change to existing declarations.	None	Not applicable
GDG 6 22 January 2014	No change to existing declarations.	None	Not applicable
GDG 7 2 April 2014	No change to existing declarations.	None	Not applicable
GDG 8 7 May 2014	No change to existing declarations.	None	Not applicable
GDG 9 12 June 2014	No change to existing declarations.	None	Not applicable
GDG 10 24 July 2014	No change to existing declarations.	None	Not applicable
GDG 11 17 September 2014	GDG member declared that she currently uses Octaplex, a drug which is used in some of the studies in the reviews at this GDG, and companies sometimes sponsor study days in her trust, but she has no personal pecuniary interest and has no declared preference for one PCC drug. GDG member also declared that there is research into dabigatran in her trust currently but that she is not directly involved in this research.	Non-personal pecuniary	Declared and participated
GDG 12 4 November 2014	No change to existing declarations.	None	Not applicable
GDG 13 10 December 2014	No change to existing declarations.	None	Not applicable
GDG 14 3 February 2015	No change to existing declarations.	None	Not applicable
GDG 15 29 July 2015			

B.7 Robert Morris

GDG meeting	Declaration of interest	Classification	Action taken

GDG meeting	Declaration of interest	Classification	Action taken
Recruitment	None	None	Not applicable
GDG 1 20 June 2013	None	None	Not applicable
GDG 2 29 July 2013	No change to existing declarations.	None	Not applicable
GDG 3 3 September 2013	No change to existing declarations.	None	Not applicable
GDG 4 22 October 2013	No change to existing declarations.	None	Not applicable
GDG 5 20 November 2013	No change to existing declarations.	None	Not applicable
GDG 6 22 January 2014	No change to existing declarations.	None	Not applicable
GDG 7 2 April 2014	No change to existing declarations.	None	Not applicable
GDG 8 7 May 2014	No change to existing declarations.	None	Not applicable
GDG 9 12 June 2014	No change to existing declarations.	None	Not applicable
GDG 10 24 July 2014	No change to existing declarations.	None	Not applicable
GDG 11 17 September 2014	No change to existing declarations.	None	Not applicable
GDG 12 4 November 2014	No change to existing declarations.	None	Not applicable
GDG 13 10 December 2014	No change to existing declarations.	None	Not applicable
GDG 14 3 February 2015	No change to existing declarations.	None	Not applicable
GDG 15 29 July 2015			

B.8 Mike Murphy

GDG meeting	Declaration of interest	Classification	Action taken
Recruitment	None	None	Not applicable
GDG 1 20 June 2013	No change to existing declarations.	None	Not applicable
GDG 2 29 July 2013	GDG member declared that he is an employee of the National Health Service Blood and Transplant, the only blood supplier for blood components in England. He has also written various articles on many aspects of Blood Transfusion and he has done extensive work in the area of electronic transfusion systems.	Personal non-pecuniary	Declared and participated
GDG 3	GDG member declared that he is	Personal non-	Declared and participated

GDG meeting	Declaration of interest	Classification	Action taken
3 September 2013	secretary of the National Blood Transfusion committee, clinical director for NHS blood and transplant and also leads the blood transfusion team in Oxford, a team which has developed electronic blood management systems to support transfusion in the NHS.	pecuniary	
GDG 4 22 October 2013	No change to existing declarations.	None	Not applicable
GDG 5 20 November 2013	GDG member declared published papers in electronic decision support and electronic patient identification systems.	Personal non-pecuniary	It was agreed that during the presentation of evidence in this area, the chair would step down and Susan Robinson would act as interim chair for this section of the agenda. The Chair will not assist with drafting recommendations for this area.
GDG 6 22 January 2014	No change to existing declarations.	None	Not applicable
GDG 7 2 April 2014	No change to existing declarations.	None	Not applicable
GDG 8 7 May 2014	No change to existing declarations.	None	Not applicable
GDG 9 12 June 2014	No change to existing declarations.	None	Not applicable
GDG 10 24 July 2014	No change to existing declarations.	None	Not applicable
GDG 11 17 September 2014	Named author on some of the studies used in the patient information review, he has no financial interest in this work.	Non-personal pecuniary	Declared and participated
GDG 12 4 November 2014	No change to existing declarations.	None	Not applicable
GDG 13 10 December 2014	Published an article in BMJ online about restrictive and liberal transfusion strategies.	Non-personal pecuniary	Withdrew from chairing, participating in discussions and drafting of recommendations in this area.
GDG 14 3 February 2015	No change to existing declarations.	None	Withdrew from discussions regarding the finalising of recommendations in these areas.
GDG 15 29 July 2015			

B.9 Helen New

GDG meeting	Declaration of interest	Classification	Action taken
Recruitment	GDG member declared her employment with the NHS Blood and Transplant service.	Non-specific personal pecuniary interest	Declared and participated
GDG 1 20 June 2013	No change to existing declarations.	None	Not applicable
GDG 2 29 July 2013	GDG member declared that her husband is a consultant for a bio-technology company, ReNeuron PLC, currently developing stem cell therapies for diagnostic and therapeutic applications.	Non-specific personal pecuniary	Declared and participated
	GDG member declared that she is the lead on a writing group for the new British Committee for Standards in haematology (BCSH) guidelines on neonatal and paediatric transfusion in preparation.	Personal non-pecuniary	Declared and participated
	GDG member declared that she is a member of the Serious Hazards of Transfusion working expert group and steering group and a member of the scientific committee of Network for advances of Transfusion Alternatives.	Personal non-pecuniary	Declared and participated
GDG 3 3 September 2013	No change to existing declarations.	None	Not applicable
GDG 4 22 October 2013	No change to existing declarations.	None	Not applicable
GDG 5 20 November 2013	No change to existing declarations.	None	Not applicable
GDG 6 22 January 2014	No change to existing declarations.	None	Not applicable
GDG 7 2 April 2014	No change to existing declarations.	None	Not applicable
GDG 8 7 May 2014	No change to existing declarations.	None	Not applicable
GDG 9 12 June 2014	No change to existing declarations.	None	Not applicable
GDG 10 24 July 2014	No change to existing declarations.	None	Not applicable
GDG 11 17 September 2014	No change to existing declarations.	None	Not applicable
GDG 12 4 November 2014	No change to existing declarations.	None	Not applicable
GDG 13 10 December 2014	No change to existing declarations.	None	Not applicable
GDG 14 3 February 2015	No change to existing declarations.	None	Not applicable

GDG meeting	Declaration of interest	Classification	Action taken
GDG 15 29 July 2015			

B.10 Susan Robinson

GDG meeting	Declaration of interest	Classification	Action taken
Recruitment	None	None	Not applicable
GDG 1 20 June 2013	No change to existing declarations.	None	Not applicable
GDG 2 29 July 2013	No change to existing declarations.	None	Not applicable
GDG 3 3 September 2013	No change to existing declarations.	None	Not applicable
GDG 4 22 October 2013	No change to existing declarations.	None	Not applicable
GDG 5 20 November 2013	No change to existing declarations.	None	Not applicable
GDG 6 22 January 2014	No change to existing declarations.	None	Not applicable
GDG 7 2 April 2014	No change to existing declarations.	None	Not applicable
GDG 8 7 May 2014	No change to existing declarations.	None	Not applicable
GDG 9 12 June 2014	No change to existing declarations.	None	Not applicable
GDG 10 24 July 2014	No change to existing declarations.	None	Not applicable
GDG 11 17 September 2014	No change to existing declarations.	None	Not applicable
GDG 12 4 November 2014	No change to existing declarations.	None	Not applicable
GDG 13 10 December 2014	No change to existing declarations.	None	Not applicable
GDG 14 3 February 2015	No change to existing declarations.	None	Not applicable
GDG 15 29 July 2015			

B.11 Dafydd Thomas

GDG meeting	Declaration of interest	Classification	Action taken
Recruitment	None	None	Not applicable
GDG 1 20 June 2013	No change to existing declarations.	None	Not applicable
	GDG member declared one instance of an honorarium paid for keynote lecture given at the 1st Danish meeting	Personal pecuniary interest	Declared and participated

GDG meeting	Declaration of interest	Classification	Action taken
	on blood transfusion to launch national guideline development document.		
	Chair of Network for advancement of transfusion alternatives, a scientific society which holds annual symposia and delivers on line learning in transfusion related interests. They rely on commercial support to run conferences. GDG member also declared his role as chair of SHOT steering group supported by UK forum (NHSBT/WBS/SNBTS/NIBTS)	Non- Personal pecuniary and personal non-pecuniary interest	Declared and participated
	GDG member declared that he is involved in previous blood transfusion guidelines for BCSH and AAGBT. Currently involved in 2 guidelines for BSCH, 1) Cell Salvage and Preoperative Anaemia and recently completed the BCSH on transfusion in clinical care.	Personal non-pecuniary interest	Declared and participated
	GDG member declared that he is seconded 1 day per week to work for the Welsh Blood service.	Non-specific personal pecuniary interest	Declared and participated.
GDG 2 29 July 2013	No change to existing declarations.	None	Not applicable
GDG 3 3 September 2013	GDG member declared that he chairs the network for alternatives to transfusion.	Personal non-pecuniary	Declared and participated
GDG 4 22 October 2013	No change to existing declarations.	None	Not applicable
GDG 5 20 November 2013	No change to existing declarations.	None	Not applicable
GDG 6 22 January 2014	No change to existing declarations.	None	Not applicable
GDG 7 2 April 2014	No change to existing declarations.	None	Not applicable
GDG 8 7 May 2014	No change to existing declarations.	None	Not applicable
GDG 9 12 June 2014	No change to existing declarations.	None	Not applicable
GDG 10 24 July 2014	No change to existing declarations.	None	Not applicable
GDG 11 17 September 2014	No change to existing declarations.	None	Not applicable
GDG 12 4 November 2014	Attended a study day on 01/11/2014 run by CSL Behring about setting up an educational resource related to the coagulation of trauma patients, for which payment of expenses was received.	Personal pecuniary	Declared and participated as allowable reasonable expenses

GDG meeting	Declaration of interest	Classification	Action taken
GDG 13 10 December 2014	No change to existing declarations.	None	Not applicable
GDG 14 3 February 2015	No change to existing declarations.	None	Not applicable
GDG 15 29 July 2015			

B.12 Timothy Walsh

GDG meeting	Declaration of interest	Classification	Action taken
Recruitment	GDG member declared that he is the UK Chief investigator for the National Institute for Health Research, Health Technoclogy Assessment funded ABLE study (Age of Blood Evaluation Study).	Non-personal pecuniary and personal non-pecuniary interests	Declared and participated
	Published research in Red Blood Cell transfusion.	Personal non-pecuniary	Withdrew from discussions at Meeting 14 regarding the finalising of recommendations in this area.
GDG 1 20 June 2013	No change to existing declarations.		
GDG 2 29 July 2013	No change to existing declarations.	None	Not applicable
GDG 3 3 September 2013	GDG member declared that he is the UK Chief investigator for the National Institute for Health Research, Health Technology Assessment funded ABLE study (Age of Blood Evaluation Study).	Non-Personal pecuniary and personal non-pecuniary interests	Declared and participated.
GDG 4 22 October 2013	No change to existing declarations.	None	Not applicable
GDG 5 20 November 2013	No change to existing declarations.	None	Not applicable
GDG 6 22 January 2014	No change to existing declarations.	None	Not applicable
GDG 7 2 April 2014	No change to existing declarations.	None	Not applicable
GDG 8 7 May 2014	No change to existing declarations.	None	Not applicable
GDG 9 12 June 2014	No change to existing declarations.	None	Not applicable
GDG 10 24 July 2014	No change to existing declarations.	None	Not applicable
GDG 11 17 September 2014	No change to existing declarations.	None	Not applicable
GDG 12 4 November 2014	No change to existing declarations.	None	Not applicable

GDG meeting	Declaration of interest	Classification	Action taken
GDG 13 10 December 2014	No change to existing declarations.	None	Not applicable
GDG 14 3 February 2015	No change to existing declarations.	None	Withdrew from discussions regarding the finalising of recommendations in this area.
GDG 15 29 July 2015			

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Appendix C: Clinical review protocols

C.1 Erythropoietin and iron

Table 1: Review protocol: Erythropoietin and iron

Review question	**What is the clinical and cost effectiveness of oral iron, IV iron and erythropoietin in reducing blood transfusion requirements in surgical patients?**
REVIEW DEFINITIONS	
Definition of the guideline condition	Blood transfusion is the process of administering blood or blood component to a patient.
Major age category	Adults aged 16 years and above) Children (under 16 years of age)
Purpose of review	Purpose of review not an inclusion criterion
Line of therapy	1st line
Minimum duration of study	Not defined
PICO INCLUSION/EXCLUSION CRITERIA	
Study design	RCT Systematic Review
Unit of randomisation	Patient
Crossover study	Not permitted
Other exclusions	Surgical ICU patients
Review population	Surgical patients with anaemia or at risk of anaemia. WHO definition of anaemia- Hb level <12 g/dl for females, Hb<13 g/dl for males, Hb<11.0 g/dl for children (0.5–5.0 years). Hb <11.5 g/dl for Hb children (5–12 years), Hb<12.0 g/dl for teens (12–15 years).
Interventions: generic/class; specific/drug	Oral iron; Oral Iron IV iron; IV iron Erythropoietin; Erythropoietin (alfa) Erythropoietin; Erythropoietin (beta) Erythropoietin; Erythropoietin (zeta) Erythropoietin; Erythropoietin (theta) Placebo; Placebo Oral iron + IV iron; Oral iron + IV iron Oral iron + Erythropoietin; Oral iron + Erythropoietin IV iron +Erythropoietin; IV iron +Erythropoietin Oral iron + IV iron + Erythropoietin ; Oral iron + IV iron + Erythropoietin No treatment; No treatment
Comparison types	Intervention vs. placebo Intervention vs. no treatment Intervention 1 vs. intervention 2 (different class) 2 interventions vs. 1 intervention (adjunct) 2 interventions vs. placebo

	2 interventions vs. no treatment 2 interventions vs. 1 intervention (not adjunct) 2 interventions vs. 2 interventions (1 common) 2 interventions vs. 2 interventions (none in common) 3 interventions vs. 1 intervention (not adjunct) 3 interventions vs. 2 interventions (1 intervention in common) 3 interventions vs. 2 interventions (not adjunct)
Outcomes	Quality of life at end of follow-up (continuous; MID: Default 0.5 SD; Available case analysis, reasons: ACA is the NCGC default) IMPORTANT Number of units transfused at end of follow-up (continuous; MID: Default 0.5 SD; Available case analysis, reasons: ACA is the NCGC default) IMPORTANT Length of hospital stay at end of follow-up (continuous; MID: Default 0.5 SD; Available case analysis, reasons: ACA is the NCGC default) IMPORTANT Mortality (all causes) at 30 days (time to event; MID: Default 1.25 or 0.75; Available case analysis, reasons: ACA is the NCGC default) CRITICAL Mortality (transfusion related) at 30 days (time to event; MID: Default 1.25 or 0.75; Available case analysis, reasons: ACA is the NCGC default) CRITICAL Infections (includes pneumonia, surgical site infection, UTI and septicaemia/bacteraemia) at within 30 days of surgery (dichotomous; MID: Default 1.25 or 0.75; Available case analysis, reasons: ACA is the NCGC default) IMPORTANT Number of patients needing transfusions at end of follow-up (dichotomous; MID: Default 1.25 or 0.75; Available case analysis, reasons: ACA is the NCGC default) CRITICAL Thrombosis IMPORTANT Serious adverse events as defined by the study (includes adverse events which result in death/life threatening adverse event for example, anaphylaxis, thrombosis, or hospitalisation/ prolongation of existing hospitalisation) at end of follow-up (dichotomous; MID: Default 1.25 or 0.75; Available case analysis, reasons: ACA is the NCGC default) IMPORTANT Mortality (all causes) at 1 year (time to event; MID: Default 1.25 or 0.75; Available case analysis, reasons: ACA is the NCGC default) CRITICAL
OTHER INCLUSION CRITERIA	
Sensitivity/other analysis	Sensitivity analysis on studies with greater than 10 days oral iron /EPO treatment vs. less than 10 days oral iron/EPO treatment. Sensitivity analysis on studies with patients who were anaemic at baseline.
Subgroup analyses if there is heterogeneity	Post MI (Systematic review: mixed; Not applicable / Not stated / Unclear; Post MI ; No post MI); Increased risk of poor treatment outcomes for patients with co-morbidities Hb level at baseline (Hb level 9-10 g/dl (females); Hb level 10-11 g/dl (females); Hb level 11-12 g/dl (females); Hb level 10-11 g/dl (males); Hb level 11-12 g/dl (males); Hb level 12-13 g/dl (males); Hb level 9-10 g/dl (children 12-15 years); Hb level 10-11 g/dl (children 12-15 years); Hb level 11-12 g/dl (children 12-15 years); Hb level 8.5-9.5 g/dl (children 5-12 years); Hb level 9.5-10.5 g/dl (children 5-12 years); Hb level 10.5-11.5 g/dl (children 5-12 years); Hb level 8-9 g/dl (children 0.5-5 years); Hb level 9-10 g/dl (children 0.5-5 years); Hb level 10-11 g/dl (children 0.5-5 years)); Treatment options and response to treatment may vary with different levels of Hb at baseline Cardiac failure (Cardiac failure; No cardiac failure); Increased risk of poor treatment outcomes for patients with co-morbidities Respiratory failure (Respiratory failure; No respiratory failure); Increased risk of poor treatment outcomes for patients with co-morbidities Ischaemic heart disease (Ischaemic heart disease; No Ischaemic heart disease); Increased risk of poor treatment outcomes for patients with co-morbidities
	Type of surgery (Systematic review: mixed; Not applicable / Not stated / Unclear; Cardiac surgery; Orthopaedic surgery; Vascular surgery; Hepatic surgery; Urological

	surgery; Gynaecological surgery; Cranial surgery); Cancer surgery; Outcomes dependent on type of surgery Duration of treatment (0-2 weeks (oral iron); 2-4 weeks (oral iron); 4-6 weeks (oral iron); once a week (IV iron); Twice a week (IV iron); Three times a week (IV iron); Once a week (Erythropoietin); Two times a week (Erythropoietin); Three times a week (Erythropoietin)); To see if there is variation in outcomes based on duration of treatment Dosage (1 unit (red blood cell transfusion); 2 units (red blood cell transfusion); More than 2 units (red blood cell transfusion); Ferrous sulfate 300mg (oral iron); Ferrous sulfate 200mg -dried (oral iron); Ferrous fumarate 200 mg (oral iron); Ferrous gluconate 300 mg (oral iron); Epoetin alfa (Erythropoietin) Binocrit- 600 units/kg every week for 3 weeks before surgery and on day of surgery or 300 units/kg daily for 15 days starting 10 days before surgery; Epoetin alfa (Erythropoietin) Eprex 600 units/kg every week for 3 weeks before surgery and on day of surgery or 300 units/kg daily for 15 days starting 10 days before surgery; Epoetin beta (Erythropoietin) NeoRecormon; Epoetin theta (Erythropoietin) Eporatio; Epoetin zeta (Erythropoietin) Retacrit 600 units/kg every week for 3 weeks before surgery and on day of surgery or 300 units/kg daily for 15 days starting 10 days before surgery; Ferric carboxymaltose 50 mg/ml of iron (IV iron) ; Ferumoxytol 30 mg/ml of iron (IV iron); Iron Dextran 50 mg/ml of iron (IV iron) ; Iron Isomaltoside 1000 (100 mg/ml) of iron (IV iron) ; Iron sucrose (20 mg/ml) of iron (IV iron)); Effect of dosage on outcomes Hb trigger/threshold for transfusion (Hb threshold < 8g/dl, Hb threshold 8-10g/dl; Hb threshold 10-12g/dl; Hb threshold >12 g/dl); It is at the point which transfusion will be considered necessary. This may affect the choice of treatment and treatment outcomes The use of transfusion protocol (Pre-defined cutoff points-Transfusion protocol ; No pre-defined cut-offs-No transfusion protocol/ based on clinical judgment; Transfusion protocol +clinical need); Variation in the exposure to allogeneic RBC transfusion
Search strategy	The databases to be searched are Medline, Embase, The Cochrane Library. Studies will be restricted to English language only.

C.2 Alternatives to blood transfusion in surgical patients - combinations of cell salvage and tranexamic acid

Table 2: Review protocol: alternatives to blood transfusion

Review question	**What is the clinical and cost-effectiveness of using alternatives to blood transfusion (cell salvage or tranexamic acid alone or in combination with one another) to reduce blood transfusion requirements?**
Objective	To evaluate if the combination of cell salvage and tranexamic acid is more effective in reducing blood transfusion requirements than each treatment individually
Population	Surgical patients Adults Children
Major age category	Adults (above 16 years of age) Children (under 16 years of age)
Interventions	High and moderate risk groups (see review strategy for definitions): Intra-operative cell salvage Post-operative cell salvage Intra-operative +Post-operative cell salvage Tranexamic acid (TXA) Intra-operative cell salvage +TXA Post-operative cell salvage +TXA

<table>
<tr><td></td><td>Intra-operative cell salvage +Post-operative cell salvage +TXA
Placebo/No treatment
Low risk group (see review strategy for definitions):
Tranexamic acid
Placebo/No treatment</td></tr>
<tr><td>Comparisons</td><td>High risk and moderate risk surgeries:
All of the above compared with one another; also see comparison matrix below.
Comparison matrix
<table>
<tr><th>Comparisons</th><th>ICS</th><th>PCS</th><th>ICS + PCS</th><th>TXA</th><th>ICS +TXA</th><th>PCS +TXA</th><th>ICS+PCS+ TXA</th><th>Standard treatment</th></tr>
<tr><td>ICS</td><td></td><td>✓</td><td>✓</td><td>✓</td><td>✓</td><td>✓</td><td>✓</td><td>✓</td></tr>
<tr><td>PCS</td><td></td><td></td><td>✓</td><td>✓</td><td>✓</td><td>✓</td><td>✓</td><td>✓</td></tr>
<tr><td>ICS+PCS</td><td></td><td></td><td></td><td>✓</td><td>✓</td><td>✓</td><td>✓</td><td>✓</td></tr>
<tr><td>TXA</td><td></td><td></td><td></td><td></td><td>✓</td><td>✓</td><td>✓</td><td>✓</td></tr>
<tr><td>ICS +TXA</td><td></td><td></td><td></td><td></td><td></td><td>✓</td><td>✓</td><td>✓</td></tr>
<tr><td>PCS +TXA</td><td></td><td></td><td></td><td></td><td></td><td></td><td>✓</td><td>✓</td></tr>
<tr><td>ICS+PCS+ TXA</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td>✓</td></tr>
<tr><td>Standard treatment</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
</table>
Data from earlier reviews to be used for the NMA (if done)
Low risk surgeries:
Tranexamic acid vs. standard treatment</td></tr>
<tr><td>Outcomes</td><td>All-cause mortality at 30 days.
Quality of life.
Length of stay (hospitalisation).
Infections
Number of patients needing transfusions.
Number of units of allogeneic blood transfused / volume of allogeneic blood transfused(in ml)
Thrombotic complications
Serious adverse events (as defined by study)</td></tr>
<tr><td>Exclusions</td><td>None</td></tr>
<tr><td>Search strategy</td><td>The databases to be searched are Medline, Embase, The Cochrane Library.
Studies will be restricted to English language only.</td></tr>
<tr><td>The review strategy</td><td>Study designs:
RCTs
Systematic reviews

Strata:
High risk and moderate risk surgeries
Cell salvage is appropriate only for those surgeries where blood loss is expected to be greater than 1 unit (roughly 500 ml); so the comparison of cell salvage or tranexamic acid and their combination can only be made in surgeries where this is the case. Based on this, surgeries are classified as:
High risk surgeries- defined as surgeries where blood loss is expected to be greater than 1 litre.
Moderate risk surgeries-defined as surgeries where blood loss is expected to be between 500 ml-1 litre.</td></tr>
</table>

	A network meta-analysis (NMA) will be undertaken if appropriate, for the high and moderate risk groups. Low risk surgeries Low risk surgeries are defined as surgeries where blood loss is expected to be less than 500 ml. Cell salvage is not a feasible option in this group and only effectiveness of tranexamic acid compared with placebo will be evaluated here. Subgroups: Subgroup analysis will be conducted in both strata based on: Age (Adults, children, young people) Pre-operative anaemia management
Key papers	None reported.

