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  
Usable reports
Research funding is finite

If someone takes a slice there is less left for everybody else …
Waste occurs in all stages of research

<table>
<thead>
<tr>
<th>Questions</th>
<th>Design/conduct</th>
<th>Regulation</th>
<th>Accessibility</th>
<th>Usability</th>
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</thead>
<tbody>
<tr>
<td>Questions relevant to users of research?</td>
<td>Appropriate research design, conduct and analysis?</td>
<td>Efficient research regulation and delivery?</td>
<td>Accessible, full research reports?</td>
<td>Unbiased and usable reports?</td>
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<tr>
<td>High priority questions addressed</td>
<td>Studies designed with reference to systematic reviews of existing evidence</td>
<td>Appropriate regulation of research</td>
<td>Studies published in full</td>
<td>Trial interventions sufficiently described</td>
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<td>Important outcomes assessed</td>
<td>Studies take adequate steps to reduce biases - e.g. uncontrolled treatment allocation</td>
<td>Efficient delivery of research</td>
<td>Reporting of studies with disappointing results</td>
<td>Reported planned study outcomes</td>
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<td>Clinicians and patients involved in setting research agendas</td>
<td>Good re-use of data</td>
<td>New research interpreted in the context of systematic assessment of relevant evidence</td>
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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

Increased risk of sudden infant death
Sleeping position and sudden infant death

Cumulative effect (by year)

Clear effect by 1970

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

Wrong questions

increased risk of sudden infant death
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
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

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Myocardial infarction

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Weak designs

Heart attack

Death
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

Roberts et al *BMJ* 2002;324:474

Trial size and smallest absolute risk reduction detectable
Wasting lab animals

<table>
<thead>
<tr>
<th>Number of animals</th>
<th>Power</th>
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<tr>
<td>4</td>
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<td>81.4%</td>
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<tr>
<td>8</td>
<td>32.3%</td>
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<tr>
<td>16</td>
<td>56.4%</td>
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<tr>
<td>32</td>
<td>85.1%</td>
<td>14.9%</td>
</tr>
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Chances of wasting an animal in 2-group study seeking 30% reduction in infarct volume with SD = 40%
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 design in animal studies over-estimates effect size

Vesterinen et al *MS* 2010;16:1044

Review of 1117 studies in multiple sclerosis
Much research is never published

Figure 2: Reporting of completed trials, by study characteristic
Data taken from Ross and colleagues’ analysis\textsuperscript{11} of a random sample of 677 completed trials registered with ClinicalTrials.gov between 2000 and 2007.
50% of clinical trials unpublished

Of EU-funded health research 1998-2006

- 50% unpublished

- 570 million Euros of research had “no detectable academic output”

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

Galsworthy et al *Lancet* 2012;380:971

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 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.

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)

Wrong questions
Weak designs
Publication bias
Unusable reports
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

Wrong questions
Weak designs
Publication bias
Unusable reports
Links

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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