

PAPER C

A SUMMARY OF WORK BY THE SYSTEMATIC REVIEW INITIATIVE : 2012/13

The Systematic Review Initiative was established in 2002, following concern about the lack of a supporting infrastructure for the development of the evidence base for transfusion in England. The need for an evidence base had been highlighted in the successive 'Better Blood Transfusion' Health Service Circulars. In the second of these, 'systematic review and research into the clinical and cost-effectiveness of transfusion practice including alternatives to donor transfusion' was included as a recommendation that required specific work. In the third, a specific objective was to "increase the evidence base for transfusion practice".

The Systematic Review Initiative (SRI) is based in Oxford and has a remit to perform systematic reviews of the literature covering randomised trials in transfusion medicine. Approximately half of the work of the SRI is undertaken in collaboration with The Cochrane Collaboration. The SRI was initially funded by the NBA Trust Funds but since 2005 the SRI has been funded through the blood pricing mechanism. The SRI has one full time and four part time core members of staff. All other staff members (for full details please see Appendix 4) contribute a set number of hours on a weekly basis to the SRI.

EXECUTIVE SUMMARY

The focus of our work over the last year has been to complete the large number of reviews that were in progress at the 2012 Steering Group meeting and to pursue the development of our Transfusion Evidence Library (TEL).

In 2012/13

- three systematic reviews were completed and published;
- five additional publications were completed and published;
- five systematic reviews are currently undergoing the peer review process;
- we explored the impact of all our published reviews (PAPER D);
- fourteen systematic reviews are ongoing, (PAPER E), of which five are new this year and six are in the final stages of being written up ahead of submission for peer review;
- we began the process of redeveloping the Transfusion Evidence Library with a commercial partner: Evidentia Publishing;
- the Transfusion Evidence Library now contains references to 945 high-quality transfusion medicine systematic reviews, plus 1566 fully indexed, hand searched randomised controlled trials;
- we have begun a working relationship with the Centre for Statistics in Medicine, Oxford.

ACTIVITY OF THE SYSTEMATIC REVIEW INITIATIVE: 2012-13

1. Systematic Reviews

Published 2012-2013- see appendix 1 for full citation details.

Systematic Reviews

- A systematic review of the effect of red blood cell transfusion on mortality: evidence from large-scale observational studies published between 2006 and 2010. *BMJ Open* 2013 May 2; 3(5).
- Pathogen reduced platelets for the prevention of bleeding. *Cochrane Database of Systematic Reviews: issue 2013: Issue 3.*
- What factors lead to deferral of blood donors due to failure to meet Hb standards? A systematic review of longitudinal studies. *Transfusion Medicine (in press). Accepted for publication: May 2013.*

Associated Papers

- Bone marrow stem cell treatment for ischemic heart disease patients with no option for revascularization: a systematic review and meta analysis. *PloS One. Accepted for publication April 2013.*
- How we decide when a neonate needs a transfusion. *British Journal of Haematology* 2013 Feb; 160(4):421-33.
- How to further develop the evidence base for Transfusion Medicine. *Blood Transfusion* 2012; 10:436-439
- Long-term effects of autologous bone marrow stem cell treatment in acute myocardial infarction: factors that may influence outcomes. *PLoS One. 2012;7(5):e37373*
- The challenges of measuring bleeding outcomes in clinical trials of platelet transfusions. *Transfusion* 2013; Jan 10 doi: 10.1111/trf.12058. [Epub ahead of print]

Currently undergoing peer review

- Antifibrinolytics for the prevention of bleeding in patients with haematological malignancies (Cochrane: Haematological Malignancies Group).
- Does bleeding affect patient related outcome measures in patients with myelodysplasia or haematological malignancies? (Transfusion)
- Desferrioxamine mesylate for managing transfusional iron overload in people with transfusion-dependent thalassaemia [update]. (Cochrane: Cystic Fibrosis & Genetic Diseases Group).
- Oral deferiprone for iron chelation in people with thalassaemia [update]. (Cochrane: Cystic Fibrosis & Genetic Diseases Group).
- The use of stem cells as treatment for chronic heart failure. (Cochrane Heart Group).

