

Randomised Controlled Trials in Surgery: Experience of recruitment in the AMAZE multicentre trial

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AMAZE trial design

- Radio-frequency ablation as an adjunct to elective cardiac surgery
- Patients with pre-existing atrial fibrillation
- Intermediate clinical endpoint – return to SR
- Final patient/NHS endpoint – quality-adjusted survival and costs

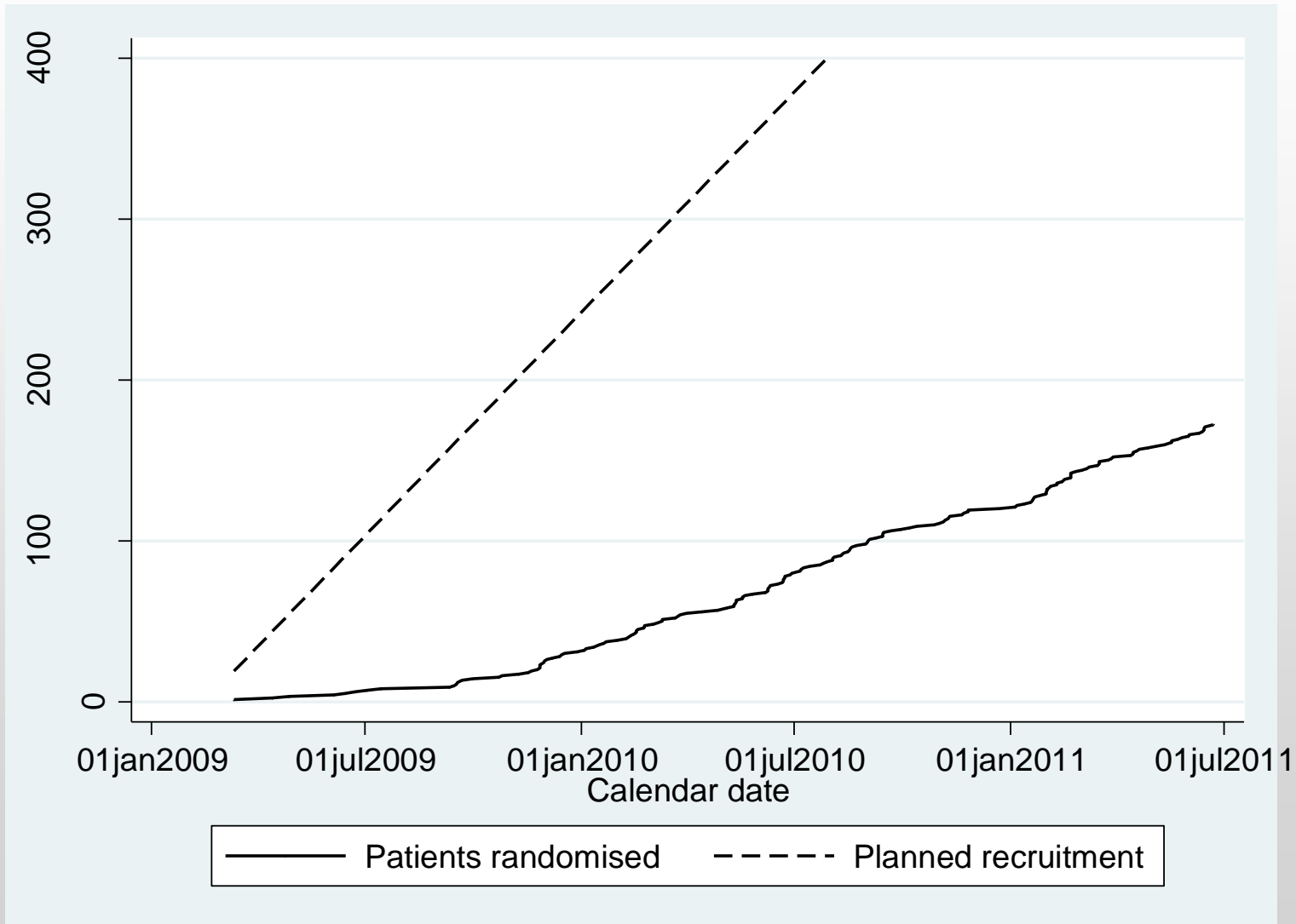
AMAZE trial design

- Multicentre trial
- Total sample size 352 for intermediate endpoint, 400 for final endpoint
- Recruit at pre-surgery clinics, randomise in theatre
- Target recruitment Papworth 3-4 per month, other centres 2-3 per month
- Plan to recruit 400 in 18 months

