PAPER C: SRI outcome and Impact report for September 2017 to November 2018

EXECUTIVE SUMMARY. Since September 2017: Fifteen systematic reviews were completed and published; Eight further systematic reviews are completed and undergoing peer review (see PAPER G). We successfully completed (on time and on budget) our first NIHR Cochrane Programme Grant: "Safe and Appropriate Use of Blood Components". We were successful in our application for a second NIHR Cochrane programme grant: "Alternatives and adjuncts to transfusion to prevent and treat bleeding in people who are at risk of serious or life-threatening bleeding "and have appointed four new members of staff to complete this work. We completed a James Lind Alliance Priority Setting Partnership and are in the process of disseminating the findings - a 'top ten' of research priority questions (see PAPER F). We updated our prioritisation strategy to include the questions derived from the James Lind Alliance Priority Setting Partnership project (see PAPER I). We launched the Stem Cell Evidence Library [http://www.stemcellevidence.com/] on 29th March 2018 with development monies awarded through the Oxford Biomedical Research Council for 3 years to March 2020 and staffing and other costs from the UK Forum through to March 2022. ☐ The Transfusion Evidence Library [http://www.transfusionevidencelibrary.com/] now contains references to over 1,600 high-quality transfusion medicine systematic reviews and over 7,000 fully indexed randomised controlled trials; Use are continuing to work towards 'free at the point of access' for the Transfusion Evidence Library and the Stem Cell Evidence Library which will require sponsorship from external sources (see PAPER H2). We launched Twitter accounts for the group and electronic libraries [@TransfusionLib, @sritransfusion and @stemcell] to increase our dissemination activities. On request, we have undertaken specialist search activities for professional societies [for example BSH guidelines] and received payment for this work. We have appointed four new steering group members. Two SRI members [Susan Brunskill and Lise Estcourt] were to join NHSBT R&D's new Patient and Public Advisory Group. We have begun talks with Professor Rafael Perera from University of Oxford's Nuffield Department of Primary Care Health Sciences Medical Sciences Division with regards to providing statistical support on an as-and-when basis for the group.

Section	Our Evidence
Publications since September 1 2017 [last face to face SRI steering group meeting]; listed alphabetically by first author.	Carson J, Stanworth S , Alexander JH, Roubinian N, Fergusson DA, Triulzi DJ, Goodman SG, Rao SV, Doree C , Hebert PC. Clinical trials evaluating red blood cell transfusion thresholds: An updated systematic review and with additional focus on patients with cardiovascular disease. <i>American Heart Journal</i> 2018: 200; 96-101. https://doi.org/10.1016/j.ahj.2018.04.007
[Authors in bold are members of the SRI]	
* Systematic reviews that were undertaken as part of our NIHR Cochrane programme grant 13/89/09	Estcourt LJ, Malouf R, Doree C, Trivella M, Hopewell S, Birchall J. Prophylactic platelet transfusions prior to surgery for people with a low platelet count. Cochrane Database of Systematic Reviews 2018, Issue 9. Art. No.: CD012779. DOI: 10.1002/14651858.CD012779.pub2. * https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD012779.pub2/full
	Estcourt LJ, Malouf R, Hopewell S, Doree C, Van Veen J. Use of platelet transfusions prior to lumbar punctures or epidural anaesthesia for the prevention of complications in people with thrombocytopenia. <i>Cochrane Database of Systematic Reviews 2018</i> , Issue 4. Art. No.: CD011980. DOI: 10.1002/14651858.CD011980.pub3.* https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD011980.pub3/full
	Estcourt LJ, Malouf R, Murphy M. Pathogen-Reduced Platelets for the Prevention of Bleeding in People of Any Age. JAMA Oncology Clinical Evidence Synopsis; 2018;4(4):571-572 https://jamanetwork.com/journals/jamaoncology/article-abstract/2670375
	Fisher SA, Doree C , Mathur A, Taggert DP, Martin-Rendon E. Cochrane Corner: stem cell therapy for chronic ischaemic heart disease and congestive heart failure. <i>Heart</i> Published Online First: 12 June 2017. doi: 10.1136/heartjnl-2017-311684 http://dx.doi.org/10.1136/heartjnl-2017-311684
	Fortin PM, Fisher SA, Madgwick KV, Trivella M, Hopewell S, Doree C, Estcourt LJ. Interventions for improving adherence to iron chelation therapy in people with sickle cell disease or thalassaemia. <i>Cochrane Database of Systematic Reviews</i> 2018, Issue 5. Art. No.: CD012349. DOI: 10.1002/14651858.CD012349.pub2. https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD012349.pub2/full *
	Fortin PM, Hopewell S, Estcourt LJ. Red blood cell transfusion to treat or prevent complications in sickle cell disease: an overview of Cochrane reviews. <i>Cochrane Database of Systematic Reviews</i> 2018, Issue 8. Art. No.: CD012082. DOI:

10.1002/14651858.CD012082.pub2.

https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD012082.pub2/full *

Huber J, **Stanworth SJ, Doree C,** Trivella M, **Brunskill SJ,** Hopewell S, Wilkinson KL, **Estcourt LJ.** Prophylactic plasma transfusion for patients undergoing non-cardiac surgery (Protocol). *Cochrane Database of Systematic Reviews* 2017, Issue 8. Art. No.: CD012745. DOI: 10.1002/14651858.CD012745.

http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD012745/full *

Estcourt LJ, Malouf R, Doree C, Trivella M, Hopewell S, Birchall J. Prophylactic platelet transfusions prior to surgery for people with a low platelet count (Protocol). Cochrane Database of Systematic Reviews 2017, Issue 9. Art. No.: CD012779. DOI: 10.1002/14651858.CD012779.

