The Queen's Anniversary Prizes
For Higher and Further Education
2017

HSRU
Promoting Excellence in Health Services Research

Quality matters: why randomised trials are essential and how we can make them better

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TRIAL FORGE

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MRC | Hubs for Trials Methodology Research

OK to ask about clinical research

NHS National Institute for Health Research

Trials Change Lives

"Clinical trials are the backbone of primary research that informs clinical practice in the NHS in the UK"

Prof Hywel Williams, Director, Health Technology Assessment Programme (NIHR)

Listen to the podcast

Clinical Trials for the NHS

www.methodologyhubs.mrc.ac.uk/trials-change-lives/

Photo reference,
Queen's University Belfast

What questions do randomised trials do really well?

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1. In people with x
2. ..does Treatment A increase/reduce/make no important difference
3. ..to y
4. ..compared to Treatment B?

What questions do randomised trials do really well?

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1. In people with sore throat
2. ..do antibiotics reduce
3. ..throat soreness
4. ..compared to no antibiotics?

The wisdom of Donald Rumsfeld..

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"[T]here are known knowns; there are things we know we know. We also know there are known unknowns; that is to say we know there are some things we do not know.

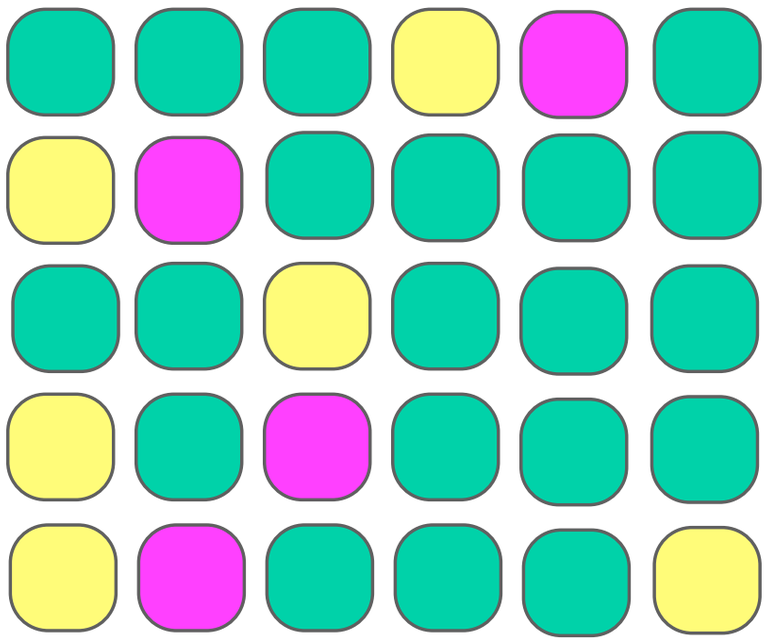
But there are also unknown unknowns – the ones we don't know we don't know."

