Guy's and St Thomas' NHS
NHS Foundation Trust

NICE Guidance on Spectra Optia for automated red cell exchange in patients with Sickle Cell Disease

Dr Jo Howard

Guy's and St Thomas' NHS Foundation Trust

Conflicts of interest

- Co-investigator/Key opinion leader for Aes-103 and GBT 440 trials
- Paid consultancies for Aes-Rx, Imara and Bluebird Bio
- Speaker bureau for Novartis and Terumo BCT

What is NICE?

NICE National Institute for Health and Care Excellence

- National Institute for Health and Care Excellence
- Set up in 1999 as a special health authority to reduce variation in availability and quality of National Health Service (NHS) treatments and care
- Subsequent changes
  - Responsibility for developing public guidelines to prevent ill health and promote healthier lifestyles
  - Development of guidance and quality standards in social care
- Accountable to Dept of Health but independent

What is NICE?

- Medical technologies guidance
  - Address specific technologies notified to NICE by the manufacturers
  - The ‘case for adoption’ recommendations are based on the claimed advantages of introducing the specific technology compared with current management of the condition
  - This ‘case’ is reviewed against evidence submitted and expert advice

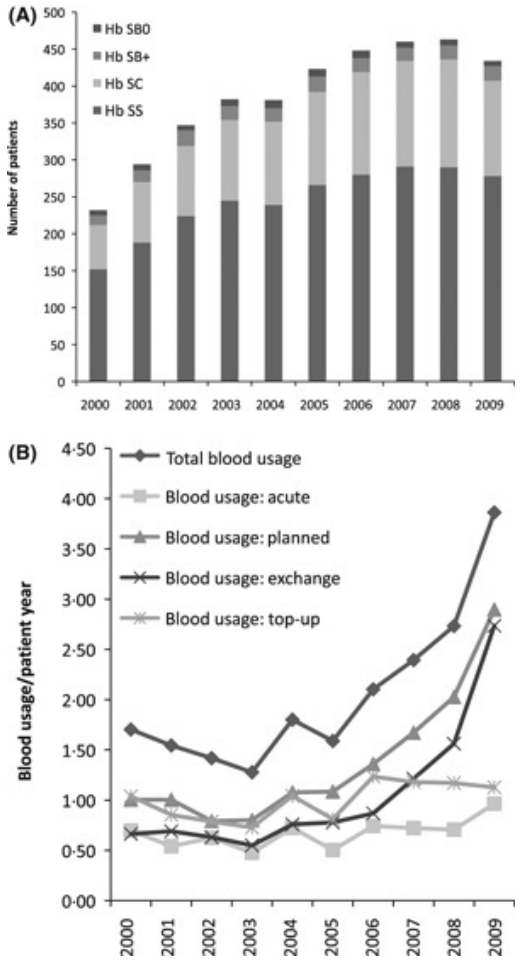
Medical technologies evaluation programme

- MTEP committee
- Expert Advisers
- Patient and carer organisation
- Sponsor
- External assessment centre

What is the Spectra Optia and why is it important?

- Apheresis and cell collection platform
- Automated red blood cell exchange, depletion or depletion exchange
- Benefits of less iron loading for patients on long term transfusion

Why is Spectra Optia important?



- Increasing use of red cell transfusion to treat the complications of SCD

Drasar et al 2011

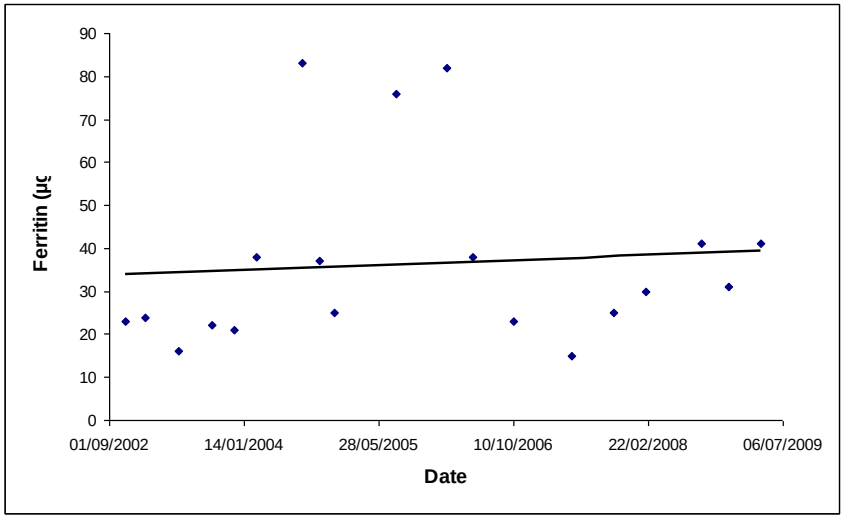
American Society for Apheresis indications for red cell exchange

