The “double standard” in consent

Iain Chalmers
Coordinator, James Lind Initiative

Contribution to
“Governing medical research and medical practice: what’s the difference?”

ESRC Science in Society Workshop
London, 18 January 2007

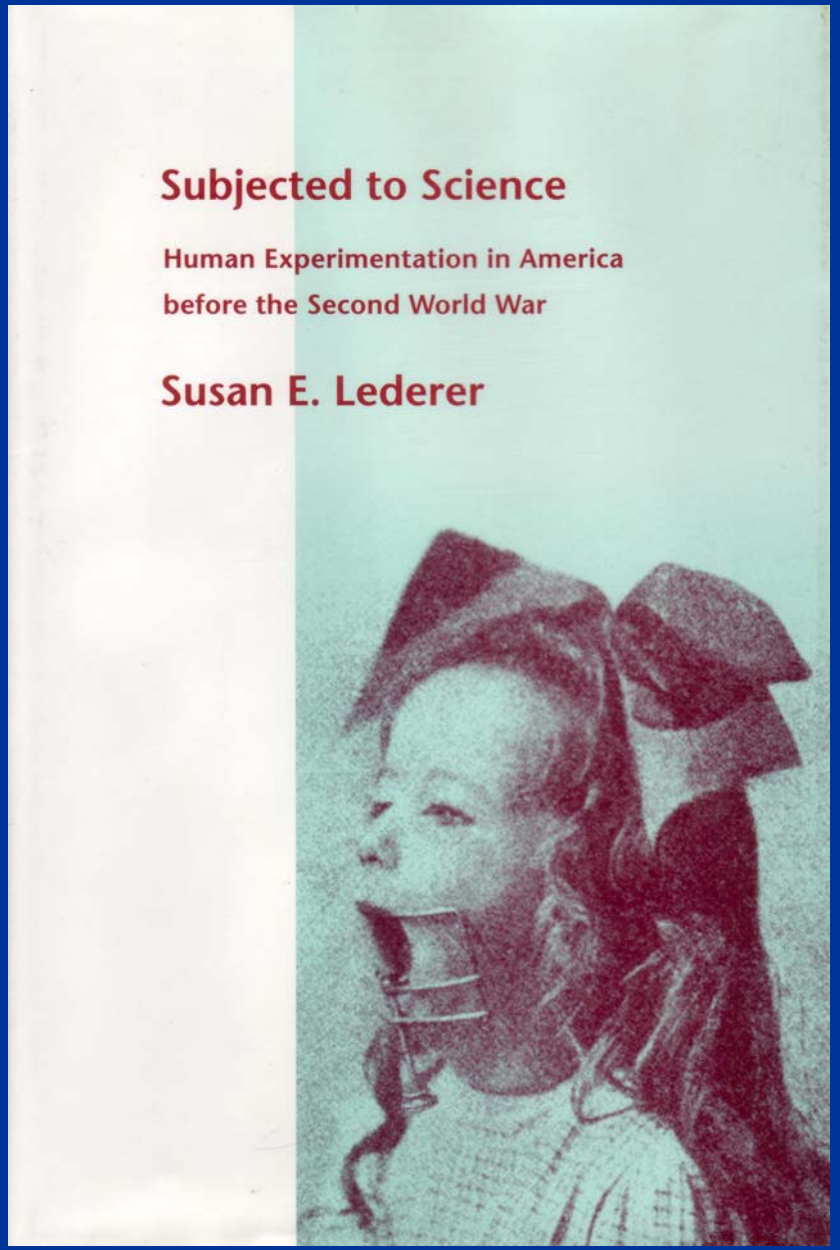
What am I **not** going to talk about?

I am not going to refer to the examples discussed by:

Beecher 1966,
Pappworth 1967…

…and many others since,

for example,
Lederer 1995.



So I am <u>not</u> talking about consent for:

known effective treatment to be withheld
(e.g. Tuskegee; **+** ***<u>numerous current examples</u>***)

physiologic studies
(e.g. Ellen Roche, Johns Hopkins 2001)

studies to improve understanding of disease
(e.g. Tickton & Zimmerman 1962 - Willowbrook)

technical (invasive) **study of disease**
(e.g. Samet, Bernstein & Litwak 1961).

'first in human' studies of potential therapies
(e.g. Jesse Gelsinger 1999; TGN 1412 2006)

The double standards to which I will refer concern informed consent to **treatment already in use within 'normal/routine' clinical practice**

“I need permission to give a drug to half of my patients, but not to give it to them all.”

Richard Smithells 1975

Double standards applied to treatment given within and outwith formal efforts to assess the effects of treatments have been recognised for at least 200 years.