—Former US Secretary of Defence, Donald Rumsfeld

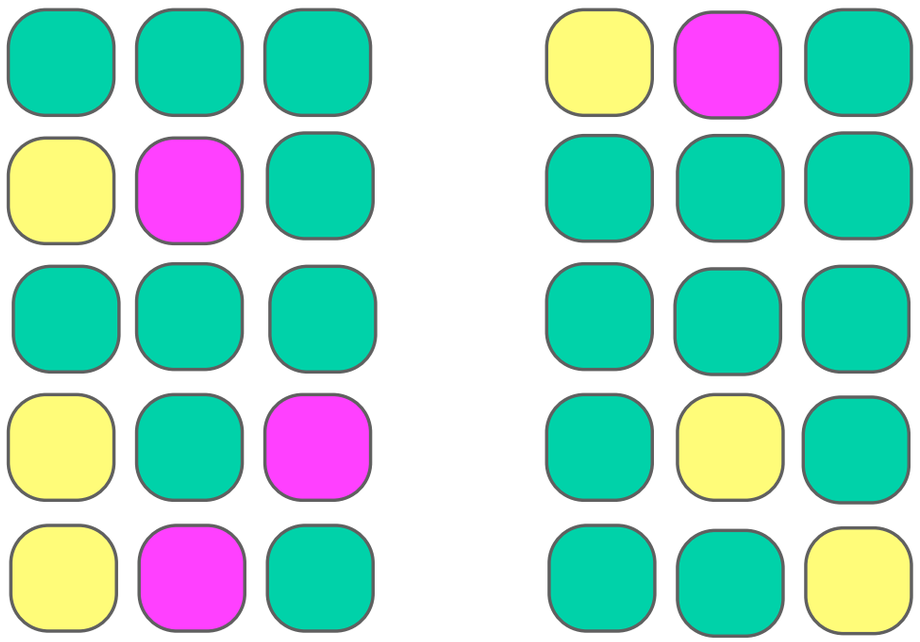
Creating your trial groups

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Community population



Your trial population

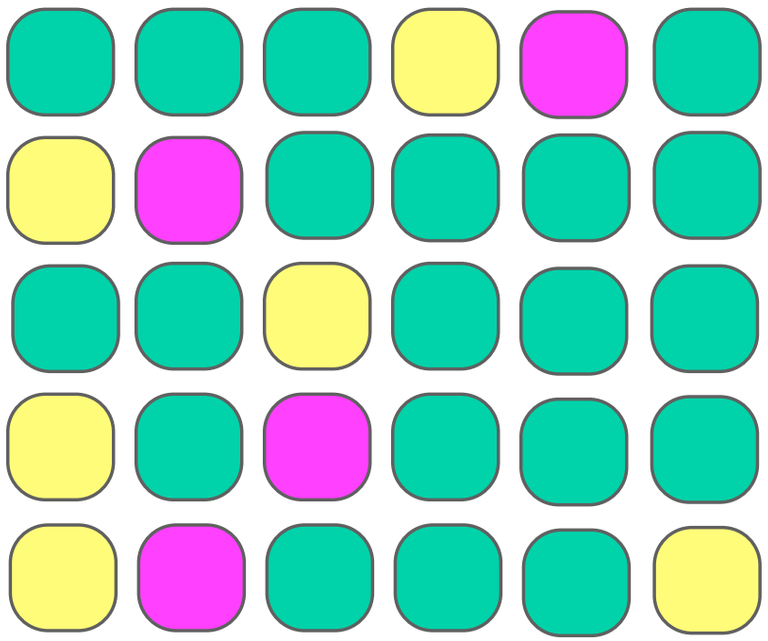


You can match the groups for thing you know about (green and yellow).

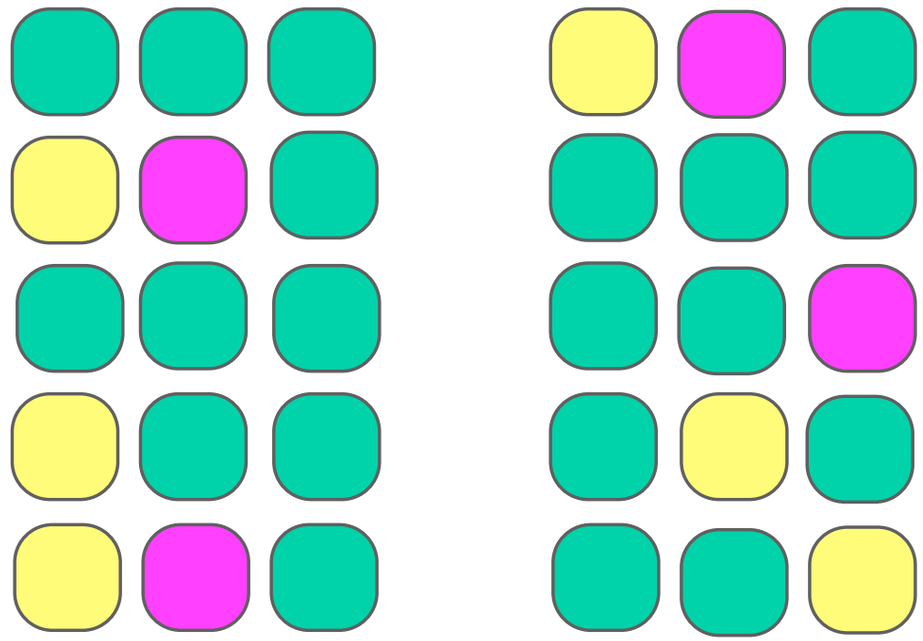
Creating your trial groups

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Community population



Your trial population



Randomly allocate to groups, which deals with green, yellow and the purple (i.e. an unknown unknown).

Randomisation does something other methods don't–

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It fairly distributes things you don't know are important. Great stuff.

Randomisation does something other methods don't–

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It fairly distributes things you don't know are important. Great stuff.

There are now plenty of ways of messing things up.

Trials– important but not always efficient

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*'There is a peculiar paradox that exists in trial execution - we perform clinical trials to generate evidence to improve patient outcomes; however, we conduct clinical trials like anecdotal medicine.'**

*Monica Shah in 'Site selection in global clinical trials in patients hospitalized for heart failure: perceived problems and potential solutions'. Heart Failure Review 2014; 19:135-52.

What is an efficient trial?

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- Scientific efficiency: right question, right design
- Process efficiency: do what is needed to answer question, keeps focused, results made public in a way people can understand

Scientific efficiency

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- Who am I designing my trial for and what do they need?
- How do you know someone hasn't already answered their questions?
- What have you done to make sure the intended users of your results don't have to dismiss your trial as irrelevant?

Design for your users, not yourself

Scientific (in)efficiency

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BMJ 2014;349:g5219 doi: 10.1136/bmj.g5219

RESEARCH

Ability of a meta-analysis to prevent redundant research: systematic review of studies on pain from propofol injection

OPEN ACCESS

Céline Habre *research fellow*[1], Martin R Tramèr *professor in anaesthesia*[2 3], Daniel M Pöpping *anaesthetist*[4], Nadia Elia *public health epidemiologist*[2 5]

[1]Department of Radiology, Geneva University Hospitals, 4 rue Gabrielle-Perret-Gentil, CH-1211 Geneva 14, Switzerland; [2]Division of Anaesthesiology, Geneva University Hospitals, Geneva, Switzerland; [3]Faculty of Medicine, University of Geneva, Geneva, Switzerland; [4]Department of Anaesthesiology and Intensive Care, University Hospital Münster, Münster, Germany; [5]Institute of Global Health, Faculty of Medicine, University of Geneva, Geneva, Switzerland