Ongoing through 2012-13: for further details see Paper E.

Key: * = Started 2012/2013 ** = In the final stages of being written up.

- Age of blood – efficacy and safety of fresher versus older red blood cells across all clinical conditions. (Cochrane: Injuries Group).*
- Antifibrinolytics for the prophylaxis of variceal haemorrhage in patients with liver cirrhosis. (Cochrane Hepato-Billary Group). *
- Effectiveness of red cell transfusion support for patients with hip fracture – a systematic review. (Cochrane Bone, Joint & Muscle Trauma Group).**
- Fresh frozen plasma for cardiovascular surgery (Cochrane Heart Group).
- Intracranial haemorrhage in haematology patients receiving myeloblative chemotherapy or stem cell transplantation. **
- Iron supplementation (oral and/ or parenteral) for iron deficiency and/ or anaemia in blood donors. (Cochrane Injuries Group).**
- Patient Blood Management: an update of the National Blood Authority, Australia Module 1 guidelines.*
- POTS 5: Interventions to reduce wrong blood in tube (WBIT) errors in transfusion.**
- Platelets in haematological malignancy: (Cochrane: Haematological Malignancies Group).*
 - Platelets vs. placebo;
 - Platelets: prophylactic vs. therapeutic;
 - Platelets: dose A vs. dose B;
 - Platelets: prophylactic vs. alternative agents.
- Pro-coagulant haemostatic factors for the prevention and treatment of bleeding in patients without haemophilia. (Cochrane Injuries Group).
- Red blood cell transfusion for patients undergoing surgery for congenital heart disease. (Cochrane Heart Group).**
- Restrictive versus liberal red blood cell transfusion triggers for patients with a haematological malignancy treated with intensive chemotherapy and/or stem cell transplantation. (Cochrane Haematological Malignancies Group).*
- Reporting of “longer term” harms data in randomised controlled trials of blood transfusion.**
- The evidence for the effectiveness and safety of mesenchymal stromal cells in treating GVHD, transplant rejection and autoimmune disease (principally Crohn’s disease). (Cochrane Haematological Malignancies Group).

2. Searching Activities

a. Hand searching

Since 2006 we have only undertaken the prospective hand searching of conference abstracts, and since 2008 have retrieved only those abstracts addressing areas within the SRI Group scope. See Appendix 2 for a list of publications hand searched. The findings of this hand searching provide

an excellent resource for people interested in the practice of transfusion medicine. An in-house database of all RCTs, systematic reviews (SRs) and other relevant studies identified from our hand searching currently contains 4560 entries [3772 RCTs, 413 CCTs and 376 SRs]. Details of all SRs and RCTs identified through hand searching have been indexed and are now available on the Transfusion Evidence Library (www.transfusionevidencelibrary.com). Despite the plan stated in the Steering Group Paper C 2011 for the SRI entirely to cease handsearching from January 2011, the addition of conference proceedings to EMBASE from mid-2009 onwards has proved slow and unreliable. As a result, the handsearching of several transfusion-related conference proceedings has been continued by the SRI Assistant Information Specialist for abstracts of SRs and RCTs relevant to our scope, with the results added to the Transfusion Evidence Library.

b. Additional Searching

The information science workload continues to grow. One aspect of this workload is updating search results while a review is in preparation. Our policy has always been to run a full search at the beginning of the review process and another full search close to expected submission. Frequently Carolyn has been running 2 or 3 additional searches during the course of the review preparation. During the past year, Carolyn has been encouraging review authors to set up PubMed auto alerts to highlight any new studies published during the course of the review so that only two full searches per review are required.

