Why is waste in research an ethical issue?

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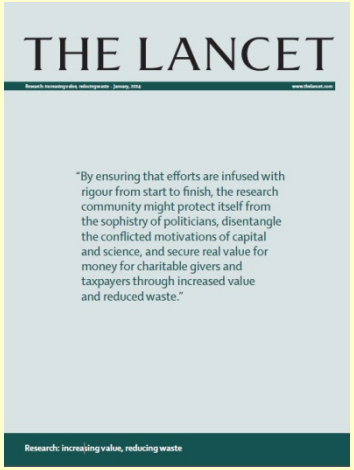
Themes



- Why does research waste matter?
- When / how does waste occur?
- What harm does research waste do?
- How can we reduce waste in research?

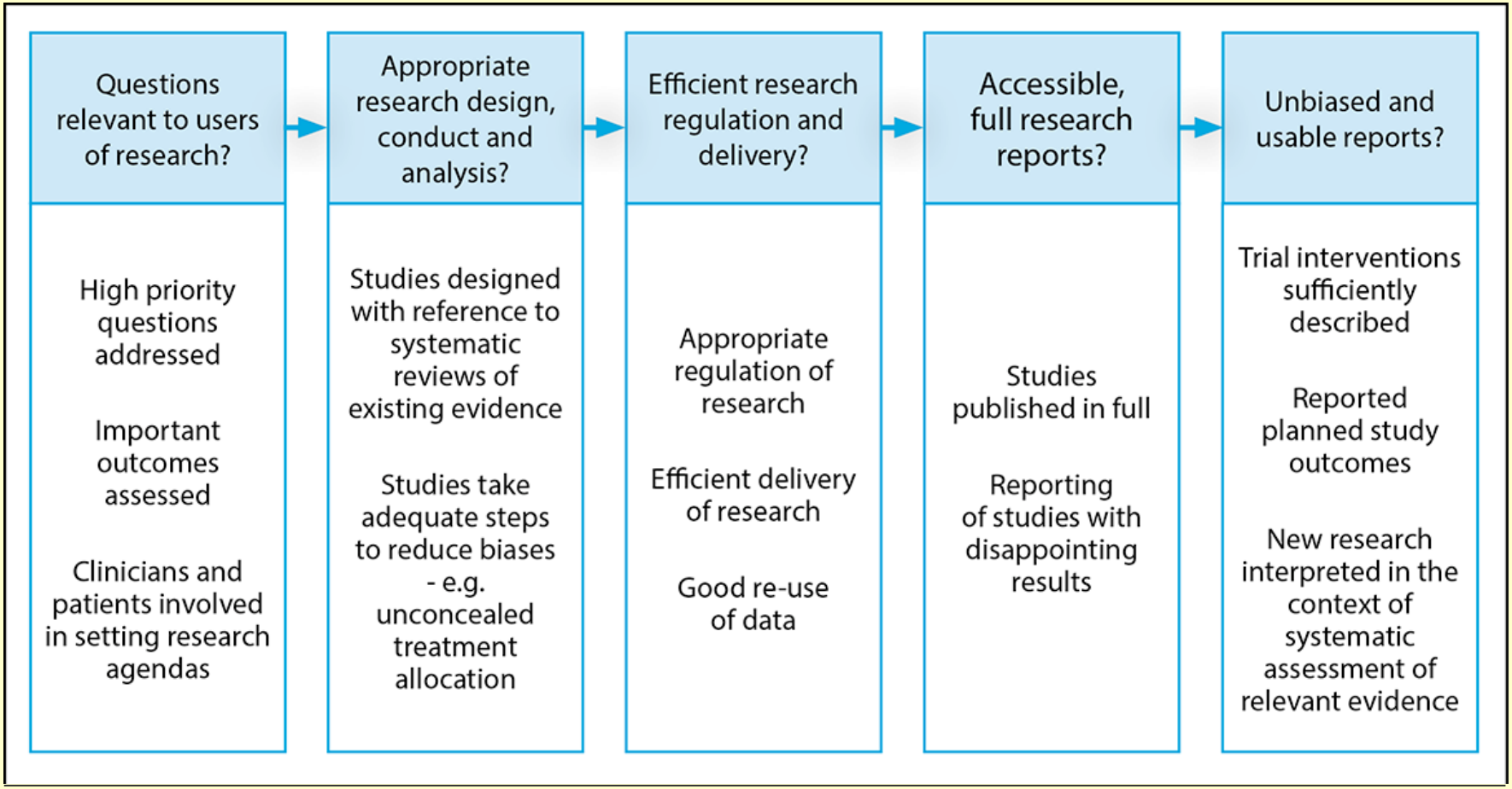
Wrong questions | Weak designs | Publication bias | Unusable reports