Reasons to be optimistic

- At least 400 eligible patients per year at initial centres – recruitment targets seemed conservative
- Pragmatic trial with few exclusions
- Patients having surgery anyway
- No requirement for additional referrals/changes in pathway
- RFA widely used, little training required
- Control groups also have surgery
- No direct evidence of patient benefit
- General enthusiasm of surgeons across several centres

Proposed vs. Actual Recruitment



Trial launch – January 2009(!)



Initial delays

- 3 month waiting lists – first randomisation March 09
- Local approvals 5-16 months
 - Local R&D bureaucracy
 - Appointment of research staff
 - Lack of dedicated research staff
 - Lack of local ownership
 - CLRN support variable

Trial centres during planning



Additional trial centres – hurrah!



Trial centres pulled out – boo!



Trial centres' recruitment to date



Centre	Number randomised
Newcastle	2
Blackpool	2
Northern General, Sheffield	19
Glenfield, Leicester	42
Coventry	2
Papworth*	93
Brompton**	2
Guys & St Thomas	5
Brighton	2
Derriford, Plymouth	12

*Co-ordinating centre

** Brompton withdrew from study

Recruitment strategies

- Initiation of new centres
- Trials on agenda at monthly surgical management meetings
- Internal trial promotion - AF cases highlighted by cardiologists, SpRs, nurses
- Screening of all medical notes
- Presentation at local and national research meetings (probably not enough)
 - Consider cardiology meetings
 - National specialty groups not considered helpful so not contacted
- Leaflets/adverts
- Promotion at specialist training courses

It's good to talk!

- Initiation and monitoring visits
- Trial Steering Group meetings
 - Attach to scientific meetings
 - Face to face with telecon option
 - Vary venue – encourage ownership
- Monthly fixed telecon primarily for research nurses
- Telephone helpline

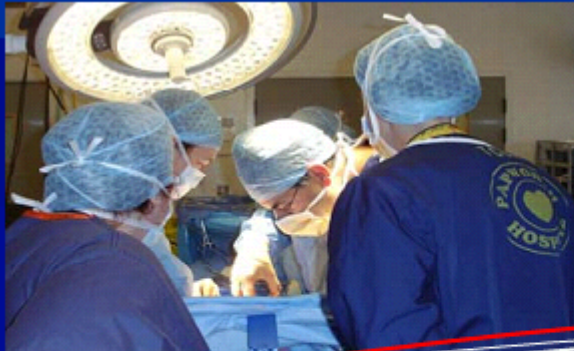


Newsletters

ISSUE

03

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The Amaze Trial



Our Aim! 280 by 2012!

Progress – nearly half way there!

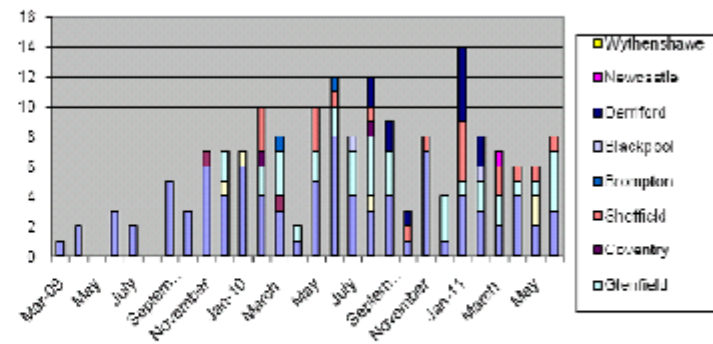
Amaze has now recruited over 43% (173/400) of the required patients. We would like to say a special thanks to our top recruiters, Prof Spyt and Donna Alexander from Glenfield (38 patients recruited). You have played a significant role in helping us reach our goal and your support is greatly appreciated.