Scientific (in)efficiency

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thebmj

BMJ 2014;349:g5219 doi: 10.1136/bmj.g5219

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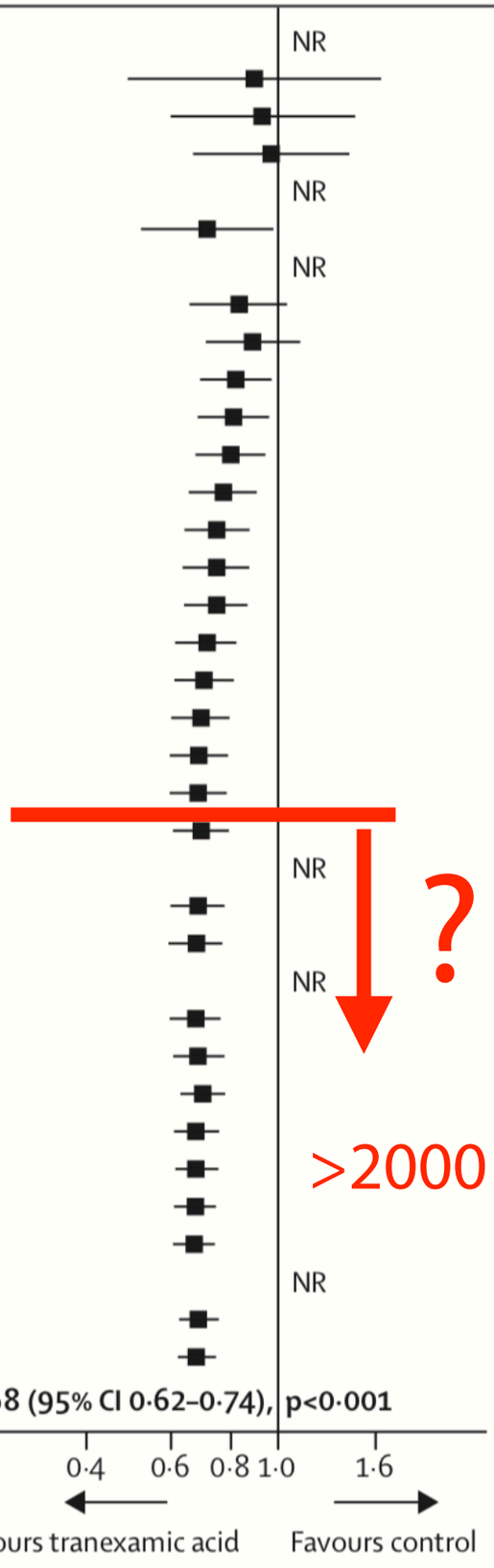
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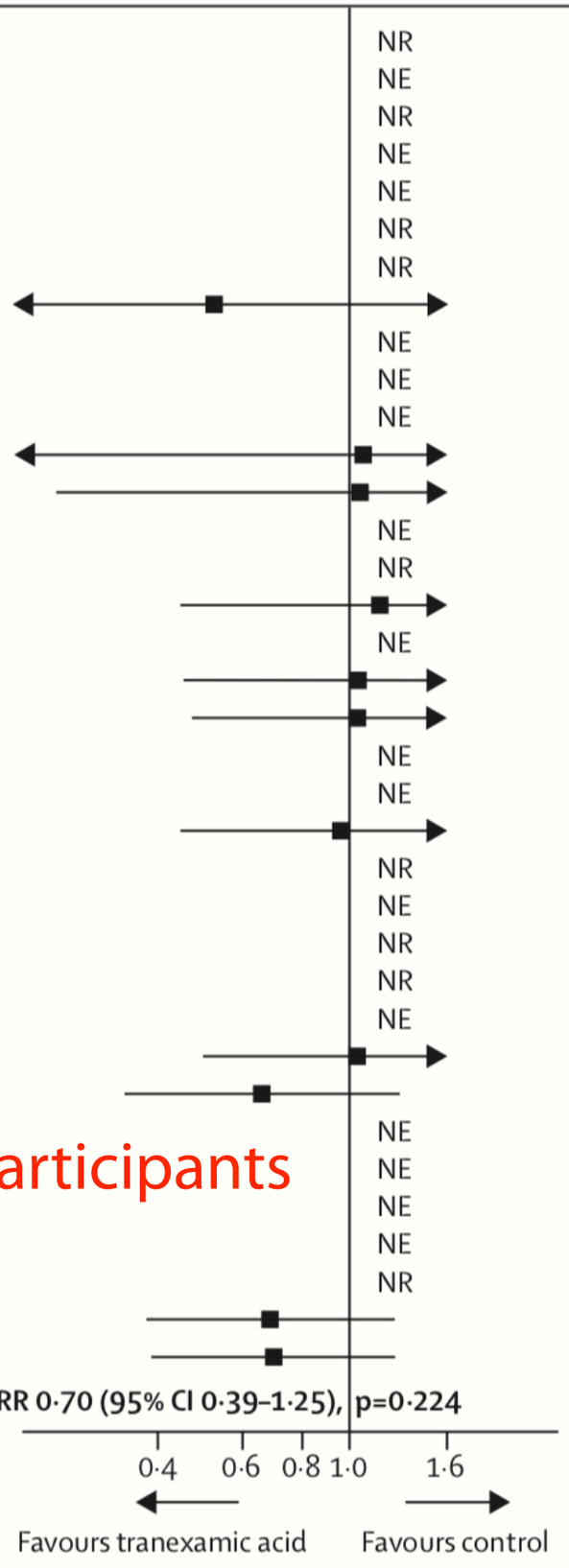
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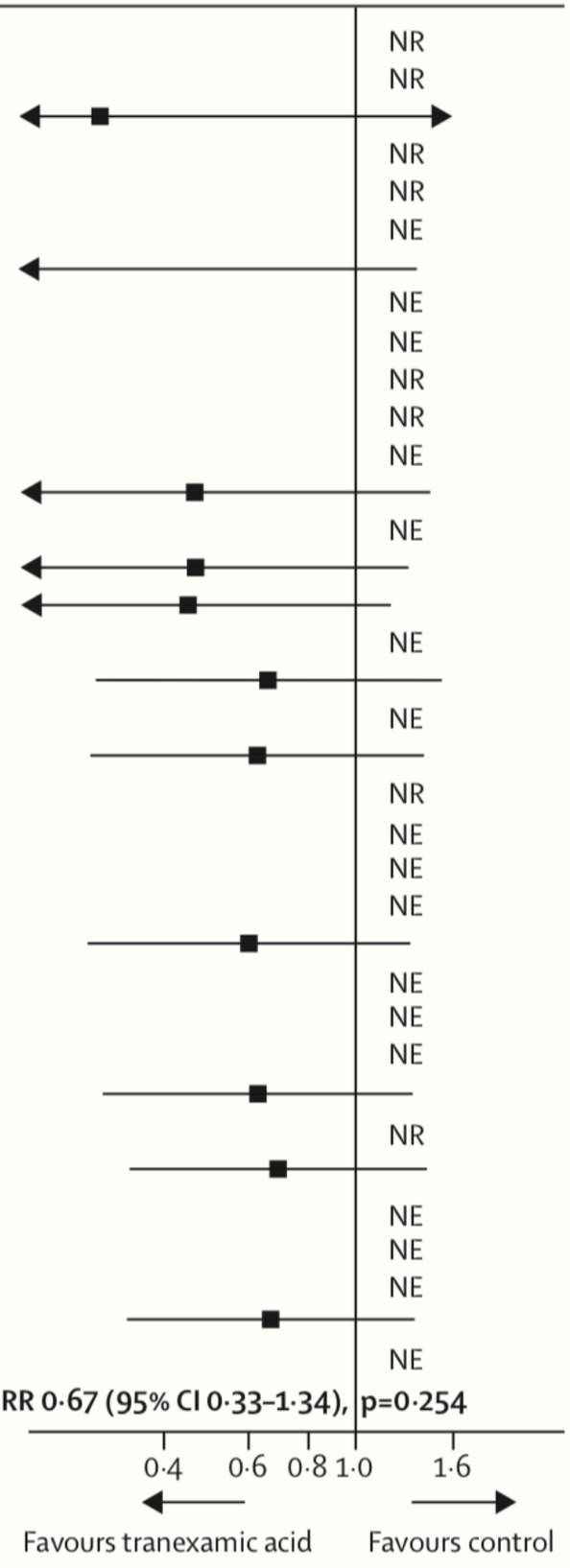
Number of clinically irrelevant trials:

87 of 136 (64%)

Year of study	Number of patients	Blood transfusion RR (95% CI)	Myocardial infarction RR (95% CI)	Death RR (95% CI)
1990	38	NR	NR	NR
1991	81		NE	NR
1995	30		NR	
1995	145		NE	NR
1995	147	NR	NE	NR
1996	86		NR	NE
1996	45	NR	NR	
1998	86			NE
2000	39		NE	NE
2001	99		NE	NR
2001	40		NE	NR
2001	38			NE
2002	58			
2003	40		NE	NE
2004	102		NR	
2005	120			
2005	100		NE	NE
2005	312			
2005	40			NE
2006	62		NE	
2006	29		NE	NR
2006	100			NE
2007	222	NR	NR	NE
2007	50		NE	NE
2007	67		NR	
2008	55	NR	NR	NE
2008	64		NE	NE
2008	147			NE
2009	202			
2009	100		NE	NR
2010	110		NE	
2010	660		NE	NE
2011	39		NE	NE
2011	44	NR	NR	NE
2011	63			
2011	200			NE
Total	**3860**	**RR 0·68 (95% CI 0·62–0·74), p<0·001**	**RR 0·70 (95% CI 0·39–1·25), p=0·224**	**RR 0·67 (95% CI 0·33–1·34), p=0·254**







Process efficiency

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How do we know that the way we propose to do something is the most effective way of doing it?

Recruitment

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- Generally accepted that around 50% of trials fail to recruit to target (and it's probably worse than this).

- Rated as Methods Problem #1 by UK Clinical Trials Unit Directors.

Cochrane Library

Cochrane Database of Systematic Reviews

Strategies to improve recruitment to randomised trials (Review)

Treweek S, Pitkethly M, Cook J, Fraser C, Mitchell E, Sullivan F, Jackson C, Taskila TK, Gardner H

TRIAL FORGE

http://onlinelibrary.wiley.com/doi/10.1002/14651858.MR000013.pub6/full

What improves trial recruitment?