Research funding is finite

If someone takes a slice there is less left for everybody else …

Waste occurs in all stages of research

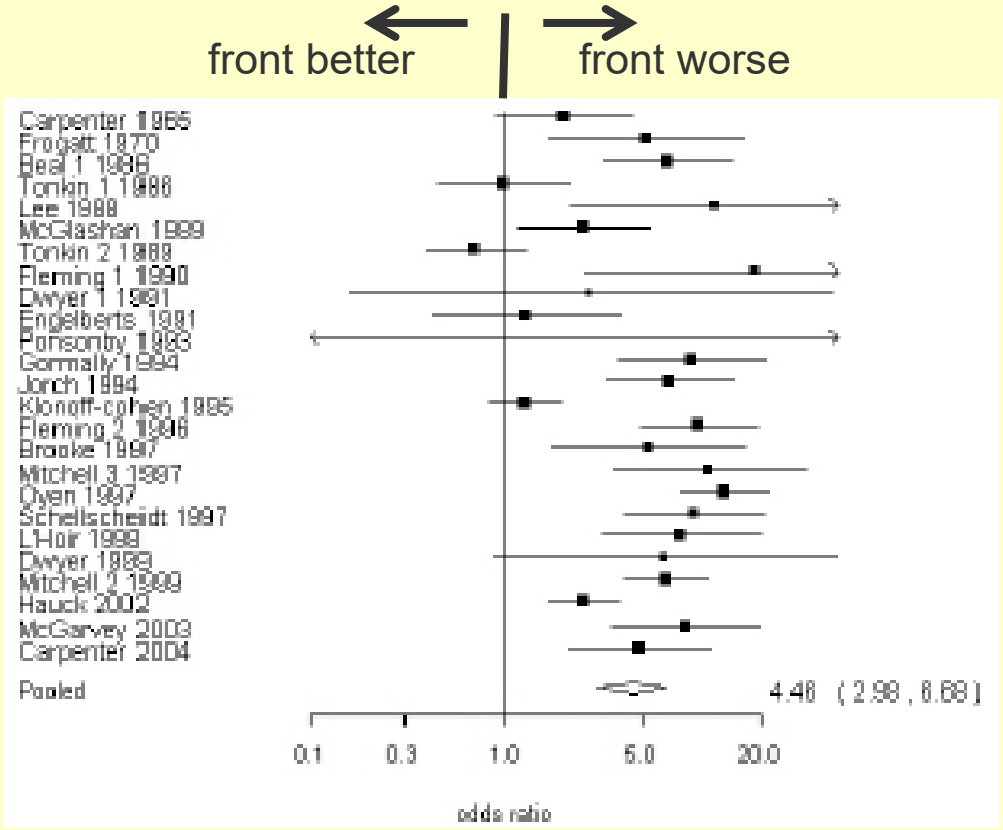
Questions | Design/conduct | Regulation | Accessibility | Usability



Ethical impacts

1. Asking the wrong questions
2. Weak study designs
3. Not publishing all research
4. Poor reporting quality

Sleeping position and sudden infant death



Individual studies (by year) 1965-2004

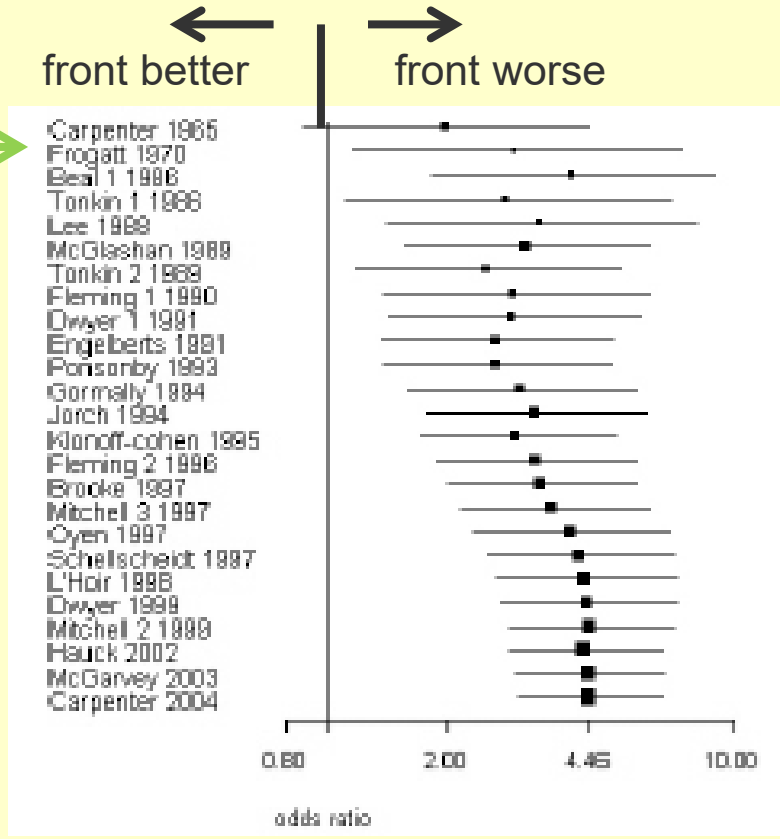
Gilbert et al *Int J Epidemiol* 2005;**34:**874

