

Reducing waste from inappropriate ethics analysis and hyper-regulation of research

**Iain Chalmers
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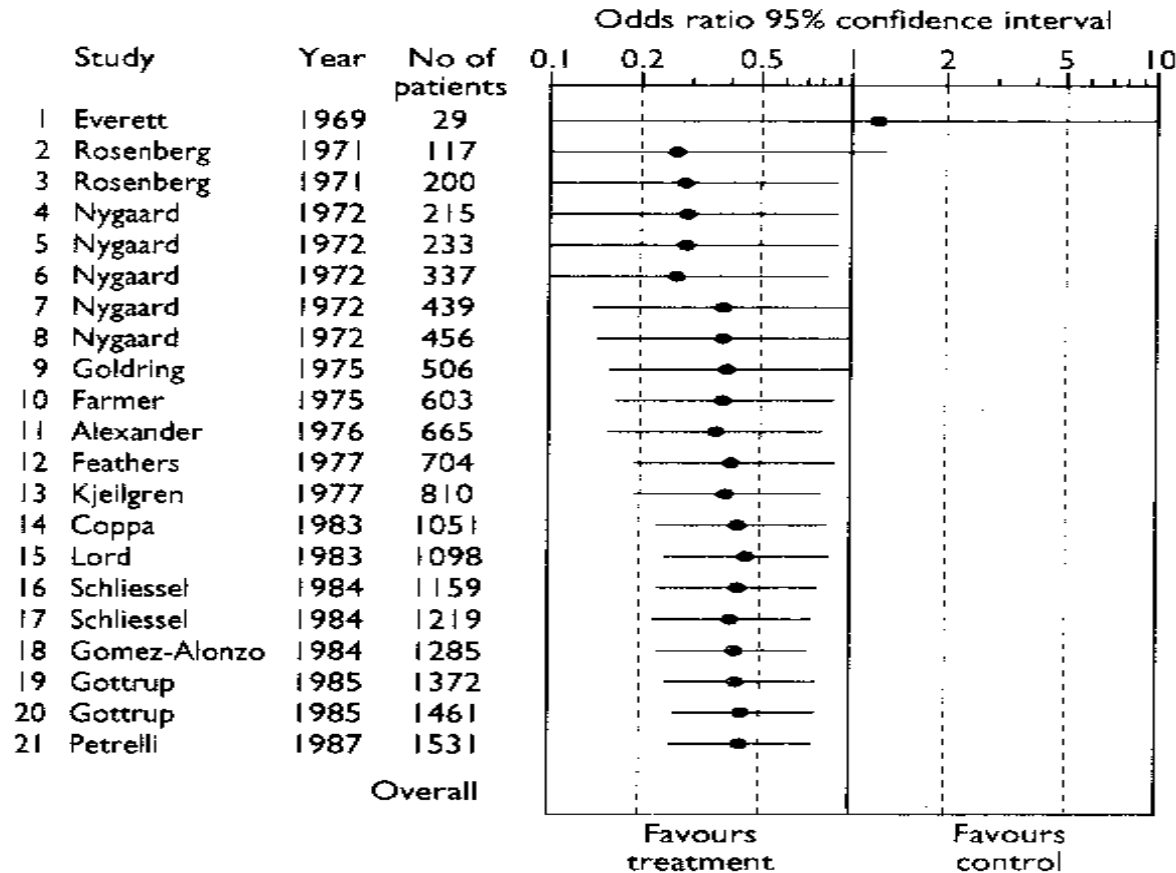
**World Congress on Research Integrity,
Amsterdam, 29 May 2017**

Are research ethics committees behaving unethically? Some suggestions for improving performance and accountability

Julian Savulescu, Iain Chalmers, Jennifer Blunt

The results of recent empirical investigations in research synthesis imply that research ethics committees are behaving unethically by endorsing new research which is unnecessary and by acquiescing in biased under-reporting of research which they have approved.