OPEN TRIAL

10%

(95% CI = 7% to 13%)

(an increase)



2 studies; 4833 participants

TELEPHONE REMINDERS

6%

(95% CI = 3% to 9%)

(an increase)



2 studies; 978 participants

USER-TESTED PATIENT INFORMATION LEAFLET

1%

(95% CI = -1% to 3%)

(little or no increase)



3 studies; 8935 participants

What further research is needed?

- More replication is needed across a range of trials.
- See the Cochrane review's *Implication for methodological research* section for prioritised recruitment interventions in need of evaluation.

Published Feb 2018

www.trialforge.org

What might help?

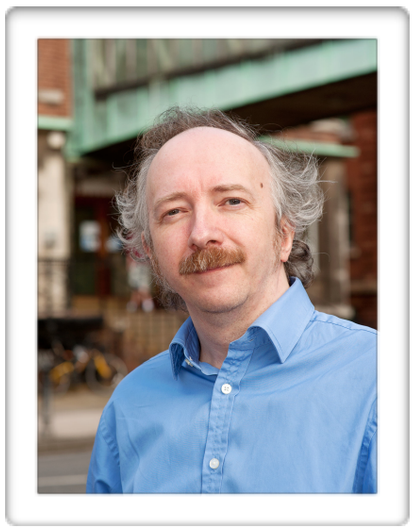
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1. SWATs – a Study Within A Trial
2. Co-operation

SWATs– why bother?

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It is essential that trials are done in the most effective and efficient ways and one way to do this is to use the same types of evaluation to investigate and improve the processes of how we do randomised trials.



Mike Clarke,
Belfast, UK

What is a SWAT?

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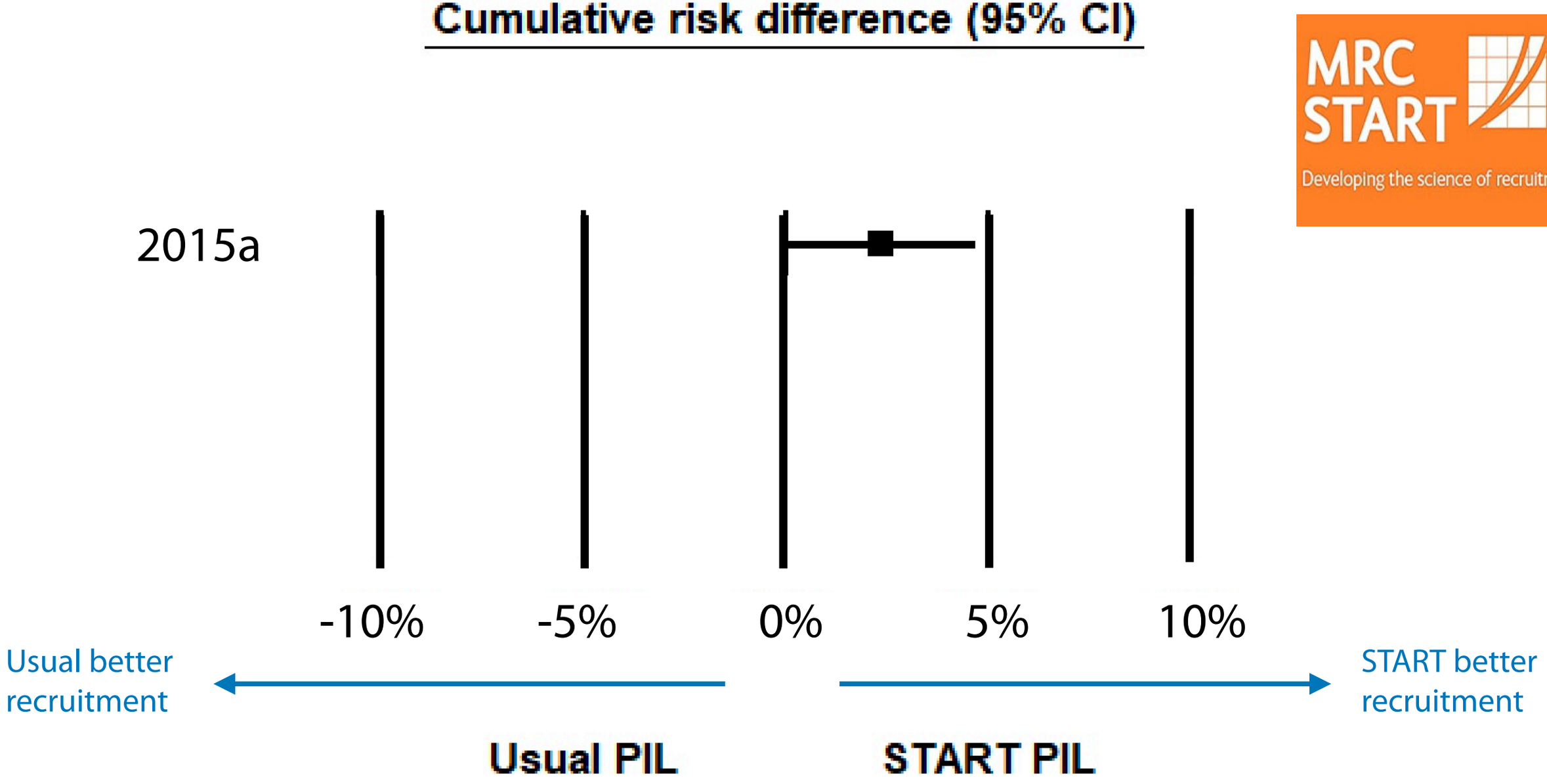
A SWAT is a self-contained research study that has been embedded within a host trial with the aim of evaluating or exploring alternative ways of delivering or organising a particular trial process.*

