

Putting the R into Randomisation

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R user conference 2011

Warwick

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Introduction

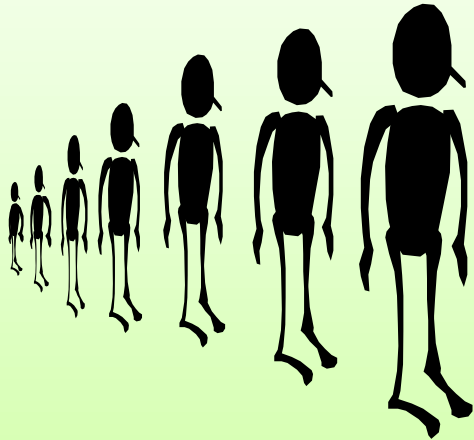
- R in clinical trials
- Dynamic adaptive randomisation
- Simulations
- Interactive web system
- Automated report generating



R in clinical trials

- R becoming more widely used in clinical trials
- Validation and Quality Assurance of the coding is an issue
- Introducing R to a clinical trials unit more used to using other packages

Simple randomisation



A

B

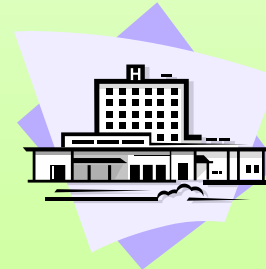
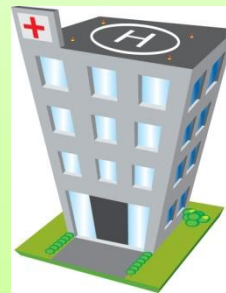
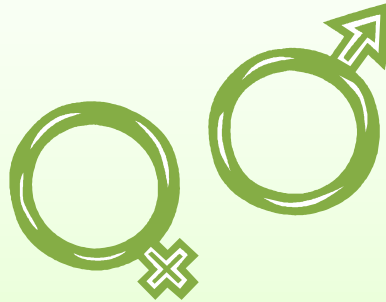
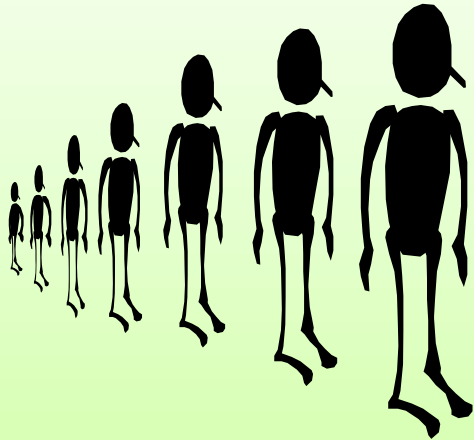


Dynamic adaptive randomisation

“Generalized method for adaptive randomization in clinical trials” *D. Russell, Z. Hoare et al.*

- Takes into account the participants already randomised
- Adjusts the probability boundary based on this information
- Takes into account overall balance, stratification level balance and stratum balance simultaneously
- Can accommodate various allocation ratios and number of treatment groups
- Assessment of loss and bias of the method