In addition to the comprehensive searching undertaken for all in-house systematic reviews, the SRI (through Carolyn) acts as an occasional resource for individuals/ research groups wanting to undertake searching on a given topic by developing and amending search strategies, running the searches on a wide range of relevant databases and screening the hits generated for relevance to the given topic. During 2012/13 Carolyn devised and/ or updated the search strategies and performed searches for the following:

- Critical Care Guideline: search strategies & searches run (BCSH)
- WHO Global Blood Safety & Availability: search consultancy (WHO)
- Paediatric & Neonate Guideline: search strategies & searches run (BCSH)
- Blood Donation & Haemoglobin Levels: DTA search consultancy (PenTAG)
- Anticoagulation & Head Injury: search strategies & full search for systematic review (ORH Trust)
- Adverse events post-RBC transfusion in Neonates: search consultancy (Canadian Blood Services)

3. The Transfusion Evidence Library.

a. Re-development

In January 2013, our funders the UK Blood Forum agreed that we could seek a commercial partner for the re-development of the Transfusion Evidence Library. During the summer of 2012 we had

had discussions with two companies and the advantages and disadvantages of working with these or staying with our current provider were presented in a business case to the UK Forum in September 2012. Agreement was given for us to work with Evidentia Publishing, a company specialising in developing, marketing and selling bespoke electronic specialist libraries. Those involved with this company have seventeen years experience in the electronic evidence market having worked for Wolters Klower (Ovid) and other similar companies. To date contracts have been signed and a new Transfusion Evidence Library is being developed with a planned launch date for August 2013.

The benefits of working with Evidentia are twofold: increased functionality and the opportunity to market our library internationally. The library will be made freely available to UK blood service staff and the wider NHS, but will be sold, through Evidentia to academic institutions and professional societies within the UK. Internationally, it will be marketed and sold to health services., professional societies, blood transfusion organisations, academic institutions and individuals. We are working with Evidentia Publishing to get endorsements by specific agencies and to identify an appropriate marketing strategy.

At the launch of the library, it will contain:

- all systematic reviews in transfusion medicine, that meet our inclusion criteria;
- transfusion medicine relevant randomised controlled trials from 2002 onwards;
- the results of our ongoing hand searching project

An ongoing project will be to identify transfusion medicine relevant randomised controlled trials, published pre 2002 (and not already identified from our handsearching project).

b. Content

Currently, the Transfusion Evidence Library contains all high quality systematic reviews (945 at June 2013) relevant to transfusion medicine and is updated monthly. It also contains over 1,500 randomised controlled trials that have been hand searched from journals and conference proceedings from 1980 onwards by the SRI, which continue to be added throughout the year.

4. Links with groups outside the NHSBT

We have continued to develop the national and international links established over the previous years during 2011/12. This has predominantly been collaboration on systematic reviews:

- Sandra Gray, Douglas Watson and Susan Cottrell from the SNBTS Better Blood Transfusion Group and Dr Toby Eyre, Haematology Registrar, Oxford (POTS 5: wrong blood in tube);
- Dr Liz Glidewell, a psychologist and Debbie Pinchon, a transfusion practitioner (bleeding and patient related outcomes);

- Dr Kirstin Wilkinson, a Consultant Cardiac Anaesthetist (red blood cell and congenital heart failure review);
- Dr Richard Gregg, Haematology Registrar, Birmingham (fresher versus older red blood cells);
- Dr Douglas Wardrop, Haematology Registrar, Oxford (anti-fibrinolytics for the prevention of bleeding in patients with haematological malignancies);
- Drs Clare Pulford and Sarah Cook, Consultant Physician, Trauma/ Geratology and Registrar in Geriatrics, Oxford and Dr Ali Shokoohi, Haematology Locum Consultant, Bath (hip fracture);
- Dr Ravinder Sandu, Cardiac Registrar, Liverpool (FFP for cardiovascular surgery);
- Drs Erica Wood, Sunelle Englebrecht and Ieva Oozolins and colleagues, Monash University, Melbourne, Australia (Patient Blood Management);
- Drs Graham Barker and Jez Fabes, Intensivist Registrars, Oxford and London (prohaemostatic coagulant factors);
- Drs Dean Fergusson, Alan Tinmouth and Jason Tay, Canada (transfusion triggers for patients with a haematological malignancy);
- Graham Smith, Blood Transfusion Service Manager, Barnet and Chase Farm Hospital (iron supplementation in donors& donor deferral);
- Ly-Mee Yu and Omar Omar, senior statisticians at the Centre for Statistics in Medicine, Oxford (observational studies of the use of red blood cell transfusion).