Wrong questions

Sleeping position and sudden infant death

Cumulative effect (by year)

Clear effect by 1970



increased risk of sudden infant death

Gilbert et al *Int J Epidemiol* 2005;**34:**874

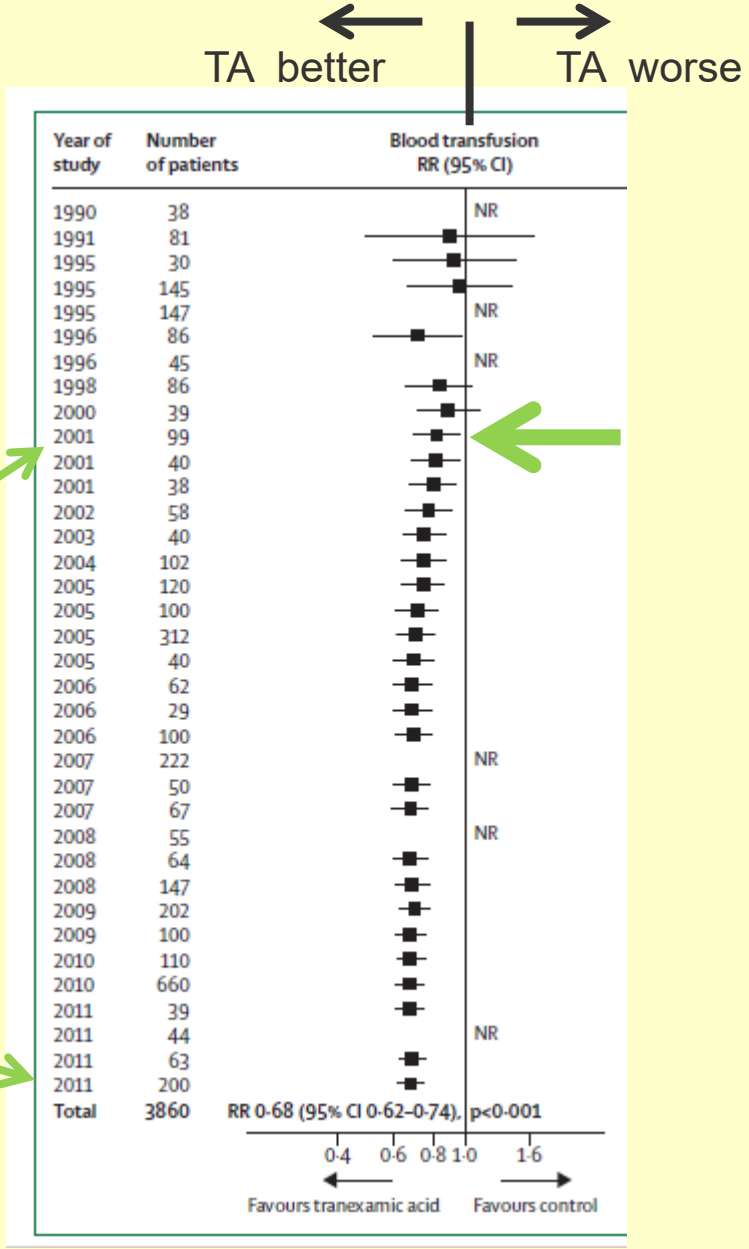
Wrong questions

This mother was right!