It's also fantastic to see two sites vying for the second recruiter spot. Well done to Mr Dalrymple-Hay and Linda March from Derriford and Mr Peter Bradley and Ratna Ray from Northern General.

We are also grateful to all our collaborators who gave up their time to attend our recent Trial Steering Committee meeting, which provided a useful


Recruitment figures

All Sites Randomisation breakdown - total 172



Last 18 month Randomisation figures
Jan 10 - June 11 (172)

Maintaining awareness



Uncle Sam Wants You!!

*To refer patients in AF to
Christine Thomas ex 4614 bleep 340*

ISSUE 2

The Amaze Trial

First correct solution wins the champagne!
All other entries win a mouse mat!

fax solution to 01480 364744

1	2		3	4	5	6
		7				
8				9		
10			11			
	12				13	
14						15
16	17			18		
19			20			
					22	

Across

- 1 Temper reversal of fate (4)
- 3 They sound like they have a chest infection in the treasury (7)
- 8 Where one may vanish into the stratosphere? (4,3)
- 9 Sightless Austrian or Venetian (5)
- 10 Surprise 14 (5)
- 11 Stupid papers I love, jerk (7)
- 12 Rumbled she-devil led astray (11)
- 16 Pruner after diet (7)
- 18 At first the vet should examine the box (2,3)
- 19 Manufacture losing attempt to get Asian river (5)
- 20 Pressing groin in crisis (7)
- 21 The French team trick is in the dictionary (7)
- 22 Amazing feat to produce cheese (4)

Down

- 1 Some martial art image rising in one's heart (6)
- 2 I'm a cheque, bouncing and folding into shapes (7)
- 3 Soar in divorce poor treatment for 14 4 (13)
- 4 See 14
- 5 Be first to follow lover once (5)
- 6 Get off with short bird - see about that (6)
- 7 Conductor usually does accept the consequences (4,3,5)
- 13 Private facility set in EU regulation (2,5)
- 14/4 Subject of brilliant trial? I may be! (6,12)
- 15 Mark unites secretive racing driver with mother (6)
- 17 List of mind-expanding ingredients (5)

Royal College of Surgeons 1st September 2011

Getting tough!

THE
Amaze
TEAM!

Are looking to abolish the mystery behind the troublesome AF!
If you have a problem, no one else can help, and if you can find them,
maybe you can hire... The Amaze-Team.
Refer any potential trouble makes to R&D