*Trial Forge Guidance 1: What is a Study Within A Trial (SWAT)? Trials 2018, 19: 139

SWATs– e.g. presenting information to potential participants

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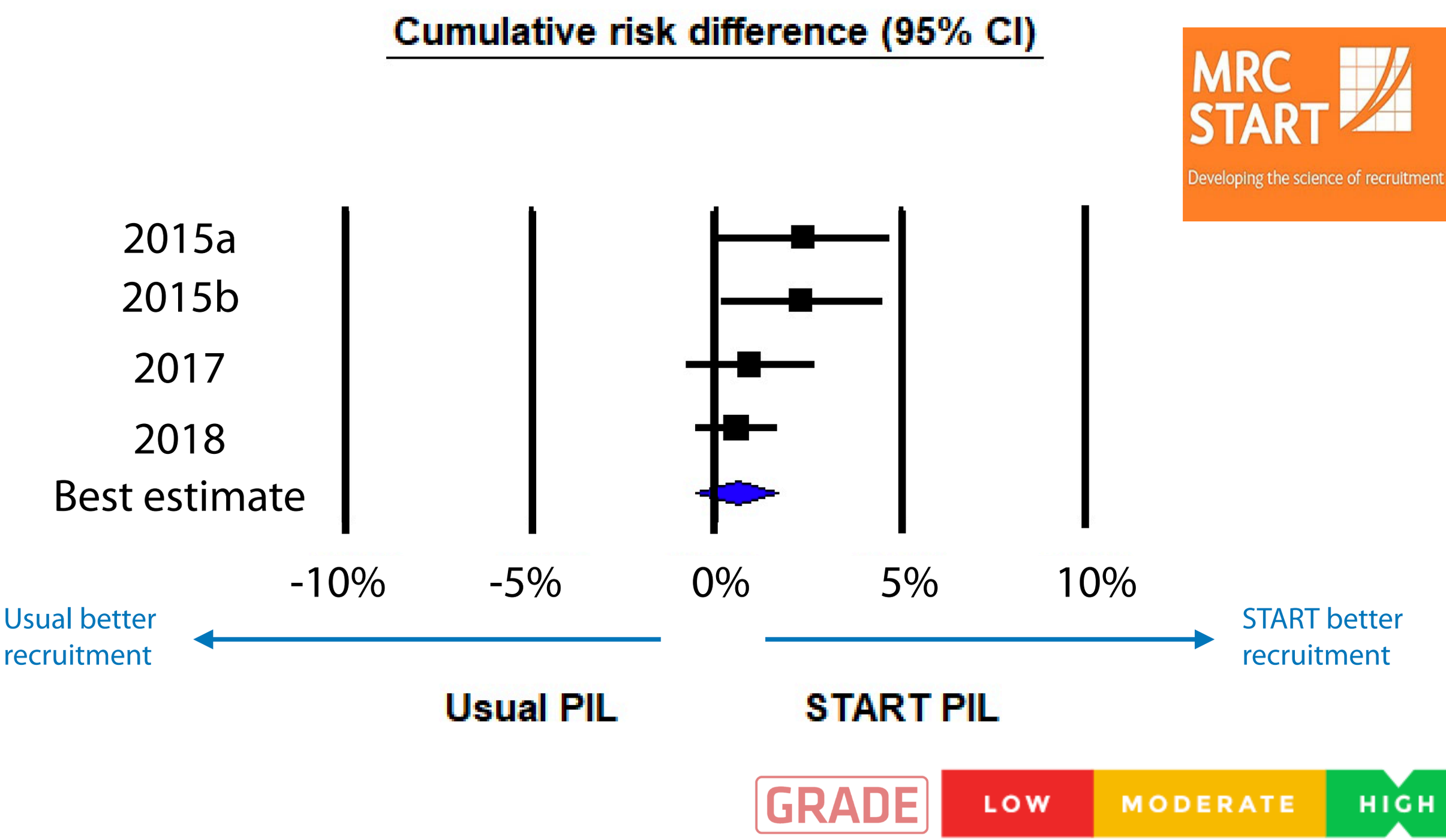
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Developing the science of recruitment