- Up to 1988 UK & US books recommended babies should sleep on their front
- But since 1970 there was clear evidence that front sleeping significantly **increased** sudden infant death
- Earlier recognition of risk of front sleeping could have prevented >60,000 infant deaths

Effect of tranexamic acid (TA) on blood loss during surgery

Cumulative meta-analysis shows effect by 2001 but trials continue until 2011



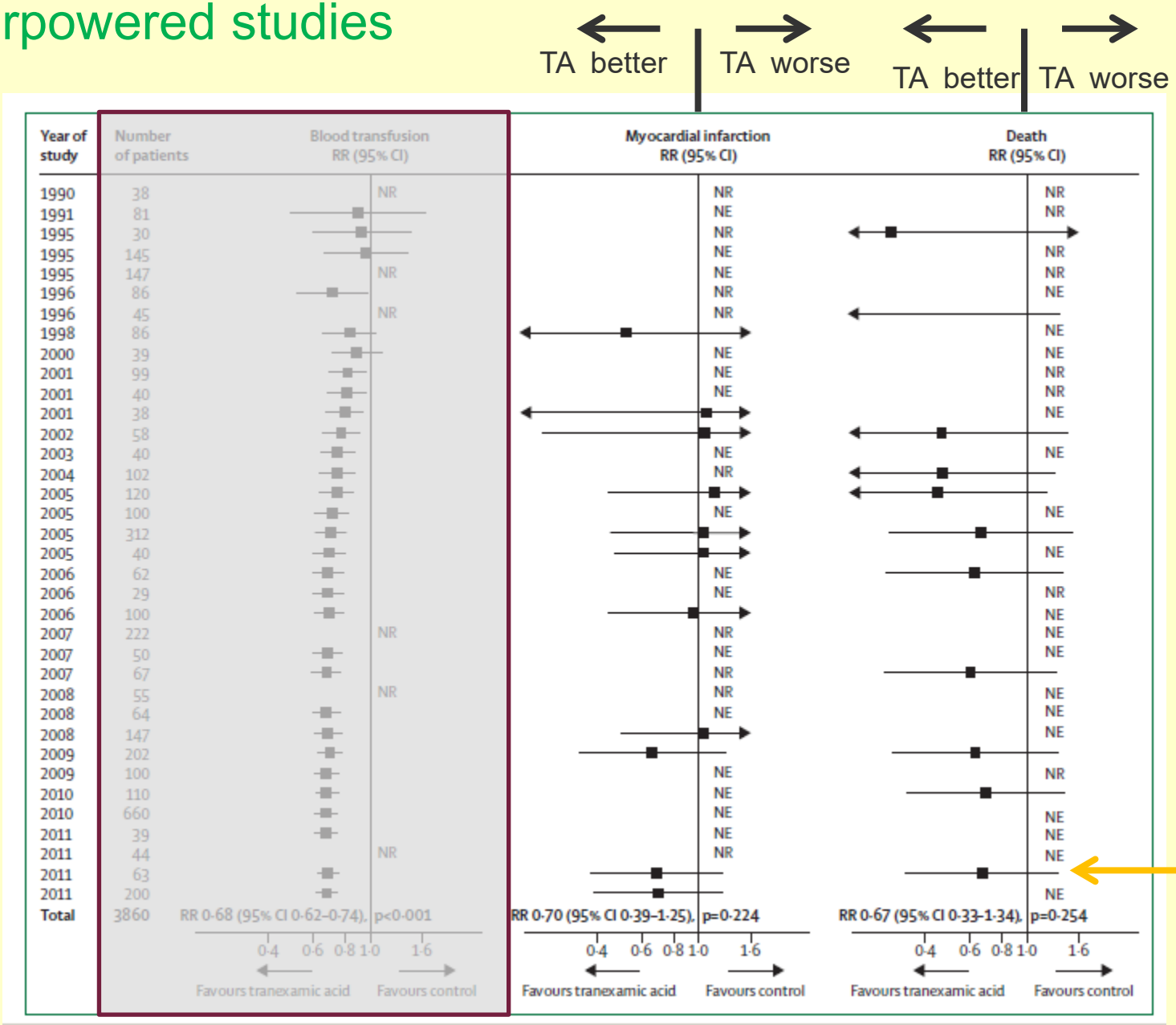
Based on Ker et al *BMJ* 2012;**344**:e3054

Wrong questions

Asking the wrong question
Weak study design

- Patients undergoing surgery involved in unnecessary trials, some receiving sub-optimal treatment, despite clear evidence that tranexamic acid reduces blood loss
- BUT, despite all the studies, they were too small to show whether tranexamic acid also reduced heart attacks and death