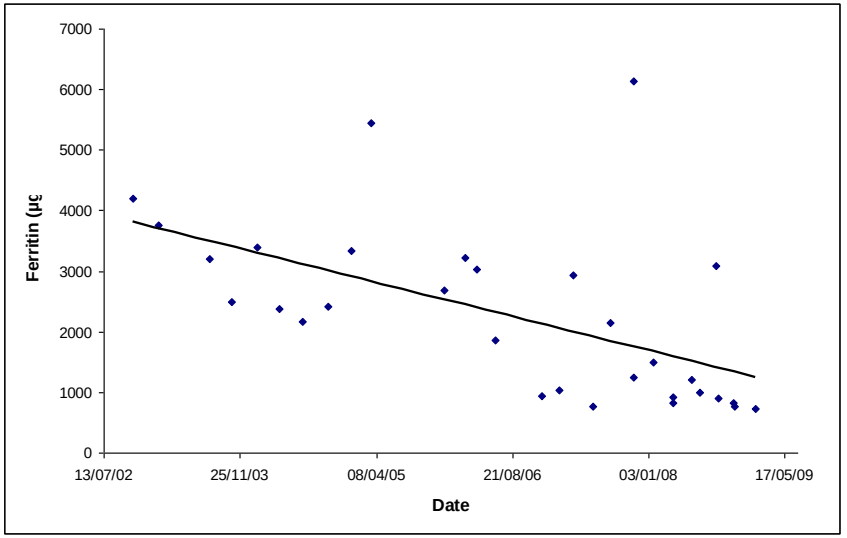
Disease name	TA Modality	Indication	Category	Grade
Sickle cell disease, acute	RBC Exchange	Acute stroke	I	1C
	RBC Exchange	Acute chest syndrome, severe	II	1C
	RBC Exchange	Priapism	III	2C
	RBC Exchange	Multiorgan failure	III	2C
	RBC Exchange	Splenic/ hepatic sequestration; intrahepatic cholestasis	III	2C
Sickle cell disease, non-acute	RBC exchange	Stroke prophylaxis/iron overload prevention	I	1A
	RBC exchange	Recurrent vaso-occlusive pain crisis	III	2C
	RBC exchange	Pre- operative management	III	2A
	RBC exchange	Pregnancy	III	2C

Indications for automated red cell exchange at GSTT

Indication	2013	2016
Disease severity	17	45
Secondary stroke prevention	22	36
Primary stroke prevention	4	7
Priapism	2	3
Hepatopathy	1	3
Pulmonary hypertension	1	1
Leg ulcers	0	3
	47	98

Automated apheresis ensures good control of iron balance





Patients who are not iron loaded at commencement of transfusion do not become iron loaded

Patients who are iron loaded can be iron depleted by a combination of iron chelation and automated exchange

NICE National Institute for Health and Care Excellence

Spectra Optia for automatic red blood cell exchange in patients with sickle cell disease