SWATs– e.g. presenting information to potential participants

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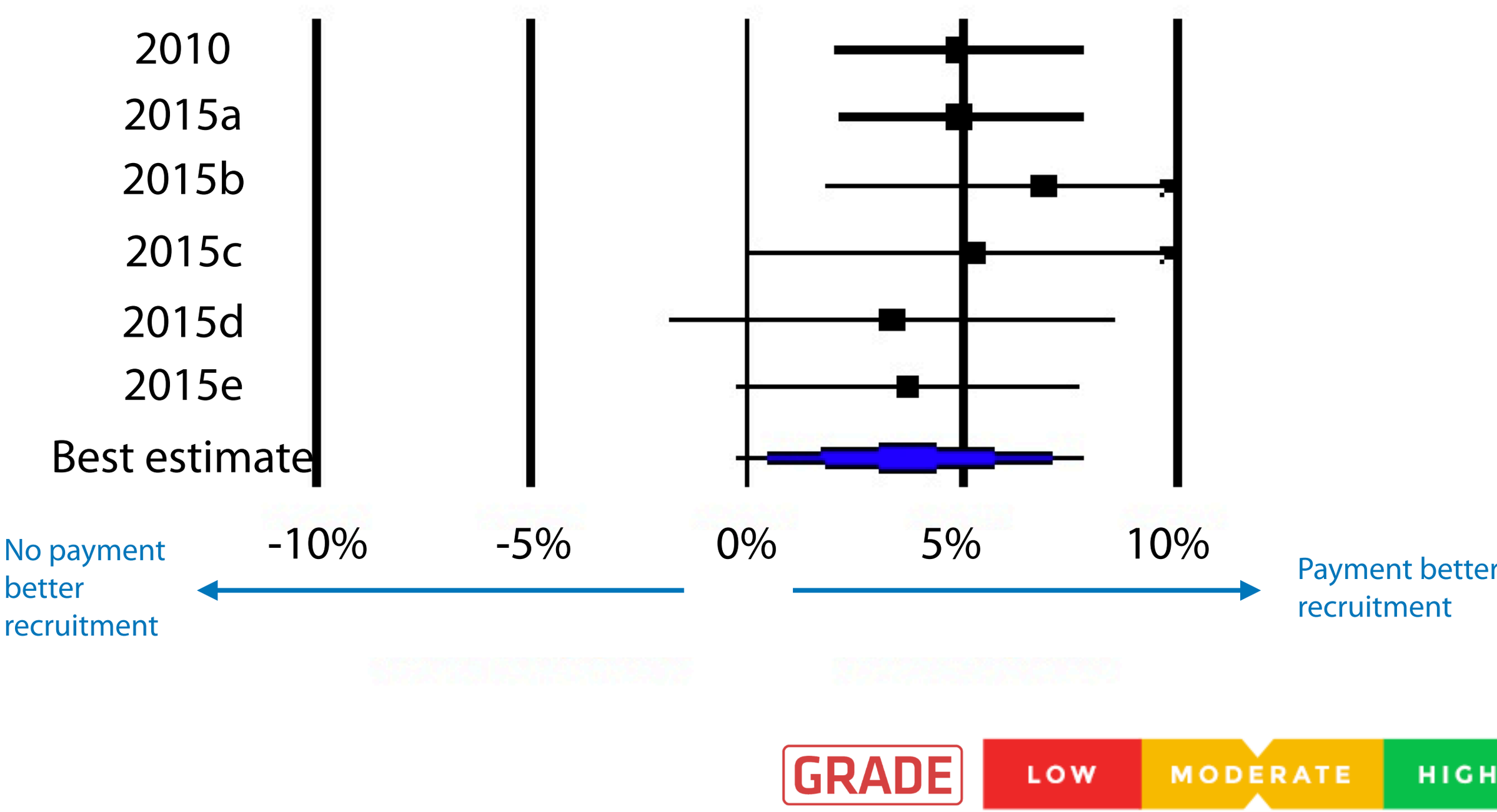
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GRADE LOW MODERATE HIGH

SWAT– financial incentives

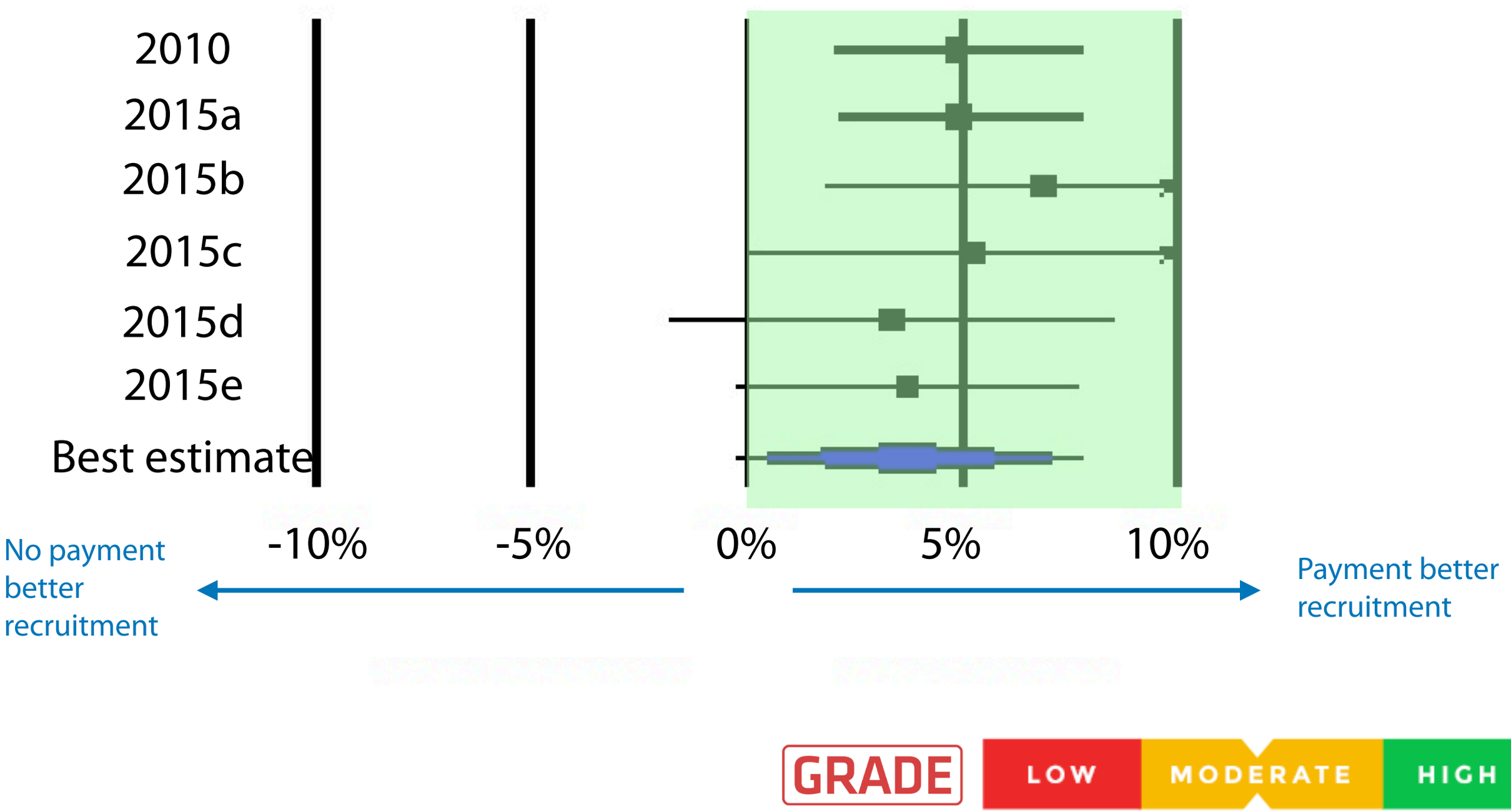
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GRADE LOW MODERATE HIGH