https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD012779/full *

Hunt H, Pollock A, Campbell P, **Estcourt L**, Brunton G. An introduction to overviews of reviews: planning a relevant research question and objective for an overview. *Systematic Reviews* 2018; 7:39 https://doi.org/10.1186/s13643-018-0695-8

McQuilten ZK, Crighton G, **Brunskill S**, Morison JK, Richter TH, Waters N, **Murphy MF**, Wood EM. Optimal Dose, Timing and Ratio of Blood Products in Massive Transfusion: Results from a Systematic Review. *Transfusion Medicine Reviews* 2018; 32 [1]: 6-15. https://doi.org/10.1016/j.tmrv.2017.06.003

Malouf R, Ashraf A, Hadjinicolaou AV, Doree C, Hopewell S, Estcourt LJ. Comparison of a therapeutic-only versus prophylactic platelet transfusion policy for people with congenital or acquired bone marrow failure disorders. *Cochrane Database of Systematic Reviews* 2018, Issue 5. Art. No.: CD012342. DOI: 10.1002/14651858.CD012342.pub2. https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD012342.pub2/full

Murphy MF, Estcourt LJ, Goodnough LT. Blood transfusion strategies in elderly patients. *Lancet Haematology* 2017 Oct;4(10):e453-e454 https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026(17)30173-4/fulltext

Oakland K, Isherwood J Lahiff C Goldsmith P **Desborough M** Colman KS Guy R Uberoi R **Murphy MF** East JE Hopewell S Jairath V. Diagnostic and therapeutic treatment modalities for acute lower gastrointestinal bleeding: a systematic review. *Endoscopy International Open.* 2017. 5 (10) E959-E973. https://www.thieme-connect.com/DOI/DOI?10.1055/s-0043-117958

	Oakland K, Jairath V, Murphy MF. Advances in transfusion medicine: gastrointestinal bleeding. Transfusion Medicine 2018; 9: 132-139. https://doi.org/10.1111/tme.12446
Collaborations with people outside the SRI. These have been grouped by type of project.	We have collaborated with many clinicians and researchers over the last 14 months. Their names and affiliations are provided here:
	Stem Cell Evidence:
New collaborators this year are identified by an * at the beginning of their details.	Dr Jenny Byrne - Nottingham City Hospital, Nottingham, UK and President of the British Society of Blood and Marrow Transplantation;
, ,	Professor Charles Crawley – Addenbrooke's, Cambridge, UK;
	Dr Rob Danby - Oxford University Hospitals NHS Foundation Trust, UK;
	Dr James Griffin – NHSBT Bristol, UK;
	Dr Andrew Hadley – NHSBT, UK;
	Mr John Muth - Evidentia Publishing, UK;
	Mr Mark Schregardus – Evidentia Publishing, The Netherlands;
	Professor Paresh Vyas – Oxford BRC & University of Oxford, UK;
	NIHR Cochrane Programme Grant
	Cochrane Heart Group [co-applicant];
	Cochrane Injuries Group [co-applicant];
	Cochrane Vascular Group;
	Dr Nikki Curry - Oxford University Hospitals NHS Foundation Trust, UK [co-applicant];
	Dr Neil Hawkins - Cochrane Complex Reviews Unit, UK;
	Professor Nicky Welton – University of Bristol;
	Dr Kirstin Williamson - University Hospital Southampton, UK [co-applicant];
	Dr Olivia Wu - Cochrane Complex Reviews Unit, UK;
	Systematic review collaborators:
	Professor Doug Altman - Centre for Statistics in Medicine, University of Oxford, Oxford, UK;
	Dr Asma Ashraf - University of Newcastle, Waratah, Australia;
	*Dr Janet Birchall – Medical Director, Welsh Blood Service, UK;
	*Dr Catherine Booth – Barts Health NHS Trust, UK;
	Dr Jeff Carson - Rutgers Robert Wood Johnson Medical School, New Brunswick, New Jersey, USA;

Dr Katherine Colman - Monash University Medical School, Melbourne, Australia Dr Gemma Crighton - Monash University, Melbourne, Australia; Dr Nikki Curry - Oxford University Hospitals NHS Foundation Trust, UK; Dr Antony Cutler - NHSBT, Cambridge, UK and University of Cambridge, UK Dr Ross Davenport - Barts and the London School of Medicine and Dentistry, Queen Mary University of London, UK; *Paula Dhiman – University of Oxford, Oxford, UK; Dr Jez Fabes - Oxford University Hospitals NHS Foundation Trust, UK; Dr Dean Fergusson - Ottawa Hospital Research Institute, Canada; Dr Betty Gratition - Oxford University Medical School, University of Oxford, Oxford, UK; Dr John Girdlestone - NHSBT, UK; *Professor L Tim Goodnough – Stanford Blood Centre, USA; *Dr Laura Green - NHSBT & Barts Health NHS Trust, UK; *Kennedy Hao – Medical Student, University of Toronto, Canada; Dr Andreas Hadjinicolaou - University of Oxford, UK; Dr Stephen Hibbs - University of Oxford, UK; Dr Paul C Hebert - Centre de recherché du Centre hospitalier de l'Université de Montréal, Montreal, QC, Canada; Dr Sally Hopewell –University of Oxford, Oxford, UK; Ms Harriet Hunt - University of Exeter Medical School, Exeter, UK; Dr Jonathan Huber - University Hospital Southampton, UK; Dr Abi Lamikanra - NHSBT, & University of Oxford, Oxford, UK; Dr Lani Lieberman - University Health Network & University of Toronto, Canada; *Dr Ed Litton - The University of Western Australia, Perth, Australia; *Jo Mccullagh - Barts Health NHS Trust, UK; Mrs Karen Madgwick - North Middlesex University Hospitals NHS Trust, London, UK; Dr Enca Martin-Rendon – University of Oxford, Oxford, UK; Professor Anthony Mathur - Barts and the Royal London, UK; Dr Stuart McKechnie - Oxford University Hospitals NHS Foundation Trust, UK; Dr Zoe McQuilten - Monash University, Melbourne, Australia; *Dr Rebecca Mellor - NHSBT, UK; Dr Jessica Morrison - Monash University, Melbourne, Australia; Dr Suzy Morton - NHSBT & University Hospitals Birmingham NHS Foundation Trust, UK; Dr Jack Pottle - Oxford University Hospitals NHS Foundation Trust, UK; Ms Tania Richter – Monash University, Melbourne, Australia;