Medical technology guidance

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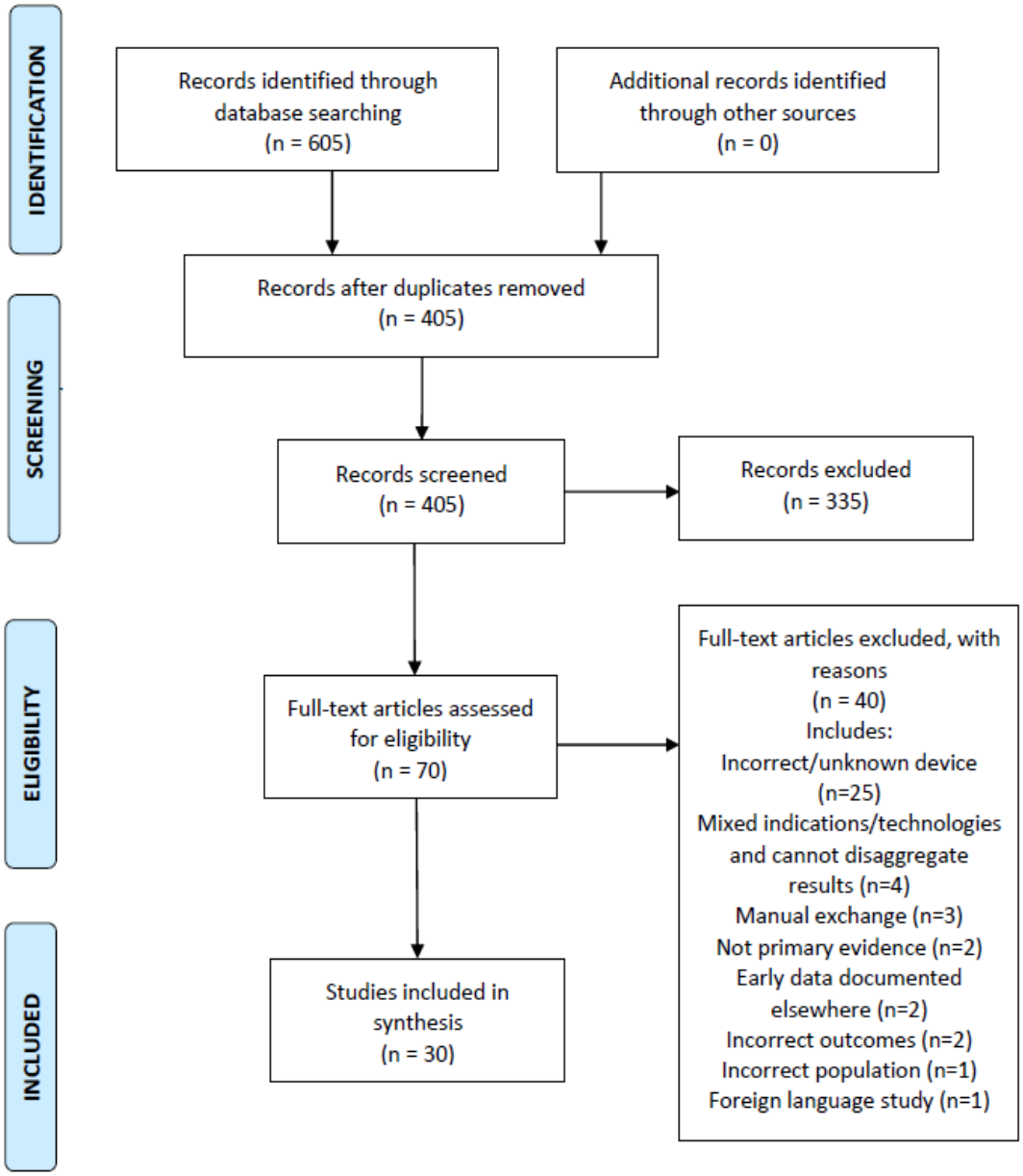
nice.org.uk/guidance/mtg28

Clinical Evidence Review



Clinical Evidence Review

Hb S levels (%)	No consistent evidence of effect
Duration of procedure	Strong evidence of reduced duration
Frequency of treatment	Strong evidence of reduced frequency
Patient haematocrit	No evidence of difference
Iron overload and requirement for chelation therapy	Significant uncertainty about whether ferritin levels are reduced
Clinical outcomes, quality of life, staff time and grade, BMI and growth in children, alloimmunisation, hospital admissions	Not reported