C.3 Red blood cell transfusion

C.3.1 RBC thresholds

Table 3: Review protocol: RBC thresholds

Review question	**What is the clinical and cost effectiveness of red blood cell transfusion at different haemoglobin concentrations?**
Guideline condition and its definition	Blood transfusion. Definition: Blood transfusion is the process of administering blood or blood component to a patient.
Review population	Patients receiving red blood cell transfusion
Major age category	Adults and young people (aged 16 years and above) Children (under 16 years of age)
Interventions and comparators: generic/class; specific/drug (All interventions will be compared with each other, unless otherwise stated)	Low (restrictive) haemoglobin thresholds for transfusion High (liberal) haemoglobin thresholds for transfusion
Outcomes	- Quality of life at end of follow-up (Continuous) IMPORTANT - Number of units transfused (all blood components- red cells, platelets, FFP and Cryoprecipitate)/Volume in ml in children at end of follow-up (Continuous) CRITICAL - Length of hospital stay at end of follow-up (Continuous) IMPORTANT - All cause mortality at 30 days at 30 days (Dichotomous) CRITICAL - Infections (includes pneumonia, surgical site infection, UTI and septicaemia/bacteremia) at 30 days of surgery (Dichotomous) IMPORTANT - Number of patients needing allogeneic transfusions (Dichotomous) CRITICAL - Acute and delayed serious adverse events as reported in study (TACO and TRALI, iron overload at End of follow-up (Dichotomous) IMPORTANT - New cardiac events (Myocardial infarction, Cardiac failure) at end of follow-up (Dichotomous) IMPORTANT
Study design	RCT

	Systematic Review
Unit of randomisation	Patient
Other exclusions	Trauma patients Patients receiving exchange transfusions Patients with haemoglobinopathies
Population stratification	Adults Children
Subgroup analyses if there is heterogeneity	- Gender (Male; Female); Outcomes may vary depending on male/female gender - Co-existing ischaemic heart disease (Co-existing ischaemic heart disease; No Co-existing ischaemic heart disease); Outcomes may vary depending on presence/absence of co-existing ischaemic heart disease - Acute Coronary syndrome (Not applicable/stated; Acute coronary syndrome; No acute coronary syndrome); Outcomes may vary depending on presence/absence of Acute Coronary syndrome - Congenital cardiac disease (Congenital cardiac disease; No Congenital cardiac disease); Outcomes may vary depending on presence/absence of Congenital cardiac disease - Stroke (stroke; No stroke); Outcomes may vary depending on presence/absence of stroke - Neurological disease (Neurological disease; No neurological disease); Outcomes may vary depending on presence/absence of neuorological disease - Traumatic brain injury (Traumatic brain injury; No traumatic brain injury); Outcomes may vary depending on presence/absence of Traumatic brain injury - Critical care (In critical care; Not in critical care); Outcomes may vary if patients in critical care - Peri-operative surgical patients (Peri-operative surgical patients; Not Peri-operative surgical patients); Outcomes may vary if Peri-operative surgical patients - Patients receiving radiotherapy (Patients receiving radiotherapy; Patients not receiving radiotherapy); Outcomes may vary if patients receiving radiotherapy - Patients undergoing chemotherapy and stem-cell transplants. (Patients undergoing chemotherapy and stem-cell transplants. ; Patients not undergoing chemotherapy and stem-cell transplants.); Outcomes may vary if patients undergoing chemotherapy and stem-cell transplants.
Search criteria	The databases to be searched are Medline, Embase, The Cochrane Library. Studies will be restricted to English language only.

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C.3.2 RBC targets

Table 4: Review protocol: RBC targets

Review question	What is the clinical and cost effectiveness of different target levels of post-transfusion haemoglobin concentrations for red blood cell transfusion?
Guideline condition and its definition	Blood transfusion. Definition: Blood transfusion is the process of administering blood or blood component to a patient.
Review population	Patients undergoing red blood cell transfusion
Major age category	Adults and young people (aged 16 years and above) Children (under 16 years of age)
Interventions and comparators: generic/class; specific/drug (All interventions will be compared with each other, unless otherwise stated)	High haemoglobin target levels for transfusion Low haemoglobin target levels for transfusion
Outcomes	- Quality of life at End of follow-up (Continuous) IMPORTANT - Number of units transfused (all blood components- red cells, platelets, FFP and Cryoprecipitate)/volume in ml in children at End of follow-up (Continuous) CRITICAL - Length of hospital stay at End of follow-up (Continuous) IMPORTANT - All cause mortality at 30 days at 30 days (Dichotomous) CRITICAL - Infections (includes pneumonia, surgical site infection, UTI and septicaemia/bacteremia) at Within 30 days of surgery (Dichotomous) IMPORTANT - Number of patients needing allogeneic transfusions at End of follow-up (Dichotomous) CRITICAL - Acute and delayed serious adverse events as reported in study (TACO and TRALI, iron overload at End of follow-up (Dichotomous) IMPORTANT
Study design	RCT Systematic Review
Unit of randomisation	Patient
Other exclusions	Trauma patients Patients receiving exchange transfusions Patients with haemoglobinopathies
Population stratification	Adults Children
Subgroup analyses if there is heterogeneity	- Gender (Male; Female); Outcomes may vary depending on male/female gender - Co-existing ischaemic heart disease (Co-existing ischaemic heart disease; No Co-existing ischaemic heart disease); Outcomes may vary depending on presence/absence of co-existing ischaemic heart disease - Acute Coronary syndrome (Not applicable/stated; Acute coronary syndrome; No acute coronary syndrome); Outcomes may vary depending on presence/absence of Acute Coronary syndrome - Congenital cardiac disease (Congenital cardiac disease; No Congenital cardiac disease); Outcomes may vary depending on presence/absence of

	Congenital cardiac disease - Stroke (stroke; No stroke); Outcomes may vary depending on presence/absence of stroke - Neurological disease (Neurological disease; No neurological disease); Outcomes may vary depending on presence/absence of neuorological disease - Traumatic brain injury (Traumatic brain injury; No traumatic brain injury); Outcomes may vary depending on presence/absence of Traumatic brain injury - Critical care (In critical care; Not in critical care); Outcomes may vary if patients in critical care - Peri-operative surgical patients (Peri-operative surgical patients; Not Peri-operative surgical patients); Outcomes may vary if Peri-operative surgical patients - Patients receiving radiotherapy (Patients receiving radiotherapy; Patients not receiving radiotherapy); Outcomes may vary if patients receiving radiotherapy - Patients undergoing chemotherapy and stem-cell transplants. (Patients undergoing chemotherapy and stem-cell transplants. ; Patients not undergoing chemotherapy and stem-cell transplants.); Outcomes may vary if patients undergoing chemotherapy and stem-cell transplants.
Search criteria	The databases to be searched are Medline, Embase, The Cochrane Library. Studies will be restricted to English language only.

C.3.3 RBC dose

Table 5: Review protocol: RBC doses

Review question	**What is the clinical and cost effectiveness of different doses of red blood cell transfusion?**
Guideline condition and its definition	Blood transfusion. Definition: Blood transfusion is the process of administering blood or blood component to a patient.
Review population	Patients undergoing red blood cell transfusion
Major age category	Adults and young people (aged 16 years and above) Children (under 16 years of age)
Interventions and comparators: generic/class; specific/drug (All interventions will be compared with each other, unless otherwise stated)	Low dose OR single unit High dose OR multiple units
Outcomes	- Quality of life at End of follow-up (Continuous) IMPORTANT - Number of units transfused (all blood components- red cells, platelets, FFP and Cryoprecipitate)/volume in ml in children at End of follow-up (Continuous) CRITICAL - Length of hospital stay at End of follow-up (Continuous) IMPORTANT

	- All cause mortality at 30 days at 30 days (Dichotomous) CRITICAL - Infections (includes pneumonia, surgical site infection, UTI and septicaemia/bacteremia) at Within 30 days of surgery (Dichotomous) IMPORTANT - Number of patients needing transfusions at End of follow-up (Dichotomous) CRITICAL - Serious adverse events (Acute transfusion reactions) at End of follow-up (Dichotomous) IMPORTANT
Study design	RCT Systematic Review
Unit of randomisation	Patient
Other exclusions	Trauma patients Patients who are actively bleeding Patients with haemoglobinopathies Patients undergoing exchange transfusions
Population stratification	Adults Children
Subgroup analyses if there is heterogeneity	None specified
Search criteria	The databases to be searched are Medline, Embase, The Cochrane Library. Studies will be restricted to English language only.

C.4 Platelet transfusion

C.4.1 Platelet thresholds

Table 6: Review protocol: platelet thresholds

Review question	**What is the clinical and cost effectiveness of platelet transfusion at different platelet count thresholds?**
Guideline condition and its definition	Blood transfusion. Definition: Blood transfusion is the process of administering blood or blood component to a patient.
Review population	Bleeding patients and non-bleeding patients receiving platelet transfusions. Bleeding is defined as WHO grade 2 and above.
Major age category	Adults and young people (aged 16 years and above) Children (under 16 years of age)
Interventions and comparators: generic/class; specific/drug (All interventions will be compared with each other, unless otherwise stated)	**Interventions in bleeding patients:** • Low platelet thresholds for transfusion (as defined by the trial) • High platelet thresholds for transfusion (as defined by the trial) **Interventions in non-bleeding patients:** • Low platelet thresholds for prophylactic transfusion (as defined by the trial) • High platelet thresholds for prophylactic transfusion (as defined by the trial) • No Prophylactic transfusion Comparisons: • Prophylactic platelet transfusions (high/low threshold) vs. No Prophylactic platelet transfusion Low threshold vs. High threshold (in bleeding and non-bleeding patients)

Outcomes	- Quality of life at End of follow-up (Continuous) CRITICAL - Number of units transfused (all blood components- red cells, platelets, FFP and Cryoprecipitate)/volume in ml in children at End of follow-up (Continuous) IMPORTANT - Length of hospital stay at End of follow-up (Continuous) IMPORTANT - All cause mortality at 30 days at 30 days (Dichotomous) CRITICAL - Infections (includes pneumonia, surgical site infection, UTI and septicaemia/bacteremia) at Within 30 days of surgery (Dichotomous) CRITICAL - Number of patients needing transfusions at End of follow-up (Dichotomous) IMPORTANT - Serious adverse events as reported in study at End of follow-up (Dichotomous) CRITICAL - Bleeding (reported as WHO Grade 2 and above or equivalent) at End of follow-up (Continuous) CRITICAL o Occurrence of bleeding (in non-bleeding patients) o Cessation of bleeding (in bleeding patients)
Study design	RCT Systematic Review
Unit of randomisation	Patient
Other exclusions	Patients receiving exchange transfusions
Population stratification	Adults who are haematology patients -bleeding patients Adults who are non-haematology patients -bleeding patients Children who are haematology patients- bleeding patients Children who are non- haematology patients-bleeding patients Adults who are haematology patients -non-bleeding patients Adults who are non-haematology patients -non-bleeding patients Children who are haematology patients- non-bleeding patients Children who are non- haematology patients-non-bleeding patients
Subgroup analyses if there is heterogeneity	- Infections (Presence of Infections; Absence of infections); may affect outcomes - Sepsis (Presence of sepsis; Absence of sepsis); may affect outcomes - Type of treatment (Allogeneic transplant; Autologous transplant; Chemotherapy); may affect outcomes - Procedures such as bone marrow biopsy, lumbar puncture, intravenous line insertion and surgery (Procedures such as bone marrow biopsy, lumbar puncture, intravenous line insertion and surgery; No procedures); may affect outcomes - Patients receiving antiplatelet treatment (Patients receiving antiplatelet treatment; Patients not receiving antiplatelet treatment); may affect outcomes
Search criteria	The databases to be searched are Medline, Embase, The Cochrane Library. Studies will be restricted to English language only.

C.4.2 Platelet targets

Table 7: Review protocol: platelet targets

Review question	**What is the clinical and cost effectiveness of different target levels of post-transfusion platelet counts?**

Guideline condition and its definition	Blood transfusion. Definition: Blood transfusion is the process of administering blood or blood component to a patient.
Review population	Patients receiving prophylactic platelet transfusions (non- bleeding) and therapeutic platelet transfusions (bleeding). Bleeding is defined as WHO grade 2 and above.
Major age category	Adults and young people (aged 16 years and above) Children (under 16 years of age)
Interventions and comparators: generic/class; specific/drug (All interventions will be compared with each other, unless otherwise stated)	Low target platelet counts High target platelet counts Prophylactic transfusion No transfusion
Outcomes	- Quality of life at End of follow-up (Continuous) CRITICAL - Number of units transfused (all blood components- red cells, platelets, FFP and Cryoprecipitate)/volume in ml in children at End of follow-up (Continuous) IMPORTANT - Length of hospital stay at End of follow-up (Continuous) IMPORTANT - All cause mortality at 30 days (all causes) at 30 days (Dichotomous) CRITICAL - Infections (includes pneumonia, surgical site infection, UTI and septicaemia/bacteremia) at Within 30 days of surgery (Dichotomous) CRITICAL - Number of patients needing transfusions at End of follow-up (Dichotomous) IMPORTANT - Serious adverse events as reported in study at End of follow-up (Dichotomous) CRITICAL - Bleeding reported as WHO Grade 2 and above or equivalent'. at End of follow-up (Continuous) CRITICAL o Occurrence of bleeding (in non-bleeding patients) o Cessation of bleeding (in bleeding patients)
Study design	RCT Systematic Review
Unit of randomisation	Patient
Other exclusions	Patients receiving exchange transfusions
Population stratification	Adults who are haematology patients - bleeding patients Adults who are non-haematology patients -bleeding patients Children who are haematology patients-bleeding patients Children who are non- haematology patients-bleeding patients Adults who are haematology patients - non-bleeding patients Adults who are non-haematology patients -non-bleeding patients Children who are haematology patients-non-bleeding patients Children who are non- haematology patients-non-bleeding patients
Subgroup analyses if there is heterogeneity	- Infections (Presence of Infections; Absence of infections); may affect outcomes - Sepsis (Presence of sepsis; Absence of sepsis); may affect outcomes - Type of treatment (Allogeneic transplant; Autologous transplant; Chemotherapy); may affect outcomes - Procedures such as bone marrow biopsy, lumbar puncture, intravenous line insertion and surgery (Procedures such as bone marrow biopsy, lumbar

	puncture, intravenous line insertion and surgery; No procedures); may affect outcomes - Patients receiving antiplatelet treatment (Patients receiving antiplatelet treatment; Patients not receiving antiplatelet treatment); may affect outcomes
Search criteria	The databases to be searched are Medline, Embase, The Cochrane Library. Studies will be restricted to English language only.

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2 ## C.4.3 Platelet doses

3 **Table 8: Review protocol: platelet doses**

Topic B - Review question 3	What is the clinical and cost effectiveness of different doses of platelet transfusion?
Guideline condition and its definition	Blood transfusion. Definition: Blood transfusion is the process of administering blood or blood component.
Review population	Patients receiving prophylactic platelet transfusions (non- bleeding) and therapeutic platelet transfusions (bleeding).Bleeding is defined as WHO grade 2 and above or equivalent.
Major age category	Adults and young people (aged 16 years and above) Children (under 16 years of age)
Interventions and comparators: generic/class; specific/drug (All interventions will be compared with each other, unless otherwise stated)	Low dose; Low dose was defined as 1.1 x 1011 platelets per square metre of body surface area per transfusion or administration of 3 platelet units. Medium dose; Medium dose was defined as 2.2 x 1011 platelets per square metre of body surface area per transfusion or, 5 platelet units, or, 0.5 x 1011/10 kg. High dose; High dose was defined as 4.4 x 1011 platelets per square metre of body surface area per transfusion or, 1.0 x 1011/10 kg.
Outcomes	- Quality of life at Define (Continuous) CRITICAL - Length of stay (hospitalisation) at End of follow up (Continuous) IMPORTANT - Infections eg, pneumonia at End of follow up (Dichotomous) CRITICAL - All cause mortality at 30 days (Dichotomous) CRITICAL - Bleeding at End of follow up (Dichotomous) CRITICAL - Serious adverse events as defined by study at End of follow up (Dichotomous) CRITICAL - Number of patients needing platelet transfusions at End of follow up (Dichotomous) IMPORTANT - Number of units of platelets transfused at End of follow up (Continuous) IMPORTANT
Study design	Systematic Review RCT
Unit of randomisation	Patient
Population stratification	Adult haematology patients who are not bleeding Adult non-haematology patients who are not bleeding Children haematology patients who are not bleeding Children non-haematology patients who are not bleeding Adult haematology patients who are bleeding Adult non-haematology patents who are bleeding

	Children haematology patients who are bleeding Children non-haematology patients who are bleeding
Reasons for stratification	Platelet transfusions are given at different doses taking into account if the patient is a haematology patient or a non-haematology patient, is an adult or a child and is bleeding (therapeutic) or not bleeding (prophylactic). Haematology patents include patients undergoing intensive chemotherapy or haemopoietic stem cell transplant and patients with platelet function disorders, ITP, aplastic anaemia or myelodysplasia. Non-haematology patients include patients with sepsis, liver failure or renal failure, patients in critical care and surgical patients.
Subgroup analyses if there is heterogeneity	- Type of treatment (Autologous transplant; Allogeneic transplant; Chemotherapy); Dose may differ based on type of treatment haematology patients are receiving - Infections (Presence of infections; Absence of infections); Dose may differ based on presence or absence of infections in haematology patients - Procedures such as bone marrow biopsy, lumbar puncture, intravenous line insertion and surgery. (Patients undergoing procedures; Patients not undergoing procedures); Dose may differ based on whether the patient is undergoing procedures or not. - Anti-platelet treatment (Patients receiving anti-platelet treatment; Patients not receiving anti-platelet treatment); Dose may differ based on whether patient is receiving anti-platelet treatment or not - Sepsis (Presence of sepsis ; Absence of sepsis); Dose of platelet transfusion may differ based on whether a haematology patient has sepsis or not
Search criteria	The databases to be searched are Medline, Embase, The Cochrane Library. Studies will be restricted to English language only.

C.5 Fresh frozen plasma transfusion

C.5.1 FFP thresholds

Table 9: Review protocol: FFP thresholds

Review question	**What is the clinical and cost effectiveness of transfusions of fresh frozen plasma (FFP) to treat and prevent bleeding?**
Guideline condition and its definition	Blood transfusion. Definition: Blood transfusion is the process of administering blood or blood component to a patient.
Population	Strata: Adults who are bleeding Adults receiving prophylaxis and undergoing procedures Adults receiving prophylaxis and not undergoing procedures Children who are bleeding Children receiving prophylaxis and undergoing procedures Adults receiving prophylaxis and not undergoing procedures
Major age category	Adults and young people (aged 16 years and above) Children (under 16 years of age)

Interventions and comparators	FFP transfusions at the following International Normalised Ratio (INR) levels/range of INR levels will be compared to one another. INR ≤1.5 INR 1.6- 2.0 INR 2.1 – 2.5 INR ≥2.6 Transfusions of FFP will also be compared to no transfusion of FFP at each of the above INR levels. FFP transfusions based on different levels of prothrombin ration (PT) and activated partial thromboplastin time (APTT) will also be compared to one another. These will be compared according to data reported in trials.
Outcomes	Occurrence of bleeding (WHO Grade 2 and above or equivalent) at End of follow-up (Dichotomous) CRITICAL Cessation of bleeding in bleeding patients at End of follow-up (Dichotomous) CRITICAL All cause mortality at 30 days (Dichotomous) CRITICAL Quality of life at End of follow-up (Continuous) CRITICAL Infections (for example, pneumonia) at End of follow-up (Dichotomous) CRITICAL Serious adverse events (as defined by study) at End of follow-up (Dichotomous) CRITICAL Adverse events related to the transfusion at End of follow-up (Dichotomous) CRITICAL Number of patients needing red cell transfusions at End of follow-up (Dichotomous) IMPORTANT Number or volume of red cells transfused at End of follow-up (Continuous) IMPORTANT Length of stay (hospitalisation) at End of follow-up (Continuous) IMPORTANT. Correction of abnormal coagulation test at End of follow-up (Dichotomous) IMPORTANT.
Exclusion	Plasma exchange
Study designs to be considered	RCTs Systematic reviews Observational studies
Subgroups to be considered in case of heterogeneity	Patients with liver disease Patients on anti-coagulants Disseminated Intravascular Coagulation
Search criteria	The databases to be searched are Medline, Embase, The Cochrane Library, CINAHL. Studies will be restricted to English language only.

C.5.2 FFP targets

Table 10: Review protocol: FFP targets

Review question	**What is the clinical and cost effectiveness of different target levels of post-transfusion haemostasis tests with the use of fresh frozen plasma FFP for prophylactic transfusions?**
Guideline condition and its definition	Blood transfusion. Definition: Blood transfusion is the process of administering blood or blood component to a patient.

Population	Strata: Adults who are bleeding Adults receiving prophylaxis and undergoing procedures Adults receiving prophylaxis and not undergoing procedures Children who are bleeding Children receiving prophylaxis and undergoing procedures Adults receiving prophylaxis and not undergoing procedures
Major age category	Adults and young people (aged 16 years and above) Children (under 16 years of age)
Interventions and comparators	FFP transfusion to achieve the following target INR levels will be compared to one another: FFP transfusion to high target levels of INR (as defined by trial) FFP transfusion to low target levels of INR (as defined by trial) FFP transfusion to achieve high target INR levels will be compared with FFP transfusion to achieve low target INR levels.
Outcomes	Occurrence of bleeding (WHO Grade 2 and above or equivalent) in non-bleeding patients at End of follow-up (Dichotomous) CRITICAL Cessation of bleeding in bleeding patients at End of follow-up (Dichotomous) CRITICAL All cause mortality at 30 days (Dichotomous) CRITICAL Quality of life at End of follow-up (Continuous) CRITICAL Infections (for example, pneumonia) at End of follow-up (Dichotomous) CRITICAL Serious adverse events (as defined by study) at End of follow-up (Dichotomous) CRITICAL Adverse events related to the transfusion at End of follow-up (Dichotomous) CRITICAL Number of patients needing red cell transfusions at End of follow-up (Dichotomous) IMPORTANT Number or volume of red cells transfused at End of follow-up (Continuous) IMPORTANT Length of stay (hospitalisation) at End of follow-up (Continuous) IMPORTANT. Correction of abnormal coagulation test at End of follow-up (Dichotomous) IMPORTANT
Exclusion	None
Study designs to be considered	RCTs Systematic reviews
Subgroups to be considered in case of heterogeneity	Patients with liver disease Patients on anti-coagulants Disseminated Intravascular Coagulation
Search criteria	The databases to be searched are Medline, Embase, The Cochrane Library, CINAHL. Studies will be restricted to English language only.

C.5.3 FFP doses

Table 11: Review protocol: FFP doses

Review question	**What is the clinical and cost effectiveness of different doses of fresh frozen**

	plasma (FFP) for transfusion to treat and prevent bleeding?
Guideline condition and its definition	Blood transfusion. Definition: Blood transfusion is the process of administering blood or blood component to a patient.
Population	Strata: Adults who are bleeding Adults receiving prophylaxis and undergoing procedures Adults receiving prophylaxis and not undergoing procedures Children who are bleeding Children receiving prophylaxis and undergoing procedures Adults receiving prophylaxis and not undergoing procedures
Major age category	Adults and young people (aged 16 years and above) Children (under 16 years of age)
Interventions and comparators	Standard dose of FFP as reported by trial* High dose of FFP as reported by trial *The standard dose used in clinical practice in the UK is equivalent to 15ml/kg. It was noted that doses reported as 'standard' in studies may differ from this. FFP transfusions at standard doses will be compared with FFP transfusion at high doses.
Outcomes	Occurrence of bleeding (WHO Grade 2 and above or equivalent) at End of follow-up (Dichotomous) CRITICAL Cessation of bleeding in bleeding patients at End of follow-up (Dichotomous) CRITICAL All-cause mortality at 30 days (Dichotomous) CRITICAL Quality of life at End of follow-up (Continuous) CRITICAL Infections (for example, pneumonia) at End of follow-up (Dichotomous) CRITICAL Serious adverse events (as defined by study) at End of follow-up (Dichotomous) CRITICAL Adverse events related to the transfusion at End of follow-up (Dichotomous) CRITICAL Number of patients needing red cell transfusions at End of follow-up (Dichotomous) IMPORTANT Number or volume of red cells transfused at End of follow-up (Continuous) IMPORTANT Length of stay (hospitalisation) at End of follow-up (Continuous) IMPORTANT. Correction of abnormal coagulation test at End of follow-up (Dichotomous) IMPORTANT.
Exclusion	None
Study designs	RCTs Systematic reviews
Subgroups to be considered in case of heterogeneity	Patients with liver disease Patients on anti-coagulants Disseminated Intravascular Coagulation
Search strategy	The databases to be searched are Medline, Embase, The Cochrane Library, CINAHL. Studies will be restricted to English language only.