	Dr N Roubinian - University of California at San Francisco, San Francisco, California, USA;
	Dr Akshay Shah - Oxford University Hospitals NHS Foundation Trust, UK;
	Dr Marialena Trivella - Centre for Statistics in Medicine, University of Oxford, Oxford, UK;
	Dr David Taggert - Oxford University Hospitals NHS Foundation Trust, UK;
	Dr Darryl Triulzi - University of Pittsburgh, Institute for Transfusion Medicine, Pittsburgh, Pennsylvania, USA;
	*Dr Joost Van Veem, Sheffield Haemophilia and Thrombosis Centre, UK;
	Mr Neil Waters - Monash University, Melbourne, Australia;
	Dr Kirstin Williamson - University Hospital Southampton, UK;
	Dr Henna Wong - Oxford University Hospitals NHS Foundation Trust, UK;
	Dr Erica Wood - Monash University, Melbourne, Australia;
	James Lind Alliance, Priority Setting Partnership:
	4 x Patient representatives, support and guidance from the The James Lind Alliance [Beccy Maseo & Caroline Whiting]
	and survey support from John Grant-Casey, NHSBT Oxford, UK.
	Clinical representatives:
	Dr Stephen Hibbs (Core Medical Trainee, London)
	Dr Bill Martin (Royal College of Obstetricians & Gynaecologists)
	Professor Mike Murphy (NHS Blood and Transplant, Oxford)
	Dr Claire Pulford (Acute Medicine/Trauma Geriatrics, OUH Oxford)
	Dr Toby Richards (Vascular Surgery, University College London)
	Professor Tim Walsh (Intensive Care Medicine, Edinburgh)
Further Funding	We made no funding applications between September 2017 and November 2018. We have focused on implementing
	the additional funding which we received in 2017:
	1) NIHR Cochrane Programme Grant: Alternatives to transfusion to prevent and treat bleeding in people who are at
	risk of serious or life-threatening bleeding.
	Grant applicant: Dr Lise Estcourt
	Start date: 1 st June 2018
	The grant is a 3-year grant with maximum funding of £420,000 over the 3 years.
	Proposal: The theme for this grant application is 'Alternatives to transfusion to prevent and treat bleeding in people who
	are at risk of serious or life-threatening bleeding'. The reason for this theme was summarised in our expression of interest:
	"Bleeding remains a serious condition related to surgery, child birth, and trauma. Bleeding accounts for 40% of all trauma

deaths and is the most common cause of maternal death worldwide. In managing patients, it is crucial to stop the source of blood loss. Blood loss may be exacerbated by abnormal blood coagulation and a number of local or systemic adjuvant treatments, or replacement therapies are available. The optimal use of these interventions is poorly understood. NICE guidelines have assessed the use of TXA but did not assess the use of other alternatives to reduce bleeding. They recommend TXA use in all surgery expected to have moderate blood loss. Their analysis and those of other systematic reviews did not differentiate between route (topical, oral or intravenous), timing (before, during, or after surgery), or dose of TXA. Most of the included studies in previous systematic reviews have compared the intervention versus placebo or no treatment. None of the previous systematic reviews have compared the use of different alternatives (e.g. fibrinogen concentrate, fibrin glue, antifibrinolytics, desmopressin) within the same review."

Relationship to SRI priorities and 5-year strategic plan: In our priority setting work thus far, we (the SRI clinical team) identified that this area - Alternatives to transfusion to prevent and treat bleeding in people who are at risk of serious or life-threatening bleeding - was a priority area for future work. However, further standard methodology systematic reviews of the available interventions will not necessarily be able to establish the best treatment, or combination of treatments, to prevent or treat bleeding in people who are at risk of serious bleeding, or death due to bleeding. What is needed is a more complex methodology and this programme grant will enable the performance of network meta-analyses for individual patients' groups to identify the most appropriate management. We do not have the resources to do this work within the SRI, so this programme grant would give us the resources and the access to the required methodological and statistical support, through the Cochrane Complex Reviews Support Unit.

External support for the programme grant:

- Cochrane Complex Reviews Unit oversight on the methodologies that are being used, review of the protocols and final manuscripts;
- Professor Nicky Welton, University of Bristol training on Network Meta-Analysis methodologies, advice and support on these methods for the duration of the grant;
- Specialist clinicians
- Cochrane Injuries, Vascular and Heart Groups.

Staffing: During the spring of 2018 we recruited 4 new members of staff [Fixed term for 2 years] whom all started in post during August 2018. They are:

- Clinical Research Fellows [both are full time posts]: Dr Anair Beverly, specialist anaesthetist registrar and Dr Victoria Gibbs orthopaedic surgeon registrar.
- Systematic Reviewers [both are 0.5 WTE posts]: Rita Solanki and Dr Giok Ong.

