



BASIL Trials



NIHR HTA funded RCTs comparing vein bypass and different endovascular revascularisation strategies for SLI

BASIL-2 – open and recruiting since September 2014

BASIL-3 – funded since 1 August 2015

Andrew W. Bradbury

**Chief Investigator & Sampson Gamgee Professor of Vascular Surgery
University of Birmingham, UK**



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NICE PAD Guidelines 2012

CG147 Lower limb peripheral arterial disease (CG147)



Lower limb peripheral arterial disease pathway

Fast, easy summary view of NICE guidance on 'lower limb peripheral arterial disease'

NICE PAD GDG

Lower limb peripheral arterial disease: Diagnosis and management

Clinical guidelines, CG147 - Issued: August 2012

Research Recommendations SLI

This guidance has been incorporated into the following NICE

Lower limb peripheral arterial disease

Diagnosis and management

NICE Clinical Guideline 147

Methods, evidence and recommendations

August 2012

Final version
Commissioned by the National Institute for
Health and Clinical Excellence



Applications to NIHR HTA

Multi-centre RCTs to compare the clinical and cost-effectiveness of:

- **Vein Bypass vs Best Endovascular Treatment for SLI due to *infra-popliteal* disease (**BASIL-2**) (NIHR HTA Surgical Call / Board)**
- **POBA+/-BMS vs DCB+/-BMS vs DES for SLI due to *femoro-popliteal* disease (**BASIL-3**) (NIHR HTA commissioned research)**



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BASIL 2/3 Co-applicants

Southampton (Professor Shearman, Dr Odurny)

St George's (Mr Hinchliffe and Professor Belli)

Imperial (Professor Davies, Dr Burfitt)

Oxford (Mr Perkins, Dr Uberoi)

Birmingham (Mr Claridge, Dr Ganeshan)

Leicester (Professor Naylor, Dr Adair)

Hull (Professors Chetter and Ettles)

Leeds (Professor Scott, Dr Patel)

Sheffield (Professor Beard, Dr Cleveland)

Newcastle (Professor Stansby, Dr Jackson)

Scotland (Professor Brittenden, Dr Yadavaldi

Mr Stuart, Professor Moss)

VSGBI

BSIR

ESVS

CF

Diabetes-UK



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B-2 Overview



- Detect a one-third reduction in AFS (HR = 0.66) (B1)
- 90% power at 5% significance level
- Allowing for 10% drop-out (1% in BASIL-1)
- Target recruitment: 600 over 3 years
- UK centres: 55
- Recruitment started: September 2014
- Currently open sites: 41 (24 recruited)
- Current recruitment: **95 patients**
- Internal pilot criteria met (Monitoring Visit Sept 2015)
- **Next target: 207 by May 2016 (3/16 November)**

Randomisation



Randomisation (**IP arteries only**)

↓
Vein Bypass (VB) **first**
(n = 300)

↓
Best Endovascular
Treatment (BET) **first**
(n = 300)