RESULTS OF AN INVESTIGATION,

RESPECTING

EPIDEMIC AND PESTILENTIAL

DISEASES;

INCLUDING

RESEARCHES IN THE LEVANT,

CONCERNING

The Plague.

BY

CHARLES MACLEAN, M.D.

LECTURER ON THE DISEASES OF HOT CLIMATES TO THE HONOURABLE EAST INDIA COMPANY.

IN TWO VOLUMES.

VOL. II.

London:

PRINTED FOR THOMAS AND GEORGE UNDERWOOD,

32, FLEET-STREET;

By R. & R. Gilbert, St. John's Square, Clerkenwell.

1818.

my opponents should take patient for patient, under similar circumstances, of constitution and disease; confident of an easy victory, if they would abstain from applying the very means, which they were so strenuous to condemn. This proposition could only be evaded, by pretending a reluctance to try experiments with the lives of men; as if it were not manifest, that *my* experiments, *which were always first tried upon myself*, were capable of being conducted with perfect safety; or, as if the practice of medicine, in its conjectural state, were any thing else, than *a continued series of experiments, upon the lives of our fellow-creatures.*

Claude Bernard, 1865:

"Many physicians attack experimentation, believing that medicine should be a science of observation. But physicians make therapeutic experimentation daily on their patients so this inconsistency cannot stand careful thought. Medicine by its nature is an experimental science, but it must apply the experimental method systematically."

Professional and Public Double Standards on Clinical Experimentation

Iain Chalmers

National Perinatal Epidemiology Unit, Radcliffe Infirmary, Oxford, England and

William A. Silverman

90 La Cuesta Drive, Greenbrae, California, U.S.A.

Yet there is another, more pervasive way in which double standards operate to promote poorly controlled experiments on uninformed patients. Illogically, and with no empirical evidence to support it, a mischievous view has been promoted that the interests of the vast number of patients involved in the poorly controlled experiments of informal medical "tinkering" are less in need of protection than are those of the relatively small number of patients who are involved in planned, properly controlled clinical experiments.

Controlled Clinical Trials 8:388–391 (1987)

APRIL 22, 2002 $4.95 (INCL. GST)

Powell's Mission Impossible

TIME

HOW MEDICAL TESTING HAS TURNED MILLIONS OF US INTO ...

HUMAN GUINEA PIGS

9 770818 062026

Outcomes of patients who participate in randomised controlled trials compared to similar patients receiving similar interventions who do not participate (Review)

Vist GE, Hagen KB, Devereaux PJ, Bryant D, Kristoffersen DT, Oxman AD

Plain language summary

This review assessed whether there are harmful or beneficial effects from participating in randomised controlled trials (RCTs). The outcomes of patients who participated in RCTs were compared with outcomes of patients who were eligible for the trial and received similar clinical interventions, but did not participate. On average, the outcomes of patients participating and not participating in RCTs were similar, suggesting that participation in RCTs, independent of the effects of the clinical interventions being compared, is unlikely to be harmful. In addition, these results challenge the assertion that the results of RCTs are not applicable to usual clinical practice.

For ethical as well as scientific reasons, when there is properly informed uncertainty about the relative merits of alternative treatments:

“the trial is the treatment.”

Ashcroft R (2000).
Giving medicine a fair trial.
BMJ;320:1686.

In the UK, the development of what John Lantos (1994) has referred to as **“a confused ethical analysis”** and its application by research ethics committees seems likely to have reflected Maurice Pappworth’s influence.

MEDICAL ETHICAL COMMITTEES

A REVIEW OF THEIR FUNCTIONS

by M. H. Pappworth

World Medicine 22 Feb 1978, pp 19-

Medical experimentation.

I share much of Dr Pappworth's concern about medical experimentation (February 22, p.19). However, I am not so sure as he seems to be that the medical world can be neatly divided into clinical experimenters ("the bad guys") and altruistic clinicians ("the good guys").

It seems very possible that there is a more urgent need to protect patients from the uncontrolled experimentation which characterises much "accepted medical practice" by altruistic, but scientifically uncritical, clinicians. Certainly the number of patients "at risk" is much larger than those whose interests are protected, to a greater or lesser extent, by ethical committees.

Cardiff IAIN CHALMERS, MB, BS, MRCOG

World Medicine 5 April 1978, p 18

"Human guinea pigs"—a history

M H Pappworth

London NW3 1AX
M H Pappworth, MD, *retired*

Br Med J 1990;**301**:1456-60

Human guinea pigs

Thirteen years ago, prompted by an article published by Dr Pappworth in *World Medicine* in which he used the words experiment and experimentation,[2] I tried to encourage him to clarify what he meant by these words.[3] Because he did not respond to my questions at that time, and because he uses these words in his more recent article, I would like to invite him again to make his position clearer.