Clinical Evidence Review

Length of hospital stay	Not reported directly but reduced hospital stay highly likely
Ease of venous access, bruising and haematoma	Peripheral venous access more difficult using Spectra Optia system
Device related adverse events	Weak evidence for increased catheter related complications with Spectra Optia
Donor blood usage	Strong evidence of increased requirement

Ultrasound guided peripheral vascular access (USG-PIVA)

	Upper arm			Antecubital fossa		Lower arm	
	Basilic	Brachial	Ceph	Basilic	MedC	Ceph	Rad
Number of cannulation episodes	22	33	2	3	7	2	2
Cannula size	18g	18g	18g	18g	18/20g	20/22g	20g

Abbreviations: Ceph, cephalic; MedC, median cubital; Rad, radial.

- 16/12 single centre observational study
- 84 USG-PIVA procedures in 38 patients
- 71 (85%) were successful

Putensen et al, J Clin Apheresis 2015

Iron overload and requirement for chelation therapy

- Cabibbo et al (2005) : poor quality data
  - 7/7 patients on manual exchange had increasing ferritin level
  - 7/13 on automated exchange had decreased ferritin (stable in 5/13, increased in 1/13)
- Dedeken et al (2014)
  - Ferritin levels decreased from 666ug/l (182-1512) to 148ug/l (9-622) and 255ug/l (52-811) after 12 and 24 months of automated exchange
  - No parallel control group

Iron overload and requirement for chelation therapy

- Fasano et al (2015)
  - Ferritin decreased by -61ng/ml/month with automated exchanged compared with an increase of 19ng/ml/month in control group
  - Liver iron concentration: -5.7mg/g/year vs +1.6mg/g/year in control group
  - Controls were mixture of top up and partial manual
- Woods et al
  - No difference in ferritin between automated and manual exchange
- Single armed studies – many showed iron neutrality with automated exchange, but no control arm and confounded by use of iron chelation

Clinical Evidence Review

- Automated exchanges procedures are shorter and have a longer clinical benefit
- Spectra Optia is the only reliably iron-neutral transfusion therapy currently available and this is particularly important as chelation therapy is costly and poorly tolerated (expert opinion)

Population	No overload	Mild overload	Moderate overload	Severe overload
0% capital costs for SCD				
Adults	−£25,011	−£96,512	−£24,874	−£10,867
Children (2° prevention)	−£12,439	−£46,294	−£12,374	−£5,742
Children (1° prevention)	−£10,005	−£43,860	−£9,940	−£3,307
50% capital costs for SCD				
Adults	−£16,555	−£88,056	−£16,418	−£2,410
Children (2° prevention)	−£3,983	−£37,838	−£3,918	£2,715
Children (1° prevention)	−£1,548	−£35,404	−£1,484	£5,149

Economic analysis

- The results of the cost modelling show that the Spectra Optia is cost saving compared with manual exchange and top-up transfusion in most patients with SCD
- Cost savings varied from >£90,000 to <£1500 depending on scenario

Recommendations

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- The case for adopting Spectra Optia for automated red blood cell exchange in patients with sickle cell disease is supported by the evidence. Specta Optia is faster to use and needs to be done less often than manual red blood cell exchange
- Spectra Optia should be considered for automated red blood cell exchange in patients with sickle cell disease who need regular transfusion

Recommendations

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- NICE recommends collaborative data collection to generate further clinical evidence
- Cost modelling shows that in most cases using Spectra Optia is cost saving compared with manual red blood cell exchange or top up transfusion
- Estimated cost savings are £18,100 per patient per year. Potential savings to NHS in England are £12.9 million each year

Do Not Do Recommendation

Top-up transfusion is not generally suitable as a long-term regime for sickle cell disease because it is iron positive

June 2016

Peer Review of Services for patients with Haemoglobin Disorders showed marked inequality in access to automated exchange

WM QRS West Midlands Quality Review Service

UK Forum on Haemoglobin Disorders

Health Services for People with Haemoglobin Disorders

Conclusions

- Patients with SCD who are being treated with long term transfusion therapy should have access to automated red cell exchange technology

- Further data collection is required to aid decision making about optimal transfusion practice