Grant Co-applicants: The guidance for this grant application requests that there is at least one NHS clinician as a coapplicant. The following are the current co-applicants:

Dr Simon Stanworth - Consultant Haematologist, NHSBT;

Dr Nikki Curry - Consultant Haematologist, Oxford Haemophilia and Thrombosis Centre;

Dr Kirstin Wilkinson - Consultant Cardiac Anaesthetist, Southampton General Hospital;

Dr Juan-Pablo Casas - Co-ordinating Editor Cochrane Heart Group & Professor in Clinical Epidemiology and Informatic, University College London.

Susan Brunskill - SRI manager and line manager for any programme grant staff.

2) Stem Cell Evidence Project

Grant applicant: Mike Murphy and Susan Brunskill on behalf of the SRI Start date: The project has started but funds are required to keep it going.

Budget: £290,834.42 over 5 years.

Funding secured:

- a) We received £10,000 towards set up costs in January 2017. This money was used [for the 2017 calendar year] to increase our current Assistant Information Specialist's hours from 15 to 25 per week.
- b) We were partially successful with our bid to Oxford BioMedical Research Centre: they will provide £25,000 per year for 3 years, from April 1st, 2017 to March 2020. This money is being used for our annual technical development costs: initial development and testing and ongoing maintenance and development through to March 2020. In 2019, we need to reapply to the Oxford BioMedical Research Centre for years 4 and 5 of the additional bid monies [totalling £50,000].
- c) It was agreed in August 2017 that we would receive a one-off contribution of £25,000 from DTS to enable the recruitment of an additional Assistant Information Specialist for a fixed term of one year. This covered the salary of Chris Cooper, [who was employed with NHSBT between Jan and July 2018] and will be used to pay the salary of Alicia Plaza who is due to start with us on 15th January 2019.
- d) UK Forum agreed in September 2017 that they would support any other costs for the Stem Cell Evidence project over a 4-year period from April 2018 to March 2022. This could amount to £180,834.42 during this timeframe.

Next Destination & Skills

There have been changes to SRI core staff – see organogram [Paper D] for full details.

Three members of staff who worked with SRI during the last year have moved on to new roles during this period:

Patricia Fortin was a systematic reviewer on our first Cochrane Programme grant "Safe and appropriate use of blood components" returned to her native Canada at the end of her contract and is happy in her retirement.

Dr Reem Malouf was a systematic reviewer on our first Cochrane Programme grant "Safe and appropriate use of blood components", working part time with NHSBT until December 2017 has returned to her role as a Health Services Researcher in the National Perinatal Epidemiology Unit at the University of Oxford.

Chris Cooper worked with us for six months as an Assistant Information Specialist with responsibility for our Transfusion Evidence Library. He is now working as an Information Specialist with the homeless charity, CRISIS.

Their publications:

Estcourt LJ, **Malouf R,** Doree C, Trivella M, Hopewell S, Birchall J. Prophylactic platelet transfusions prior to surgery for people with a low platelet count. Cochrane Database of Systematic Reviews 2018, Issue 9. Art. No.: CD012779. DOI: 10.1002/14651858.CD012779.pub2.

https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD012779.pub2/full

Estcourt LJ, **Malouf R**, Hopewell S, Doree C, Van Veen J. Use of platelet transfusions prior to lumbar punctures or epidural anaesthesia for the prevention of complications in people with thrombocytopenia. *Cochrane Database of Systematic Reviews 2018*, Issue 4. Art. No.: CD011980. DOI: 10.1002/14651858.CD011980.pub3. https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD011980.pub3/full

Estcourt LJ, **Malouf R,** Murphy M. Pathogen-Reduced Platelets for the Prevention of Bleeding in People of Any Age. JAMA Oncology Clinical Evidence Synopsis; 2018;4(4):571-572 https://jamanetwork.com/journals/jamaoncology/article-abstract/2670375

Fortin PM, Fisher SA, Madgwick KV, Trivella M, Hopewell S, Doree C, Estcourt LJ. Interventions for improving adherence to iron chelation therapy in people with sickle cell disease or thalassaemia. *Cochrane Database of Systematic Reviews* 2018, Issue 5. Art. No.: CD012349. DOI: 10.1002/14651858.CD012349.pub2. https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD012349.pub2/full

Fortin PM, Hopewell S, Estcourt LJ. Red blood cell transfusion to treat or prevent complications in sickle cell disease: an overview of Cochrane reviews. Cochrane Database of Systematic Reviews 2018, Issue 8. Art. No.: CD012082. DOI: 10.1002/14651858.CD012082.pub2. https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD012082.pub2/full Malouf R, Ashraf A, Hadjinicolaou AV, Doree C, Hopewell S, Estcourt LJ. Comparison of a therapeutic-only versus prophylactic platelet transfusion policy for people with congenital or acquired bone marrow failure disorders. Cochrane Database of Systematic Reviews 2018, Issue 5. Art. No.: CD012342. DOI: 10.1002/14651858.CD012342.pub2. https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD012342.pub2/full **Engagement Activities** Social media activity: We run 3 Twitter accounts, one for each of our electronic libraries and one for the SRI overall. Our activity on these accounts is one of the aspects of our online presence strategy Talks or Presentations: Members of the SRI have given the following talks over the last year: • [Lise Estcourt]: MSc lecture on systematic reviews, University of Bristol 10th November 2017 • [Mike Murphy]: Guidelines and standards for perioperative anaemia, Royal College of Anaesthetists, London, 31st January 2018 • [Lise Estcourt]: Lecture in Utrecht, Netherlands on Patient Blood Management 8th February 2018 • [Mike Murphy]: Implementation of Patient Blood Management (PBM), EBA Consensus Conference on PBM, Frankfurt, 24th April 2018, • [Mike Murphy & Lise Estcourt]: Review of PBM Consensus Conference, NHSBT PBM Team, Birmingham, 8th May 2018 • [Mike Murphy]: Patient Blood Management, Milton Keynes Hospital, 31st July 2018 • [Lise Estcourt]: Platelet research and audits. London deanery teaching 15th August 2018. • [Susan Brunskill]: Research priorities in Blood Donation and Blood Transfusion: James Lind Alliance project at the inaugural NHSBT Patient and Public Advisory Group (PPAG) meeting in Bristol on 25th September 2018. • [Mike Murphy]: Top 10 priorities for research in blood donation and transfusion: outcome of the James Lind Alliance Priority Setting Partnership, British Blood Transfusion Society, Brighton, 5th October 2018 • [Akshay Shah]: INtravenous Iron to Treat Anaemia following CriTical Care (INTACT): Rationale for a feasibility study", presented at Thames Valley and Wessex Regional NIHR CRN Event, 31st October 2018