Underpowered studies



Heart attack

Death

Weak designs

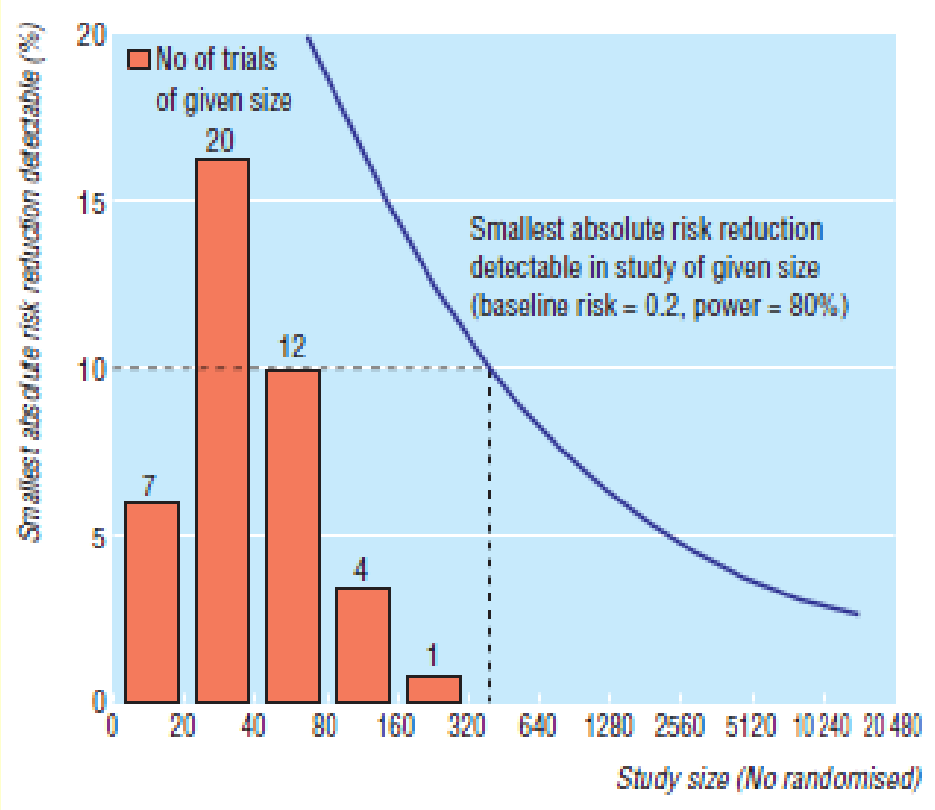
Underpowered studies

- Big problem in preclinical (animal) research
- Risk of not detecting true effect and reporting 'false positive' effect

- Systematic reviews found:
  3% animal studies in stroke
  0% in Alzheimer's / Parkinson's disease
  reported sample size calculation

Underpowered studies

- Meta-analysis of 44 animal studies of fluid resuscitation
- Average number of animals / treatment group was 13
- No trial was large enough to reliably detect a 10% absolute difference (halving) in risk of death

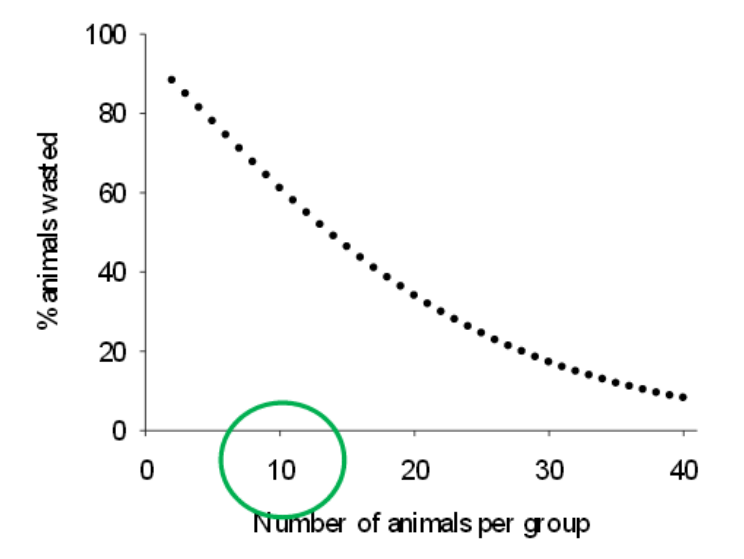


Trial size and smallest absolute risk reduction detectable

Roberts et al *BMJ* 2002;**324**:474

Wasting lab animals

Number of animals	Power	% animals wasted
4	18.6%	81.4%
8	32.3%	67.7%
16	56.4%	43.6%
32	85.1%	14.9%



Chances of wasting an animal in 2-group study seeking 30% reduction in infarct volume with SD = 40%

From CAMARADES

Weak designs

Poor design in animal studies on multiple sclerosis

- Meta-analysis of 1117 publications
  - 9% reported random allocation to group
  - 16% had blinded assessment of outcome
  - <1% had sample size calculation