C.6 Cryoprecipitate

C.6.1 Cryoprecipitate thresholds

Table 12: Review protocol: cryoprecipitate thresholds

Review question	What is the clinical and cost effectiveness of transfusions of cryoprecipitate to treat and prevent bleeding?
Guideline condition and its definition	Blood transfusion. Definition: Blood transfusion is the process of administering blood or blood component to a patient.
Population	Adults who are bleeding Adults receiving prophylaxis and undergoing procedures Children who are bleeding Children receiving prophylaxis and undergoing procedures
Major age category	Adults and young people (aged 16 years and above) Children (under 16 years of age)
Interventions and comparators	Cryoprecipitate transfusions administered at different thresholds will be compared to one another. Cryoprecipitate transfusions administered at low thresholds will be compared with cryoprecipitate transfusions administered at high thresholds. Cryoprecipitate transfusions at low thresholds include: Cryoprecipitate transfusions at low fibrinogen levels. Fibrinogen levels which are considered as low thresholds for cryoprecipitate transfusion include: ≤1 g/L As defined by trial Cryoprecipitate transfusions administered at prothrombin time ratio (PT) or activated partial thromboplastin time (APTT) >1.5 times of the control or as defined by trial. Cryoprecipitate transfusions at high thresholds include: Cryoprecipitate transfusions at high fibrinogen levels. Fibrinogen levels which are considered as high thresholds for cryoprecipitate transfusion include: >1g/L As defined by trial Cryoprecipitate transfusions administered at prothrombin time ratio (PT) or activated partial thromboplastin time (APTT) >2 times of the control or as defined by trial.
Outcomes	Occurrence of bleeding (WHO Grade 2 and above or equivalent) at End of follow-up (Dichotomous) CRITICAL Cessation of bleeding in bleeding patients at End of follow-up (Dichotomous) CRITICAL All cause mortality at 30 days (Dichotomous) CRITICAL Quality of life at End of follow-up (Continuous) CRITICAL Infections (for example, pneumonia) at End of follow-up (Dichotomous) CRITICAL Serious adverse events (as defined by study) at End of follow-up (Dichotomous) CRITICAL Adverse events related to the transfusion at End of follow-up (Dichotomous) CRITICAL Number of patients needing red cell transfusions at End of follow-up (Dichotomous) IMPORTANT

	Number or volume of red cells transfused at End of follow-up (Continuous) IMPORTANT Length of stay (hospitalisation) at End of follow-up (Continuous) IMPORTANT Correction of abnormal coagulation test at End of follow-up (Dichotomous) IMPORTANT.
Exclusion	Plasma exchange
Study designs to be considered	RCTs Systematic reviews Observational studies
Subgroups to be considered in case of heterogeneity	Patients with liver disease Disseminated Intravascular Coagulation
Search strategy	The databases to be searched are Medline, Embase, The Cochrane Library. Studies will be restricted to English language only.

C.6.2 Cryoprecipitate targets

Table 13: Review protocol: cryoprecipitate targets

Review question	**What is the clinical and cost effectiveness of different target levels of post-transfusion haemostasis tests with the use of cryoprecipitate for prophylactic transfusions?**
Guideline condition and its definition	Blood transfusion. Definition: Blood transfusion is the process of administering blood or blood component to a patient.
Population	Adults who are bleeding Adults receiving prophylaxis and undergoing procedures Children who are bleeding Children receiving prophylaxis and undergoing procedures
Major age category	Adults and young people (aged 16 years and above) Children (under 16 years of age)
Interventions and comparators	Cryoprecipitate transfusion to achieve low target levels of fibrinogen levels/Prothrombin time/Activated Partial Thromboplastin Time (as defined by trial) Cryoprecipitate transfusion to achieve high target levels of fibrinogen levels/ Prothrombin time/Activated Partial Thromboplastin Time as defined by trial Cryoprecipitate transfusions to achieve low target levels will be compared with cryoprecipitate transfusion to achieve high target levels of above coagulation test results.
Outcomes	Occurrence of bleeding (WHO Grade 2 and above or equivalent) at End of follow-up (Dichotomous) CRITICAL Cessation of bleeding in bleeding patients at End of follow-up (Dichotomous) CRITICAL All cause mortality at 30 days (Dichotomous) CRITICAL Quality of life at End of follow-up (Continuous) CRITICAL Infections (for example, pneumonia) at End of follow-up (Dichotomous) CRITICAL Serious adverse events (as defined by study) at End of follow-up (Dichotomous) CRITICAL

	Adverse events related to the transfusion at End of follow-up (Dichotomous) CRITICAL Number of patients needing red cell transfusions at End of follow-up (Dichotomous) IMPORTANT Number or volume of red cells transfused at End of follow-up (Continuous) IMPORTANT Length of stay (hospitalisation) at End of follow-up (Continuous) IMPORTANT. Correction of abnormal coagulation test at End of follow-up (Dichotomous) IMPORTANT.
Exclusion	None
Study designs to be considered	RCTs Systematic reviews Observational studies
Subgroups to be considered in case of heterogeneity	Patients with liver disease Disseminated Intravascular Coagulation
Search strategy	The databases to be searched are Medline, Embase, The Cochrane Library Studies will be restricted to English language only.

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2 ### C.6.3 Cryoprecipitate doses

3 **Table 14: Review protocol: Cryoprecipitate doses**

Review question	What is the clinical and cost effectiveness of different doses of cryoprecipitate for transfusion?
Guideline condition and its definition	Blood transfusion. Definition: Blood transfusion is the process of administering blood or blood component to a patient.
Population	Adults who are bleeding Adults receiving prophylaxis and undergoing procedures Children who are bleeding Children receiving prophylaxis and undergoing procedures
Major age category	Adults and young people (aged 16 years and above) Children (under 16 years of age)
Interventions and comparators	Standard dose of cryoprecipitate for transfusion will be compared with high dose of cryoprecipitate for transfusion. The doses are defined as follows: Standard adult dose (where 1 dose of cryoprecipitate will increase fibrinogen count by about 1g/L) High dose (adults)- where 1 dose of cryoprecipitate will increase fibrinogen count by greater than 1g/L Doses in children will be considered separately (10-15 ml/kg)
Comparisons	Standard dose of cryoprecipitate vs. High dose of cryoprecipitate
Outcomes	Occurrence of bleeding (WHO Grade 2 and above or equivalent) at End of follow-up (Dichotomous) CRITICAL Cessation of bleeding in bleeding patients at End of follow-up (Dichotomous) CRITICAL

	All cause mortality at 30 days (Dichotomous) CRITICAL Quality of life at End of follow-up (Continuous) CRITICAL Infections (for example, pneumonia) at End of follow-up (Dichotomous) CRITICAL Serious adverse events (as defined by study) at End of follow-up (Dichotomous) CRITICAL Adverse events related to the transfusion at End of follow-up (Dichotomous) CRITICAL Number of patients needing red cell transfusions at End of follow-up (Dichotomous) IMPORTANT Number or volume of red cells transfused at End of follow-up (Continuous) IMPORTANT Length of stay (hospitalisation) at End of follow-up (Continuous) IMPORTANT. Correction of abnormal coagulation test at End of follow-up (Dichotomous) IMPORTANT.
Exclusion	None
The review strategy	Study designs to be considered: RCTs Systematic reviews Observational studies
Subgroups to be considered in case of heterogeneity	Patients with liver disease Disseminated Intravascular Coagulation
Search strategy	The databases to be searched are Medline, Embase, The Cochrane Library Studies will be restricted to English language only.

C.7 Prothrombin complex concentrates

C.7.1 PCC thresholds

Table 15: Review protocol: PCC thresholds

Review question	**What is the clinical and cost effectiveness of transfusions of prothrombin complex concentrates (PCC) to treat and prevent bleeding?**
Guideline condition and its definition	Blood transfusion. Definition: Blood transfusion is the process of administering blood or blood component to a patient.
Population	Strata: Adults who are bleeding Adults receiving prophylaxis and undergoing procedures Patients on Vitamin K antagonists Patients on novel anticoagulants Children who are bleeding Children receiving prophylaxis and undergoing procedures Children on Vitamin K antagonists Children on novel anticoagulants
Major age category	Adults and young people (aged 16 years and above) Children (under 16 years of age)

Interventions and comparators	PCC transfusions at different INR/PT/APTT thresholds will be compared to one another. In patients receiving Vitamin K antagonists, PCC transfusions at the following INR levels will be compared to one another. INR ≤1.5 INR 1.6- 2.0 INR 2.1 – 2.5 INR ≥2.6 In patients receiving novel anticoagulants, PCC transfusion at high and low threshold levels of the following coagulation tests will be compared to one another. Prothrombin time ratio (PT) Activated Partial Thromboplastin time (APTT) High and low thresholds of PT and APTT for PCC transfusion will be as defined by the trial.
Outcomes	Occurrence of bleeding (WHO Grade 2 and above or equivalent) at End of follow-up (Dichotomous) CRITICAL Cessation of bleeding in bleeding patients at End of follow-up (Dichotomous) CRITICAL All cause mortality at 30 days (Dichotomous) CRITICAL Quality of life at End of follow-up (Continuous) CRITICAL Infections (for example, pneumonia) at End of follow-up (Dichotomous) CRITICAL Serious adverse events (as defined by study) at End of follow-up (Dichotomous) CRITICAL Adverse events related to the transfusion at End of follow-up (Dichotomous) CRITICAL Number of patients needing red cell transfusions at End of follow-up (Dichotomous) IMPORTANT Number or volume of red cells transfused at End of follow-up (Continuous) IMPORTANT Length of stay (hospitalisation) at End of follow-up (Continuous) IMPORTANT. Correction of abnormal coagulation test at End of follow-up (Dichotomous) IMPORTANT.
Exclusion	Plasma exchange
Study designs to be considered	RCTs Systematic reviews Observational studies
Subgroups to be considered	Patients with liver disease
Search strategy	The databases to be searched are Medline, Embase, The Cochrane Library Studies will be restricted to English language only.

C.7.2 PCC targets

Table 16: Review protocol: PCC targets

Review question	**What is the clinical and cost effectiveness of different target levels of post-transfusion haemostasis tests with the use of prothrombin complex concentrates**

	(PCC) for prophylactic transfusions?
Guideline condition and its definition	Blood transfusion. Definition: Blood transfusion is the process of administering blood or blood component to a patient.
Population	Strata: Adults who are bleeding Adults receiving prophylaxis and undergoing procedures Patients on Vitamin K antagonists Patients on novel anticoagulants Children who are bleeding Children receiving prophylaxis and undergoing procedures Children on Vitamin K antagonists Children on novel anticoagulants
Major age category	Adults and young people (aged 16 years and above) Children (under 16 years of age)
Interventions and comparators	In patients receiving Vitamin K antagonists, the interventions are PCC transfusion to achieve low target levels of INR (as defined by trial) PCC transfusion to achieve high target levels of INR (as defined by trial) PCC transfusions to achieve low target levels of INR will be compared with PCC transfusions to achieve high target levels of INR. In patients receiving novel anticoagulants, the interventions are PCC transfusion to achieve low target levels of PT/APTT (as defined by trial) PCC transfusion to achieve high target levels of PT/APTT (as defined by trial) PCC transfusions to achieve low target levels of PT/APTT will be compared with PCC transfusions to achieve high target levels of PT/APTT.
Outcomes	Occurrence of bleeding (WHO Grade 2 and above or equivalent) at End of follow-up (Dichotomous) CRITICAL Cessation of bleeding in bleeding patients at End of follow-up (Dichotomous) CRITICAL All cause mortality at 30 days (Dichotomous) CRITICAL Quality of life at End of follow-up (Continuous) CRITICAL Infections (for example, pneumonia) at End of follow-up (Dichotomous) CRITICAL Serious adverse events (as defined by study) at End of follow-up (Dichotomous) CRITICAL Adverse events related to the transfusion at End of follow-up (Dichotomous) CRITICAL Number of patients needing red cell transfusions at End of follow-up (Dichotomous) IMPORTANT Number or volume of red cells transfused at End of follow-up (Continuous) IMPORTANT Length of stay (hospitalisation) at End of follow-up (Continuous) IMPORTANT Correction of abnormal coagulation test at End of follow-up (Dichotomous) IMPORTANT
Exclusion	None
Study designs to be considered	RCTs Systematic reviews Observational studies
Subgroups to be considered	Patients with liver disease

Search strategy	The databases to be searched are Medline, Embase, The Cochrane Library, CINAHL. Studies will be restricted to English language only.

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2 ### C.7.3 PCC doses

3 **Table 17: Review protocol: PCC doses**

Review question	What is the clinical and cost effectiveness of different doses of prothrombin complex concentrates (PCC) for transfusion?
Guideline condition and its definition	Blood transfusion. Definition: Blood transfusion is the process of administering blood or blood component to a patient.
Population	Strata: Adults who are bleeding Adults receiving prophylaxis and undergoing procedures Patients on Vitamin K antagonists Patients on novel anticoagulants Children who are bleeding Children receiving prophylaxis and undergoing procedures Children on Vitamin K antagonists Children on novel anticoagulants
Major age category	Adults and young people (aged 16 years and above) Children (under 16 years of age)
Intervention and comparators	High dose of PCC for transfusion will be compared with low dose of PCC for transfusion. The interventions are defined as follows: Low dose PCC for transfusion (as defined by trial) High dose PCC for transfusion (as defined by trial)
Outcomes	Occurrence of bleeding (WHO Grade 2 and above or equivalent) at End of follow-up (Dichotomous) CRITICAL Cessation of bleeding in bleeding patients at End of follow-up (Dichotomous) CRITICAL All-cause mortality at 30 days (Dichotomous) CRITICAL Quality of life at End of follow-up (Continuous) CRITICAL Infections (for example, pneumonia) at End of follow-up (Dichotomous) CRITICAL Serious adverse events (as defined by study) at End of follow-up (Dichotomous) CRITICAL Adverse events related to the transfusion at End of follow-up (Dichotomous) CRITICAL Number of patients needing red cell transfusions at End of follow-up (Dichotomous) IMPORTANT Number or volume of red cells transfused at End of follow-up (Continuous) IMPORTANT Length of stay (hospitalisation) at End of follow-up (Continuous) IMPORTANT. Correction of abnormal coagulation test at End of follow-up (Dichotomous) IMPORTANT.
Exclusion	None
Study designs to be considered	RCTs Systematic reviews

Subgroups to be considered	Patients with liver disease
Search strategy	The databases to be searched are Medline, Embase, The Cochrane Library Studies will be restricted to English language only.

C.8 Monitoring for acute reactions

Table 18: Review protocol: Monitoring

Review question	**What is the clinical and cost effectiveness of monitoring for acute reactions at different times in relation to the transfusion*?** *** Acute transfusion reactions (ATR) are defined as those occurring within 24 hours of transfusion including: acute reactions due to transfusion of the incorrect component, haemolytic reactions, transfusion-related acute lung injury (TRALI), transfusion related circulatory overload (TACO) and those due to bacterial contamination of the component, febrile type reaction, allergic type reaction, reaction with both allergic and febrile features, hypotensive reaction.**
Population	Adults Children
Major age category	Adults (aged16 years and over) Children (under 16 years of age)
Intervention	Standard practice of monitoring for acute transfusion reactions (ATR). Alternative monitoring practices for acute transfusion reactions at different times.
Comparisons	Standard monitoring practice vs. alternative monitoring practice. Standard practice includes: Frequency Initial 15-30 minutes after start of transfusion End of transfusion Components (clinical signs to be monitored) Temperature Pulse Blood pressure Respiration Alternative (change in frequency and components of monitoring from standard practice) including: Frequency Any increase or decrease in frequency of monitoring Components (clinical signs to be monitored) Additional or less monitoring of clinical signs
Outcomes	-Quality of life-IMPORTANT -Length of hospital stay-IMPORTANT -Mortality (all causes) at 30 days-CRITICAL -Transfusion related mortality at 30 days-CRITICAL -Acute transfusion reaction/serious adverse events of transfusion-CRITICAL -Morbidity (ICU admission, renal failure, DIC) (dichotomous)-IMPORTANT -Admission to hospital or ICU post transfusion (day or in-patient)-IMPORTANT
Exclusion	None

Search strategy	The databases to be searched are Medline, Embase, The Cochrane Library, CINAHL. Studies will be restricted to English language only.
The review strategy	RCTs Systematic reviews Before and after studies Cohort studies Critical outcomes: acute transfusion reactions, mortality, morbidity
Key papers	None reported.

C.9 Electronic decision support

Table 19: Review protocol: electronic decision support

Review question	**What is the clinical and cost effectiveness of electronic decision-support blood order systems to reduce inappropriate blood transfusions?**
Population	Adults and young people (aged 16 years and above) Children (under 16 years of age)
Intervention	Electronic decision-support blood order systems (blood ordering is done in an online system and alerts are sent to doctors, for example, an alert may point out that, based on Hb level or platelet count, the Hb level is above thresholds) Standard care (no decision-support blood order systems) Non-electronic decision support systems (for example, staff review of requests and discussions between laboratory and clinicians; not electronic, may include checklists)
Comparisons	Electronic decision-support blood order systems vs. standard care Electronic decision-support blood order systems vs. non-electronic decision support systems
Outcomes	Proportion of inappropriate transfusions Proportion of patients transfused Number of units transfused Hospital length of stay Quality of life Mortality Pre-transfusion haemoglobin levels/platelet count/coagulation result
Exclusion	None
Search strategy	The databases to be searched are Medline, Embase, The Cochrane Library, HMIC. Studies will be restricted to English language only.
The review strategy	Study designs to be considered: RCTs Systematic reviews Before and after studies Cohort studies
Key papers	Cochrane review- A. Tinmouth, D. Fergusson.

C.10 Electronic patient identification systems

Table 4: Review protocol: Electronic patient identification systems

Review question	What are the clinical and cost effectiveness of electronic patient identification systems such as patient identification band, bar code or radiofrequency identification (RFID) to ensure patient safety during blood transfusions?
Guideline condition and its definition	Blood transfusion. Definition: Blood transfusion is the process of administering blood or blood component to a patient.
Review population	Adults and Children
Major age category	Adults and young people (Aged 16 years and above) Children (under 16 years of age)
Interventions and comparators: generic/class; specific/drug (All interventions will be compared with each other, unless otherwise stated)	Electronic patient identification systems (including bar codes and Radio frequency Identification tags) Non-electronic patient identification systems; Non -electronic patient identification systems (standard practice of checking wrist bands) Non-electronic patient identification systems; Non -electronic patient identification systems (standard practice of checking wrist bands +use of checklists by one nurse) Non-electronic patient identification systems; Non -electronic patient identification systems (standard practice of checking wrist bands +use of checklists by 2 nurses) Non-electronic patient identification systems; Non -electronic patient identification systems (use of checklists by 2 nurses) Non-electronic patient identification systems; Non -electronic patient identification systems (use of checklists by one nurse) No patient identification system
Outcomes	- Quality of life at End of follow-up (Continuous) IMPORTANT - Mortality (all causes) at 30 days (Dichotomous) CRITICAL - Transfusion related mortality at 30 days (Dichotomous) CRITICAL - Incorrect blood component transfused. at End of follow-up (Dichotomous) CRITICAL - Incorrect labelling (Incorrect blood in tube and Rejected blood samples) at End of follow-up (Dichotomous) CRITICAL - Morbity (ICU admission, renal failure, DIC) at End of follow-up (Dichotomous) IMPORTANT
Study design	RCT Systematic Review Non randomised study Quasi-RCT Before and after study
Unit of randomisation	Patient
Subgroup analyses if there is heterogeneity	- Type of patient identification (Bar codes; Radio frequency identification; Standard practice (check wrist band); Use of check list by nurse (one nurse); Standard practice + use of check list (one nurse); Standard practice + use of check list (2 nurses); Use of check list by nurse (2 nurses); Any other patient identification system); Outcomes may be dependent on the type of identification system
Search strategy	The databases to be searched are Medline, Embase, The Cochrane Library, CINAHL, HMIC.

	Studies will be restricted to English language only.

C.11 Patient information

Table 20: Review protocol: patient information

Review question	What is the information and support patients under consideration for a blood transfusion and their family members or carers would value and how would they prefer to receive it?
Objective	To consider people's experience of and preferences for various types of information and support provided before receiving a blood transfusion
Population	Adults and children under consideration for a blood transfusion and their family members and carers.
Intervention	Patients' experience of and preferences for information and support prior to a transfusion. Specific information and support that patients would value (for example, type of information - written or verbal information or information from websites, including videos).
Outcomes	The information that patients value (that is, want or found useful) Patient preference for type of information Patient/carer satisfaction HRQoL
Exclusion	None
Search strategy	The databases to be searched are Medline, Embase, The Cochrane Library, CINAHL, PsycINFO. Studies will be restricted to English language only.
Search terms	
The review strategy	Study designs to be considered: Qualitative studies (interviews, focus groups, observations) Surveys Review strategy: Population size and directness: No limitations on sample size Studies with indirect populations will not be considered, for example, Patients receiving IV fluids Setting: Any setting where patients receive blood transfusions relevant to the NHS Appraisal of methodological quality The methodological quality of each study will be assessed using NICE checklists and the quality of the evidence will be assessed by a modified GRADE approach for each outcome. Data synthesis Thematic analysis of the data will be conducted and findings presented.

Appendix D: Economic review protocol

Table 21: Health economic review protocol

Review question	All questions – health economic evidence
Objectives	To identify economic evaluations relevant to the review questions set out above.
Criteria	• Populations, interventions and comparators must be as specified in the individual review protocols above. • Studies must be of a relevant economic study design (cost–utility analysis, cost–benefit analysis, cost-effectiveness analysis, cost–consequence analysis, comparative cost analysis). • Studies must not be an abstract only, a letter, editorial or commentary, or a review of economic evaluations. Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English. • Studies must not be published before 2003. *The GDG agreed that there have been substantial changes in transfusion practice over the last 10 years. In addition, increased transfusion safety over time will have had an impact on the overall cost and resource use associated with transfusion. As a result, it was agreed that health economic evidence published prior to 2003 would not be applicable to current practice.*
Search strategy	An economic study search will be undertaken using population-specific terms and an economic study filter – see Appendix G
Review strategy	Each study fulfilling the criteria above will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in Appendix G of the NICE guidelines manual (2012).[3] **Inclusion and exclusion criteria** • If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. An economic evidence table will be completed and it will be included in the economic evidence profile. • If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded then an economic evidence table will not be completed and it will not be included in the economic evidence profile. • If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included. **Where there is discretion** The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the GDG if required. The ultimate aim is to include studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and methodological quality that they could all be included, then the health economist, in discussion with the GDG if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded on the basis of applicability or methodological limitations will be listed with explanation as excluded economic studies in Appendix Q. The health economist will be guided by the following hierarchies. *Setting:* • UK NHS

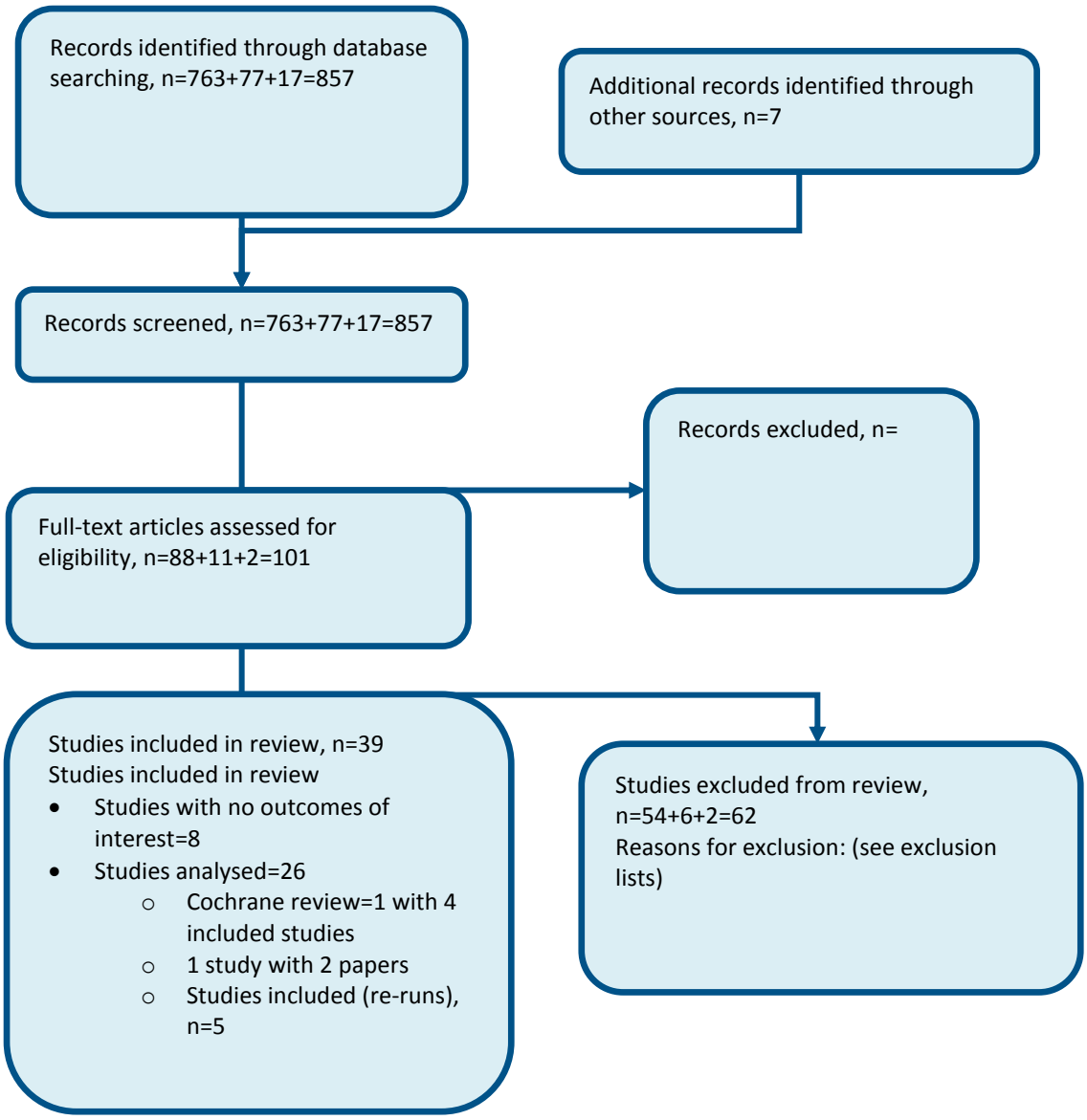
	• OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden) • OECD countries with predominantly private health insurance systems (for example, USA, Switzerland) • non-OECD settings (always 'Not applicable'). *Economic study type:* • cost–utility analysis • other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequence analysis) • comparative cost analysis • non-comparative cost analyses including cost-of-illness studies (always 'Not applicable'). *Year of analysis:* • The more recent the study, the more applicable it is. *Quality and relevance of effectiveness data used in the economic analysis:* • The more closely the effectiveness data used in the economic analysis matches with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.