	 [Akshay Shah]: "Iron in critical illness: a double-edged sword", Oxford Regional Intensive Care Society (ORICS), 14th November 2018 [Lise Estcourt]: Blood 2018 Brisbane Australia. The combined Annual Scientific Meeting of the: Haematology Society of Australia and New Zealand, Australian and New Zealand Society of Blood Transfusion and Thrombosis and Haemostasis society of Australia and New Zealand. Appropriate platelet transfusions October 21st, 2018 [Lise Estcourt]: Blood 2018 Brisbane Australia. The combined Annual Scientific Meeting of the: Haematology Society of Australia and New Zealand, Australian and New Zealand Society of Blood Transfusion and Thrombosis and Haemostasis society of Australia and New Zealand. Systematic Review Masterclass October 22nd, 2018
	Poster Presentation
	• [Susan Brunskill]: Treatment uncertainties in blood donation and blood transfusion: involvement of patients and donors as well as clinicians at the Cochrane Collaboration annual meeting on 18 th September 2018.
	Provision of training to external collaborators:
	We have provided on-the-project training to all our new [identified by an asterix in the Collaborations section above] collaborators as required. For systematic reviews this included an understanding of the review process and methodology as well as training on how to use Covidence and Review Manager software packages.
Influence on Policy	We recorded the number of citation s [SCOPUS, Science Citation Index and Altmetric Score] for our systematic reviews at November 2018. Please refer to PAPER C1 for this information.
	Guidelines published in 2018 that have been informed by SRI systematic reviews:
	1). Green L, Bolton-Moggs P, Beattie C, Cardigan R, Kallis Y, Stanworth SJ, Thachill J, Zahra S (2018) British Society of Haematology Guidelines on the spectrum of fresh frozen plasma and cryoprecipitate products: their handling and use in various patient groups in the absence of major bleeding. British Journal of Haematology, 181:54-67. https://doi.org/10.1111/bjh.15167
	 Stanworth, S.J., Brunskill, S.J., Hyde, C.J., McClelland, D.B. & Murphy, M.F. (2004) Is fresh frozen plasma clinically effective? A systematic review of randomized controlled trials. <i>British Journal of Haematology</i>, 126, 139–152. Yang, L., Stanworth, S., Hopewell, S., Doree, C. & Murphy, M. (2012) Is fresh-frozen plasma clinically effective? An update of a systematic review of randomized controlled trials. <i>Transfusion</i>, 52, 1673–1686.

- 2) Sibson KR, Biss TT, Furness CL, Grainger JD, Hough RE, Mccartney C, Payne JH, Chalmers EA on behalf of the British Society for Haematology (2018) BSH Guideline: management of thrombotic and haemostatic issues in paediatric malignancy. British Journal of Haematology, 184: 511-525. https://doi.org/10.1111/bjh.15112
 - Estcourt, L., Stanworth, S., Doree, C., Hopewell, S., Murphy, M.F., Tinmouth, A. & Heddle, N. (2012) Prophylactic platelet transfusion for prevention of bleeding in patients with haematological disorders after chemotherapy and stem cell transplantation (Review). *Cochrane Database of Systematic Reviews*, **5**, CD004269.
- 3) Robinson S, Harris A, Atkinson S, Atterbury C, Bolton-Moggs P, Elliott C, Hawkins T, Hazra E, Howell C, New H, Shackleton T, Shreeve K, Taylor C. (2018) The administration of blood components: a British Society for Haematology Guideline. Transfusion Medicine, 28: 3-21. ps://doi.org/10.1111/tme.12481
 - Blest, A., Roberts, M., Murdock, J., Watson, D. & Brunskill, S. (2008) How often should a red blood cell
 administration set be changed while a patient is being transfused? A commentary and review of the
 literature. *Transfusion Medicine*, 18 (2), 121–133
 - Brunskill, S., Thomas, S., Whitmore, E. *et al.* (2012) What is the maximum time that a unit of red blood cells can be safely left out of controlled temperature storage? *Transfusion Medicine Reviews*, **26** (3), 209–223.
 - Murdock, J., Watson, D., Dorée, C., Blest, A., Roberts, M. & Brunskill, S. (2009) Drugs and blood transfusions: Dogma- or evidenced-based practice? *Transfusion Medicine*, **19** (1), 6–15.
 - Watson, D., Murdock, J., Dorée, C., Murphy, M., Roberts, M., Blest, A. & Brunskill, S. (2008) Blood transfusion administration 1 or 2-person checks, which is the safest method? *Transfusion*, **48** (4), 783–789.
- 4) Mak LY, Lau CW, Hui YT, Leung WK (2018). Joint recommendations on management of anaemia in patients with gastrointestinal bleeding in Hong Kong. Hong Kong Medical Journal, 24(4):416-422. DOI: 10.12809/hkmj187348.
 - Odutayo A, Desborough MJR, Trivella M, Stanley AJ, Doree C, Collins GS, Hopewell S, Brunskill SJ, Kahan BC, Logan RA, Bakrun AN, Murphy MF, Jairath V.(2017). Restrictive versus liberal blood transfusion for gastrointestinal bleeding: a systematic review and meta-analysis of randomised controlled trials. The Lancet Gastroenterology & Hepatology 2(5). DOI 10.1016/S2468-1253(17)30054-7.
- 5) Cicchetti A, Coretti S, Sacco F, Rebulla P, Fiore A, Rumi F, Di Bidino R, Urbina LI, Refolo P, Sacchini D, Spagnolo AG, Midolo E, Marano G, Farina B, Pati I, Veropalumbo E, Pupella S, Liumbruno GM