Follow-up
Minimum 24 months
Mean 39 months (3.3 years)
Maximum 60 months

First = at point of clinical equipoise

Inclusion Criteria

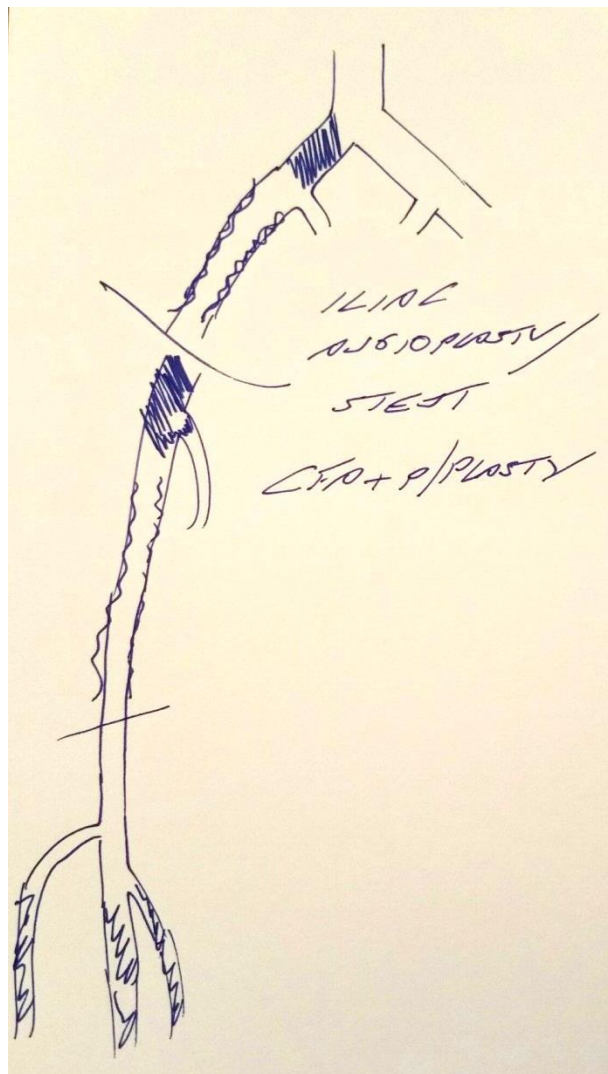


SLI due to IP +/- INFLOW disease

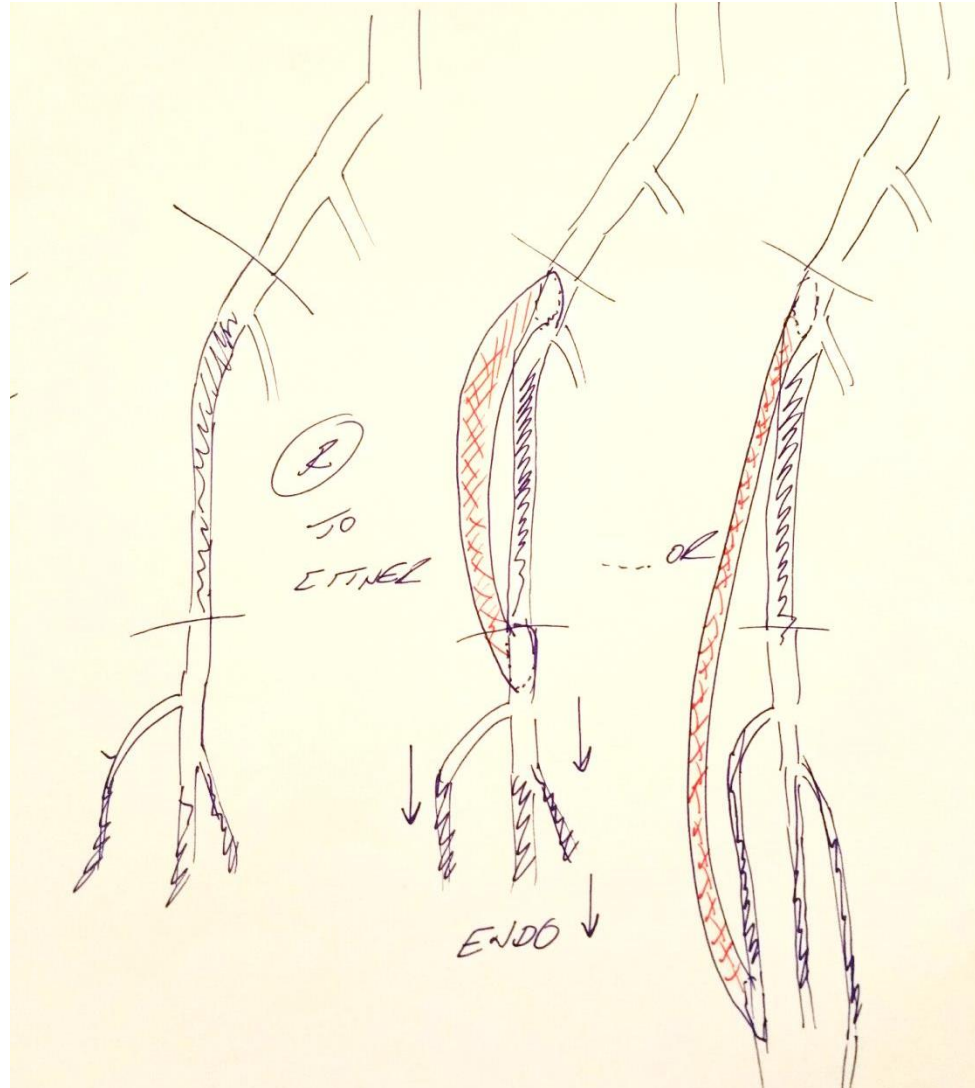
Judged by at least one **VS** and one **IR** to require **early IP +/- INFLOW** revascularisation **in addition to** BMT, foot and wound care

Have '**INFLOW**' adequate to support **IP** VB and BET

Inflow Correction (AI)



Inflow Correction (FP)



Exclusion Criteria



Anticipated **life expectancy** < 6 months

Judged **unsuitable** for either of the two revascularisation strategies by the responsible consultant VS and IR

Insufficient **English / translation** facilities to guarantee informed consent

Unable to provide consent due to **incapacity** (as defined by Mental Capacity Act 2005 or Adults with Incapacity [Scotland] Act 2000)

Outcome Data Collection

Gareth Bate

BASIL Senior Research Nurse

Outcomes



- 1° **Amputation free survival, AFS**
- 2° **Overall Survival (OS)**
- 2° **In-hospital and 30-day morbidity and mortality**
- 2° **Major Adverse Limb Events (MALE)**
- 2° **Major Adverse Cardiovascular Events (MACE)**
- 2° **Relief of ischaemic pain (VAS, medication usage)**
- 2° **HRQL and functional status (EQ-5D-5L, SF-12, ICECAP-O, HADS, VascuQoL)**
- 2° **Re- and cross-over intervention rates**
- 2° **Healing tissue loss / minor amputations (PEDIS / WiFi)**
- 3° **Haemodynamic changes (patency)**