Inappropriate continued use of placebo controls in clinical trials assessing the effects on death of antibiotic prophylaxis for colorectal surgery



Reprinted from the *BMJ*, 30 November 1996, Vol 313, p 1390-1393

Are research ethics committees behaving unethically?
Some suggestions for improving performance and accountability

"By ensuring that efforts are infused with rigour from start to finish, the research community might protect itself from the sophistry of politicians, disentangle the conflicted motivations of capital and science, and secure real value for money for charitable givers and taxpayers through increased value and reduced waste."

Lancet Adding Value, Reducing Waste 2014
www.researchwaste.net

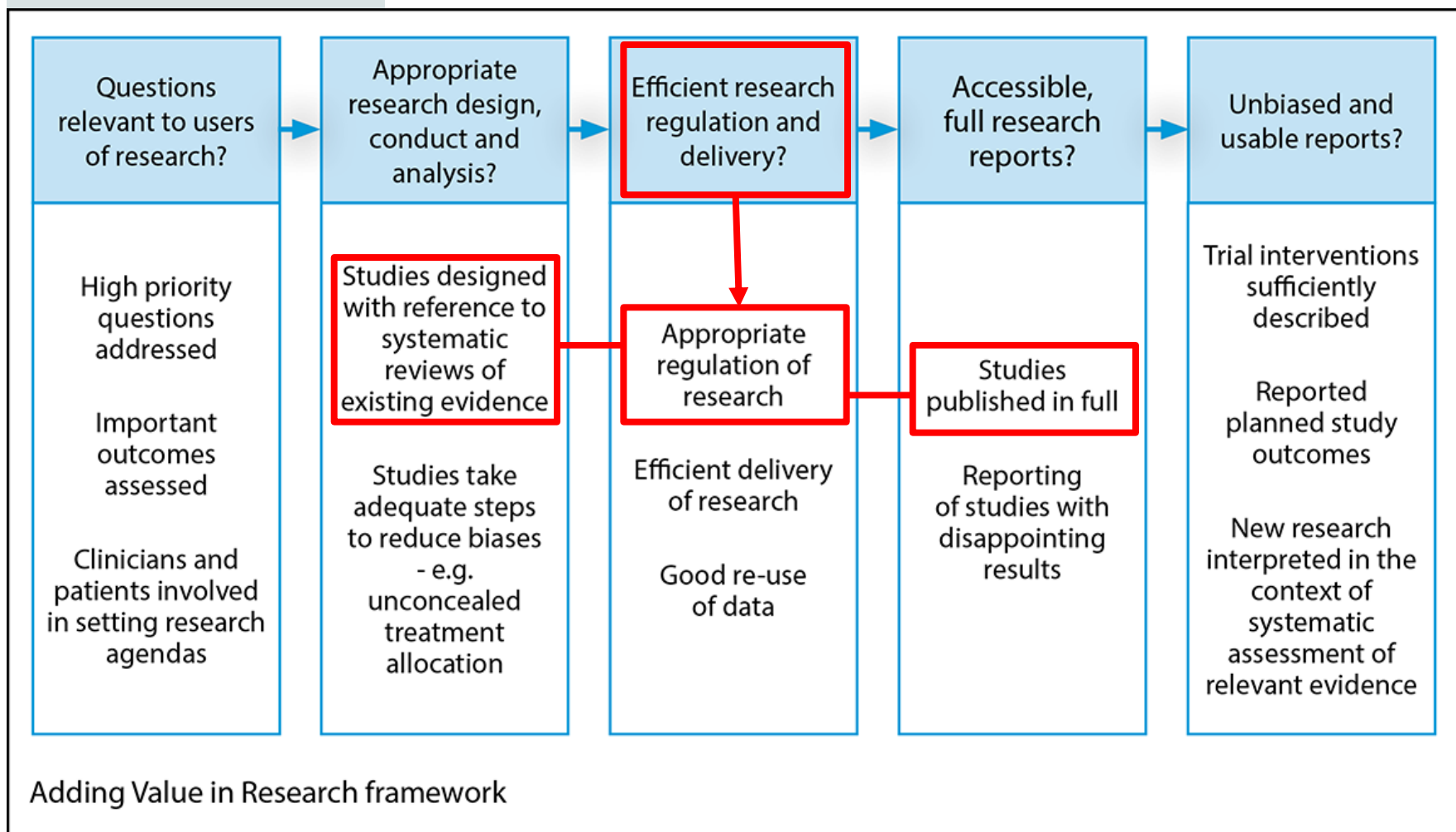
Five stages of waste in research



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Five stages of waste in research NETSCC's Adding Value in Research framework



**Reports of new research
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**Ignoring these principles
has resulted in avoidable
suffering and death!**

Because research ethics committees and many research 'ethicists' have ignored these principles, **they have contributed to avoidable suffering and deaths**

(i) by endorsing unnecessary research

7500 stroke patients participated in unjustified drug trials

STUDIES IN ANIMALS

Nimodipine in Animal Model Experiments of Focal Cerebral Ischemia

A Systematic Review

J. Horn, MD; R.J. de Haan, PhD; M. Vermeulen, MD; P.G.M. Luiten, PhD; M. Limburg, MD

20 animal studies: “The results of this review did not show convincing evidence to substantiate the decision to perform trials with nimodipine in large numbers of patients.

Stroke 2001;32:2433-8

STUDIES IN HUMANS

Horn J, Limburg M.

Calcium antagonists for acute ischemic stroke.

The Cochrane Database of Systematic Reviews.

“46 trials were identified of which 28 were included (7521 patients). No effect of calcium antagonists on poor outcome at the end of follow-up (OR 1.07, 95% CI 0.97/1.18), or on death at end of follow-up (OR 1.10, 95% CI 0.98/1.24) was found.”



TGN 1412: 13 March 2006



Establishing risk of human experimentation with drugs: lessons from TGN1412

M J H Kenter, A F Cohen