(2018).Budget impact of implementing platelet pathogen reduction into the Italian blood transfusion system. Blood Transfusion 16(6):483-489. doi: 10.2450/2018.0115-18.

• Estcourt LJ, Malouf R, Hopewell S, Trivella M, Doree C, Stanworth SJ, Murphy MF. Pathogen-reduced platelets for the prevention of bleeding. Cochrane Database of Systematic Reviews 2017, Issue 7. Art. No.: CD009072. DOI: 10.1002/14651858.CD009072.pub3.

6) Viberg B, Gundtoft PH, Schønnemann J, Pedersen L, Anderson LR, Titlestad K, Madsen CF, Lauritsen J, Overgaard S (2018). Introduction of national guidelines for restrictive blood transfusion threshold for hip fracture patients—a consecutive cohort study based on complete follow-up in national databases. Journal of Orthopaedic Surgery and Research 13:116 https://doi.org/10.1186/s13018-018-0828-8

- Brunskill SJ, Millette SL, Shokoohi A, Pulford EC, Doree C, Murphy MF, et al. Red blood cell transfusion for people undergoing hip fracture surgery. Cochrane Database Systematic Reviews. 2015;4:CD009699
- Carson JL, Stanworth SJ, Roubinian N, Fergusson DA, Triulzi D, Doree C, et al. Transfusion thresholds and other strategies for guiding allogeneic red blood cell transfusion. Cochrane Database Systematic Reviews. 2016;10:CD002042
- Docherty AB, O'Donnell R, Brunskill S, Trivella M, Doree C, Holst L, et al. Effect of restrictive versus liberal transfusion strategies on outcomes in patients with cardiovascular disease in a non-cardiac surgery setting: systematic review and meta-analysis. BMJ. 2016;352: i1351.

7) Pagano D, Milojevic M, Meestersa MI, Benedetto U, Bolligera D, von Heymanna C, Jeppsson A, Kostera A, Osnabrugge RL, Ranuccia M, Ravna HB, Vonk ABA, Wahba A, Boera C (2017) 2017 EACTS/EACTA Guidelines on patient blood management for adult cardiac surgery The Task Force on Patient Blood Management for Adult Cardiac Surgery of the European Association for Cardio-Thoracic Surgery (EACTS) and the European Association of Cardiothoracic Anaesthesiology (EACTA). European Journal of Cardio-Thoracic Surgery 01–33 https://doi:10.1093/ejcts/ezx325

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- Stanworth SJ, Brunskill SJ, Hyde CJ, McClelland DB, Murphy MF. Is fresh frozen plasma clinically effective? A systematic review of randomized controlled trials. British Journal of Haematology 2004;126:139–52

	 8) Kohli N, Bhaumik S, Jagadesh S, Sales RK, Bates I. (2018). Packed red cells versus whole blood transfusion for severe paediatric anaemia, pregnancy-related anaemia and obstetric bleeding: an analysis of clinical practice guidelines from sub-Saharan Africa and evidence underpinning recommendations. Trop Med Int Health. 2018 Oct 22. doi: 10.1111/tmi.13173. Yang L, Stanworth S, Hopewell S, Doree C, Murphy M. Is fresh-frozen plasma clinically effective? An update of a systematic review of randomized controlled trials. Transfusion. 2012;52(8):1673-86
Research Tools & Methods	NIHR Cochrane programme grant [1]. We completed all 28 reviews by the agreed deadline of 31 st December 2017. However, although all completed, there were 4 reviews that were not published by the end of 2017 primarily because of the Cochrane peer review process. All but one of these reviews has now been published in full. This grant will also be delivered on budget.
	NIHR Cochrane programme grant [2]. We will be using a form of analysis: network meta-analysis that has not been used by the core group before. All working on the programme grant will be attending specific NMA training during the next year. We will receive support from both the Cochrane Complex Reviews Unit and Professor Nicky Welton from the University of Bristol in writing about, performing and analysis network meta-analyses.
	We purchased five individual licences for the software STATA : this package is required to undertake network meta- analyses but can also complement the other systematic review software we have in the department.
	We have started using the software package Covidence for our data extraction activities.
Research Databases & Models	See section below: Software & Technical Products
Intellectual Property & Licensing	Nothing to report. We have talked about this for our electronic libraries, but the only aspect that we could consider would be the database and Evidentia Publishing does not think it is appropriate to apply for intellectual property for the database structure.
Medical Products, Interventions and Clinical Trials	 Clinical Trials that have developed from one of our systematic reviews*: REVIEW: Granulocytes for treating infection [2016]: CLINICAL TRIAL: PROGRES: An observational study of the incidence of infectious episodes eligible for granulocyte transfusion and outcomes. Awarding Body: NHSBT.