(a) Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.

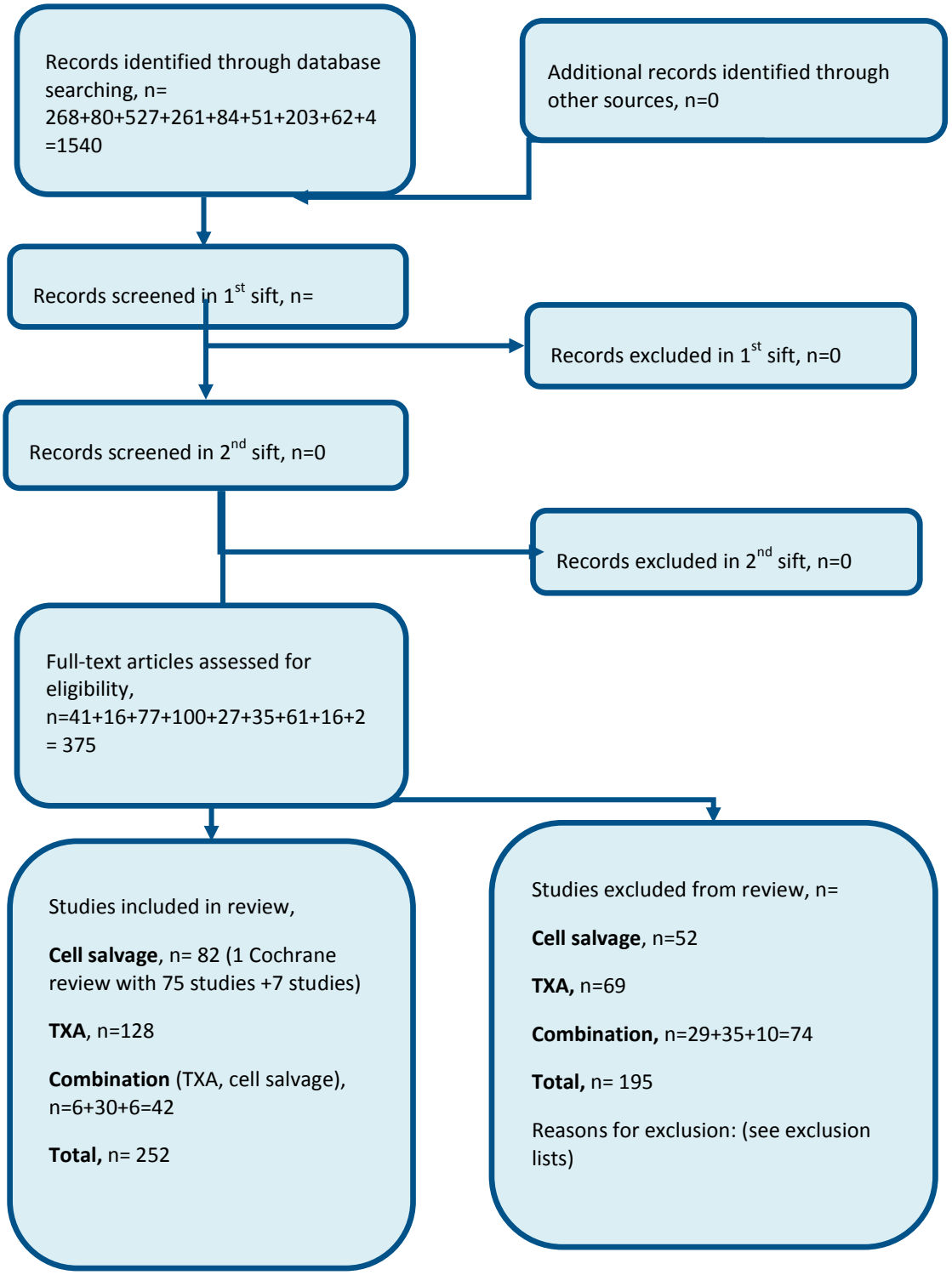
1 Appendix E: Clinical article selection

2 E.1 Erythropoietin and iron

Figure 1: Flow diagram of clinical article selection for iron and EPO review



E.2 Alternatives to blood transfusion



E.3 Red blood cells

Figure 2: Flow chart of clinical article selection for the review of RBC dose

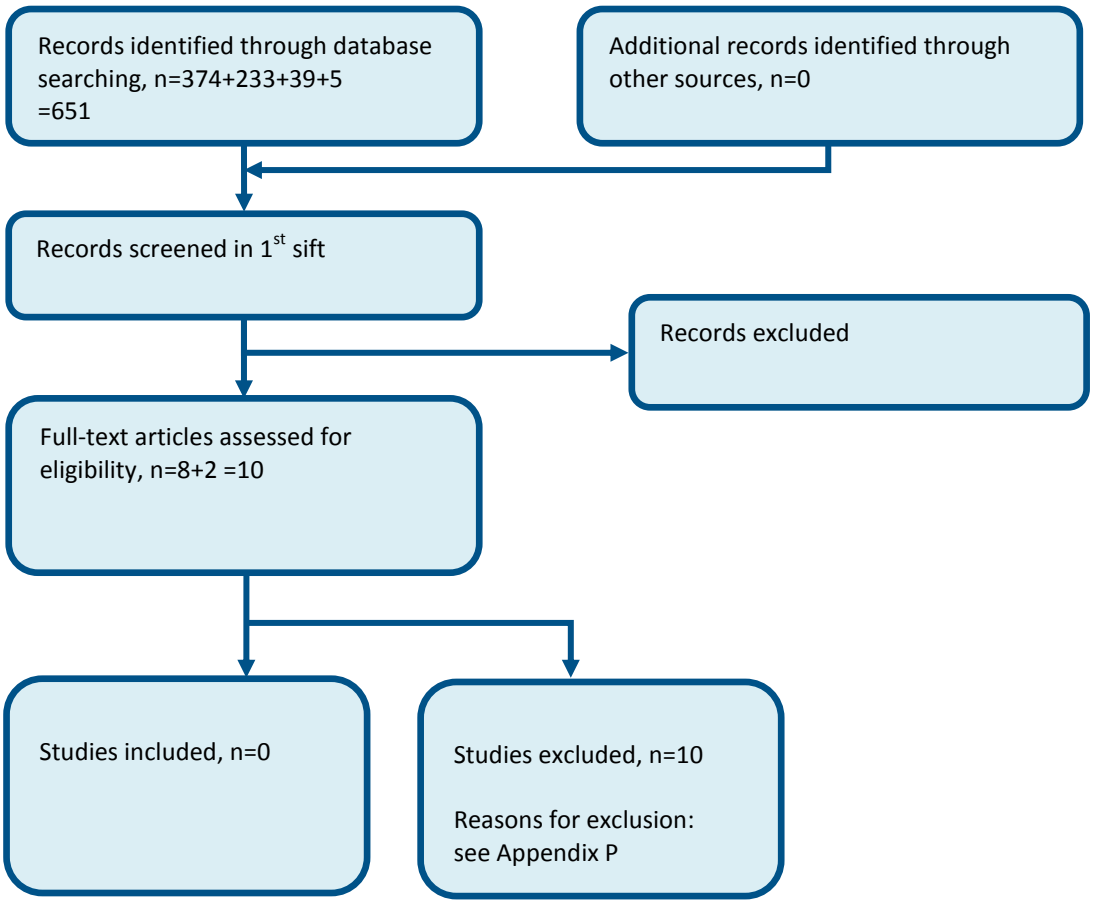
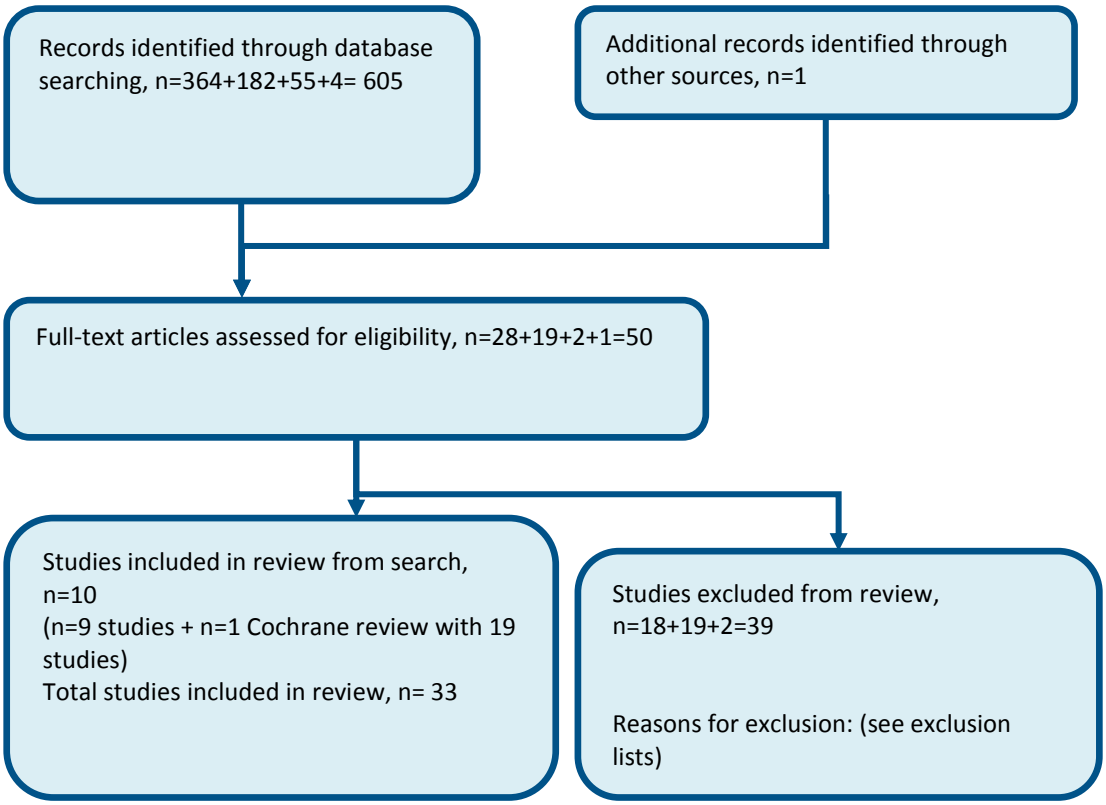


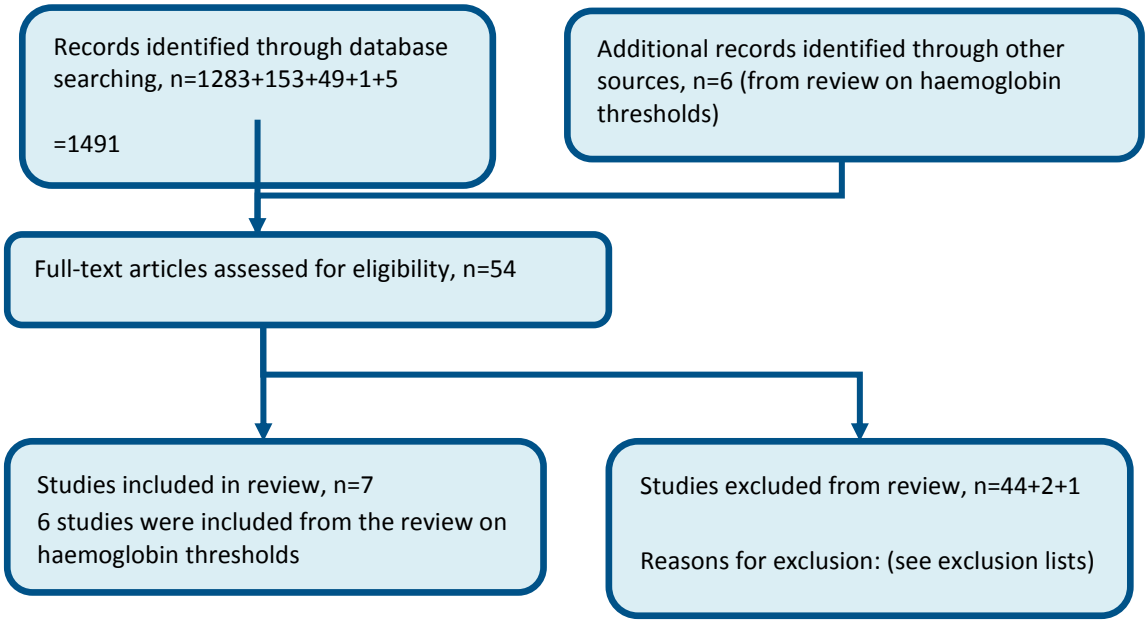
Figure 3: Flow chart of clinical article selection for the review of RBC thresholds



1

2

Figure 4: Flow chart of clinical article selection for the review of RBC targets



1

2

E.4 Platelets

Figure 5: Flow chart of clinical article selection for the review of platelet dose

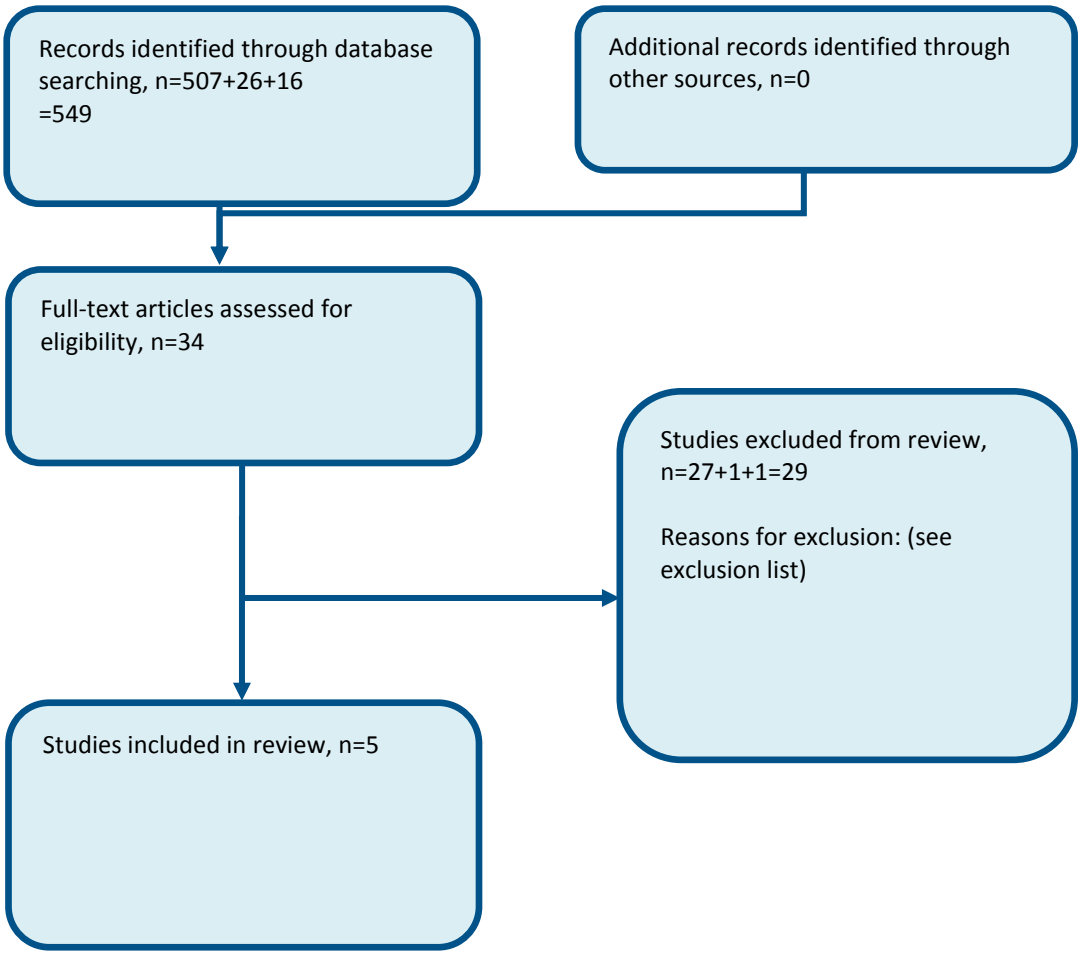
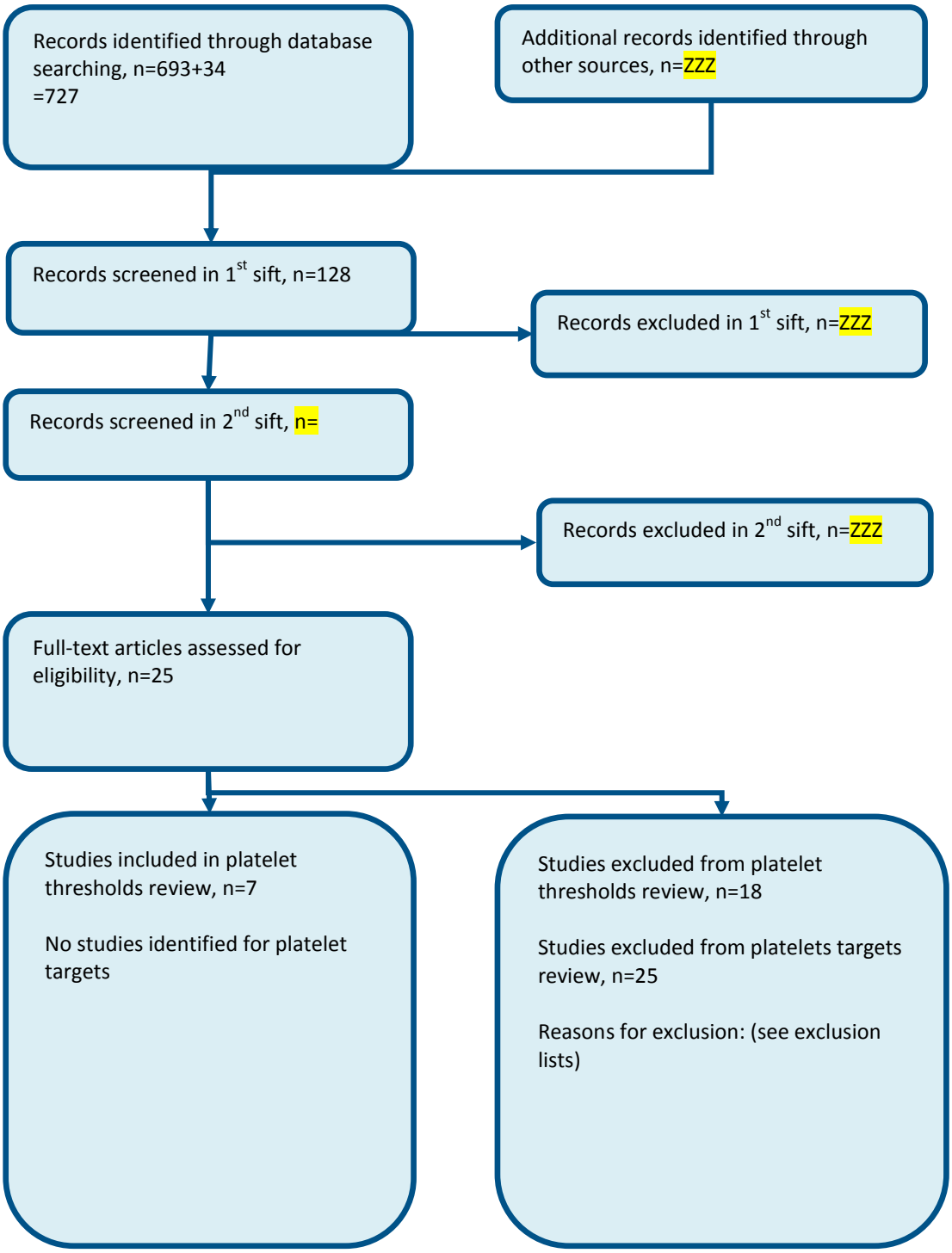


Figure 6: Flow chart of clinical article selection for the review of platelet thresholds and platelet targets



E.5 Fresh frozen plasma

Figure 7: Flow chart of clinical article selection for the review

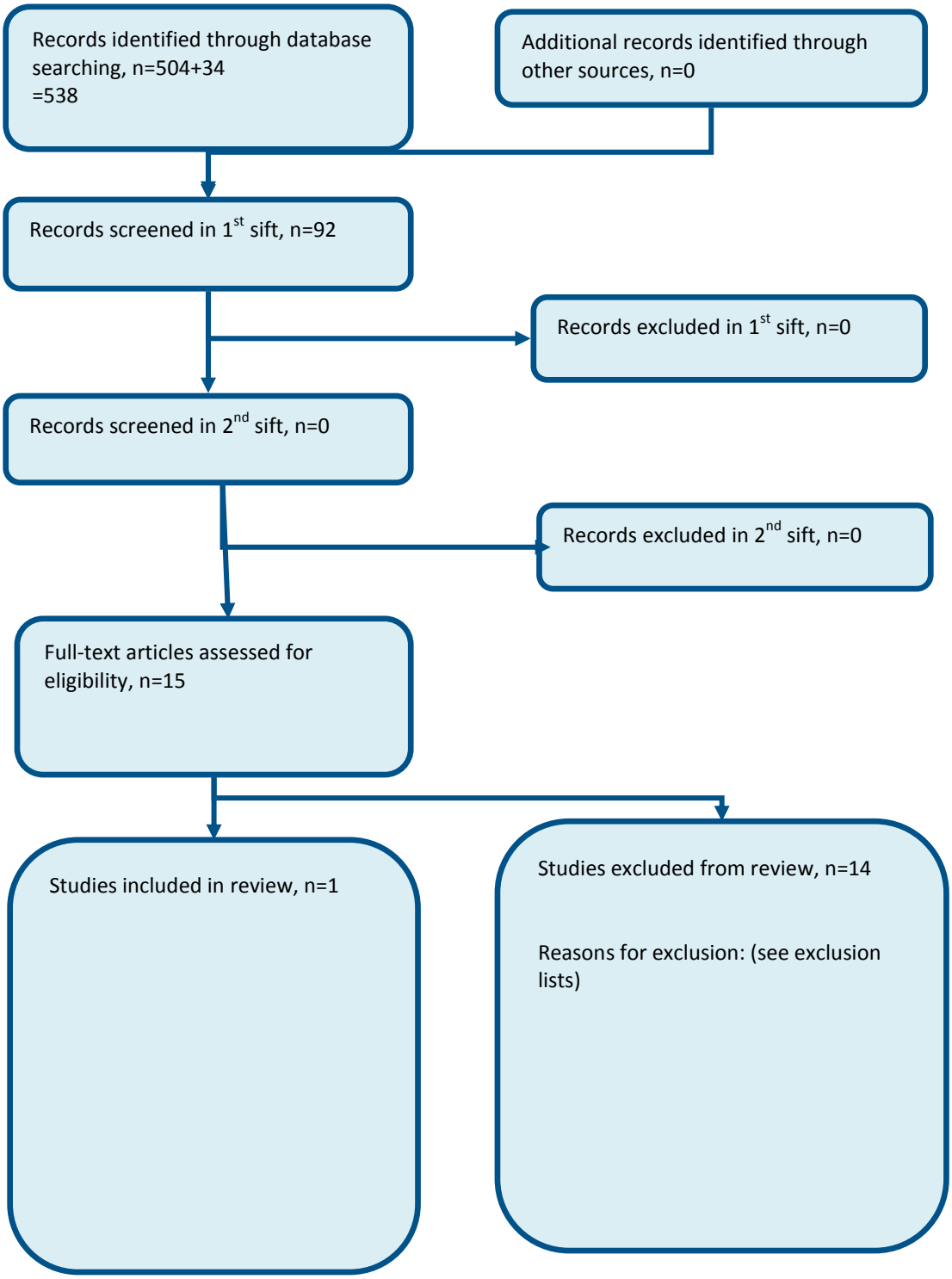
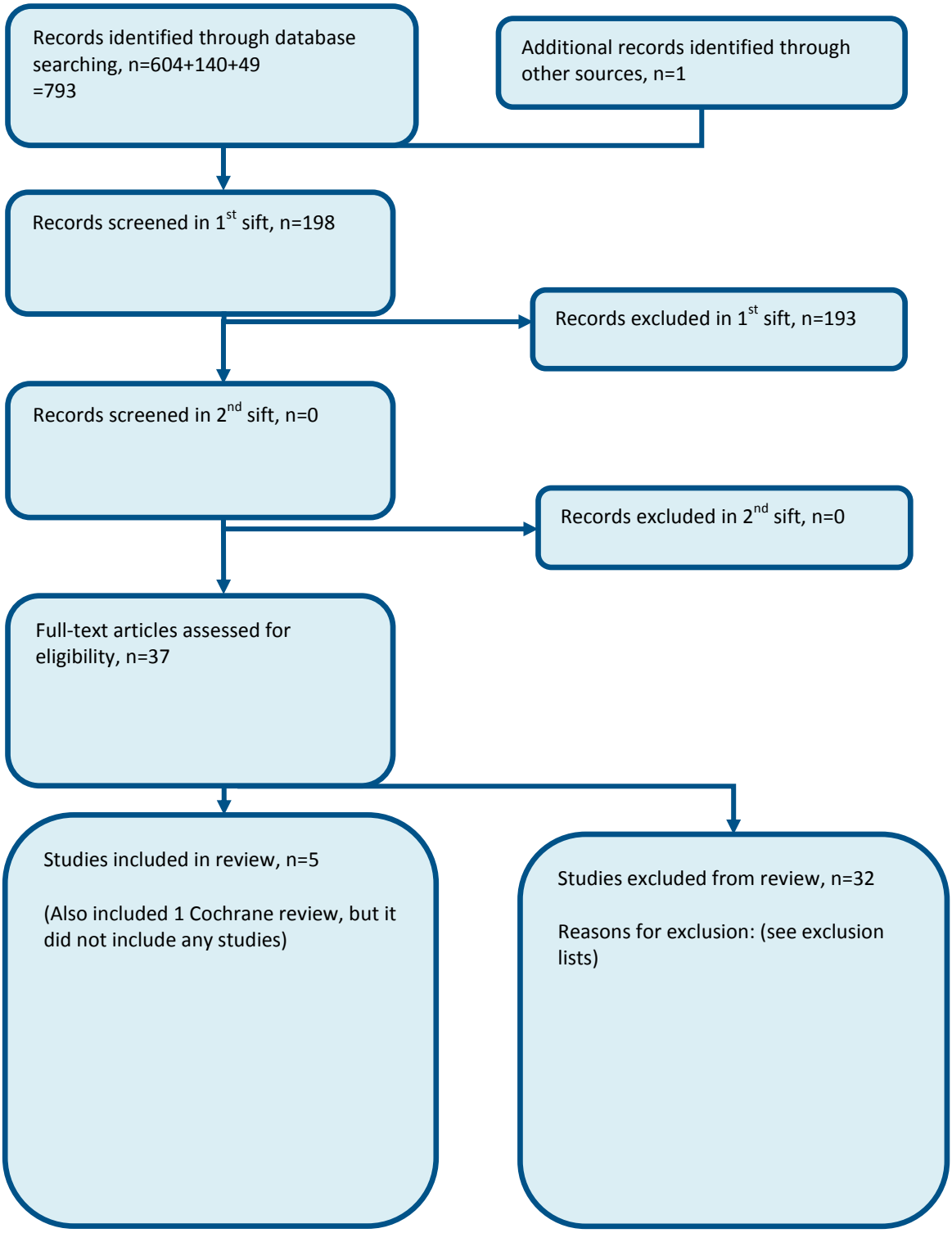