Lancet 2006; 368: 1387-91

Discussion

The above risk analysis, undertaken with data available in the research file and public domain before the TGN1412 trial started, shows that essential information was absent and the antibody was a high-risk compound unlikely to be suitable for administration to healthy people without additional preclinical experiments.

- 3 Research funders and regulators should demand that proposals for additional primary research are justified by systematic reviews showing what is already known, and increase funding for the required syntheses of existing evidence
- Monitoring—audit proposals for and reports of new primary research

Some research funders and regulators now require reference to systematic reviews of existing evidence from applicants for research funds or research approval

The **National Institute for Health Research** advises researchers applying for support for new primary research as follows:



“Where a systematic review already exists that summarises the available evidence this should be referenced, as well as including reference to any relevant literature published subsequent to that systematic review. Where no such systematic review exists it is expected that the applicants will undertake an appropriate review of the currently available and relevant evidence. All applicants must also include reference to relevant on-going studies.”

The **Health Research Authority** states:



“Any project should build on a review of current knowledge. Replication to check the validity of previous research is justified, but unnecessary duplication is unethical.”

Because research ethics committees and many research 'ethicists' have ignored these principles, **they have contributed to avoidable suffering and deaths**

(i) by endorsing unnecessary research

(ii) by acquiescing in biased under-reporting of research



TGN 1412: 13 March 2006



EXPERT SCIENTIFIC GROUP ON PHASE ONE CLINICAL TRIALS

Professor Terry Hamblin, Professor Martin Gore and Dr. Monica Preuss,
representing the Gene Therapy Advisory Committee (GTAC).

presented unpublished data regarding a study he had carried out in a single patient subject
in 1994 using a tri-specific anti-CD3/CD2/CD28 antibody.