- REVIEW Granulocytes for preventing infection [2016]: CLINICAL TRIAL: PROGRES: An observational study of the incidence of infectious episodes eligible for granulocyte transfusion and outcomes. Awarding Body: NHSBT
- REVIEW: Anti-fibrinolytics for the prevention of bleeding in patients with haematological malignancies [2016]: The recent update of this review was referenced in the updated TREATT [An ongoing, international trial "to evaluate anti-fibrinolytic therapy in patients with haematological malignancies] trial documentation.
- REVIEW: Desmopressin for the treatment of platelet dysfunction and reversal of antiplatelet agents [2017]: 2 new CLINICAL TRIALS: (1) DRIVE: a pilot, randomised trial of desmopressin versus placebo prior to procedure in intensive care patients. Awarding Body: NHSBT [ISRCTN12845429] and (2) DASH (desmopressin for reversal of antiplatelet drugs in stroke due to haemorrhage) trial from the National Institute for Health Research, Research for Patient Benefit funding stream Trial aims to start in April 2018.
- REVIEW: Iron supplementation to treat anaemia in adult critical care patients [2016]: 1 new clinical trial: INtravenous Iron to Treat Anaemia following CriTical Care (INTACT): a randomised feasibility study

Clinical Audits that have developed from one of our systematic reviews*:

- *REVIEW:* Is fresh frozen plasma clinically effective? [2012]: National Comparative Audit of FFP and Cryoprecipitate use in children in planning for Spring 2019.
- *REVIEW:* Management of trauma haemorrhage [[2011]: National Comparative Audit of major haemorrhage (all conditions) October 2018.
- REVIEW: Gaps in the evidence for prevention & treatment of maternal anaemia [2012]: National Comparative Audit of maternal anaemia in November 2018

GRANT APPLICATIONs that have developed from one of our systematic reviews*:

• REVIEW: Pro-coagulant haemostatic factors for the prevention and treatment of bleeding in patients without haemophilia [not yet complete] informed a ssuccessful application for a NIHR Cochrane programme grant on "What is the best treatment or combination of treatments to prevent or treat bleeding in people who are at high risk of

	serious bleeding or death due to bleeding?". Grant awarded August 2017: work in the form of network meta- analyses of specific clinical groups (cardiac surgery, trauma) began in the summer of 2018.
	REVIEW: Electronic decision support for the appropriate use of blood [2015] informed a Innovate grant application for a scalable AI platform for blood service demand planning. NHSBT/Kortical. £1.3 million. 2018/19.
	REVIEW: Iron supplementation to treat anaemia in adult critical care patients [2016]. Erythroferrone in critical illness anaemia: an opportunity for novel mechanistic insights and developing clinical prediction models - grant application for Human Iron Research Oxford (H.I.R.O). Awaiting outcome.
	Previous REVIEWs in maternity [Gaps in the evidence for prevention & treatment of maternal anaemia, 2012] have informed a large funding application to NIHR entitled: Primary prevention of maternal ANaemia to avoid preterm Delivery and other Adverse outcomes (PANDA). Awaiting Outcome.
	REVIEW: Transfusion of fresher versus older red blood cells for all conditions [2016] has informed a NIHR application for an individual patient data meta-analysis. Awaiting outcome.
	* These being trials, audits and grant applications that the PI's working with the SRI have been involved with.
Artistic & Creative Products	Nothing to report
Software & Technical Products	Transfusion Evidence Library (www.transfusionevidencelibrary.com). As of November 2018, the library contains 7,255 RCTs, 1,695 Systematic Reviews and 78 Economic studies. We are half was through our current contract, which will expire in December 2018. Evidentia Publishing is aware that when we look to renew it, TEL will have to be available as a 'free at the point of access database'. We currently have 41 independent subscribers to the TEL (an increase of 9 from last year). Four institutions have not renewed their annual subscription; 5 have renewed for the fourth year running Royalties earnt this year are £8,766.29 Annual maintenance bill = £ 10,000 (with VAT = £12,100.00). We still have over 14,000 subscribers to our monthly Transfusion Evidence Alerts.
	TEL usage (taken from Google Analytics data) Since the beginning of 2018 (1 st Jan – 31 st October 2018), 7067 individual users have used TEL. They have viewed 23,870 pages in just over 10,000 sessions.

	This reflects a static rate of usage, with fewer new users this year than last year (17% v. 40% in 2017). The reasons for this is partly that that TEL has a more established user base year on year, but more particularly because of the reduced staff time available for publicity since July 2018. **Stem Cell Evidence** (using the domain name, www.stemcellevidence.com) was launched in April 2017 and now contains 3,267 records. The Stem Cell Evidence Alert is being sent out monthly to 706 subscribers. **Stem Cell Evidence** is a 'free at the point of access' database that supports best evidence-based practice in haematopoietic stem cell transplantation. *Stem Cell Evidence** will be a database of systematic reviews, randomised controlled trials, overviews of systematic reviews, observational studies and registry-based studies relevant to haematopoietic stem cell transplantation. Full details on funding are available in item 3 of *Further Funding* above. The third annual steering group meeting for Stem Cell Evidence was held on 19th September 2018. We have recruited a 0.6 WTE Band 6 Assistant Information Specialist starting January 2019 to support the population of the database.
Spin Outs	Nothing to report
Awards and Recognition	Lise Estcourt became the Coordinating Editor of the Cochrane Haematological Malignancies Review Group.
	Lise Estcourt became a member of the International Society of Blood Transfusion [ISBT] Clinical Transfusion Working Party.
	Lise Estcourt became a member of the International Collaboration for Transfusion Medicine Guidelines [ICTMG] Committee.
	Lise Estcourt became a member of the Transfusion Specialist Advisory Committee [SAC] of the Royal College of Pathologists.
	Akshay Shah won the best oral presentation award at the NIHR Thames Valley - Celebrating Urgent Care Research Conference (31st October 2018).
	Akshay Shah was appointed an <i>Anaesthesia [journal]</i> trainee fellow.