We have also continued our relationship with the 'International Collaboration for the Development, Implementation and Evaluation of Transfusion Medicine Guidelines' in Canada with the view to communicating ideas and sharing best practice in the transfusion medicine research field.

5. Talks and Presentations

Over the last year, members of, and reviewers within the SRI have been asked to give talks and presentations at national and international conferences. See appendix 3 for a full list of talks, presentations and conference abstracts.

6. Other activities

- We have made contact with the lead authors(s) of all our published reviews in a bid to assess the impact of these reviews. The results of these contacts are summarised in PAPER D.

- Our relationship with the UK Cochrane Centre ended, by mutual consent on 31 December 2013. Since 1 January 2013 we have been working with the Centre for Statistics in Medicine to provide review methodology and statistical support. Fortunately, Marialena Trivella who had been providing this support through the UK Cochrane Centre since January 2012 has continued to seamlessly provide this support through the transition in her new role with the Centre for Statistics in medicine.
- Since early 2012 we have been registering all non-Cochrane systematic reviews on Prospero, an International prospective register of systematic reviews developed by the Centre for reviews and Dissemination in York in collaboration with an advisory group and following an international consultation.

7. Where next - work plan for 2013/14

To accompany this report there is an additional paper which will be discussed at the SRI Steering Group meeting:

PAPER E) A summary of work activities for 2013/14.

APPENDIX 1: SRI Publications 2012-2013

Butler C, Doree C, Estcourt LJ, Trivella M, Hopewell S, Brunskill SJ, Stanworth S, Murphy MF.

Pathogen reduced platelets for the prevention of bleeding.

Cochrane Database of Systematic Reviews: 2013 Mar 28;3:CD009072.

Clifford DM, Fisher SA, Brunskill SJ, Doree C, Mathur A, Clarke MJ, Watt SM, Martin-Rendon E.

Long-term effects of autologous bone marrow stem cell treatment in acute myocardial infarction: factors that may influence outcomes. .

PLoS One; 2012; 7(5): e7373

Estcourt LJ, Heddle N, Kaufman R, McCullough J, Murphy MF, Slichter S, Wood EM, Stanworth SJ; Biomedical Excellence for safer Transfusion (BEST) Collaborative.

The challenges of measuring bleeding outcomes in clinical trials of platelet transfusions.

Transfusion 2013 Jan 10 doi: 10.1111/trf.12058. [Epub ahead of print]

Fisher SA, Doree C, Brunskill SJ, Mathur A, Martin-Rendon E.

Bone marrow stem cell treatment for ischaemic heart disease patients with no option for revascularization: a systematic review and meta analysis.

PloS One. Accepted for publication April 2013.

Hopewell S, Omar O, Hyde C, Yu LM, Murphy MF.

A systematic review of the effect of red blood cell transfusion on mortality: evidence from large-scale observational studies published between 2006 and 2010.

BMJ Open 2013; May 2; 3(5).

Murphy MF, Brunskill S, Estcourt L, Stanworth S, Doree C.

How to further develop the evidence base for Transfusion Medicine.

Blood Transfusion 2012; 10:436-439

Smith G, Fisher SA, Doree C, Roberts DJ.

A systematic review of factors associated with the deferral of donors failing to meet low haemoglobin thresholds

Transfusion Medicine (in press). Accepted for publication: May 2013.

Venkatesh V, Khan R, Curly A, New H, Stanworth S.

How we decide when a neonate needs a transfusion.

British Journal of Haematology 2013 Feb;160(4):421-33.

APPENDIX 2: Journals and Conference Abstracts Hand searched by the SRI: June 2013