Trial Exit and “Lost to Follow-up”

ISRCTN: 27728889 BASIL-2 Trial Version 2.0 (12th November, 2015)

BASIL-2 Exit Form	
TO BE COMPLETED IF THE PATIENT HAS DIED OR WITHDRAWN CONSENT	
BASIL-2 Trial Number:	2 <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>
Patient initials:	<input type="text"/> <input type="text"/> <input type="text"/>
Date of Birth:	___ / ___ / ___ (dd/mmm/yyyy)
Patient exit from the trial:	

Has the patient withdrawn? No Yes

Date of withdrawal: ___ / ___ / ___ (dd/mmm/yyyy)

Patient has withdrawn from: (tick all that apply)

- Randomised treatment
- Attendance at clinic
- Completion of HRQoL
- Collection of all NHS data

Has patient been lost to follow-up? No Yes

If yes, give reason: _____

HEFT Data

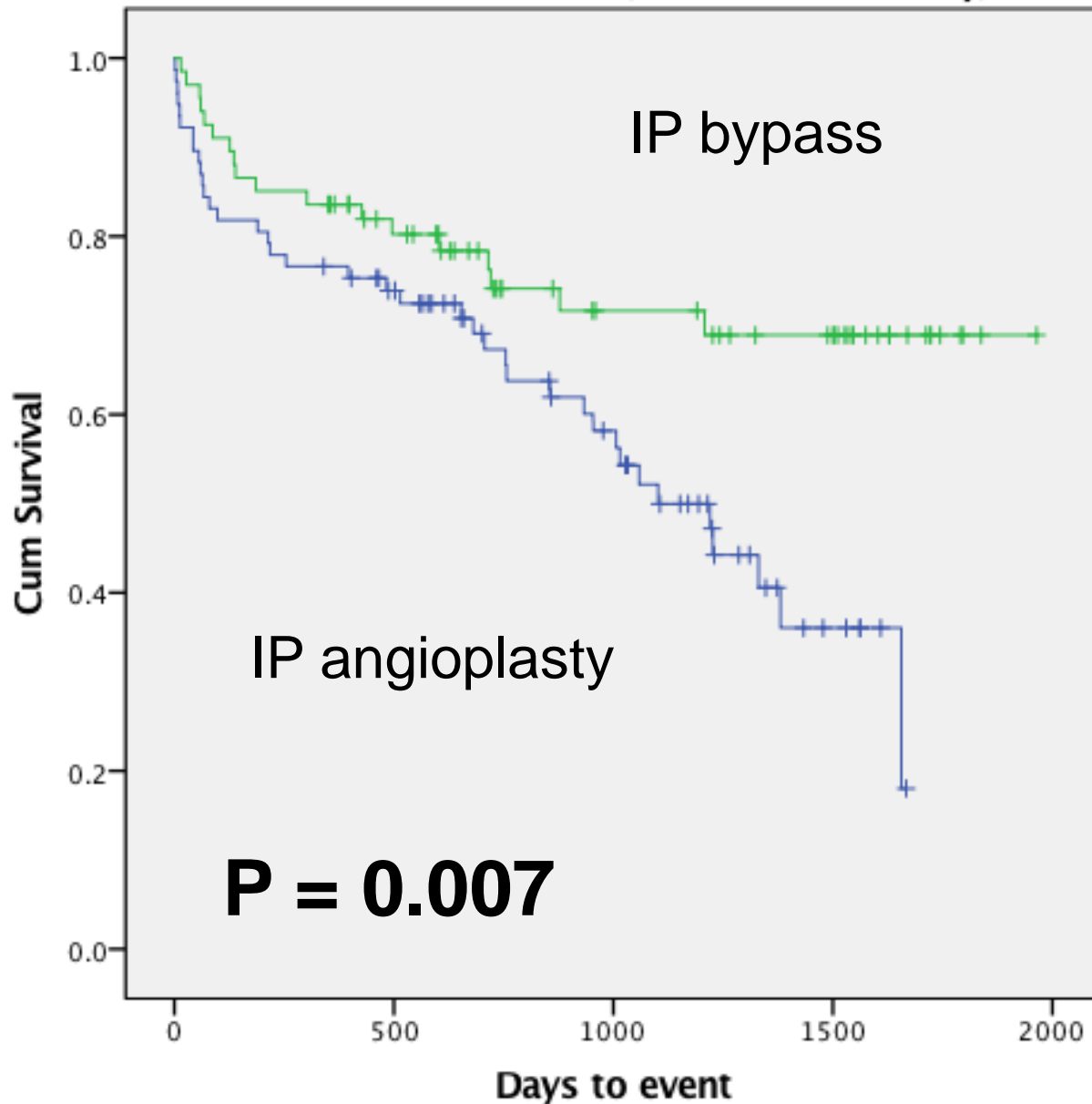
Matt Popplewell

Vascular Research Registrar

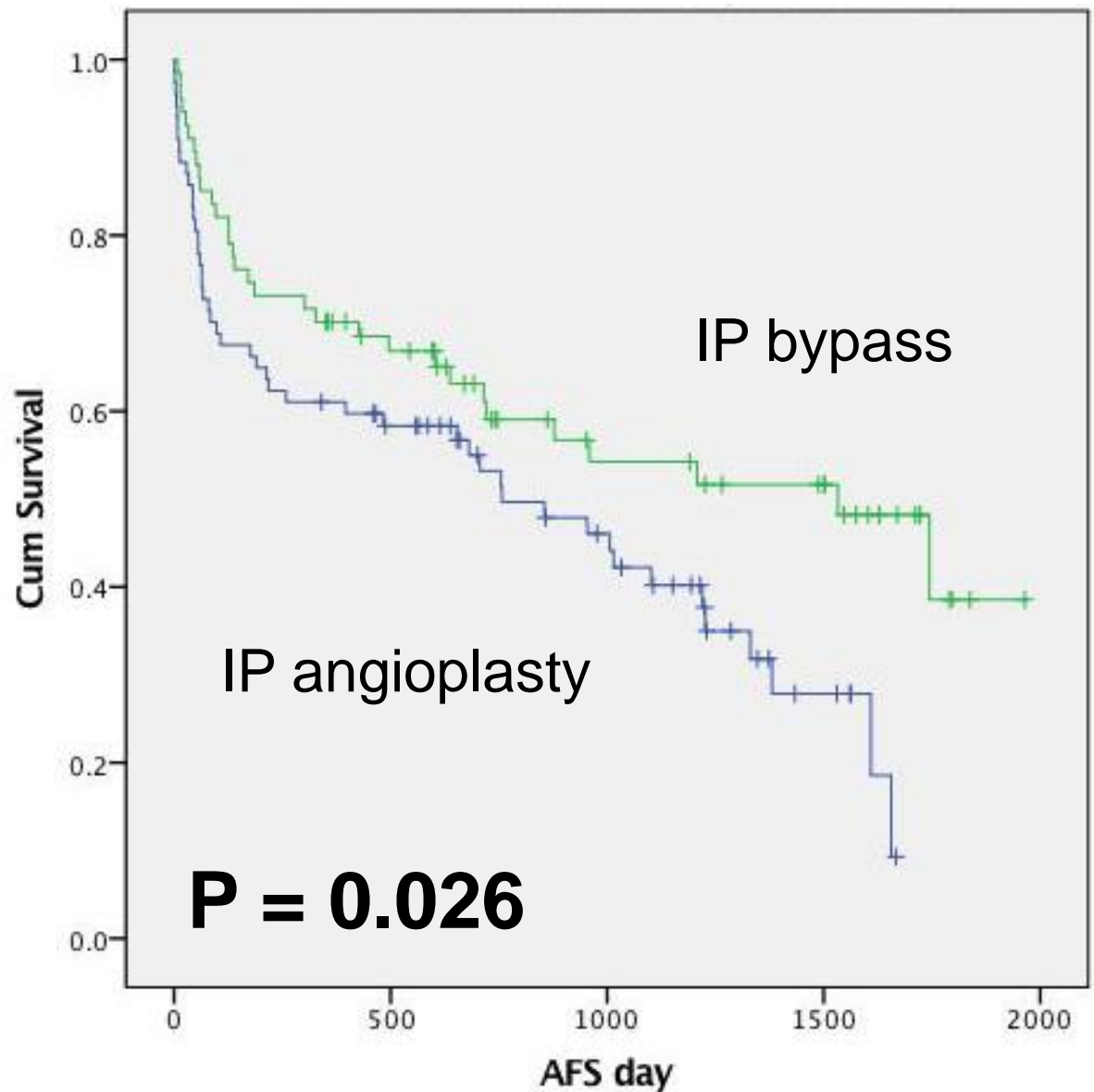
HEFT Retrospective Study

- Retrospective analysis of IP bypass (n = 67) and angioplasty (n = 77) in 142 consecutive SLI patients between 01-07-2009 and 30-06-2013 with at least 12 months follow up
- Primary outcome: amputation free survival
- Secondary outcomes:
 - All cause mortality
 - Length of hospital stay
 - Index admission
 - Out to 12 months

All cause mortality



Amputation-free Survival



Length of Stay

	Angioplasty	Bypass
Index Admission	10.3 days	14.1 days
Over 12 months (including index)	21.8 days	22.6 days

No difference in re-intervention

BASIL - HEFT PCS

24/06/2014 to 31/08/2015 - 161 new SLI patients

82/161 (51%) **IP +/- INFLOW** disease



Primary amputation
12

Revascularisation attempted
48 (59%)

Conservative
22

7 other surgery

Vein bypass
(outside trial)
8

“No equipoise” – 2
Thrombosed PAA – 1
FP/Al only – 3
No MDT (emergency) - 2

Endovascular
(outside trial)
25

“No equipoise” – 12
Unfit for bypass – 7
FP/Al only – 3
No vein – 2
Patient choice - 1