Trial scenario

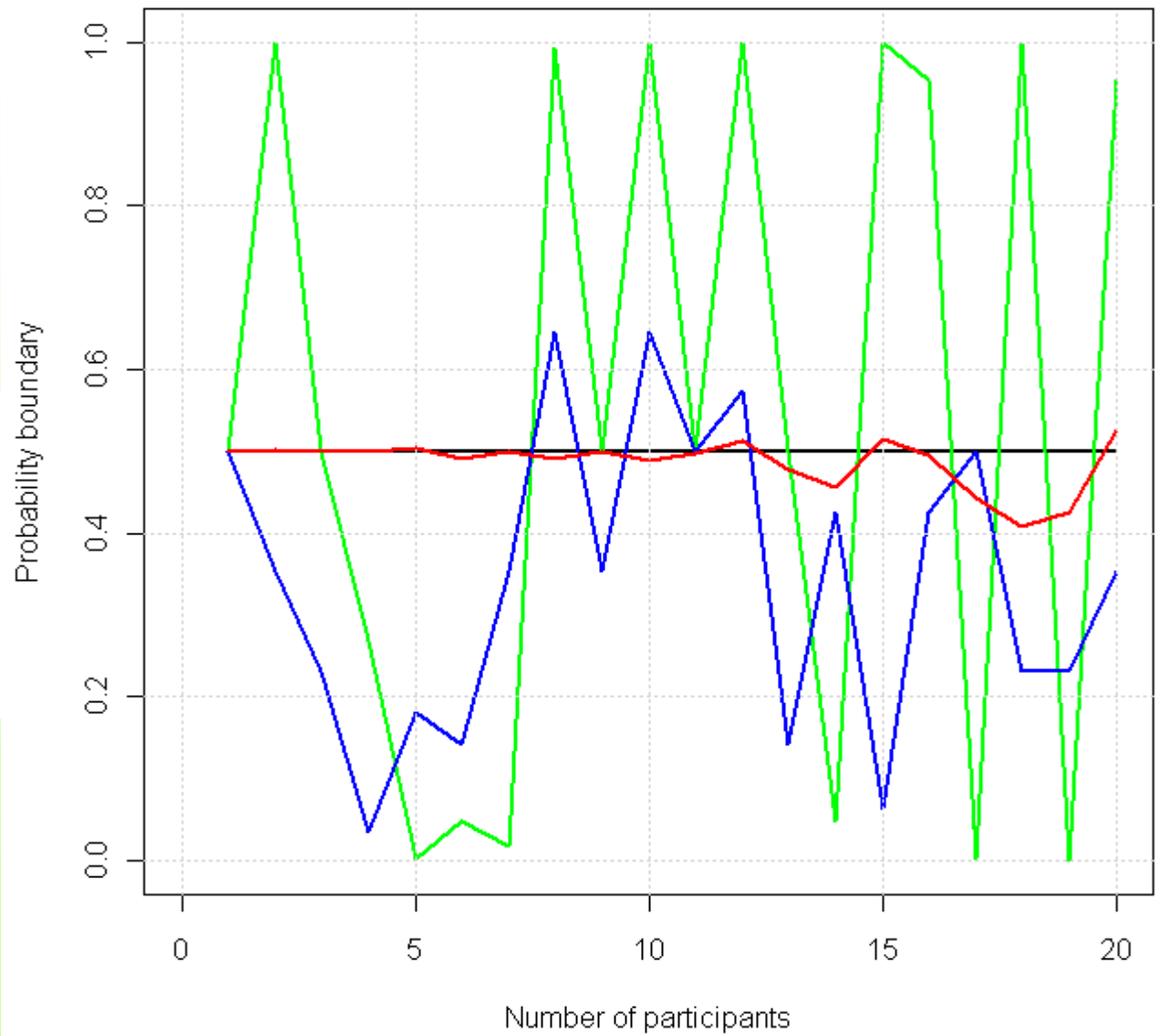


A

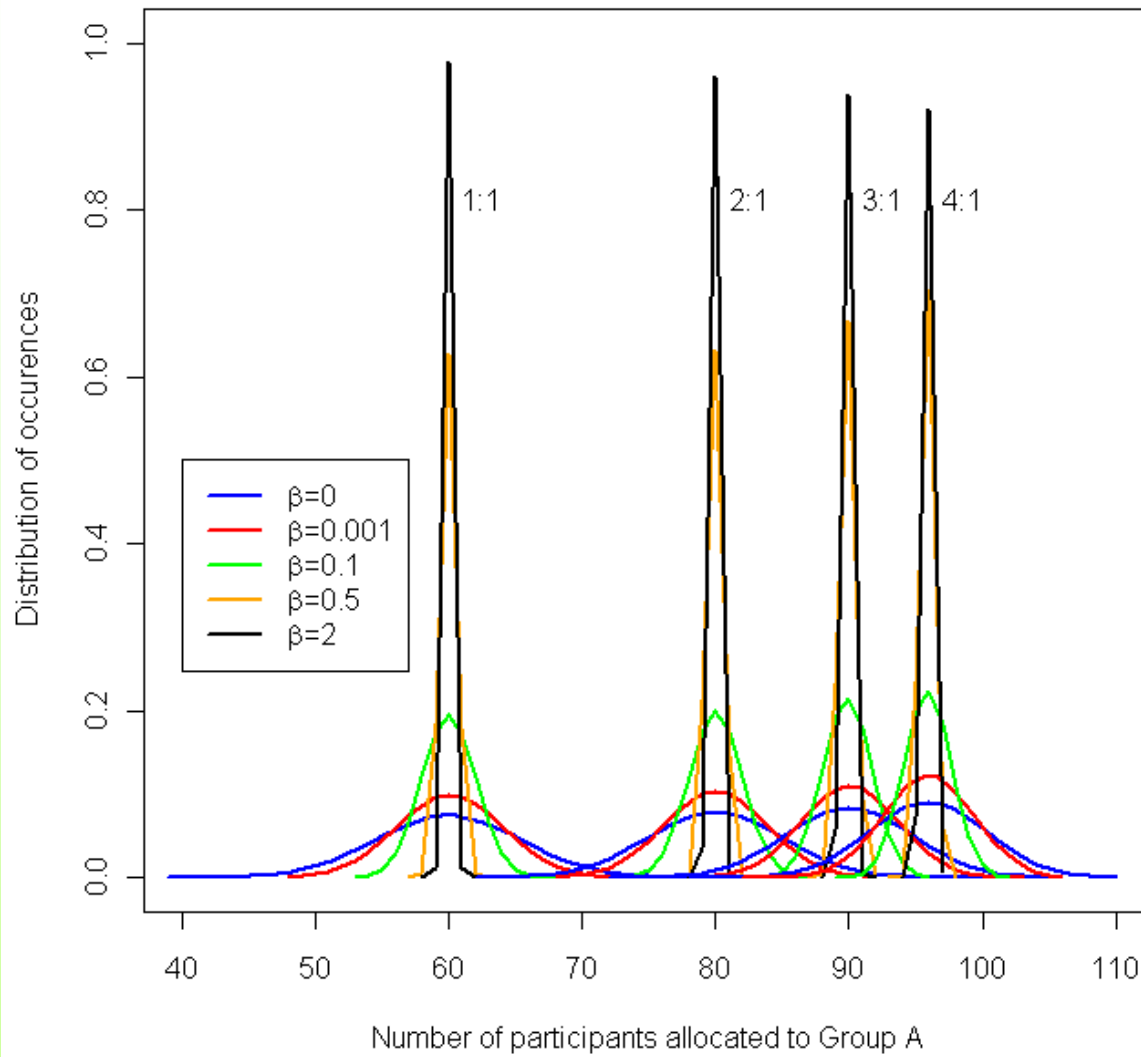
B

Parameters

- All 0
- Order of 0.01
- Order of 0.1
- Order of 1



Simulation of allocation for 120 participants (1000 replicates)





Simulation system

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q
2																	
3			Trial size	Variation			Number of simulations to repeat						File name for simulation to be saved to				
4			5	0			5000						sim5.Rdata				
5																	
6			Number of Groups to randomise into				Number of stratification variables										
7			2				1										
8																	
9			Group ratios (integers)				Number of levels in stratification variables										
10			A	1			Strat 1	2									
11			B	1													
12																	
13																	
14																	
15																	
16																	
17			PARAMETER SETS														
18			Up to 10 parameter sets may be entered at once														
19	4	CELL	TOTAL	STRAT 1													
20	1	0	0	0													
21	2	0.01	0.002	0.005													
22	3	0.3	0.3	0.3													
23	4	4	1	2													
24																	
25																	

Starting set up				
Update this field with current counts for a continuation simulation				
Cell	s1	GroupA	GroupB	
1	1	0	0	
2	2	0	0	



Simulation system output

- Provides the overall breakdown of allocation to treatment group
- Provides the information by each stratification level
- Provides the probability boundary frequency counts
- Provides the maximum sequence runs
- Allows generation of time point view
- Report generated using R2Word



Web based randomisation system

- Dynamic allocation algorithm now implemented using a web based system
- Allows trials ability to use a centralised randomisation 24hrs a day



Automation

- Data extraction via script / code
- Process data using Sweave / latex / R
 - High quality output
 - Repeatable
- Jenkins to control everything
- Subversion to manage versions
- Apache maven to glue it together