AMAZE

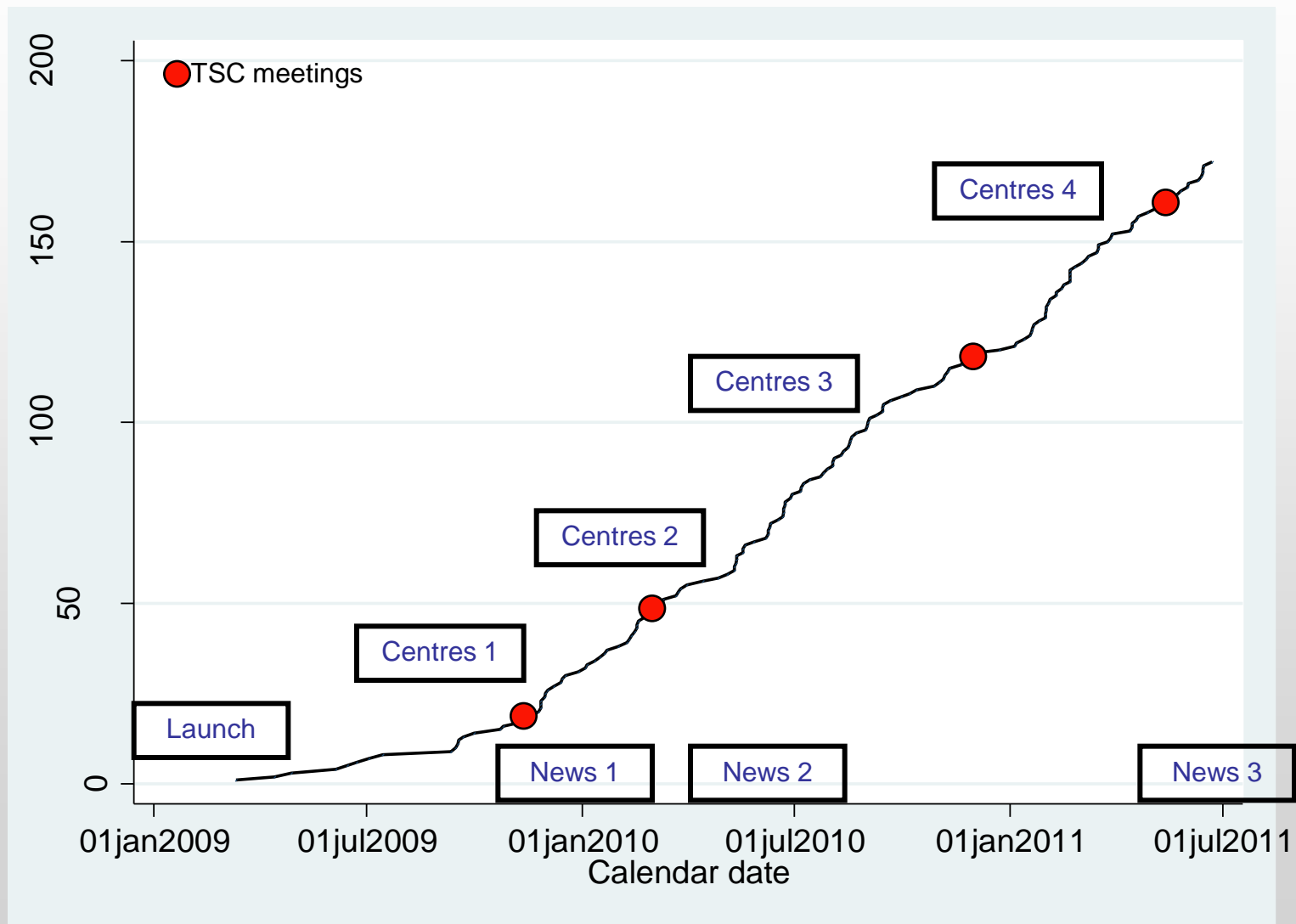
Centre issues

- Concerns about blinding
- Lack of personal equipoise
- Number of surgeons/Isolated surgeons
- Support from other clinical colleagues
- CLRN
 - Papworth, Coventry, Derriford, Blackpool full support
 - Other centres minimal or no support
- Variable research experience/academic backgrounds and support
- Pressure of service provision

Reasons for not recruiting

- Surgeons were "optimistic" when target setting
- Notes not screened
 - At Papworth CLRN screen 20 notes to get 2 eligible, 1 recruit
- Staff turnover or lack of research staff
- Short waiting lists
- Long waiting lists
- Lack of ITU beds

Effects on Recruitment



Some general recommendations

- Complexity of surgery suggests multicentre trials crucial – strong CI leadership
- Good research nurse crucial
- SpR, CLRN support important
- Recruit groups of surgeons at each centre if possible
- Realistic funding
- Involve colleagues from other disciplines (especially if on the diagnosis-treatment-follow up pathway)

Pragmatic vs. explanatory



Pragmatic trials are

- Inclusive
- Reflect practice
- Allow flexibility
- Measure effectiveness

Explanatory trials are

- Selective
- Reflect ideal conditions
- Require strict protocols
- Measure efficacy

Pragmatic trials = quicker recruitment

Expect the unexpected!



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