Figure 8: Flow chart of clinical article selection for the review of FFP thresholds and targets



1

E.6 Prothrombin complex concentrates

Figure 9: Flow chart of clinical article selection for the review of PCC doses

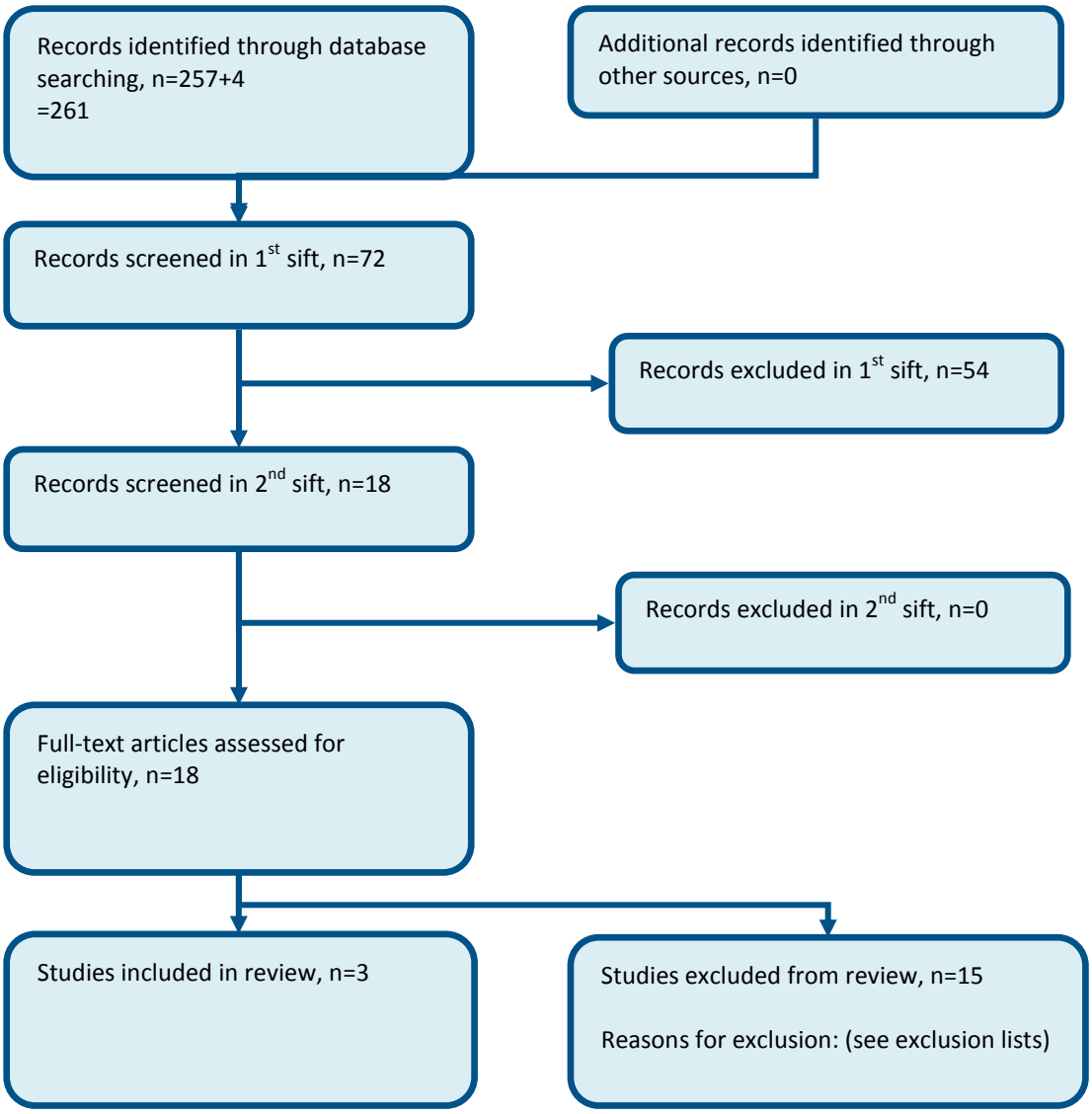
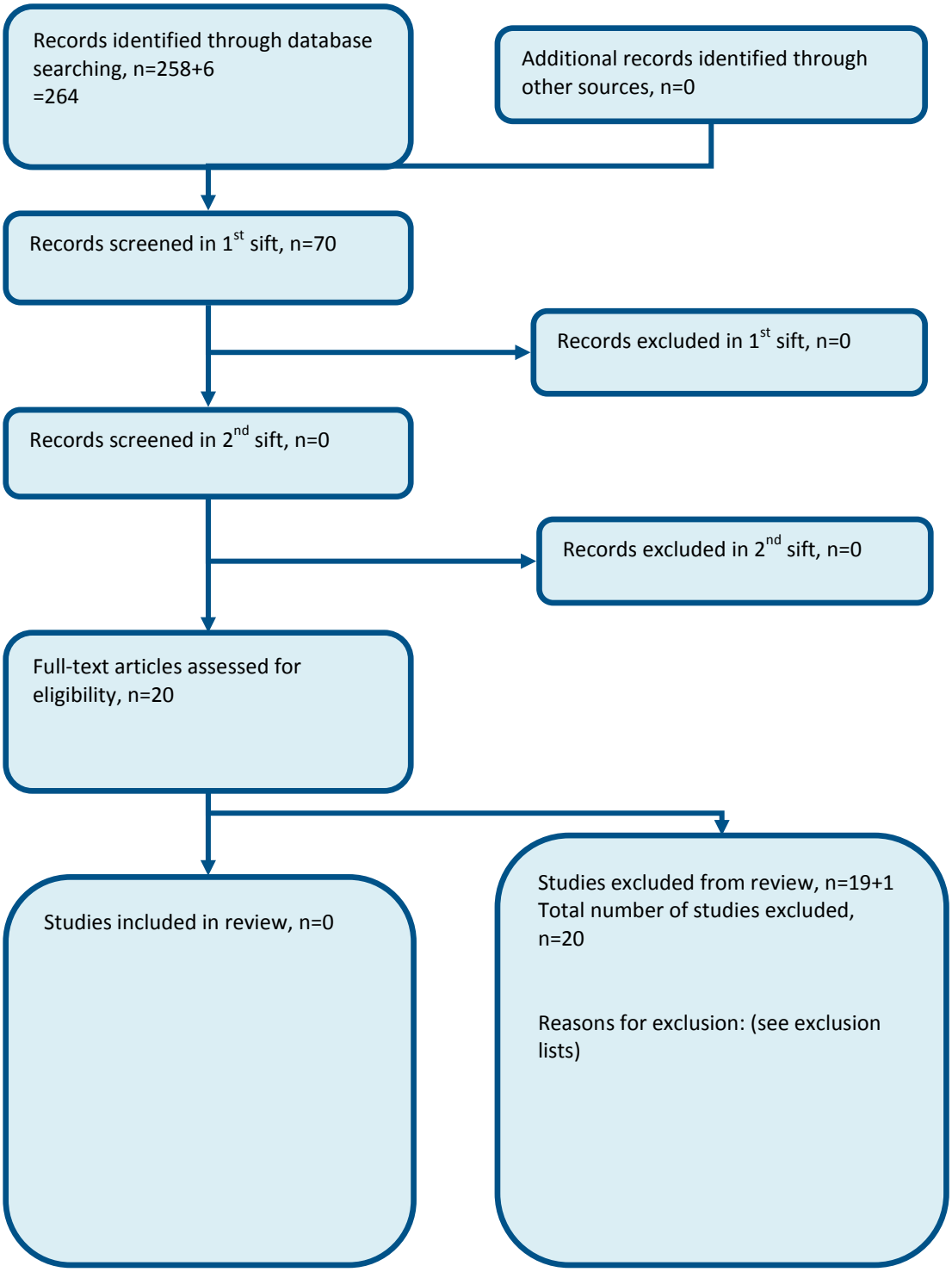


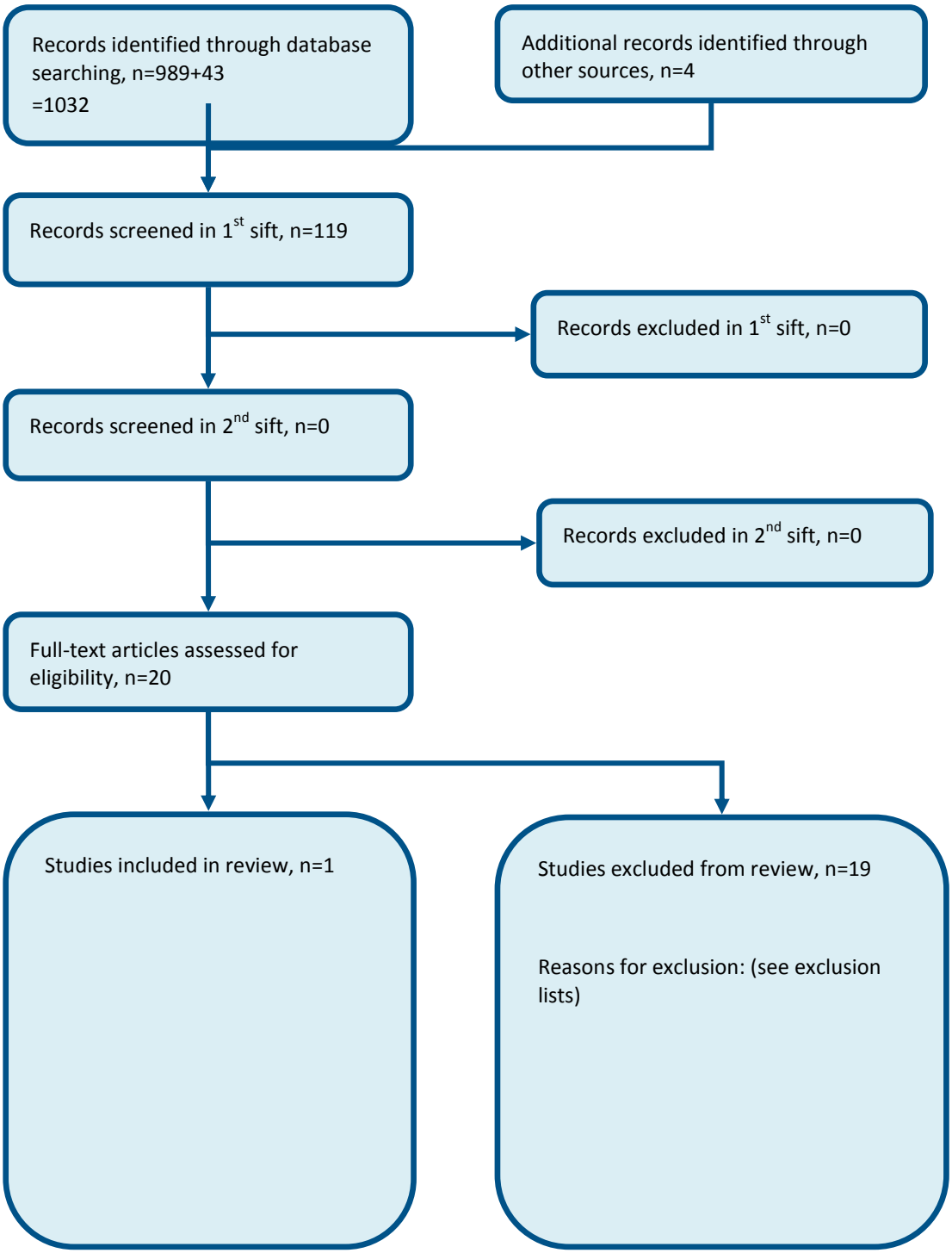
Figure 10: Flow chart of clinical article selection for the review of PCC thresholds and targets



1

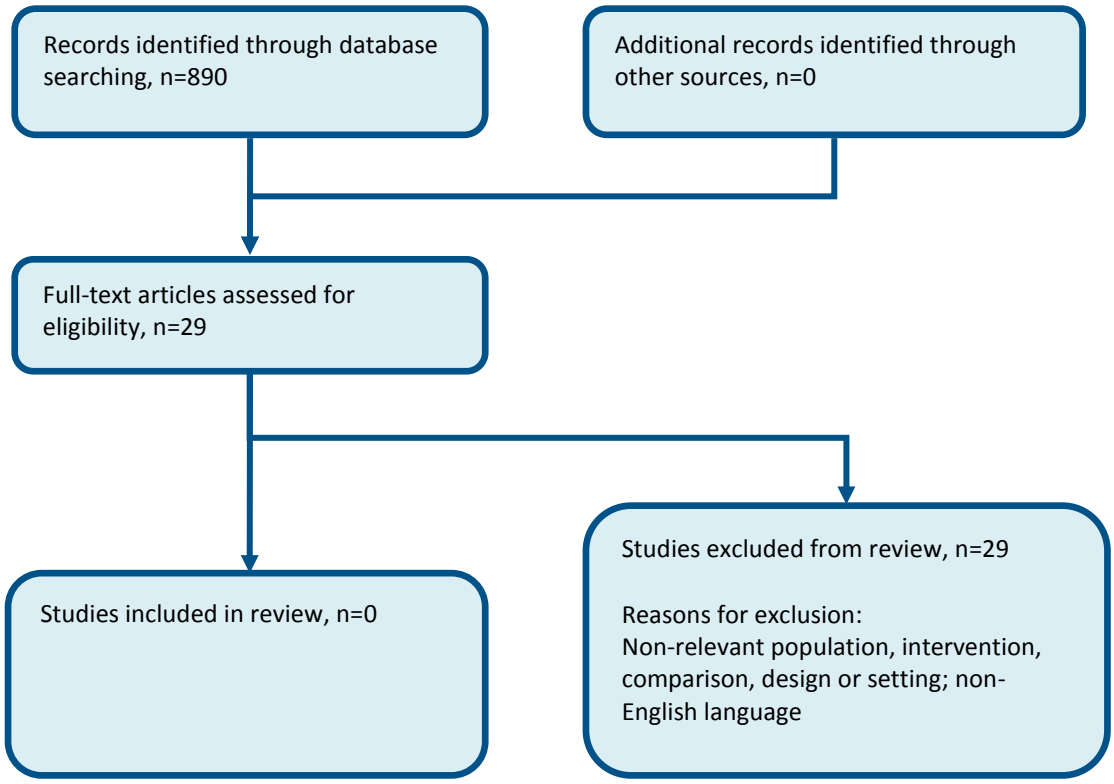
E.7 Cryoprecipitate

Figure 11: Flow chart of clinical article selection for the review of cryoprecipitate doses, thresholds and targets



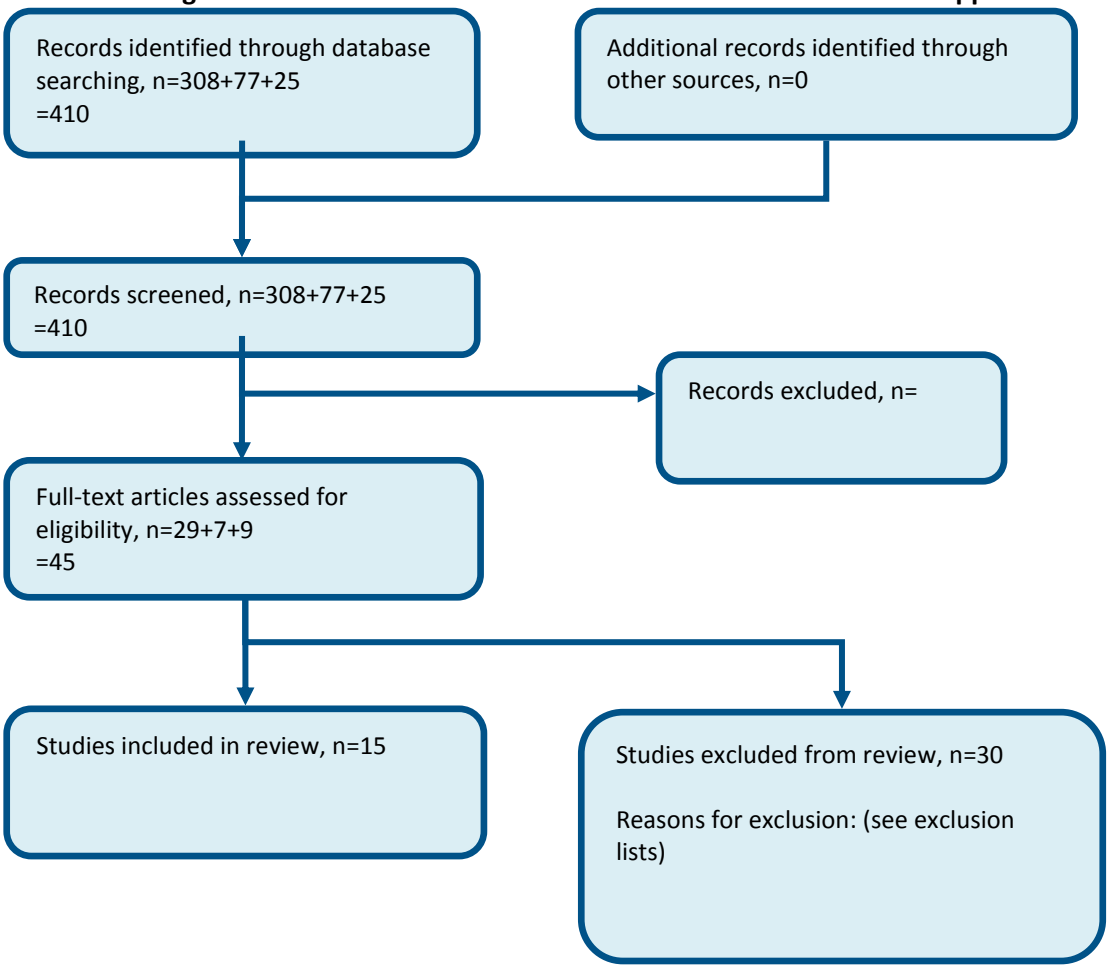
E.8 Monitoring for acute reactions

Figure 12: Flow diagram of clinical article selection for the review of monitoring



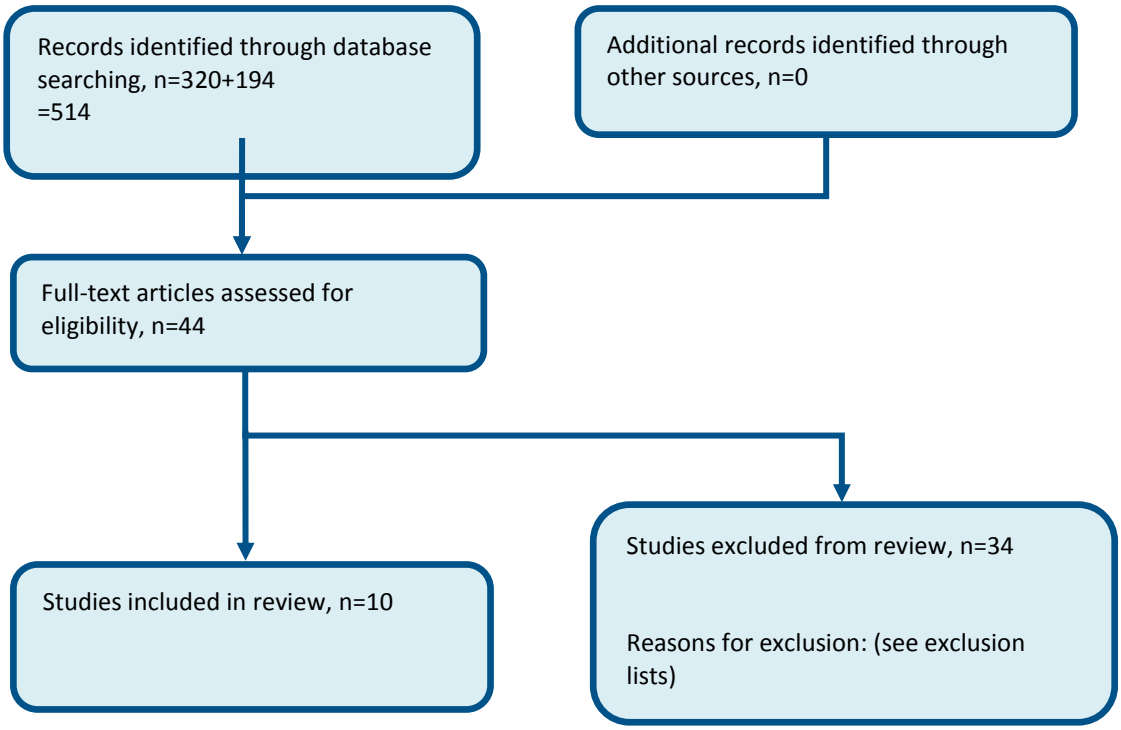
E.9 Electronic decision support

Figure 13: Flow diagram of article selection for the review of electronic decision support



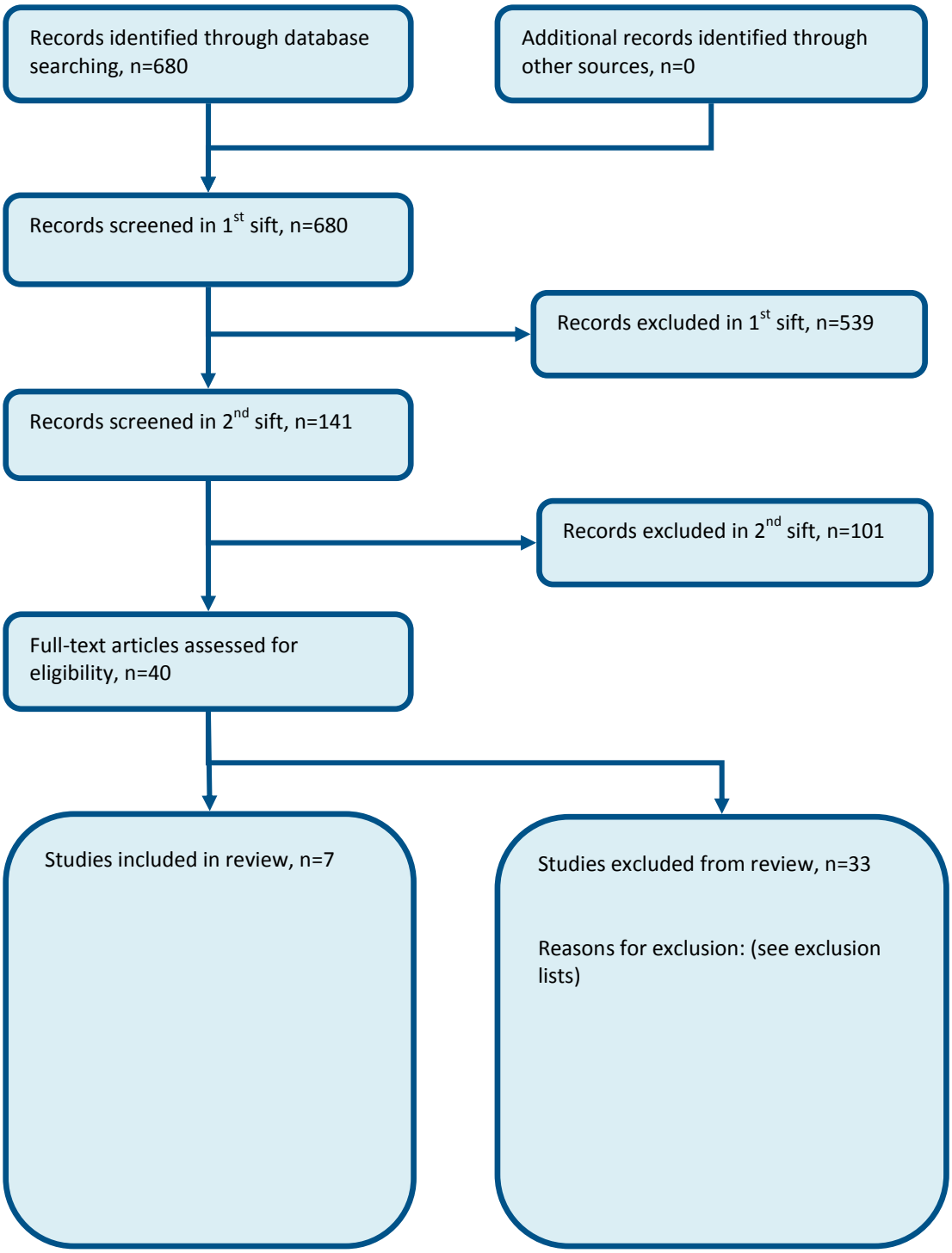
E.10 Electronic patient identification systems