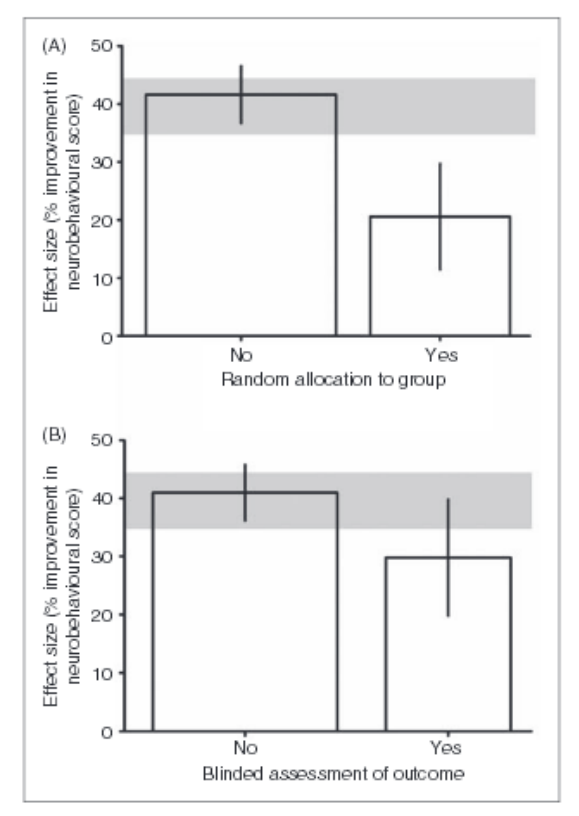
Vesterinen et al *MS* 2010;**16:**1044

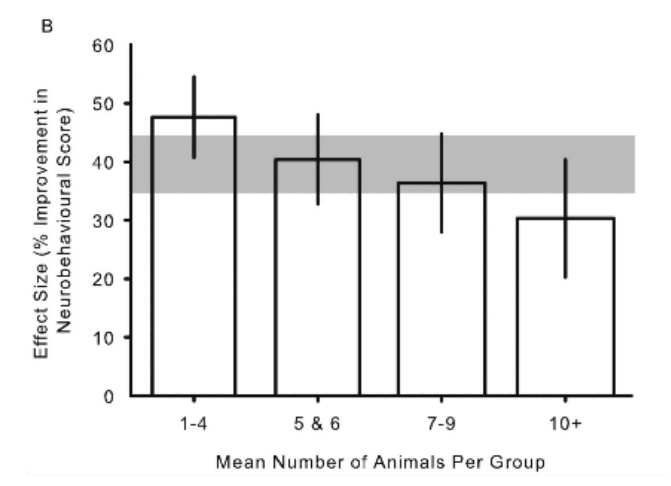
Weak designs

Weak design in animal studies over-estimates effect size

Randomization

Blinded assessment





Group size

Review of 1117 studies in multiple sclerosis

Vesterinen et al *MS* 2010;**16:**1044

Weak designs

Much research is never published

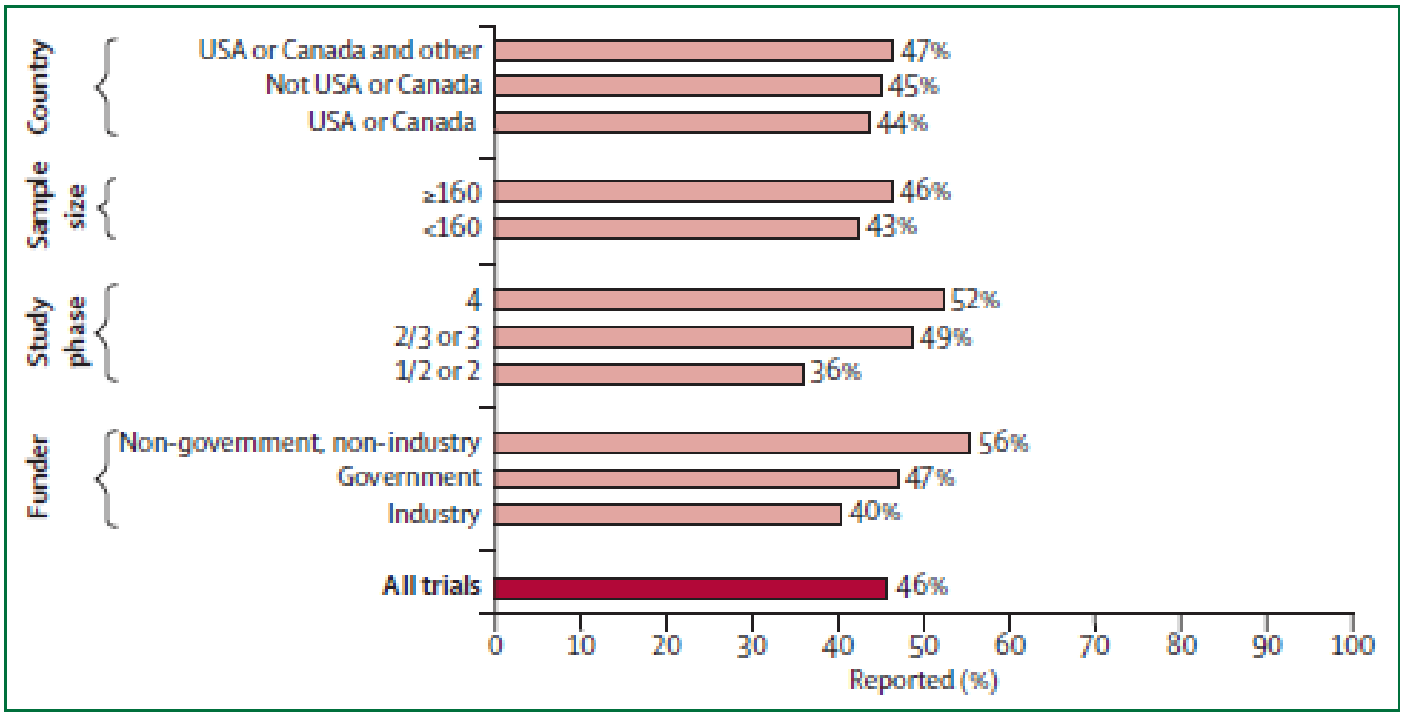


Figure 2: **Reporting of completed trials, by study characteristic**
Data taken from Ross and colleagues' analysis[11] of a random sample of 677 completed trials registered with ClinicalTrials.gov between 2000 and 2007.

Publication bias

50% of clinical trials unpublished

Of EU-funded health research 1998-2006

- 50% unpublished
- 570 million Euros of research had "no detectable academic output"

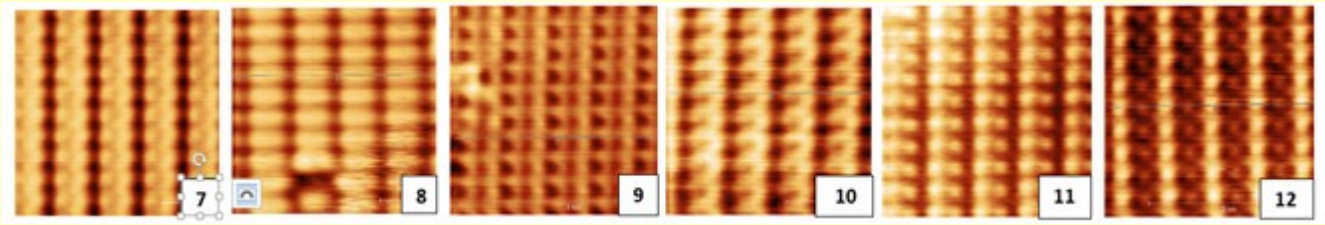
Galsworthy et al *Lancet* 2012;**380**:971

- Situation may be improving but evidence-base for most prescribed medicines is badly affected by non-publication

Publication bias

Non-publication of negative studies also a problem in physics

- Scanning probe microscopy (SPM) uses a ‘single atom tip’ to map structures
- Many SPM images are discarded because they don’t show the “correct” image (because the tip isn’t in the right state)



Effect of tip state on images (same sample and conditions)
Acknowledgement: Philip Moriarty / Morten Moller, Univ Nottingham

- How do researchers decide on what the “correct” image is ….?

Publication bias

Publication bias affects the social sciences

- 221 social science experiments (NSF funded, rigorous quality review)
- Strong results 40% more likely to be published than null results
- 60% more likely to be written up at all
- Authors concluded: ***"Authors do not write up and submit null findings"***