The presentation covered two main areas, first dosing in man, healthy volunteers versus patients and the first in man study of a tri-specific anti-CD3/CD2/CD28 antibody which was performed in 1994. The effects of this antibody had parallels with the effects of TGN1412.

3 Funders, sponsors, regulators, research ethics committees, journals, and legislators should endorse and enforce study registration policies, wide availability of full study information, and sharing of participant-level data for all health research

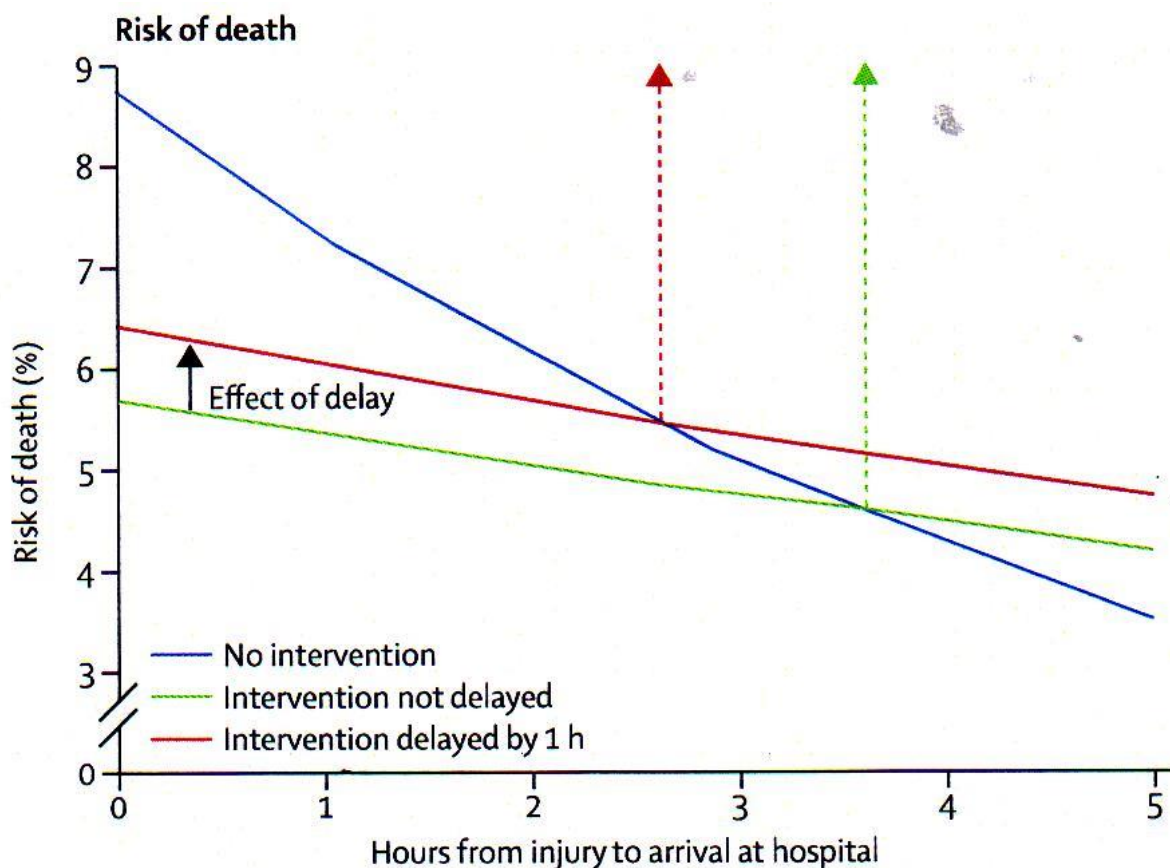
- Monitoring—assessment of the proportion of stakeholder policies that endorse dissemination activities, and the proportion of studies that are registered and reported with available protocols, full study reports, and participant-level data

Is there evidence that, on balance, research ethics regulation is doing more good than harm?