Figure 14: Flow diagram of clinical article selection for the review of electronic patient identification systems



E.11 Patient information

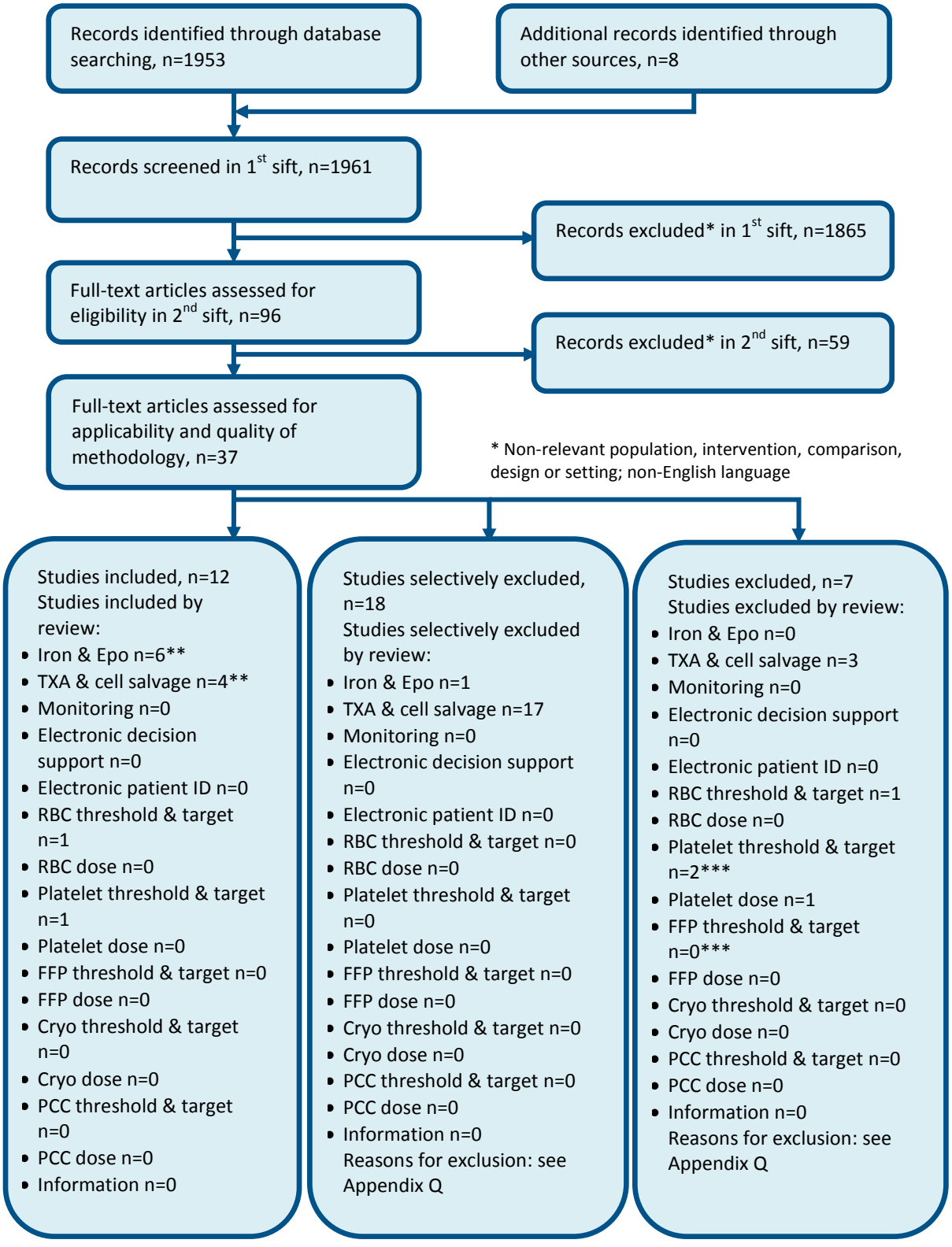
Figure 15: Flow chart of clinical article selection for the review of patient information



1

Appendix F: Economic article selection

Figure 16: Flow chart of economic article selection for the guideline



** One article identified was applicable to cell salvage and erythropoietin, for purposes of this diagram it has been included under erythropoietin only.

*** One article identified was applicable to platelet and FFP threshold and target, for purposes of this diagram it has been included under platelet threshold and target only.

Appendix G: Literature search strategies

Contents:

Search strategies used for the Transfusion guideline are outlined below and were run in accordance with the methodology in the NICE guidelines manual 2012.[3] All searches were run up to **29 January 2015** unless otherwise stated. Any studies added to the databases after this date (even those published prior to this date) were not included unless specifically stated in the text. We do not routinely search for electronic, ahead of print or "online early" publications. Where possible, searches were limited to retrieve material published in English.

Table 22: Database date parameters

Database	Dates searched
Medline	1946 to 28 January 2014
Embase	1980 to January 2015 (week 4)
The Cochrane Library	Cochrane Reviews to 2015 Issue 1 of 12 CENTRAL to 2014 Issue 12 of 12 DARE, HTA and NHSEED to 2014 Issue 4 of 4
CINAHL	1981 to January 2015
PsycINFO	1806 to January 2015 (week 4)
HMIC	1979 to November 2014

Searches for the **clinical reviews** were run in Medline (OVID), Embase (OVID) and the Cochrane Library (Wiley). Additional searches were run in CINAHL, PsycINFO and HMIC for some questions.

Searches for **intervention and diagnostic studies** were usually constructed using a PICO format where population (P) terms were combined with Intervention (I) and sometimes Comparison (C) terms. An intervention can be a drug, a procedure or a diagnostic test. Outcomes (O) are rarely used in search strategies for interventions. Search filters were also added to the search where appropriate.

Searches for the **health economic reviews** were run in Medline (OVID), Embase (OVID), the NHS Economic Evaluations Database (NHS EED), the Health Technology Assessment (HTA) database and the Health Economic Evaluation Database (HEED). Searches in NHS EED and HEED were constructed using population terms only. For Medline and Embase an economic filter (instead of a study type filter) was added to the same clinical search strategy.

G.1 Population search strategies

There was no single population search strategy used for this guideline. The population search terms used for each question, and for the economic searches, are reported in the relevant sections below.

G.2 Study filter search terms

G.2.1 Systematic review search terms

Medline search terms

1	meta-analysis/
2	meta-analysis as topic/
3	(meta analy* or metanaly* or metaanaly*).ti,ab.
4	((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.
5	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
6	(search strategy or search criteria or systematic search or study selection or data extraction).ab.

7	(search* adj4 literature).ab.
8	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
9	cochrane.jw.
10	or/1-9

Embase search terms

1	systematic review/
2	meta-analysis/
3	(meta analy* or metanaly* or metaanaly*).ti,ab.
4	((systematic or evidence) adj2 (review* or overview*)).ti,ab.
5	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
6	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
7	(search* adj4 literature).ab.
8	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
9	((pool* or combined) adj2 (data or trials or studies or results)).ab.
10	cochrane.jw.
11	or/1-10

G.2.2 Randomised controlled trials (RCTs) search terms

Medline search terms

1	randomized controlled trial.pt.
2	controlled clinical trial.pt.
3	randomi#ed.ab.
4	placebo.ab.
5	randomly.ab.
6	clinical trials as topic.sh.
7	trial.ti.
8	or/1-7

Embase search terms

1	random*.ti,ab.
2	factorial*.ti,ab.
3	(crossover* or cross over*).ti,ab.
4	((doubl* or singl*) adj blind*).ti,ab.
5	(assign* or allocat* or volunteer* or placebo*).ti,ab.
6	crossover procedure/
7	double blind procedure/
8	single blind procedure/
9	randomized controlled trial/
10	or/1-9

G.2.3 Observational studies search terms

Medline search terms

1	epidemiologic studies/

2	exp case control studies/
3	exp cohort studies/
4	cross-sectional studies/
5	case control.ti,ab.
6	(cohort adj (study or studies or analys*)).ti,ab.
7	((follow up or observational or uncontrolled or non randomi#ed or nonrandomi#ed or epidemiologic*) adj (study or studies)).ti,ab.
8	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort*)).ti,ab.
9	or/1-8

1 **Embase search terms**

1	clinical study/
2	exp case control study/
3	family study/
4	longitudinal study/
5	retrospective study/
6	prospective study/
7	cross-sectional study/
8	cohort analysis/
9	follow-up/
10	cohort*.ti,ab.
11	9 and 10
12	case control.ti,ab.
13	(cohort adj (study or studies or analys*)).ti,ab.
14	((follow up or observational or uncontrolled or non randomi#ed or nonrandomi#ed or epidemiologic*) adj (study or studies)).ti,ab.
15	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort*)).ti,ab.
16	or/1-8,11-15

2 ### G.2.4 Health economics search terms

3 **Medline search terms**

1	economics/
2	value of life/
3	exp "costs and cost analysis"/
4	exp economics, hospital/
5	exp economics, medical/
6	economics, nursing/
7	economics, pharmaceutical/
8	exp "fees and charges"/
9	exp budgets/
10	budget*.ti,ab.
11	cost*.ti.
12	(economic* or pharmaco?economic*).ti.
13	(price* or pricing*).ti,ab.

14	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
15	(financ* or fee or fees).ti,ab.
16	(value adj2 (money or monetary)).ti,ab.
17	or/1-16

Embase search terms

1	health economics/
2	exp economic evaluation/
3	exp health care cost/
4	exp fee/
5	budget/
6	funding/
7	budget*.ti,ab.
8	cost*.ti.
9	(economic* or pharmaco?economic*).ti.
10	(price* or pricing*).ti,ab.
11	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
12	(financ* or fee or fees).ti,ab.
13	(value adj2 (money or monetary)).ti,ab.
14	or/1-13

G.2.5 Quality of life search terms

Medline search terms

1	quality-adjusted life years/
2	sickness impact profile/
3	(quality adj2 (wellbeing or well-being)).ti,ab.
4	sickness impact profile.ti,ab.
5	disability adjusted life.ti,ab.
6	(qal* or qtime* or qwb* or daly*).ti,ab.
7	(euroqol* or eq5d* or eq 5d*).ti,ab.
8	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
9	(health utility* or utility score* or disutilit*).ti,ab.
10	(hui or hui1 or hui2 or hui3).ti,ab.
11	health* year* equivalent*.ti,ab.
12	(hye or hyes).ti,ab.
13	rosser.ti,ab.
14	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
15	(sf36 or sf 36 or short form 36 or shortform 36 or shortform36).ti,ab.
16	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
17	(sf12 or sf 12 or short form 12 or shortform 12 or shortform12).ti,ab.
18	(sf8 or sf 8 or short form 8 or shortform 8 or shortform8).ti,ab.
19	(sf6 or sf 6 or short form 6 or shortform 6 or shortform6).ti,ab.
20	or/1-19

Embase search terms

1	quality adjusted life year/

2	"quality of life index"/
3	short form 12/ or short form 20/ or short form 36/ or short form 8/
4	sickness impact profile/
5	(quality adj2 (wellbeing or well-being)).ti,ab.
6	sickness impact profile.ti,ab.
7	disability adjusted life.ti,ab.
8	(qal* or qtime* or qwb* or daly*).ti,ab.
9	(euroqol* or eq5d* or eq 5d*).ti,ab.
10	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
11	(health utility* or utility score* or disutilit*).ti,ab.
12	(hui or hui1 or hui2 or hui3).ti,ab.
13	health* year* equivalent*.ti,ab.
14	(hye or hyes).ti,ab.
15	rosser.ti,ab.
16	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
17	(sf36 or sf 36 or short form 36 or shortform 36 or shortform36).ti,ab.
18	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
19	(sf12 or sf 12 or short form 12 or shortform 12 or shortform12).ti,ab.
20	(sf8 or sf 8 or short form 8 or shortform 8 or shortform8).ti,ab.
21	(sf6 or sf 6 or short form 6 or shortform 6 or shortform6).ti,ab.
22	or/1-21

G.2.6 Excluded study designs and publication types

The following study designs and publication types were removed from retrieved results using the NOT operator.

Medline search terms

1	letter/
2	editorial/
3	news/
4	exp historical article/
5	anecdotes as topic/
6	comment/
7	case report/
8	(letter or comment*).ti.
9	or/1-8
10	randomized controlled trial/ or random*.ti,ab.
11	9 not 10
12	animals/ not humans/
13	exp animals, laboratory/
14	exp animal experimentation/
15	exp models, animal/
16	exp rodentia/
17	(rat or rats or mouse or mice).ti.
18	or/11-17

Embase search terms

1	letter.pt. or letter/
2	note.pt.
3	editorial.pt.
4	case report/ or case study/
5	(letter or comment*).ti.
6	or/1-5
7	randomized controlled trial/ or random*.ti,ab.
8	6 not 7
9	animal/ not human/
10	nonhuman/
11	exp animal experiment/
12	exp experimental animal/
13	animal model/
14	exp rodent/
15	(rat or rats or mouse or mice).ti.
16	or/8-15

G.3 Searches for specific questions

G.3.1 Alternatives to transfusion: iron and EPO

What is the clinical and cost effectiveness of oral iron, IV iron and erythropoietin in reducing blood transfusion requirements in surgical patients?

Search constructed by combining the columns in the following table using the AND Boolean operator. Exclusion filter applied using NOT Boolean operator.

Population	Intervention or exposure	Comparison	Study design filter	Date parameters and other limits
Anaemia surgical patients	Iron or EPO	n/a	The following filters were used in Medline and Embase only: RCT, SR	See Table 22 English only Exclusion filter applied in Medline and Embase

Medline search terms

1	exp anemia/
2	an?emi*.ti,ab.
3	hemoglobinometry/
4	((h?emoglobin or hb) adj2 (level* or volume* or measure*)).ti,ab.
5	or/1-4
6	(surg* or operat* or preoperat* or pre-operat* or perioperat* or peri-operat* or intraoperat* or intra-operat* or postoperat* or post-operat*).ti,ab.
7	exp perioperative period/
8	exp perioperative care/
9	or/6-8
10	5 and 9

11	exp hematinics/
12	exp iron compounds/
13	iron/
14	((iron or ferrous or ferric or ferumoxytol or magnetite or "ferriferous oxide") adj5 (supplement* or therap* or treat* or oral or iv or intravenous or diet*)).ti,ab.
15	(h?ematinic* or h?ematopoieti*).ti,ab.
16	erythropoietin/
17	(erythropoie* or epoetin* or epoietin* or epo or epogen or eporatio or procrit or binocrit or eprex or mircera or neorecormon or recormon or retacrit or darbopoetin or darbepoetin or darbepoietin or aranesp or r-huepo or huepo or r-hepo or rhepo or glycol-epoetin).ti,ab.
18	(anti-an?emi* or antian?emi*).ti,ab.
19	or/11-18
20	10 and 19

1 **Embase search terms**

1	exp *anemia/
2	an?emi*.ti,ab.
3	*hemoglobin determination/
4	((h?emoglobin or hb) adj2 (level* or volume* or measure*)).ti,ab.
5	or/1-4
6	exp *surgery/
7	(surg* or operat* or preoperat* or pre-operat* or perioperat* or peri-operat* or intraoperat* or intra-operat* or postoperat* or post-operat*).ti,ab.
8	or/6-7
9	5 and 8
10	exp *antianemic agent/
11	*iron/
12	*iron derivative/
13	*iron intake/
14	((iron or ferrous or ferric or ferumoxytol or magnetite or "ferriferous oxide") adj5 (supplement* or therap* or treat* or oral or iv or intravenous or diet*)).ti,ab.
15	(h?ematinic* or h?ematopoieti*).ti,ab.
16	(erythropoieti* or epoetin* or epoietin* or epo or epogen or eporatio or procrit or binocrit or eprex or mircera or neorecormon or recormon or retacrit or darbopoetin or darbepoetin or darbepoietin or aranesp or r-huepo or huepo or r-hepo or rhepo or glycol-epoetin).ti,ab.
17	(anti-an?emi* or antian?emi*).ti,ab.
18	or/10-17
19	9 and 18

2 **Cochrane search terms**

#1	[mh anemia]
#2	(anaemi* or anemi*):ti,ab
#3	[mh hemoglobinometry]
#4	((hemoglobin or haemoglobin or hb) near/2 (level* or volume* or measure*)):ti,ab
#5	#1 or #2 or #3 or #4
#6	[mh hematinics]
#7	[mh "iron compounds"]
#8	[mh ^iron]

#9	((iron or ferrous or ferric or ferumoxytol or magnetite or "ferriferous oxide") near/6 (supplement* or therap* or treat* or oral or iv or intravenous or diet*)):ti,ab
#10	(h?ematinic* or h?ematopoieti*):ti,ab
#11	[mh ^erythropoietin]
#12	(erythropoieti* or epoetin* or epoietin* or epo or epogen or eporatio or procrit or binocrit or eprex or mircera or neorecormon or recormon or retacrit or darbopoetin or darbepoetin or darbepoietin or aranesp or r-huepo or huepo or r-hepo or rhepo or glycol-epoetin):ti,ab
#13	(anti-anemi* or antianemi* or anti-anaemi* or antianaemi*):ti,ab
#14	#6 or #7 or #8 or #9 or #10 or #11 or #12 or #13
#15	(surg* or operat* or preoperat* or pre-operat* or perioperat* or peri-operat* or intraoperat* or intra-operat* or postoperat* or post-operat*):ti,ab
#16	[mh "perioperative period"]
#17	[mh "perioperative care"]
#18	{or #15-#17}
#19	#5 and #14
#20	#19 and #18

G.3.2 Alternatives to transfusion: TXA

What is the clinical and cost effectiveness of tranexamic acid in reducing blood transfusion requirements in surgical patients?

This search was run to update a Cochrane review for studies in adults.[2] It was run from 2010 onwards to pick up studies published since the Cochrane review searches were run. The search was also run with a paediatric filter and with no date restrictions to find studies in children. See below for the paediatric search terms used.

Search constructed by combining the columns in the following table using the AND Boolean operator. Exclusion filter applied using NOT Boolean operator.

Population	Intervention or exposure	Comparison	Study design filter	Date parameters and other limits
Surgery	TXA	n/a	The following filters were used in Medline and Embase only: RCT, SR	See Table 22 English only Exclusion filter applied in Medline and Embase No date limits were applied to paediatric studies, adult studies were limited to 2010 onwards

Medline search terms

1	(surg* or operat* or preoperat* or pre-operat* or perioperat* or peri-operat* or intraoperat* or intra-operat* or postoperat* or post-operat*).ti,ab.
2	exp perioperative period/
3	exp perioperative care/
4	exp blood transfusion/
5	transfus*.ti,ab.

6	or/1-5
7	tranexamic acid/
8	(tranexamic or txa or cyklokapron).ti,ab.
9	or/7-8
10	6 and 9

Embase search terms

1	exp *surgery/
2	(surg* or operat* or preoperat* or pre-operat* or perioperat* or peri-operat* or intraoperat* or intra-operat* or postoperat* or post-operat*).ti,ab.
3	exp *blood transfusion/
4	transfus*.ti,ab.
5	or/1-4
6	*tranexamic acid/
7	(tranexamic or txa or cyklokapron).ti,ab.
8	or/6-7
9	5 and 8

Cochrane search terms

#1	(surg* or operat* or preoperat* or pre-operat* or perioperat* or peri-operat* or intraoperat* or intra-operat* or postoperat* or post-operat*):ti,ab
#2	[mh "perioperative period"]
#3	[mh "perioperative care"]
#4	[mh "blood transfusion"]
#5	transfus*:ti,ab
#6	{or #1-#5}
#7	[mh "tranexamic acid"]
#8	(tranexamic or txa or cyklokapron):ti,ab
#9	#7 or #8
#10	#6 and #9

Paediatric search terms

Medline search terms

1	exp child/
2	exp pediatrics/
3	child*.ti,ab.
4	infant/
5	infan*.ti,ab.
6	(baby or babies).ti,ab.
7	"adolescent"/
8	(pediatric*1 or paediatric*1).ti,ab.
9	or/1-8

Embase search terms

1	exp child/
2	exp pediatrics/
3	child*.ti,ab.

4	infan*.ti,ab.
5	(baby or babies).ti,ab.
6	exp adolescent/
7	(pediatric*1 or paediatric*1).ti,ab.
8	or/1-7

Cochrane search terms

#1	[mh child]
#2	[mh pediatrics]
#3	child*:ti,ab
#4	[mh ^infant]
#5	infan*:ti,ab
#6	(baby or babies):ti,ab
#7	[mh ^adolescent]
#8	(pediatric* or paediatric*):ti,ab
#9	{or #1-#8}

G.3.3 Alternatives to transfusion: cell salvage

Searches for the following two questions were run as one search:

What is the clinical and cost effectiveness of cell salvage therapy in reducing blood transfusion requirements in surgical patients?

What is the clinical and cost-effectiveness of using alternatives to blood transfusion (cell salvage or tranexamic acid alone or in combination with one another) to reduce blood transfusion requirements?

Search constructed by combining the columns in the following table using the AND Boolean operator. Exclusion filter applied using NOT Boolean operator.

Population	Intervention or exposure	Comparison	Study design filter	Date parameters and other limits
No population terms used	Cell salvage	n/a	The following filters were used in Medline and Embase only: RCT, SR	See Table 22 English only Exclusion filter applied in Medline and Embase

Medline search terms

1	operative blood salvage/
2	(autotransfus* or auto-transfus*).ti,ab.
3	(intraoperat* adj (autologous or abt)).ti,ab.
4	(drain* adj2 (transfus* or retransfus* or re-transfus* or reinfus* or re-infus*)).ti,ab.
5	(((cell or blood) adj4 (salvag* or save* or scaveng* or retransfus* or re-transfus* or reinfus* or re-infus*)) or cell-saving).ti,ab.
6	or/1-5

Embase search terms

1	blood salvage/
2	(((cell or blood) adj4 (salvag* or save* or scaveng* or retransfus* or re-transfus* or reinfus* or

	re-infus*)) or cell-saving).ti,ab.
3	(autotransfus* or auto-transfus*).ti,ab.
4	(intraoperat* adj (autologous or abt)).ti,ab.
5	(drain* adj2 (transfus* or retransfus* or re-transfus* or reinfus* or re-infus*)).ti,ab.
6	or/1-5

Cochrane search terms

#1	[mh "operative blood salvage"]
#2	((cell or blood) near/4 (salvag* or save* or scaveng* or retransfus* or re-transfus* or reinfus* or re-infus*) or cell-saving):ti,ab
#3	(autotransfus* or auto-transfus*):ti,ab
#4	(intraoperat* next (autologous or abt)):ti,ab
#5	(drain* near/2 (transfus* or retransfus* or re-transfus* or reinfus* or re-infus*)):ti,ab
#6	{or #1-#5}

G.3.4 RBC: thresholds

What is the clinical and cost effectiveness of red blood cell transfusion at different haemoglobin concentrations?

This search was as update of the search for a Cochrane review.[1] It was run from 2011 onwards to pick up studies published since the Cochrane review searches were run.

Search constructed by combining the columns in the following table using the AND Boolean operator. Exclusion filter applied using NOT Boolean operator.