Randomised to B-2
8

Angioplasty x 2
Vein Bypass x 6

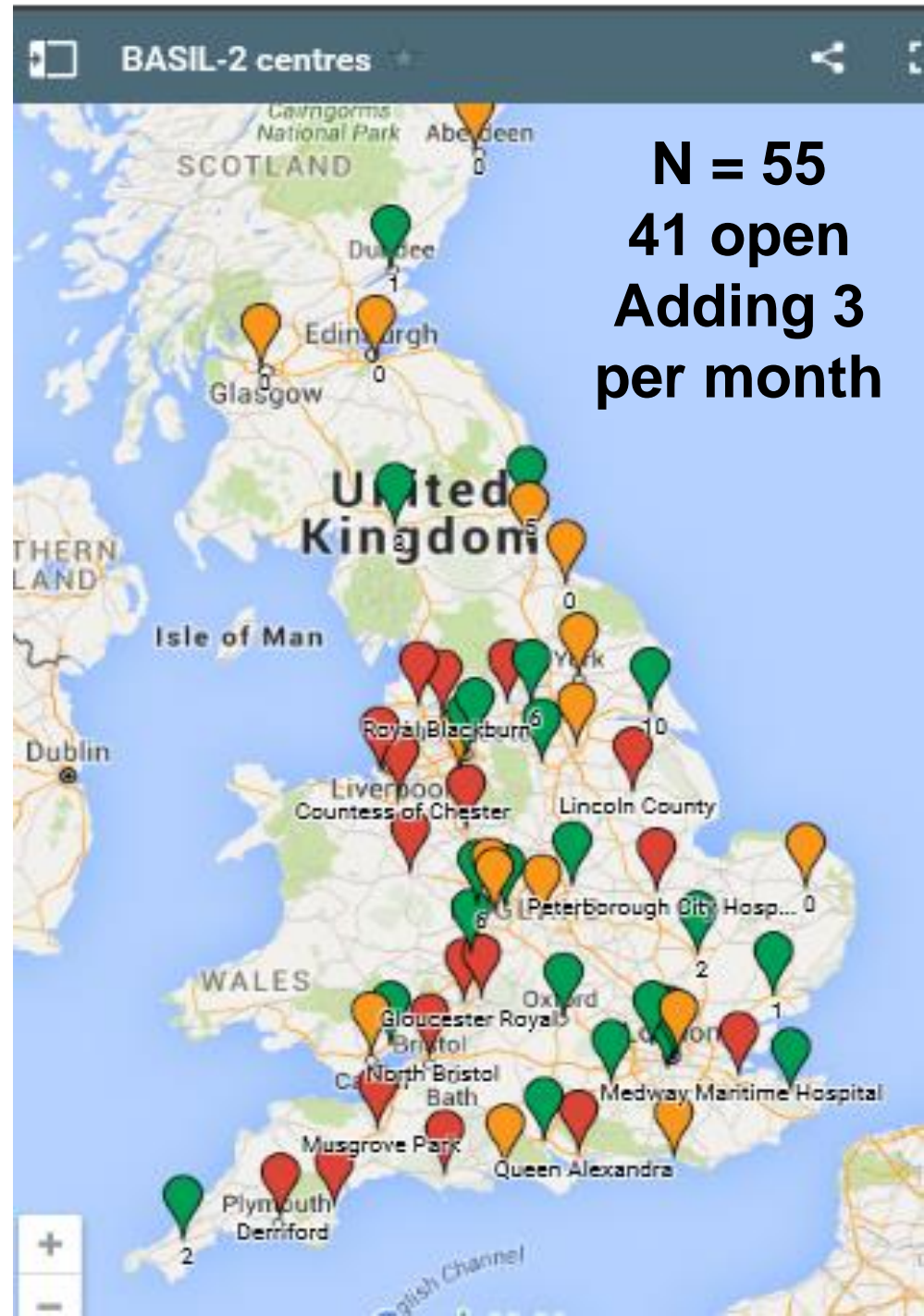
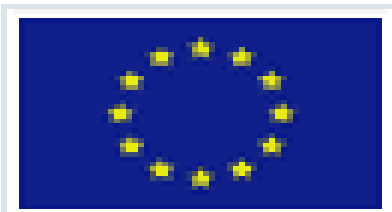
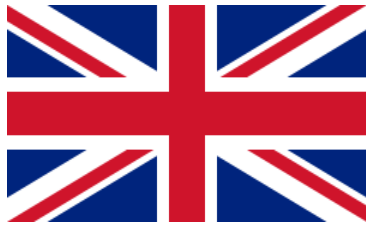
17%

8 patients randomised per 10^6 per year - 50 centres (50^6) = 400 / year
Need 520 in 2 years (260/year)