Automated report

EXAMPLE 1

Target randomisation 50

Target end date March 2012

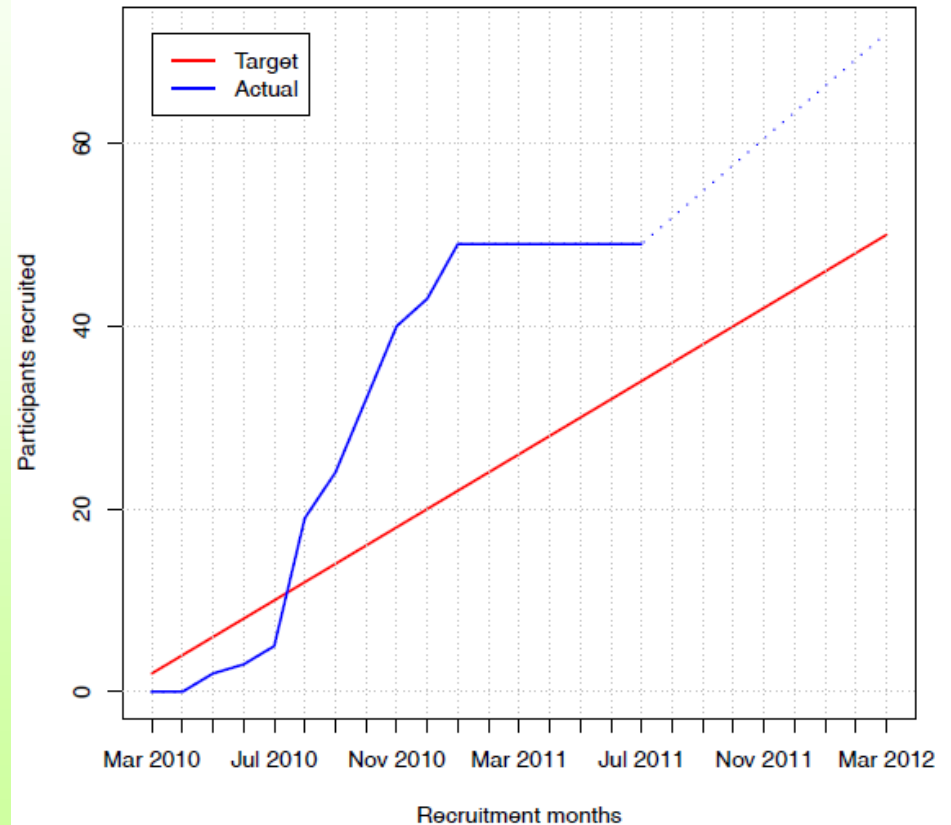
Achieved randomisation 49

Continued recruitment 66

Additional centres needed 0

Additional months needed 0

Predicted end date March 2012



Automated reporting

EXAMPLE 2

Target randomisation 300

Target end date November 2011

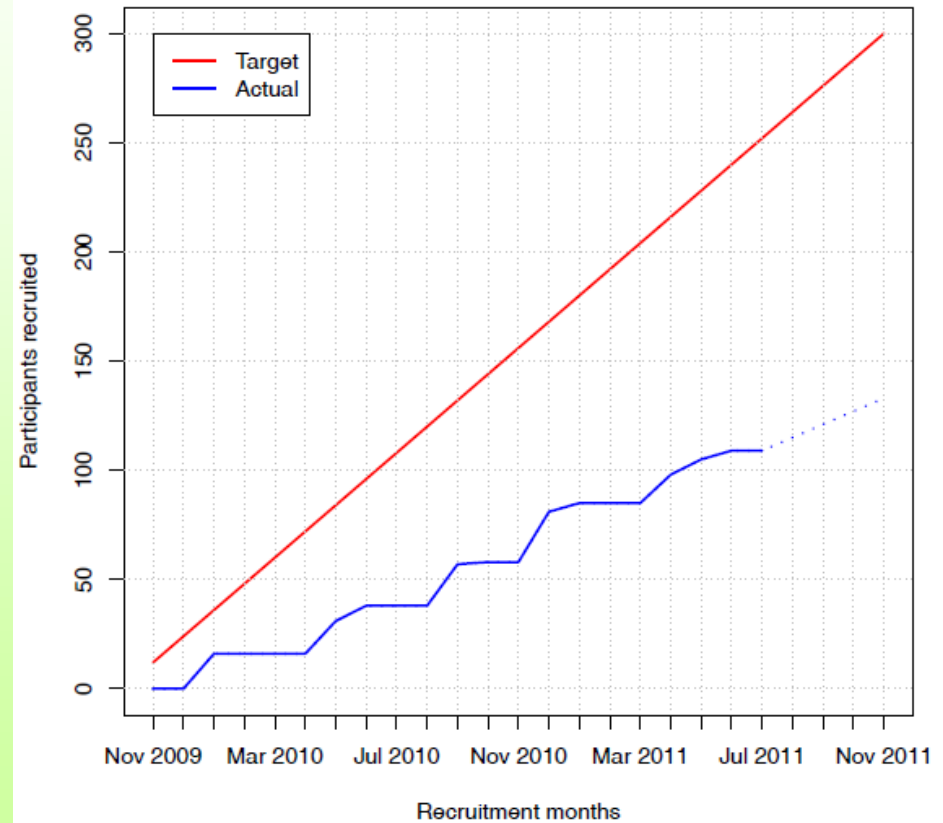
Achieved randomisation 109

Continued recruitment 133

Additional centres needed 21

Additional time needed 32 months

Predicted end of Feb 2014



Future work

- Algorithm
 - Need to update to encompass continuous valued stratification variables
- Simulation system
 - Needs to be made more robust
 - Adding to the web based system to be fully integrated
- Automation
 - Development of further automated set up and reporting functionalities

References

- Baier, T. and Neuwirth E. (April 2007) Excel::Com *Computational Statistics* 22(1) 91-108
- C.S. Group (2001) Effect of low dose mobile versus traditional epidural techniques on mode of delivery: a randomised controlled trial. *The Lancet* 358, 19-23
- Henry S., Wood D., Narasimhan B. (2009) Subject Randomization System, In *UseR! 2009 Conference* Rennes France pp.85
- Hewitt C., Torgerson D, (2006) Is restricted randomisation necessary? *BMJ* 332 1506-1508
- Russell D, Hoare Z, Whitaker Rh, Whitaker CJ, Russell IT. (2011) Generalized method for adaptive randomisation in clinical trials. *Statistics in Medicine* 30 922-934



Thank you

NWORTH

North Wales Organisation for Randomised Trials in Health
and Social Care

Bangor University

www.bangor.ac.uk/imscar/nworth