Population	Intervention or exposure	Comparison	Study design filter	Date parameters and other limits
No population terms used	Red blood cell transfusion thresholds	n/a	The following filters were used in Medline and Embase only: RCT, SR	See Table 22 English only Exclusion filter applied in Medline and Embase) 2011 onwards

Medline search terms

1	blood transfusion/ or erythrocyte transfusion/ or hemoglobins/ or hematocrit/
2	((red blood cell* or rbc or blood) adj3 (therap* or transfus*)).ti,ab.
3	or/1-2
4	reference standards/
5	3 and 4
6	hemoglobins/st
7	hematocrit/st
8	blood transfusion/st
9	erythrocyte transfusion/st
10	(transfus* adj3 (polic* or protocol* or trigger* or threshold*or indicator* or strateg* or criteri* or standard*)).ti,ab.
11	((red blood cell* or rbc) adj3 (polic* or protocol* or trigger* or threshold* or indicator* or strateg* or criteri* or standard*)).ti,ab.
12	((h?emoglobin or h?emocrit or h?ematocrit or hb or hgb or hct) adj3 (polic*or protocol* or

	trigger* or threshold*or indicator* or strateg* or criteri* or standard*)).ti,ab.
13	(transfus* adj3 (restrict* or liberal* or conserv*)).ti,ab.
14	or/5-13

Embase search terms

1	*blood transfusion/ or *erythrocyte transfusion/
2	*hemoglobin/
3	*hematocrit/
4	((red blood cell* or rbc or blood) adj3 (therap* or transfus*)).ti,ab.
5	or/1-4
6	standard/
7	5 and 6
8	(transfus* adj3 (polic* or protocol* or trigger* or threshold*or indicator* or strateg* or criteri* or standard*)).ti,ab.
9	((red blood cell* or rbc) adj3 (polic* or protocol* or trigger* or threshold*or indicator* or strateg* or criteri* or standard*)).ti,ab.
10	((h?emoglobin or h?emocrit or h?ematocrit or hb or hgb or hct) adj3 (polic* or protocol* or trigger* or threshold*or indicator* or strateg* or criteri* or standard*)).ti,ab.
11	(transfus* adj3 (restrict* or liberal* or conserv*)).ti,ab.
12	or/7-11

Cochrane search terms

#1	[mh ^"blood transfusion"]
#2	[mh ^"erythrocyte transfusion"]
#3	[mh ^hemoglobins]
#4	[mh ^hematocrit]
#5	((red blood cell* or rbc or blood) near/3 (therap* or transfus*)):ti,ab
#6	{or #1-#5}
#7	[mh ^"reference standards"]
#8	#6 and #7
#9	mesh descriptor: [hemoglobins] this term only and with qualifiers: [standards - st]
#10	mesh descriptor: [hematocrit] this term only and with qualifiers: [standards - st]
#11	mesh descriptor: [blood transfusion] this term only and with qualifiers: [standards - st]
#12	(transfus* near/3 (polic* or protocol* or trigger* or threshold*or indicator* or strateg* or criteri* or standard*)):ti,ab
#13	((red blood cell* or rbc) near/3 (polic* or protocol* or trigger* or threshold*or indicator* or strateg* or criteri* or standard*)):ti,ab
#14	((hemoglobin or haemoglobin or hemocrit or haemocrit or hematocrit or haematocrit or hb or hgb or hct) near/3 (polic* or protocol* or trigger* or threshold*or indicator* or strateg* or criteri* or standard*)):ti,ab
#15	(transfus* near/3 (restrict* or liberal* or conserv*)):ti,ab
#16	{or #8-#15}

G.3.5 RBC: targets

What is the clinical and cost effectiveness of different target levels of post-transfusion haemoglobin concentrations for red blood cell transfusion?

Search constructed by combining the columns in the following table using the AND Boolean operator. Exclusion filter applied using NOT Boolean operator.

Population	Intervention or exposure	Comparison	Study design filter	Date parameters and other limits
No population terms used	Red blood cell transfusion targets	n/a	The following filters were used in Medline and Embase only: RCT, SR	See Table 22 English only Exclusion filter applied in Medline and Embase

Medline search terms

1	blood transfusion/ or erythrocyte transfusion/
2	((red blood cell* or rbc or red cell* or blood) adj3 (therap* or transfus*)).ti,ab.
3	or/1-2
4	*hematocrit/
5	*hemoglobins/
6	((h?emoglobin or h?emocrit or h?ematocrit or hb or hgb or hct) adj3 (polic* or protocol* or target* or indicator* or strateg* or criteri* or standard* or goal* or high* or low*)).ti,ab.
7	(transfus* adj3 (restrict* or liberal* or conserv* or strateg* or criteri* or protocol* or target* or indicator* or goal* or polic*)).ti,ab.
8	or/4-7
9	3 and 8

Embase search terms

1	*blood transfusion/ or *erythrocyte transfusion/
2	((red blood cell* or rbc or red cell* or blood) adj3 (therap* or transfus*)).ti,ab.
3	or/1-2
4	*hematocrit/
5	*hemoglobin/
6	((h?emoglobin or h?emocrit or h?ematocrit or hb or hgb or hct) adj3 (polic* or protocol* or target* or indicator* or strateg* or criteri* or standard* or goal* or high* or low*)).ti,ab.
7	(transfus* adj3 (restrict* or liberal* or conserv* or strategy* or criteri* or protocol* or target* or indicator* or goal* or polic*)).ti,ab.
8	or/4-7
9	3 and 8

Cochrane search terms

#1	[mh ^"blood transfusion"]
#2	[mh ^"erythrocyte transfusion"]
#3	((red blood cell* or rbc or red cell* or blood) near/3 (therap* or transfus*)):ti,ab
#4	{or #1-#3}
#5	[mh ^hematocrit]
#6	[mh ^hemoglobins]
#7	{or #5-#6}
#8	(polic* or protocol* or target* or indicator* or strateg* or criteri* or standard* or goal* or high* or low*):ti,ab
#9	#7 and #8
#10	((hemoglobin or haemoglobin or hemocrit or haemocrit or hematocrit or haematocrit or hb or

	hgb or hct) near/3 (polic* or protocol* or target* or indicator* or strateg* or criteri* or standard* or goal* or high* or low*)):ti,ab
#11	(transfus* near/3 (restrict* or liberal* or conserv* or strategy* or criteri* or protocol* or target* or indicator* or goal* or polic*)):ti,ab
#12	{or #9-#11}
#13	#4 and #12

G.3.6 RBC: dose

What is the clinical and cost effectiveness of different doses of red blood cell transfusion?

Search constructed by combining the columns in the following table using the AND Boolean operator. Exclusion filter applied using NOT Boolean operator.

Population	Intervention or exposure	Comparison	Study design filter	Date parameters and other limits
RBC transfusion	RBC units	n/a	The following filters were used in Medline and Embase only: OBS, RCT, SR	See Table 22 English only Exclusion filter applied in Medline and Embase

Medline search terms

1	blood transfusion/ or erythrocyte transfusion/
2	((red blood cell* or rbc or prbc or red cell* or blood or packed cell* or erythroctye*) adj3 (therap* or transfus*)).ti,ab.
3	or/1-2
4	((blood or transfus*) adj3 (dose* or dosage*) adj2 (high* or low*)).ti,ab.
5	((unit* or bag*) adj3 (single or double or multiple or one or two or more) adj3 (blood or transfus*)).ti,ab.
6	(transfus* adj3 (restrict* or liberal* or conserv*)).ti,ab.
7	or/4-6
8	3 and 7

Embase search terms

1	*blood transfusion/ or *erythrocyte transfusion/
2	((red blood cell* or rbc or prbc or red cell* or blood or packed cell* or erythroctye*) adj3 (therap* or transfus*)).ti,ab.
3	or/1-2
4	((blood or transfus*) adj3 (dose* or dosage*) adj2 (high* or low*)).ti,ab.
5	((unit* or bag*) adj3 (single or double or multiple or one or two or more) adj3 (blood or transfus*)).ti,ab.
6	(transfus* adj3 (restrict* or liberal* or conserv*)).ti,ab.
7	or/4-6
8	3 and 7

Cochrane search terms

#1	[mh ^"blood transfusion"]
#2	[mh ^"erythrocyte transfusion"]
#3	((red next blood next cell* or rbc or prbc or red next cell* or packed next cell* or erythrocyte* or blood) near/3 (therap* or transfus*)):ti,ab

#4	{or #1-#3}
#5	((blood or transfus*) near/3 (dose* or dosage*) near/2 (high* or low*)):ti,ab
#6	((unit* or bag*) near/3 (single or double or multiple or one or two or more) near/3 (blood or transfus*)):ti,ab
#7	(transfus* near/3 (restrict* or liberal* or conserv*)):ti,ab
#8	{or #5-#7}
#9	#4 and #8

G.3.7 Platelets: thresholds and targets

Searches for the following two questions were run as one search:

What is the clinical and cost effectiveness of platelet transfusion at different platelet count thresholds?

What is the clinical and cost effectiveness of different target levels of post-transfusion platelet counts?

Search constructed by combining the columns in the following table using the AND Boolean operator. Exclusion filter applied using NOT Boolean operator.

Population	Intervention or exposure	Comparison	Study design filter	Date parameters and other limits
Platelet transfusion	Thresholds and targets	n/a	The following filters were used in Medline and Embase only: RCT, SR	See Table 22 English only Exclusion filter applied in Medline and Embase

Medline search terms

1	platelet transfusion/
2	((platelet* or thrombocyte*) adj3 (transfus* or prophyla* or therap* or infus* or administ*)).ti,ab.
3	blood platelets/
4	exp blood transfusion/
5	3 and 4
6	or/1-2,5
7	(transfus* adj3 (restrict* or liberal* or conserv* or strateg* or criteri* or protocol* or target* or indicator* or goal* or polic* or trigger* or threshold* or standard*)).ti,ab.
8	((platelet* or thrombocyte*) adj3 (restrict* or liberal* or conserv* or strateg* or criteri* or protocol* or target* or indicator* or goal* or polic* or trigger* or threshold* or standard*)).ti,ab.
9	st.fs.
10	((platelet* or thrombocyte*) adj1 count* adj3 (low or high)).ti,ab.
11	((platelet* or thrombocyte*) adj1 (count* or increment*) adj6 (((pre or post or before or after) adj transfus*) or pre-transfus* or post-transfus* or pretransfus* or posttransfus*)).ti,ab.
12	*platelet count/
13	or/7-12
14	6 and 13

Embase search terms

1	*thrombocyte transfusion/
2	((platelet* or thrombocyte*) adj3 (transfus* or prophyla* or therap* or infus* or administ*)).ti,ab.
3	*thrombocyte/
4	exp *blood transfusion/
5	3 and 4
6	or/1-2,5
7	(transfus* adj3 (restrict* or liberal* or conserv* or strateg* or criteri* or protocol* or target* or indicat* or goal* or polic* or trigger* or threshold* or standard*)).ti,ab.
8	((platelet* or thrombocyte*) adj3 (restrict* or liberal* or conserv* or strateg* or criteri* or protocol* or target* or indicat* or goal* or polic* or trigger* or threshold* or standard*)).ti,ab.
9	((platelet* or thrombocyte*) adj1 count* adj3 (low or high)).ti,ab.
10	((platelet* or thrombocyte*) adj1 (count* or increment*) adj6 (((pre or post or before or after) adj transfus*) or pre-transfus* or post-transfus* or pretransfus* or posttransfus*)).ti,ab.
11	*thrombocyte count/
12	or/7-11
13	6 and 12

Cochrane search terms

#1	[mh ^"platelet transfusion"]
#2	((platelet* or thrombocyte*) near/3 (transfus* or prophyla* or therap* or infus* or administ*)):ti,ab
#3	[mh ^"blood platelets"]
#4	[mh "blood transfusion"]
#5	#3 and #4
#6	#1 or #2 or #5
#7	(transfus* near/3 (restrict* or liberal* or conserv* or strateg* or criteri* or protocol* or target* or indicat* or goal* or polic* or trigger* or threshold* or standard*)):ti,ab
#8	((platelet* or thrombocyte*) near/3 (restrict* or liberal* or conserv* or strateg* or criteri* or protocol* or target* or indicat* or goal* or polic* or trigger* or threshold* or standard*)):ti,ab
#9	((platelet* or thrombocyte*) near count* near/3 (low or high)):ti,ab
#10	(((platelet* or thrombocyte*) near (count* or increment*)) near/6 (((pre or post or before or after) next transfus*) or pre-transfus* or post-transfus*or pretransfus* or posttransfus*)):ti,ab
#11	{or #7-#10}
#12	#6 and #11

G.3.8 Platelets: dose

What is the clinical and cost effectiveness of different doses of platelet transfusion?

Search constructed by combining the columns in the following table using the AND Boolean operator. Exclusion filter applied using NOT Boolean operator.

Population	Intervention or exposure	Comparison	Study design filter	Date parameters and other limits
Platelet transfusion	Platelet dose	n/a	The following filters were used in Medline and Embase only: RCT, SR	See Table 22 English only Exclusion filter applied in Medline and Embase

Medline search terms

1	platelet transfusion/
2	((platelet* or thrombocyte*) adj3 (transfus* or prophyla* or therap* or infus* or administ*)).ti,ab.
3	blood platelets/
4	exp blood transfusion/
5	3 and 4
6	or/1-2,5
7	((dose* or dosage* or dosing) adj2 (high* or low* or usual or platelet* or thrombocyte*)).ti,ab.
8	(unit* adj2 (single or double or multiple or one or two or more)).ti,ab.
9	or/7-8
10	6 and 9

Embase search terms

1	*thrombocyte transfusion/
2	((platelet* or thrombocyte*) adj3 (transfus* or prophyla* or therap* or infus* or administ*)).ti,ab.
3	*thrombocyte/
4	exp *blood transfusion/
5	3 and 4
6	or/1-2,5
7	((dose* or dosage* or dosing) adj2 (high* or low* or usual or platelet* or thrombocyte*)).ti,ab.
8	(unit* adj2 (single or double or multiple or one or two or more)).ti,ab.
9	or/7-8
10	6 and 9

Cochrane search terms

#1	[mh ^"platelet transfusion"]
#2	((platelet* or thrombocyte*) near/3 (transfus* or prophyla* or therap* or infus* or administ*)):ti,ab
#3	[mh ^"blood platelets"]
#4	[mh "blood transfusion"]
#5	#3 and #4
#6	#1 or #2 or #5
#7	((dose* or dosage* or dosing) near/2 (high* or low* or usual or platelet* or thrombocyte*)):ti,ab
#8	(unit* near/2 (single or double or multiple or one or two or more)):ti,ab
#9	#7 or #8
#10	#6 and #9

G.3.9 FFP: thresholds and targets

Searches for the following two questions were run as one search:

What is the clinical and cost effectiveness of transfusions of fresh frozen plasma (FFP) to treat and prevent bleeding?

What is the clinical and cost effectiveness of different target levels of post-transfusion haemostasis tests with the use of fresh frozen plasma FFP for prophylactic transfusions?

Search constructed by combining the columns in the following table using the AND Boolean operator. Exclusion filter applied using NOT Boolean operator.

Population	Intervention or exposure	Comparison	Study design filter	Date parameters and other limits
FFP	thresholds and targets	n/a	The following filters were used in Medline and Embase only: OBS, RCT, SR	See Table 22 English only Exclusion filter applied in Medline and Embase

Medline search terms

1	exp *plasma/
2	blood component transfusion/
3	(ffp or ((frozen or fresh) adj3 plasma)).ti,ab.
4	or/1-3
5	h?emosta*.ti,ab.
6	hemostasis/
7	(inr or international normali#ed ratio*).ti,ab.
8	exp blood coagulation tests/
9	((thromboplastin or prothrombin) adj2 time).ti,ab.
10	(ptt or aptt).ti,ab.
11	(coagul* adj2 abnormal*).ti,ab.
12	(transfus* adj3 (restrict* or liberal* or conserv* or strateg* or criteri* or protocol* or target* or indicat* or goal* or polic* or trigger* or threshold* or standard* or therap* or prophyl* or level*)).ti,ab.
13	((ffp or plasma) adj2 (therap* or prophyl*)).ti,ab.
14	or/25-33
15	24 and 34

Embase search terms

1	fresh frozen plasma/
2	plasma transfusion/
3	(ffp or ((frozen or fresh) adj3 plasma)).ti,ab.
4	or/1-3
5	*hemostasis/
6	exp *blood clotting parameters/
7	h?emosta*.ti,ab.
8	(inr or international normali#ed ratio*).ti,ab.
9	((thromboplastin or prothrombin) adj2 time).ti,ab.
10	(ptt or aptt).ti,ab.
11	(coagul* adj2 abnormal*).ti,ab.
12	(transfus* adj3 (restrict* or liberal* or conserv* or strateg* or criteri* or protocol* or target* or indicat* or goal* or polic* or trigger* or threshold* or standard* or therap* or prophyl* or level*)).ti,ab.
13	((ffp or plasma) adj2 (therap* or prophyl*)).ti,ab.
14	or/23-31
15	22 and 32

Cochrane search terms

#1	[mh plasma]
#2	[mh ^"blood component transfusion"]
#3	(ffp or ((frozen or fresh) near/3 plasma)):ti,ab
#4	{or #1-#3}
#5	[mh ^hemostasis]
#6	(hemosta* or haemosta*):ti,ab
#7	(inr or international next normalized next ratio* or international next normalised next ratio*) .ti,ab
#8	[mh "blood coagulation tests"]
#9	(coagul* near/2 abnormal*):ti,ab
#10	(transfus* near/3 (restrict* or liberal* or conserv* or strateg* or criteri* or protocol* or target* or indicat* or goal* or polic* or trigger* or threshold* or standard* or therap* or prophyl* or level*)):ti,ab
#11	((ffp or plasma) near/2 (therap* or prophyl*)):ti,ab
#12	{or #5-#11}
#13	#4 and #12

G.3.10 FFP: dose

What is the clinical and cost effectiveness of different doses of fresh frozen plasma (FFP) for transfusion?

Search constructed by combining the columns in the following table using the AND Boolean operator. Exclusion filter applied using NOT Boolean operator.

Population	Intervention or exposure	Comparison	Study design filter	Date parameters and other limits
FFP	dose	n/a	The following filters were used in Medline and Embase only: RCT, SR	See Table 22 English only Exclusion filter applied in Medline and Embase

Medline search terms

1	exp *plasma/
2	blood component transfusion/
3	(ffp or ((frozen or fresh) adj3 plasma)).ti,ab.
4	or/1-3
5	(unit* adj2 (single or double or multiple* or one or two or more or number* or plasma or "1" or "2" or "4" or "6" or additional or extra or further)).ti,ab.
6	(dose* or dosage* or dosing).ti,ab.
7	or/5-6
8	4 and 7

Embase search terms

1	fresh frozen plasma/
2	plasma transfusion/

3	(ffp or ((frozen or fresh) adj3 plasma)).ti,ab.
4	or/1-3
5	(unit* adj2 (single or double or multiple* or one or two or more or number* or plasma or "1" or "2" or "4" or "6" or additional or extra or further)).ti,ab.
6	(dose* or dosage* or dosing).ti,ab.
7	or/5-6
8	4 and 7

Cochrane search terms

#1	[mh plasma]
#2	[mh ^"blood component transfusion"]
#3	(ffp or ((frozen or fresh) near/3 plasma)):ti,ab
#4	{or #1-#3}
#5	(unit* near/2 (single or double or multiple or one or two or more or number or plasma or "1" or "2" or "4" or "6" or additional or extra or further)):ti,ab
#6	(dose* or dosage* or dosing):ti,ab
#7	#5 or #6
#8	#4 and #7

G.3.11 Cryoprecipitate

Searches for the following three questions were run as one search:

What is the clinical and cost effectiveness of transfusions of cryoprecipitate to treat and prevent bleeding?

What is the clinical and cost effectiveness of different doses of cryoprecipitate for transfusion?

What is the clinical and cost effectiveness of different target levels of post-transfusion haemostasis tests with the use of cryoprecipitate for prophylactic transfusions?

Search constructed by combining the columns in the following table using the AND Boolean operator. Exclusion filter applied using NOT Boolean operator.

Population	Intervention or exposure	Comparison	Study design filter	Date parameters and other limits
Cryoprecipitate	n/a	n/a	The following filters were used in Medline and Embase only: OBS, RCT, SR	See Table 22 English only Exclusion filter applied in Medline and Embase

Medline search terms

1	cryoprecipitate*.ti,ab.

Embase search terms

1	cryoprecipitate/
2	cryoprecipitate*.ti,ab.
3	or/1-2

Cochrane search terms

#1	cryoprecipitate*:ti,ab

G.3.12 PCC: thresholds and targets

Searches for the following two questions were run as one search:

What is the clinical and cost effectiveness of transfusions of prothrombin complex concentrates (PCC) to treat and prevent bleeding?

What is the clinical and cost effectiveness of different target levels of post-transfusion haemostasis tests with the use of prothrombin complex concentrates (PCC) for prophylactic transfusions?

Search constructed by combining the columns in the following table using the AND Boolean operator. Exclusion filter applied using NOT Boolean operator.

Population	Intervention or exposure	Comparison	Study design filter	Date parameters and other limits
PCC	Blood coagulation tests	n/a	The following filters were used in Medline and Embase only: RCT, SR	See Table 22 English only Exclusion filter applied in Medline and Embase

Medline search terms

1	(pcc* or ppsb or beriplex or "beriplex p n" or "beriplex b-n" or " beriplex p/n" or confidex or kaskadil or kcentra or octaplex or ocplex or cofact or prothar or ppconc or "protein c concentrate").ti,ab.
2	("prothrombin complex" adj2 (concentrate* or preparation)).ti,ab.
3	("prothrombin convert*" adj2 (complex or enzyme)).ti,ab.
4	or/1-3
5	h?emosta*.ti,ab.
6	hemostasis/
7	(inr or international normali#ed ratio*).ti,ab.
8	exp blood coagulation tests/
9	((thromboplastin or prothrombin) adj2 time*).ti,ab.
10	(ptt or pt or aptt).ti,ab.
11	(coagul* adj2 abnormal*).ti,ab.
12	or/5-11
13	4 and 12

Embase search terms

1	(pcc* or ppsb or beriplex or "beriplex p n" or "beriplex b-n" or " beriplex p/n" or confidex or kaskadil or kcentra or octaplex or ocplex or cofact or prothar or ppconc or "protein c concentrate").ti,ab.
2	("prothrombin complex" adj2 (concentrate* or preparation)).ti,ab.
3	("prothrombin convert*" adj2 (complex or enzyme)).ti,ab.
4	or/1-3
5	h?emosta*.ti,ab.
6	exp *hemostasis/
7	(inr or international normali#ed ratio*).ti,ab.
8	exp *blood clotting parameters/
9	((thromboplastin or prothrombin) adj2 time$).ti,ab.
10	(ptt or pt or aptt).ti,ab.

11	(coagul* adj2 abnormal*).ti,ab.
12	or/5-11
13	4 and 12

Cochrane search terms

#1	(pcc* or ppsb or beriplex or beriplex next pn or beriplex next b-n or beriplex next pn or confidex or kaskadil or kcentra or octaplex or ocplex or cofact or prothar or ppconc or protein next c next concentrate):ti,ab
#2	(prothrombin next complex near/2 (concentrate* or preparation)):ti,ab
#3	prothrombin next convert* near/2 (complex or enzyme):ti,ab
#4	{or #1-#3}
#5	[mh ^hemostasis]
#6	(hemosta* or haemosta*):ti,ab
#7	(inr or international next normalized next ratio* or international next normalised next ratio*):ti,ab
#8	[mh "blood coagulation tests"]
#9	(coagul* near/2 abnormal*):ti,ab
#10	((thromboplastin or prothrombin) adj2 time$):ti,ab
#11	(ptt or pt or aptt):ti,ab
#12	{or #5-#11}
#13	#4 and #12

G.3.13 PCC: dose

What is the clinical and cost effectiveness of different doses of prothrombin complex concentrates (PCC) for transfusion?

Search constructed by combining the columns in the following table using the AND Boolean operator. Exclusion filter applied using NOT Boolean operator.

Population	Intervention or exposure	Comparison	Study design filter	Date parameters and other limits
PCC	dose	n/a	The following filters were used in Medline and Embase only: RCT, SR	See Table 22 English only Exclusion filter applied in Medline and Embase

Medline search terms

1	(pcc* or ppsb or beriplex or "beriplex p n" or "beriplex b-n" or " beriplex p/n" or confidex or kaskadil or kcentra or octaplex or ocplex or cofact or prothar or ppconc or "protein c concentrate").ti,ab.
2	("prothrombin complex" adj2 (concentrate* or preparation)).ti,ab.
3	("prothrombin convert*" adj2 (complex or enzyme)).ti,ab.
4	or/1-3
5	(dose* or dosage* or dosing).ti,ab.
6	(unit* adj2 (single or double or multiple* or one or two or more or number* or pcc or prothrombin or additional or extra or further)).ti,ab.
7	or/5-6
8	4 and 7

Embase search terms

1	(pcc* or ppsb or beriplex or "beriplex p n" or "beriplex b-n" or " beriplex p/n" or confidex or kaskadil or kcentra or octaplex or ocplex or cofact or prothar or ppconc or "protein c concentrate").ti,ab.
2	("prothrombin complex" adj2 (concentrate* or preparation)).ti,ab.
3	("prothrombin convert*" adj2 (complex or enzyme)).ti,ab.
4	or/1-3
5	(dose* or dosage* or dosing).ti,ab.
6	(unit* adj2 (single or double or multiple* or one or two or more or number* or pcc or prothrombin or additional or extra or further)).ti,ab.
7	or/5-6
8	4 and 7

Cochrane search terms

#1	(pcc* or ppsb or beriplex or beriplex next pn or beriplex next b-n or beriplex next pn or confidex or kaskadil or kcentra or octaplex or ocplex or cofact or prothar or ppconc or protein next c next concentrate):ti,ab
#2	(prothrombin next complex near/2 (concentrate* or preparation)):ti,ab
#3	prothrombin next convert* near/2 (complex or enzyme):ti,ab
#4	{or #1-#3}
#5	(dose* or dosage* or dosing):ti,ab
#6	(unit* near/2 (single or double or multiple* or one or two or more or number* or pcc or prothrombin or additional or extra or further)):ti,ab
#7	#5 or #6
#8	#4 and #7

G.3.14 Monitoring

What is the clinical and cost effectiveness of monitoring for acute reactions at different times in relation to the transfusion?