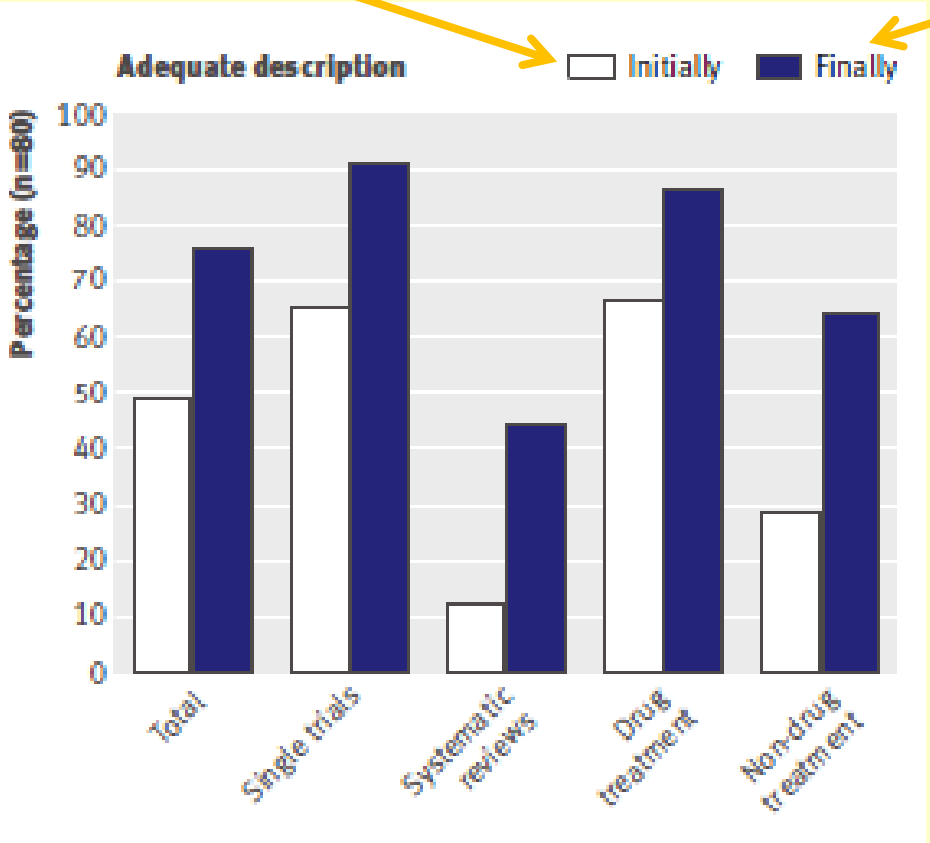
Franco et al *Science* 2014;**345**:1502

Much published research is unusable

- Of 102 journal articles reporting clinical trials, 62% had a change to the primary outcome stated in the protocol
- Of 88 studies using novel questionnaires only 8% of questionnaire could be accessed
- Of 141 studies of test accuracy, 40% did not report participants' age and sex
- Of 49 AIDS trials, only 33% reported all adverse events

All refs in Glasziou et al *Lancet*, 2014

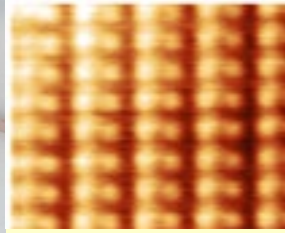
Inadequate treatment descriptions in 80 studies of medical therapies from journal article and supplementary info



Glasziou et al *BMJ*, 2008;**336**:1472

Unusable reports



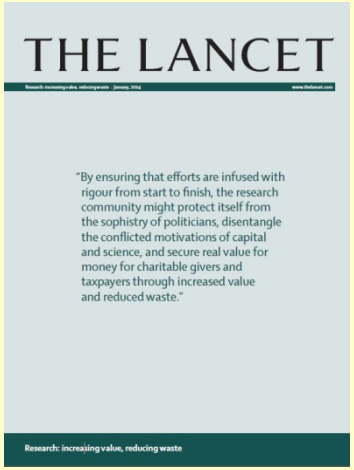


Conclusions

- Waste in research is a major problem
- Waste affects many disciplines
- Waste is an ethical issue because:
  - research resources are finite
  - patients / volunteers / animals take part in unnecessary studies
  - decisions (affecting patient treatments, public policies) are based on flawed evidence-base (incomplete, biased, misleading reporting)

How can we reduce waste in research?

- Demand justification of study question
- Support research synthesis so it's clear what is already known
- Enforce trial / study registration
- Use strong designs that maximize the effect-to-bias ratio
- Reward reproducible research
- Reward full and effective dissemination of findings (and re-use of datasets)
- Support use of reporting guidelines



Initiatives to reduce waste in medical research

- Prioritisation / question setting
- Trial registration
- Full reporting
- High quality reporting

ClinicalTrials.gov

PROSPERO

+AllTrials

equator network

REWARD

REduce research WAste and Reward Diligence

Wrong questions	Weak designs	Publication bias	Unusable reports

Links

REWARD

REduce research WAste and Reward Diligence

http://researchwaste.net/

equator network

Enhancing the QUAlity and Transparency Of health Research

www.equator-network.org/

REWARD / EQUATOR conference on research waste
Edinburgh, UK, 28-30th Sept, 2015
http://researchwaste.net/research-wasteequator-conference/

THE LANCET

Research: increasing value, reducing waste

http://www.thelancet.com/series/research

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