Year 1 st published	Years to be hand searched	Years completed
CONFERENCE ABSTRACTS		
AABB: AMERICAN ASSOCIATION OF BLOOD BANKS [IN TRANSFUSION] [1948: 1 ST CONFERENCE]	1980 – 2010	COMPLETED: 1980 – 2010
ASBMT: AMERICAN SOCIETY FOR BLOOD AND MARROW TRANSPLANTATION (BMT TANDEM MEETINGS) [ONLINE]	2010 – 2010	COMPLETED : 2010
ASH: AMERICAN SOCIETY OF HEMATOLOGY [IN BLOOD] [1958[?]: 1 ST CONFERENCE]	1958 – 2011	COMPLETED 1986 - 2011 (1958-1985 TO BE HANDSEARCHED BY HAEM MALIGNANCIES CRG)
BBTS: BRITISH BLOOD TRANSFUSION SOCIETY [IN TRANSFUSION MEDICINE] [1983: 1 ST CONFERENCE]	1990 – 2010	COMPLETED 1988, 1990 – 2010
BSH: BRITISH SOCIETY OF HAEMATOLOGY [IN BJH]	1993 – 2013	COMPLETED: 1993 – 2012
DGTI: GERMAN SOCIETY FOR TRANSFUSION MEDICINE AND IMMUNOHEMATOLOGY CONGRESS [IN VOX SANGUINIS]	2005 – 2010	COMPLETED: 2010
EBMT: EUROPEAN GROUP FOR BLOOD & BONE MARROW TRANSPLANTATION (IN BONE MARROW TRANSPLANTATION)	1997 – 2010	COMPLETED 1997 - 2010
EHA: EUROPEAN HEMATOLOGY ASSOCIATION [IN HAEMATOLOGICAL] [1994: 1 ST CONFERENCE]	1994 - 2012	COMPLETED: 1994 - 2012
HSANZ: AUSTRALIA & NZ COMBINED ANNUAL SCIENTIFIC MEETING [ONLINE]	1999 – 2012	COMPLETED 1999 - 2011
ISBT: INTERNATIONAL [IN VOX SANG.] [1950: 1 ST CONFERENCE - BIENNIAL]	1994 – 2012	COMPLETED 1988, 1994 – 2012
ISBT: REGIONAL CONGRESS, EUROPE [IN VOX SANGUINIS - BIENNIAL]	2005 – 2009	COMPLETED: 2005-2009
ISBT: REGIONAL CONGRESS, ASIA [IN VOX SANGUINIS - BIENNIAL]	2005 – 2011	COMPLETED: 2005-2011
ISTH: INTERNATIONAL SOCIETY ON THROMBOSIS AND HAEMOSTASIS [ONLINE- BIENNIAL]	2007 – 2011	COMPLETED: 2007-2011
NATA: NETWORK FOR THE ADVANCEMENT OF TRANSFUSION ALTERNATIVES [ONLINE]	2004 – 2013	COMPLETED: 2004 - 2011

APPENDIX 3: Talks, presentations and abstracts from the SRI (2012- 13).

SUBJECT	TO WHOM	DATE
TALKS AND PRESENTATIONS		
Stem cells for patients with ischaemic heart disease.	NHS Blood and Transplant Research and Development Conference.	September 2012 [Sheila Fisher]
Using platelets in Haematology Patients: New Studies	British Blood Transfusion Society [BBTS]	September 2012 [Lise Estcourt]
Challenges of changing transfusion practice.	Transfusion Conference	November 2012 [Mike Murphy]
Platelets: past, present and future.	BBTS HOT Sig meeting	May 2013 [Lise Estcourt]
CONFERENCE ABSTRACTS		
Evidence for safety and efficacy of mesenchymal stromal cells (MSC) for treating immune-mediated inflammation post-transplantation and in autoimmunity.	NHS Blood and Transplant Research and Development Conference.	September 2012 [John Girdlestone]
Interventions to reduce sampling errors in transfusions: a systematic review.	British Blood Transfusion Society [BBTS]	September 2012 [Douglas Watson]
Does bleeding affect patient-reported outcome measures in patients with myelodysplasia (MDS) or haematological malignancies? A systematic review.	3 rd Quality of Life Symptom Research and Patient Reported Outcomes in Cancer Clinical Trials Conference: 17-19 October 2012.	October 2012 [Lise Estcourt]
Anti-fibrinolytics (lysine analogues) for the prevention of bleeding in patients with haematological disorders: a systematic review.	American Society of Haematology [ASH]	December 2012 [Douglas Wardrop]

APPENDIX 4: Current SRI Staff: June 2013

Funding Streams

SRI core funding: National Commissioning Group

NHSBT core funding

NIHR funded posts