Search constructed by combining the columns in the following table using the AND Boolean operator. Exclusion filter applied using NOT Boolean operator.

Population	Intervention or exposure	Comparison	Study design filter	Date parameters and other limits
Transfusion reactions	Monitoring	n/a	The following filters were used in Medline and Embase only: OBS, RCT, SR	See Table 22 English only Exclusion filter applied in Medline and Embase

Medline search terms

1	exp *blood transfusion/
2	((blood or red cell or rbc or platelet* or plasma or ffp or cryoprecipitate or prothrombin) adj3 (transfus* or retransfus* or therap* or prescri*)).ti,ab.
3	(hemotransfus* or haemotransfus*).ti,ab.
4	((blood adj2 (management or administ*5 or component*1)) or blood support).ti,ab.
5	exp blood transfusion/ae, co, de [adverse effects, complications, drug effects]
6	(transfus* adj2 (react* or side effect* or side-effect* or adverse effect* or adverse event*)).ti,ab.

7	(((adverse or acute) adj2 (react* or respon* or effect* or event* or outcome*)) or atr or atrs).ti,ab.
8	or/1-4
9	7 and 8
10	or/5-6,9
11	monitoring, physiologic/
12	(monitor* or check up* or check-up*).ti,ab.
13	"signs and symptoms"/
14	vital signs/
15	((clinical* adj1 assess*) or "signs and symptoms" or ((vital or clinical) adj1 sign*)).ti,ab.
16	or/11-15
17	10 and 16

1 **Embase search terms**

1	exp *blood transfusion/
2	((blood or red cell or rbc or platelet* or plasma or ffp or cryoprecipitate or prothrombin) adj3 (transfus* or retransfus* or therap* or prescri*)).ti,ab.
3	(hemotransfus* or haemotransfus*).ti,ab.
4	((blood adj2 (management or administ*5 or component*1)) or blood support).ti,ab.
5	or/1-4
6	(((adverse or acute) adj2 (react* or respon* or effect* or event* or outcome*)) or atr or atrs).ti,ab.
7	5 and 6
8	exp blood transfusion reaction/
9	exp blood transfusion/ae, co [adverse drug reaction, complication]
10	(transfus* adj2 (react* or side effect* or side-effect* or adverse effect* or adverse event*)).ti,ab.
11	or/7-10
12	*monitoring/ or *patient monitoring/ or physiologic monitoring/
13	vital sign/
14	(monitor* or check up* or check-up*).ti,ab.
15	((clinical* adj1 assess*) or "signs and symptoms" or ((vital or clinical) adj1 sign*)).ti,ab.
16	or/12-15
17	11 and 16

2 **Cochrane search terms**

#1	[mh "blood transfusion"]
#2	((blood or red cell or rbc or platelet* or plasma or ffp or cryoprecipitate or prothrombin) near/3 (transfus* or retransfus* or therap* or prescri*)):ti,ab
#3	(hemotransfus* or haemotransfus*):ti,ab
#4	((blood near/2 (management or administ* or component*1)) or blood support):ti,ab
#5	{or #1-#4}
#6	(((adverse or acute) near/2 (react* or respon* or effect* or event* or outcome*)) or atr or atrs):ti,ab
#7	#5 and #6
#8	mesh descriptor: [blood transfusion] explode all trees and with qualifiers: [adverse effects - ae]
#9	(transfus* near/2 (react* or side next effect* or side-effect* or adverse next effect* or adverse next event*)):ti,ab

#10	{or #7-#9}
#11	[mh ^"monitoring, physiologic"]
#12	[mh ^"signs and symptoms"]
#13	[mh ^"vital signs"]
#14	(monitor* or check next up* or check-up*):ti,ab
#15	((clinical* next assess*) or "signs and symptoms" or ((vital or clinical) near (sign or signs))):ti,ab
#16	{or #11-#15}
#17	#10 and #16

CINAHL search terms

S1	(mh "blood transfusion+")
S2	transfus* OR hemotransfus* OR haemotransfus*
S3	((blood n2 (management or administ* or component*)) or blood support)
S4	S1 or S2 or S3
S5	(((adverse or acute) n2 (react* or respon* or effect* or event* or outcome*)) or atr or atrs)
S6	(mh "adverse health care event+")
S7	S5 or S6
S8	S4 and S7
S9	(mh "blood transfusion reaction+")
S10	(mh "blood transfusion+/ae")
S11	(transfus* n2 (react* or side effect* or side-effect* or adverse effect* or adverse event*))
S12	s8 or s9 or s10 or s11
S13	PT anecdote or PT audiovisual or PT bibliography or PT biography or PT book or PT book review or PT brief item or PT cartoon or PT commentary or PT computer program or PT editorial or PT games or PT glossary or PT historical material or PT interview or PT letter or PT listservs or PT masters thesis or PT obituary or PT pamphlet or PT pamphlet chapter or PT pictorial or PT poetry or PT proceedings or PT "questions and answers" or PT response or PT software or PT teaching materials or PT website
S14	S12 not S13
S15	(mh "monitoring, physiologic") or (mh "vital signs") or (mh "signs and symptoms (non-cinahl)")
S16	(monitor* or check up* or check-up*)
S17	((clinical* n1 assess*) or "signs and symptoms" or ((vital or clinical) n1 sign*))
S18	S15 or S16 or S17
S19	S14 and S18

G.3.15 Patient identification

What are the clinical and cost effectiveness of electronic patient identification systems such as patient identification band, bar code or radiofrequency identification (RFID) to ensure patient safety during blood transfusions?

Search constructed by combining the columns in the following table using the AND Boolean operator. Exclusion filter applied using NOT Boolean operator.

Population	Intervention or exposure	Comparison	Study design filter	Date parameters and other limits
Transfusion	Patient ID	n/a	The following filters were used in Medline and Embase only: OBS, RCT, SR	See Table 22 English only Exclusion filter applied in

Population	Intervention or exposure	Comparison	Study design filter	Date parameters and other limits
				Medline and Embase

1 **Medline search terms**

1	exp blood transfusion/
2	transfus*.ti,ab.
3	(hemotransfus* or haemotransfus*).ti,ab.
4	((blood adj2 (management or administ*5 or component*1)) or blood support).ti,ab.
5	or/1-4
6	exp patient identification systems/
7	exp medical records systems, computerized/
8	safety management/
9	blood group incompatibility/pc [prevention & control]
10	checklist/
11	(radiofrequency identification* or rfid).ti,ab.
12	(bar code* or barcode* or wristband* or wrist band*).ti,ab.
13	(checklist* or double check*).ti,ab.
14	(patient* adj2 (identification or id or misidentification)).ti,ab.
15	blood safety/mt, st [methods, standards]
16	or/6-15
17	5 and 16

2 **Embase search terms**

1	exp *blood transfusion/
2	transfus*.ti,ab.
3	(hemotransfus* or haemotransfus*).ti,ab.
4	((blood adj2 (management or administ*5 or component*1)) or blood support).ti,ab.
5	or/1-4
6	patient identification/
7	*electronic medical record/
8	blood safety/
9	blood group incompatibility/pc [prevention]
10	radiofrequency identification/
11	*checklist/
12	(radiofrequency identification* or rfid).ti,ab.
13	(bar code* or barcode* or wristband* or wrist band*).ti,ab.
14	(checklist* or double check*).ti,ab.
15	(patient* adj2 (identification or id or misidentification)).ti,ab.
16	or/6-15
17	5 and 16

3 **Cochrane search terms**

#1	[mh "blood transfusion"]
#2	transfus*:ti,ab
#3	(hemotransfus* or haemotransfus*):ti,ab

#4	((blood near/2 (management or administ* or component*)) or blood support):ti,ab
#5	{or #1-#4}
#6	[mh "patient identification systems"]
#7	[mh "medical records systems, computerized"]
#8	[mh ^"safety management"]
#9	mesh descriptor: [blood group incompatibility] this term only and with qualifiers: [prevention & control - pc]
#10	[mh ^checklist]
#11	mesh descriptor: [blood safety] this term only and with qualifiers: [methods - mt, standards - st]
#12	(radiofrequency identification* or rfid):ti,ab
#13	(bar code* or barcode* or wristband* or wrist band*):ti,ab
#14	(checklist* or double check*):ti,ab
#15	(patient* near/2 (identification or id or misidentification)):ti,ab
#16	{or #6-#15}
#17	#5 and #16

1 **Cinahl search terms**

S1	(mh "blood transfusion+")
S2	transfus* or hemotransfus* or haemotransfus*
S3	((blood n2 (management or administ* or component*)) or blood support)
S4	S1 or S2 or S3
S5	(mh "patient identification") or (mh "computerized patient record") or (mh "bar coding") or (mh "checklists")
S6	(radiofrequency identification* or rfid)
S7	(bar code* or barcode* or wristband* or wrist band*)
S8	checklist* or double check*
S9	(patient* n2 (identification or id or misidentification))
S10	S5 or S6 or S7 or S8 or S9
S11	S4 and S10
S12	PT anecdote or PT audiovisual or PT bibliography or PT biography or PT book or PT book review or PT brief item or PT cartoon or PT commentary or PT computer program or PT editorial or PT games or PT glossary or PT historical material or PT interview or PT letter or PT listservs or PT masters thesis or PT obituary or PT pamphlet or PT pamphlet chapter or PT pictorial or PT poetry or PT proceedings or PT “questions and answers” or PT response or PT software or PT teaching materials or PT website
S13	S11 not S12

2 **HMIC search terms**

1	blood transfusion/ or blood transfusion equipment/ or blood transfusion services/ or blood transfusion units/
2	transfus*.ti,ab.
3	(hemotransfus* or haemotransfus*).ti,ab.
4	((blood adj2 (management or administ*5 or component*1)) or blood support).ti,ab.
5	or/1-4
6	exp patient identification systems/ or electronic patient records/
7	(radiofrequency identification* or rfid).ti,ab.
8	(bar code* or barcode* or wristband* or wrist band*).ti,ab.
9	(checklist* or double check*).ti,ab.

10	(patient* adj2 (identification or id or misidentification)).ti,ab.
11	or/6-10
12	5 and 11

G.3.16 Electronic decision support

What is the clinical and cost effectiveness of electronic decision-support blood order systems to reduce inappropriate blood transfusions?

Search constructed by combining the columns in the following table using the AND Boolean operator. Exclusion filter applied using NOT Boolean operator.

Population	Intervention or exposure	Comparison	Study design filter	Date parameters and other limits
Transfusion	Decision support	n/a	The following filters were used in Medline and Embase only: OBS, RCT, SR	See Table 22 English only Exclusion filter applied in Medline and Embase

Medline search terms

1	exp blood transfusion/
2	transfus*.ti,ab.
3	(hemotransfus* or haemotransfus*).ti,ab.
4	((blood adj2 (management or administ*5 or component*1)) or blood support).ti,ab.
5	or/1-4
6	exp medical records systems, computerized/
7	electronic prescribing/
8	decision support systems, clinical/
9	exp medication systems/
10	medical informatics applications/ or decision making, computer-assisted/ or therapy, computer-assisted/ or medical informatics computing/
11	reminder systems/
12	clinical laboratory information systems/ or decision support systems, management/ or exp hospital information systems/
13	(((computer* or electronic*) adj3 (decision* or tool* or support* or prescri*or blood or transfus*)) or eprescri* or e-prescri*).ti,ab.
14	((computer* adj3 order entry) or cpoe).ti,ab.
15	((clinical support or decision support) adj3 system*).ti,ab.
16	reminder*.ti,ab.
17	or/6-16
18	5 and 17

Embase search terms

1	exp *blood transfusion/
2	transfus*.ti,ab.
3	(hemotransfus* or haemotransfus*).ti,ab.
4	((blood adj2 (management or administ*5 or component*1)) or blood support).ti,ab.
5	or/1-4

6	exp *electronic medical record/
7	exp computerized provider order entry/
8	decision support system/
9	*medical informatics/
10	computer assisted therapy/
11	hospital information system/ or medical information system/ or nursing information system/ or reminder system/
12	*information system/
13	*computer system/
14	(((computer* or electronic*) adj3 (decision* or tool* or support* or prescri*or blood or transfus*)) or eprescri* or e-prescri*).ti,ab.
15	((computer* adj3 order entry) or cpoe).ti,ab.
16	((clinical support or decision support) adj3 system*).ti,ab.
17	reminder*.ti,ab.
18	or/6-17
19	5 and 18

1 **Cochrane search terms**

#1	[mh "blood transfusion"]
#2	transfus*:ti,ab
#3	(hemotransfus* or haemotransfus*):ti,ab
#4	((blood near/2 (management or administ* or component*)) or blood support):ti,ab
#5	{or #1-#4}
#6	[mh "medical records systems, computerized"]
#7	[mh ^"electronic prescribing"]
#8	[mh ^"decision support systems, clinical"]
#9	[mh "medication systems"]
#10	[Mh ^"medical informatics applications"]
#11	[Mh ^"decision making, computer-assisted"]
#12	[Mh ^"therapy, computer-assisted"]
#13	[Mh ^"medical informatics computing"]
#14	[mh ^"reminder systems"]
#15	[mh ^"clinical laboratory information systems"]
#16	[mh ^"decision support systems, management"]
#17	[mh "hospital information systems"]
#18	(((computer* or electronic*) near/3 (decision* or tool* or support* or prescri*or blood or transfus*)) or eprescri* or e-prescri*):ti,ab
#19	((computer* near/3 order next entry) or cpoe):ti,ab
#20	((clinical next support or decision next support) near/3 system*):ti,ab
#21	reminder*:ti,ab
#22	{or #6-#21}
#23	#5 and #22

2 **HMIC search terms**

1	blood transfusion/ or blood transfusion equipment/ or blood transfusion services/ or blood transfusion units/
2	transfus*.ti,ab.

3	(hemotransfus* or haemotransfus*).ti,ab.
4	((blood adj2 (management or administ*5 or component*1)) or blood support).ti,ab.
5	or/1-4
6	electronic patient records/
7	electronic prescribing/
8	computer aided decision making/ or computerised control systems/ or computerised information handling/ or decision support systems/
9	medication systems/ or medication orders/
10	medical informatics/
11	information systems/ or computerised information systems/ or medical information systems/
12	(((computer* or electronic*) adj3 (decision* or tool* or support* or prescri*or blood or transfus*)) or eprescri* or e-prescri*).ti,ab.
13	((computer* adj3 order entry) or CPOE).ti,ab.
14	((clinical support or decision support) adj3 system*).ti,ab.
15	or/6-14
16	5 and 15

G.3.17 Patient information

What is the information and support patients under consideration for a blood transfusion and their family members or carers would value and how would they prefer to receive it?

Search constructed by combining the columns in the following table using the AND Boolean operator. Exclusion filter applied using NOT Boolean operator.

Population	Intervention or exposure	Comparison	Study design filter	Date parameters and other limits
Transfusion	Patient information	n/a	Qualitative terms were added to the search – see below	See Table 22 English only Exclusion filter applied in Medline and Embase

Medline search terms

1	exp blood transfusion/
2	transfus*.ti,ab.
3	(hemotransfus* or haemotransfus*).ti,ab.
4	((blood adj2 (management or administ*5 or component*1)) or blood support).ti,ab.
5	or/1-4
6	"patient acceptance of health care"/ or exp patient satisfaction/ or exp consumer satisfaction/ or personal satisfaction/
7	patient education as topic/
8	(information* adj3 (patient* or need* or requirement* or support* or seek* or access* or disseminat*)).ti,ab.
9	((client* or patient* or user* or carer* or consumer* or customer* or famil* or parent* or father* or mother*) adj2 (attitud* or priorit* or perception* or preferen* or expectation* or choice* or perspective* or view* or satisfact* or inform* or experience or experiences or opinion* or knowledge or awareness or misconception* or understanding or misunderstanding or concern* or belief* or feeling* or acceptance or need* or requirement* or support* or communication* or involvement)).ti,ab.

10	or/6-9
11	qualitative research/
12	exp interviews as topic/
13	exp questionnaires/
14	health care surveys/
15	(qualitative or interview* or focus group* or theme* or questionnaire* or survey*).ti,ab.
16	or/11-15
17	10 and 16
18	5 and 17

1 **Embase search terms**

1	exp *blood transfusion/
2	transfus*.ti,ab.
3	(hemotransfus* or haemotransfus*).ti,ab.
4	((blood adj2 (management or administ*5 or component*1)) or blood support).ti,ab.
5	or/1-4
6	patient attitude/ or patient preference/ or patient satisfaction/ or consumer attitude/
7	patient information/ or consumer health information/
8	patient education/
9	(information* adj3 (patient* or need* or requirement* or support* or seek* or access* or disseminat*)).ti,ab.
10	((client* or patient* or user* or carer* or consumer* or customer* or famil* or parent* or father* or mother*) adj2 (attitud* or priorit* or perception* or preferen* or expectation* or choice* or perspective* or view* or satisfact* or inform* or experience or experiences or opinion* or knowledge or awareness or misconception* or understanding or misunderstanding or concern* or belief* or feeling* or acceptance or need* or requirement* or support* or communication* or involvement)).ti,ab.
11	or/6-10
12	qualitative research/
13	exp interview/
14	exp questionnaire/
15	health care survey/
16	(qualitative or interview* or focus group* or theme* or questionnaire* or survey*).ti,ab.
17	or/12-16
18	11 and 17
19	5 and 18

2 **Cochrane search terms**

#1	[mh "blood transfusion"]
#2	transfus*:ti,ab
#3	(hemotransfus* or haemotransfus*):ti,ab
#4	((blood near/2 (management or administ* or component*)) or blood support):ti,ab
#5	{or #1-#4}
#6	[mh ^"patient acceptance of health care"]
#7	[mh "patient satisfaction"]
#8	[mh "consumer satisfaction"]
#9	[mh ^"personal satisfaction"]

#10	[mh ^"patient education as topic"]
#11	(information* near/3 (patient* or need* or requirement* or support* or seek* or access* or disseminat*)):ti,ab
#12	((client* or patient* or user* or carer* or consumer* or customer* or famil* or parent* or father* or mother*) near/2 (attitud* or priorit* or perception* or preferen* or expectation* or choice* or perspective* or view* or satisfact* or inform* or experience or experiences or opinion* or knowledge or awareness or misconception* or understanding or misunderstanding or concern* or belief* or feeling* or acceptance or need* or requirement* or support* or communication* or involvement)):ti,ab
#13	{or #6-#12}
#14	#5 and #13
#15	[mh ^"qualitative research"]
#16	[mh "interviews as topic"]
#17	[mh questionnaires]
#18	[mh ^"health care surveys"]
#19	(qualitative or interview* or focus group* or theme* or questionnaire* or survey*):ti,ab
#20	{or #15-#19}
#21	#14 and #20

1 **CINAHL search terms**

S1	(mh "blood transfusion+")
S2	transfus* or hemotransfus* or haemotransfus*
S3	((blood n2 (management or administ* or component*)) or blood support)
S4	S1 or S2 or S3
S5	PT anecdote or PT audiovisual or PT bibliography or PT biography or PT book or PT book review or PT brief item or PT cartoon or PT commentary or PT computer program or PT editorial or PT games or PT glossary or PT historical material or PT interview or PT letter or PT listservs or PT masters thesis or PT obituary or PT pamphlet or PT pamphlet chapter or PT pictorial or PT poetry or PT proceedings or PT “questions and answers” or PT response or PT software or PT teaching materials or PT website
S6	S4 not S5
S7	(mh "consumer satisfaction+") or (mh "patient education+") or (mh "personal satisfaction")
S8	(information* n3 (patient* or need* or requirement* or support* or seek* or access* or disseminat*))
S9	((client* or patient* or user* or carer* or consumer* or customer* or famil* or parent* or father* or mother*) n2 (attitud* or priorit* or perception* or preferen* or expectation* or choice* or perspective* or view* or satisfact* or inform* or experience or experiences or opinion* or knowledge or awareness or misconception* or understanding or misunderstanding or concern* or belief* or feeling* or acceptance or need* or requirement* or support* or communication* or involvement))
S10	S7 or S8 or S9
S11	(mh "qualitative studies+") or (mh "interviews+") or (mh "focus groups") or (mh "surveys") or (mh "questionnaires+")
S12	(qualitative or interview* or focus group* or theme* or questionnaire* or survey*)
S13	S11 or S12
S14	S10 and S13
S15	S6 and S14

2 **PsycINFO search terms**

1	blood transfusion/

2	transfus*.ti,ab.
3	(hemotransfus* or haemotransfus*).ti,ab.
4	((blood adj2 (management or administ*5 or component*1)) or blood support).ti,ab.
5	or/1-4
6	client education/
7	health education/
8	exp client attitudes/
9	consumer satisfaction/ or client satisfaction/
10	(information* adj3 (patient* or need* or requirement* or support* or seek* or access* or disseminat*)).ti,ab.
11	((client* or patient* or user* or carer* or consumer* or customer* or famil* or parent* or father* or mother*) adj2 (attitud* or priorit* or perception* or preferen* or expectation* or choice* or perspective* or view* or satisfact* or inform* or experience or experiences or opinion* or knowledge or awareness or misconception* or understanding or misunderstanding or concern* or belief* or feeling* or acceptance or need* or requirement* or support* or communication* or involvement)).ti,ab.
12	or/6-11
13	5 and 12

G.4 Health economics searches

G.4.1 Health economic reviews

Economic searches were conducted in Medline, Embase, HEED and CRD for NHS EED and HTA.

Population	Intervention or exposure	Comparison	Study design filters	Date parameters and other limits
Transfusion	n/a	n/a	The following filters were used in Medline and Embase only: HE	See Table 22 English only Medline and Embase were searched from 2012 onwards, all other databases from their date of inception No new studies were added to HEED after July 2014, and the database was taken offline in January 2015

Medline search terms

1	exp blood transfusion/
2	((blood or red cell or rbc or platelet* or plasma or ffp or cryoprecipitate or prothrombin) adj3 (transfus* or retransfus* or therap*)).ti,ab.
3	(hemotransfus* or haemotransfus*).ti,ab.
4	((blood adj2 (management or administ*5 or component*1)) or blood support).ti,ab.
5	or/1-4

Embase search terms

1	exp *blood transfusion/
2	((blood or red cell or rbc or platelet* or plasma or ffp or cryoprecipitate or prothrombin) adj3 (transfus* or retransfus* or therap*)).ti,ab.
3	(hemotransfus* or haemotransfus*).ti,ab.
4	((blood adj2 (management or administ*5 or component*1)) or blood support).ti,ab.
5	or/1-4

CRD search terms

#1	mesh descriptor blood transfusion explode all trees in NHSEED,HTA
#2	(((blood or red cell or RBC or platelet* or plasma or ffp or cryoprecipitate or prothrombin) adj3 (transfus* or retransfus* or therap*))) in NHSEED, HTA
#3	((hemotransfus* or haemotransfus*)) in NHSEED, HTA
#4	(blood adj2 (management or administ* or component*)) OR (blood support) in NHSEED, HTA
#5	#1 or #2 or #3 or #4

HEED search terms

1	ax=blood or red cell or rbc or platelet* or plasma or ffp or cryoprecipitate or prothrombin
2	ax=transfus* or retransfus*
3	cs=1 and 2
4	ax=hemotransfus* or haemotransfus*
5	ax=blood management
6	ax=blood support
7	cs=3 or 4 or 5 or 6

G.4.2 Quality of life reviews

Quality of life searches were conducted in Medline and Embase.

Population	Intervention or exposure	Comparison	Study design filters	Date parameters and other limits
Transfusion	n/a	n/a	The following filters were used in Medline and Embase only: QOL	See Table 22 English only Exclusion filter applied in Medline and Embase

Medline search terms

1	exp blood transfusion/
2	((blood or red cell or rbc or platelet* or plasma or ffp or cryoprecipitate or prothrombin) adj3 (transfus* or retransfus* or therap*)).ti,ab.
3	(hemotransfus* or haemotransfus*).ti,ab.
4	((blood adj2 (management or administ*5 or component*1)) or blood support).ti,ab.
5	or/1-4

Embase search terms

1	exp *blood transfusion/
2	((blood or red cell or rbc or platelet* or plasma or ffp or cryoprecipitate or prothrombin) adj3 (transfus* or retransfus* or therap*)).ti,ab.
3	(hemotransfus* or haemotransfus*).ti,ab.

4	((blood adj2 (management or administ*5 or component*1)) or blood support).ti,ab.
5	or/1-4

1

References

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2 Henry DA, Carless PA, Moxey AJ, O'Connell D, Stokes BJ, Fergusson DA et al. Anti-fibrinolytic use for minimising perioperative allogeneic blood transfusion. Cochrane Database of Systematic Reviews. 2011; Issue 3:CD001886

3 National Institute for Health and Clinical Excellence. The guidelines manual. London: National Institute for Health and Clinical Excellence; 2012. Available from: http://publications.nice.org.uk/the-guidelines-manual-pmg6/