	Mike Murphy became President of the American Association of Blood Banks (AABB) in October 2018 and is the outgoing Chair of the BEST Collaborative, a position he held between 2014 and 2018.
	Simon Stanworth became an Associate Professor at the University of Oxford.
Other Outputs & Knowledge / Future Steps	Information Science: The information science workload has grown considerably over the past year as the remaining systematic reviews associated with the NIHR Cochrane Programme Grant were completed and work on the new NIHR Programme Grant network meta-analyses has begun. During 2017/18 Carolyn devised and/or updated the search strategies and performed searches for the following:
	 UKHCDO Guideline search request (Rachel Rayment): 'Prophylaxis in Haemophilia' – full information science support and update search (October 2017 & September 2018) BSH Guideline search request (Nicola Curry): 'What is the evidence that supports TEG/ROTEM use in major haemorrhage?' – update search (September 2017) Cochrane review (non-SRI, J Carson et al): 'Transfusion thresholds and other strategies for guiding allogeneic red blood cell transfusion' – update search (November 2017). https://www.ncbi.nlm.nih.gov/pubmed/27731885 Systematic Review (Dr Laura Green): 'Fibrinogen & Cryoprecipitate for Post-Partum Haemorrhage' - full information science support (January/February 2018) BSH Guideline search request (Julie Staves) – 'Specification, implementation and management of information technology systems in Hospital Transfusion Laboratories' – full information science support (May/June 2018) UKHCDO Guideline search request (Nicola Curry): Management of women with inherited bleeding disorders requiring treatment for a gynaecological condition' – full information science support (July/August 2018)
	 Future Steps: 1. We are continuing to talk with the British Society for Haematology about supporting an information science service for their various guideline writing groups. The most recent discussion centred around whether we would house and provide training and support for an information specialist for BSH, but we would not line manage or employ this person. 2. We are working with NHSBT Digital to develop a website for the SRI. The website would have a domain name that included the name of our group but be housed within the NHSBT digital directory of websites.

3. We are talking with NHSBT R&D about having links to our 2 libraries on their w	ebpages.
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- 4. We are continuing to talk with Professor Rafael Perera at the Nuffield Department of Primary Care Health Sciences, University of Oxford about a provision of statistical support for our group.
- 5. We need to disseminate further the activities of the JLA PSP work that was completed in February 2018 and explore ways to assess the impact of the findings.
- 6. Catalogue the Cochrane systematic reviews that we have been involved with, with a focus on their likelihood for being eligible to update.
- 7. Explore options for increasing our workforce, principally the number of core funded systematic reviewers and how we manage our information science activities.
- 8. Work with NHSBT's new Patient and Public Advisory Group to identify lay representatives for the SRI: develop terms of reference for all projects that include lay representatives.

Use of Facilities & Resources

Resources:

We have begun using Covidence for all our screening activities. We are required to use Covidence for all our Cochrane systematic reviews and have bought a licence for use on non-Cochrane reviews although our current licence limits us to 5 separate, non-Cochrane review screening activities per year.

Training Received:

SRI team members have attended the following training activities since June 2016:

Susan Brunskill

- Attended a one-day workshop on Software Packages to Support the Systematic Review Process at York Health Economics Consortium, University of York on 19th October 2017
- Attended an NHSBT run workshop: Coaching Conversations in Birmingham on 21st February 2018
- Attended the NIHR CRSU Training Day for Cochrane Programme Grant Holders 26th April 2018
- Attended the **Transfusion Guidelines Alignment Meeting**, Toronto on 31st May 2018
- Attended the **Cochrane Colloquium** in Edinburgh from 15th to 18th September 2018 with workshops attended on narrative synthesis on systematic reviews, network meta-analysis and priority setting for systematic reviews.

• Attended the inaugural **NHSBT Patient Advisory Group on** 25th September 2018

Carolyn Doree

• Attended the **Cochrane Colloquium** in Edinburgh from 15th to 18th September 2018 with workshops attended on information retrieval, machine learning and PICO Annotation.

Catherine Kimber

- Attended the **Cochrane Colloquium** in Edinburgh from15th to 18th September 2018 with workshops in machine learning and rapid reviews.
- Completed online Endnote training

Lise Estcourt

- Attended the Cochrane Editorial Meeting Lisbon 19th to 20th March 2018
- Attended the NIHR CRSU Training Day for Cochrane Programme Grant Holders 26th April 2018
- Attended the **Transfusion Guidelines Alignment Meeting**, Toronto on 31st May 2018
- Attended the **Cochrane Colloquium** in Edinburgh from 15th to 18th September 2018

Sheila Fisher

 Attended How to understand, appraise and write a network meta-analysis, University of Oxford on 2 to 4 July 2018

Rita Solanki

- Completed Cochrane Interactive Learning: Conducting an Intervention Review during August 2018
- Attended An introduction to STATA course, University of Oxford on 24th October 2018

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Giok Ong

- Completed Cochrane Interactive Learning: Conducting an Intervention Review during August 2018
- Attended An introduction to STATA course, University of Oxford on 24th October 2018.
- Attended **Advanced STATA courses**, University of Oxford on 31st October and 7th November 2018

Anair Beverly

- Completed Cochrane Interactive Learning: Conducting an Intervention Review during September 2018
- Attended An introduction to STATA course, University of Oxford on 24th October 2018
- Attended Advanced STATA courses, University of Oxford on 31st October and 7th November 201

Naomi Gibbs

• Completed Cochrane Interactive Learning: Conducting an Intervention Review during August 2018