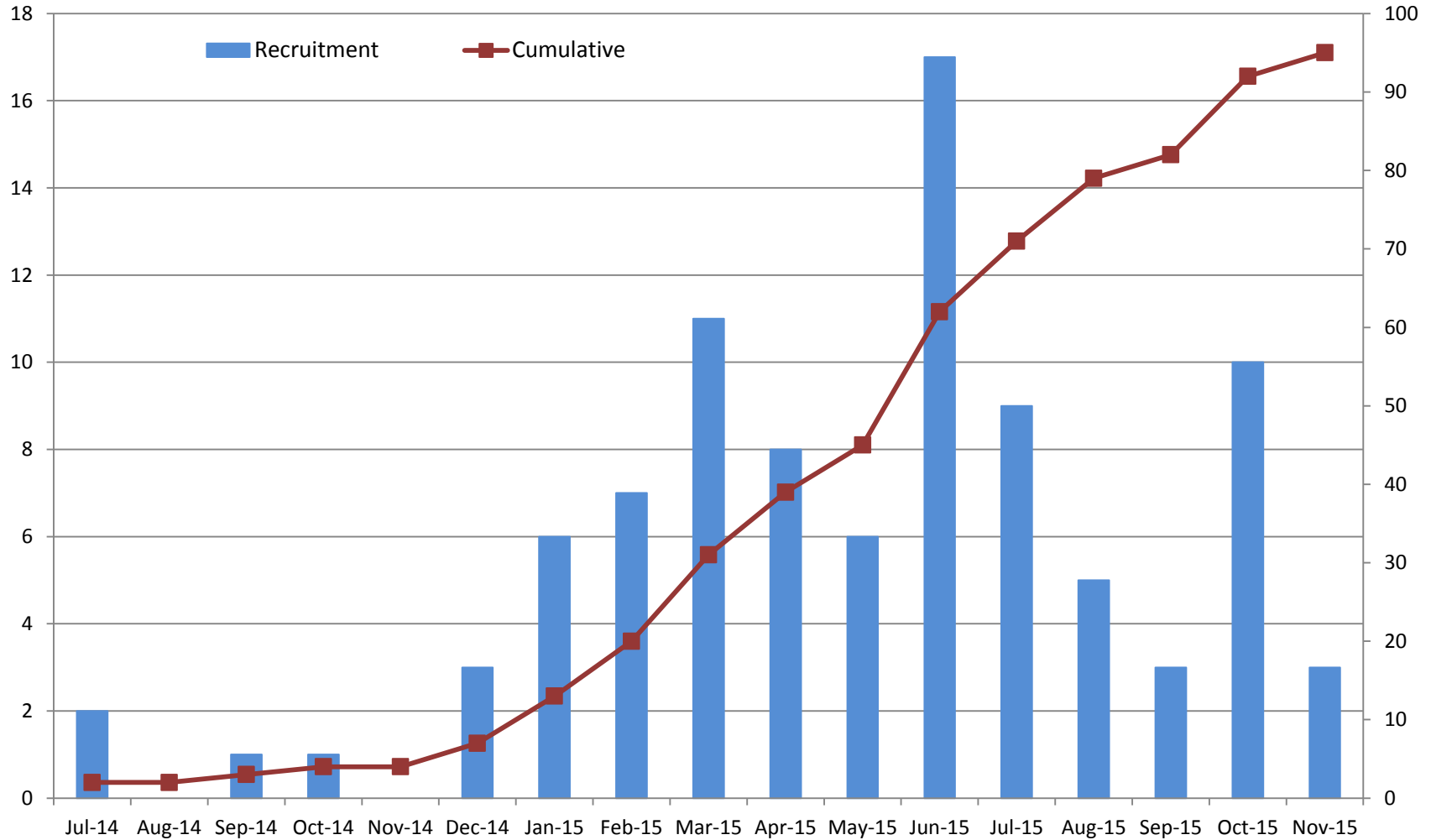
BASIL-2 Recruitment

Hugh Jarrett
Senior Clinical Trials
Co-ordinator

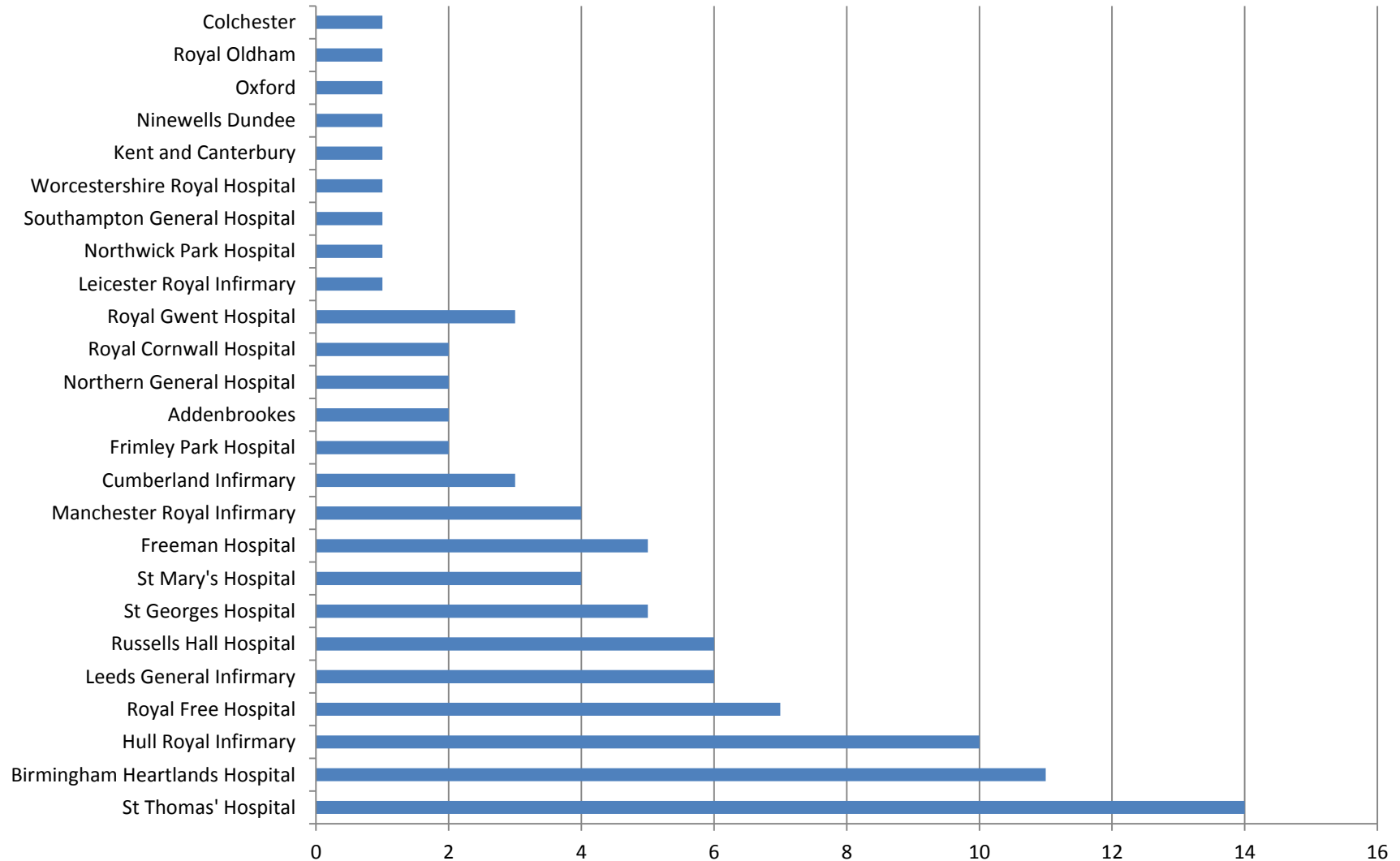




BASIL-2 Recruitment 09-11-2015



BASIL-2 Recruitment 09-11-2015



BASIL-2 eCRFs



BASIL₂


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Patient form: 2001

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Version	1.0 ▼
Paper randomisation?	Yes ▼
Randomisation Date (dd-mmm-yyyy)	22-Jul-2014
Trial intervention date (dd-mmm-yyyy)	24-Jul-2014
Current Centre	Birmingham Heartlands Hospital ▼
Current Consultant	Dr Arul Ganeshan ▼
Contact Centre (eg letters)	Birmingham Heartlands Hospital ▼
Contact Person (eg letters)	Dr Arul Ganeshan ▼
Recruiting Centre	Birmingham Heartlands Hospital ▼
Recruiting Consultant	Dr Arul Ganeshan ▼
Patient TNO	2001

Assessments

Status: ▼

Assessment	Status	
Contact: Baseline	Received	View
Medical stat: Baseline	Received	View
In-pat/Daycase : No ref	Received	View
In-pat/Daycase : New	Available	Add
Bypass : New	Available	Add
NonByps Vasc Surg : New	Available	Add
BET : No ref	Received	View
BET : New	Available	Add
BET Segmental : No ref	Received	View
BET Segmental : No ref	Received	View
BET Segmental : New	Available	Add
Amputation : No ref	Received	View
Amputation : New	Available	Add
Follow-Up: Baseline	Received	View
Follow-Up: 1 month	Received	View
Follow-Up: 3 month	Received	View
Follow-Up: 6 month	Due Now	Add
Follow-Up: 9 month	Due Now	Add
Follow-Up: 12 month	Due Now	Add
Follow-Up: 18 month	Not Due Yet	
Follow-Up: 24 month	Not Due Yet	
Follow-Up: 30 month	Not Due Yet	
Follow-Up: 36 month	Not Due Yet	
Exit : New	Available	Add
PEDIS: baseline	Received	View
PEDIS: 1 month	Received	View
PEDIS: 3 month	Due Now	Add
PEDIS: 6 month	Due Now	Add
PEDIS: 9 month	Due Now	Add
PEDIS: 12 month	Due Now	Add

COMPETITION: Win Restaurant Vouchers!