Effect of consent rituals on mortality in emergency care research

*Ian Roberts, David Prieto-Merino,
Haleema Shakur, Iain Chalmers,
Jon Nicholl
crash@lshtm.ac.uk

www.thelancet.com Vol 377 March 26, 2011



What are the implications for research regulation?

Informed consent procedures, like other well-intentioned public health interventions, should be assessed rigorously. The lethal effects we have shown might have been found decades ago had the research ethics community accepted a responsibility to provide robust evidence that its prescriptions are likely to do more good than harm.

In conclusion

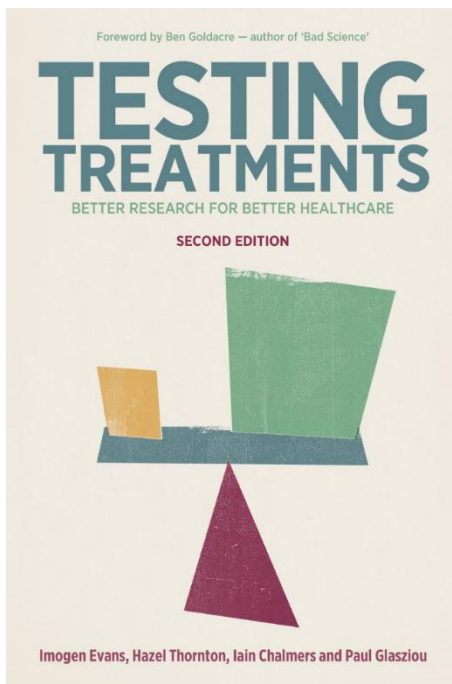
Patients continue to suffer and die unnecessarily because of both under-regulation and over-regulation of research by research ethics committees.

More needs to be done to ensure that medical ethics does more good than harm to the interests of patients in general, not only those who participate in research.

AN ACTION PLAN – THINGS YOU CAN DO

Promote research on the effects of treatments...

“Encourage and work with health professionals, researchers, research funders, and others who are try to promote research addressing inadequately answered questions about the effects of treatment which you regard as important.”



www.testingtreatments.org

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...but only if it meets scientific and ethical principles.

“Agree to participate in a clinical trial on condition that:

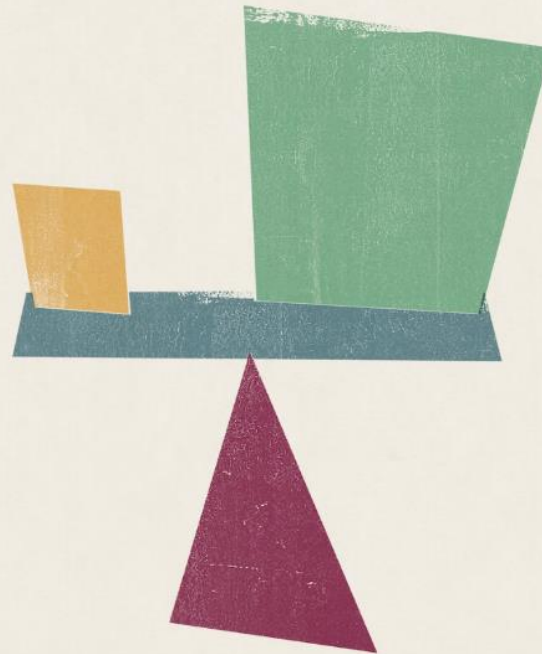
- (i) the study protocol has been registered and made publicly available
- (ii) the protocol refers to systematic reviews of existing evidence showing that the trial is justified
- (iii) you receive a written assurance that the full study results will be published.”

Foreword by Ben Goldacre — author of 'Bad Science'

TESTING TREATMENTS

BETTER RESEARCH FOR BETTER HEALTHCARE

SECOND EDITION



Imogen Evans, Hazel Thornton, Iain Chalmers and Paul Glasziou

www.testingtreatments.org