SWAT– financial incentives

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GRADE LOW MODERATE HIGH

Co-operation and networks

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ESP2
Estimating site performance

UKTMN
Trial Managers' Network

Welcome *to the*
ESP2 PROJECT

Are you setting up new trial recruitment sites?

If you are, ESP2 needs you!

Setting up trial recruitment sites takes time and effort. Not all of this effort is rewarded because not all of those sites will recruit as planned but are likely to take up just as much, if not more, of your time as sites that do recruit.

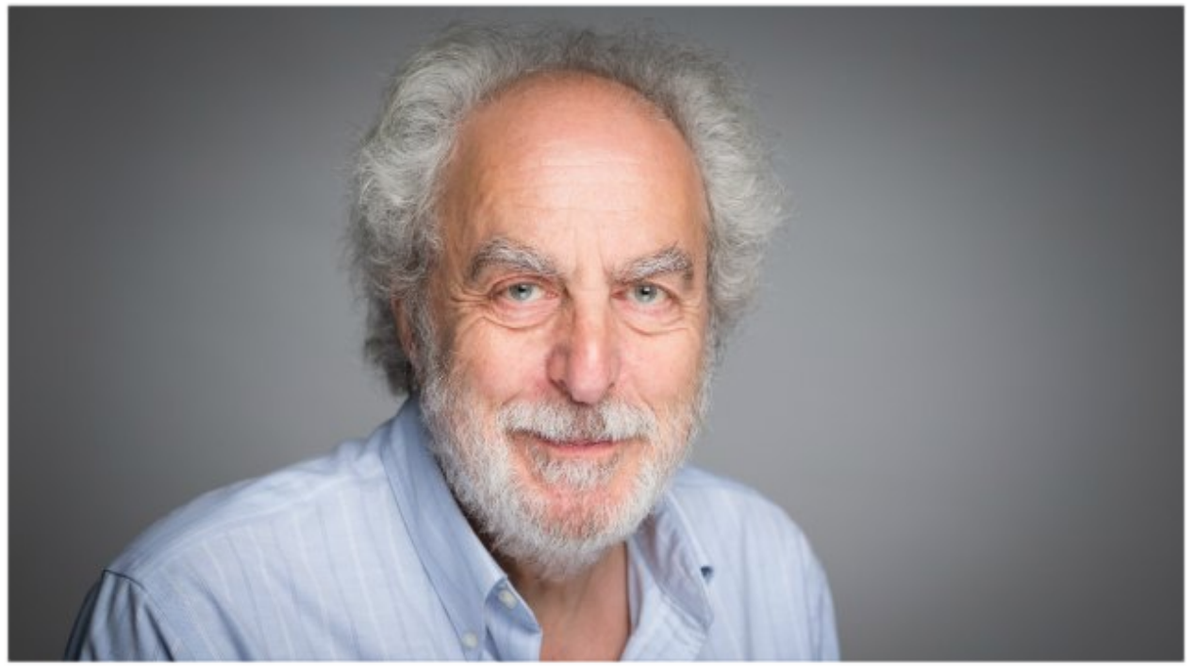


Summary–do better research, not more

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WE NEED LESS RESEARCH,
BETTER RESEARCH,
AND RESEARCH DONE
FOR THE RIGHT REASONS.

– DOUG ALTMAN



Doug Altman

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Promoting Excellence in Health Services Research

TRIAL FORGE

www.trialforge.org

If you have any further questions please contact:

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