To the end of October this month, then throughout each of November and December each time a recruiting centre recruits a patient to BASIL-2 they will get an entry into the monthly draw for £100 of restaurant vouchers of your choice to be shared by the winning team. The more patients you randomise in a calendar month, the more entries you get into the draw.

That's 3 prizes; 1 a month, from now until Jan 1st 2016.

COMPETITION



You can follow us on Twitter: @basil_trials

The screenshot shows the Twitter profile page for BASIL Trials (@basil_trial). The profile picture is a circular logo with the word 'BASIL' and a footprint icon. The bio reads: 'The BASIL trials are vascular surgery trials in the lower limb'. The page shows 16 tweets, 26 following, and 11 followers. A tweet from BASIL Trials @basil_trial, posted 5 hours ago, says 'Correction!! Tomorrow at 12:30!!'. The 'Who to follow' section includes Standard Life Invest @SLI_... with a 'Follow' button and a 'Promoted' tag. The navigation bar at the top includes Home, Notifications, Messages, a search bar, and a 'Tweet' button.

BASIL 3



Balloon vs Stenting in Severe Ischaemia of the Leg-3

Multi-centre RCT of clinical and cost-effectiveness of plain and drug coated balloon angioplasty (both +/- 'bail-out' bare metal stent) and primary drug eluting stent revascularisation strategies for SLI due to femoro-popliteal +/- infra-popliteal disease



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BASIL-3 Overview



- **Sponsor: University of Birmingham**
- **NIHR HTA: £1.98m** (awarded October 2014, deferred)
- **XS NHS costs £600K** (DCB, DES not NICE approved)
- **Funding started 1 August 2015**
- **National Target: 861 patients over 3 years**
- **No of UK centres: 69 (?)**
- **Length of recruitment: 3 years**
- **Protocol, TSC, DMEC, REC, CRFs all done**

Inclusion Criteria



SLI due to **FP +/- IP** disease

Judged by at least one IR and one VS to require **early FP +/- IP endovascular** revascularisation **in addition to** BMT, foot and wound care

Adequate '**inflow**' to support **FP +/- IP** endovascular revascularisation
(can be randomised with / after inflow procedure)

Judged suitable for **FP**
PBA+/-BMS and DCB+/-BMS and DES

Exclusion Criteria



Anticipated life expectancy < **6 months**

Judged unsuitable for any of the three endovascular revascularisation strategies

Insufficient English / translation facilities to guarantee informed consent

Unable to provide informed consent

Randomisation



Randomisation (n = 861) (FP only)



**PBA
+/- BMS
(n = 287)**



**DCB
+/- BMS
(n = 287)**



**DES
(n = 287)**

Follow-up

Minimum 24 months

Mean 39 months (3.3 years)

Maximum 60 months

Outcomes



- 1° **Amputation free survival, AFS**
- 2° **Overall Survival (OS)**
- 2° **In-hospital and 30-day morbidity and mortality**
- 2° **Major Adverse Limb Events (MALE)**
- 2° **Major cardiovascular events (MACE)**
- 2° **Relief of ischaemic pain (VAS, medication usage)**
- 2° **HRQL and functional status (EQ-5D-5L, SF-12, ICECAP-O, HADS, VascuQoL)**
- 2° **Re- and cross-over intervention rates**
- 2° **Healing tissue loss / minor amputations (PEDIS / WiFi)**
- 3° **Haemodynamic changes (patency)**

BASIL-3 Set-up

Hugh Jarrett

**Senior Clinical Trials
Co-ordinator**



Set-up / Running BASIL-3



- No need for SF-12 contract sign off
- CSAs identical to BASIL-2
- GCP / CVs collected for many staff
- Delegation logs - new PI sign off
- CRFs almost identical to BASIL-2
- Less follow-up than BASIL-2
 - (5 time points, not 9)

Progress to date

- Ethically approved
- On CSP (183761)
- Study-wide R&D approval granted
- Vast majority of BASIL-2 centres also participating in BASIL-3
- First site aims to open within weeks
- Several other sites well progressed in set-up



BASIL-2 Randomisation (n = 80)



Vein Bypass *first*
(n = 300)

**Best Endovascular
Treatment *first*** (n = 300)



BASIL-3 Randomisation (start Q4 2015)



PBA
+/- BMS
(n = 287)

DCB
+/- BMS
(n = 287)

DES
(n = 287)

Follow-up

Minimum – Mean – Maximum
24 - 39 - 60 months

UK SLI Trials Overview

Severe Limb Ischaemia (SLI) (RP +/- TL)

Correct inflow disease (endo > open)

FP disease

IP disease

Life expectancy (years) / vein?

BASIL-2

> 2 and yes

< 2 and / or no

Vein
bypass

?

BET

Vein bypass

BASIL-3

BASIL-1

PBA +/-
BMS

?

DES

?

DCB +/-
BMS

**BASIL
REGISTRY**



BRIGHAM AND
WOMEN'S HOSPITAL



MASSACHUSETTS
GENERAL HOSPITAL



BEST-CLI

Best Endovascular versus Best Surgical Therapy
in Patients with Critical Limb Ischemia



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Thank you



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