The specific example is unimportant, but the general issue that it illustrates is one which many medical ethicists seem unwilling to confront straightforwardly. Influential commentators on medical ethics like Dr Pappworth owe it to those of us who have been asking them to justify their apparent double standards for more than a decade to explain their position more clearly.

IAIN CHALMERS

Publications re informed consent, etc, 1978-2005

Chalmers I, Medical experimentation. World Medicine 1978;5 Apr:18.

Chalmers I, Baum M. Consent to randomized treatment. Lancet 1982;2:1050-1051.

Chalmers I, Grant A. Informed consent. BMJ 1983;286:1279.

Grant A, Chalmers I. Informed consent. BMJ 1983;286:1973.

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Chalmers I. The promotion of poorly controlled experimentation on children by medical ethicists. Paediatric and Perinatal Epidemiology 1988;2:104-106.

Savulescu J, Chalmers I, Blunt J. Are research ethics committees behaving unethically? BMJ 1996;313:1390-1393.

Chalmers I, Lindley R. Double standards on informed consent to treatment. In: Doyal L, Tobias JS, eds. Informed Consent in Medical Research. London: BMJ Publications, 2001:266-275.

Oxman AD, Chalmers I, Sackett DL. A practical guide to informed consent to treatment. BMJ 2001;323:1464-1466.

Chalmers I. Provision of consent. Lancet 2003;362:663-664.

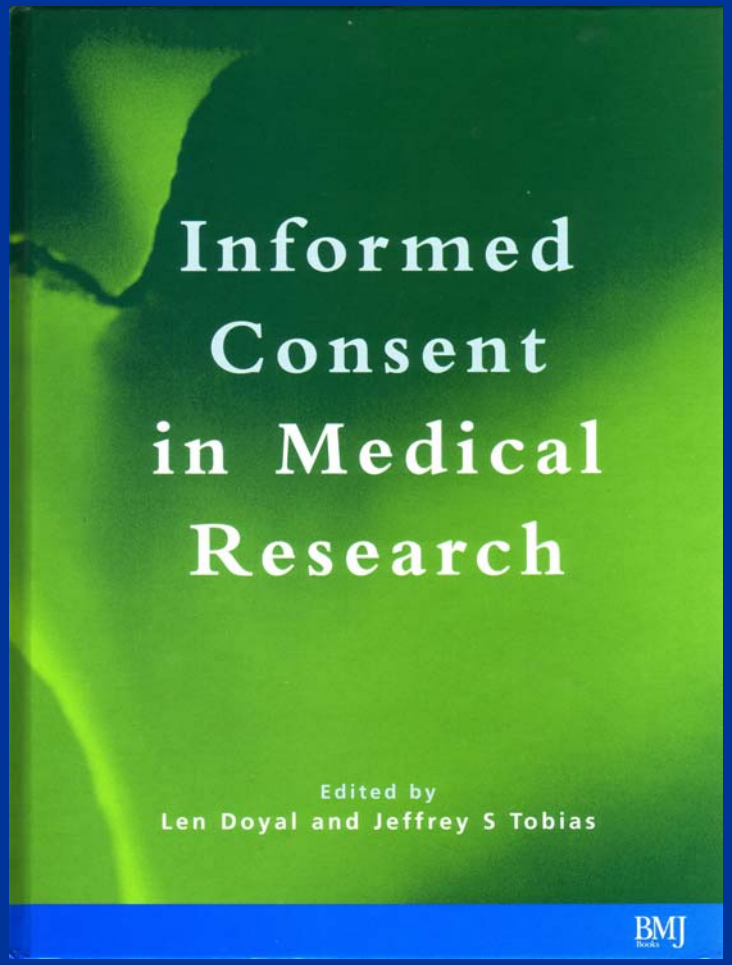
Glasziou P, Chalmers I. Ethics review roulette: what can we learn? BMJ 2004;328:121-122.

Chalmers I. Well informed uncertainties about the effects of treatments: how should clinicians and patients respond? BMJ 2004;328:475-6.

Chalmers I. Human guinea pigs, risky clinical experiments, and negative public images of fair tests of medical treatments. HealthWatch Newsletter 2004;53:3.

Chalmers I. The scandalous failure of science to cumulate evidence scientifically. Clinical Trials 2005;2:229-231.

A personal last blast in print! [two publications in 2001]



26 · Double standards on informed consent to treatment

Iain Chalmers and Richard I Lindley

Iain Chalmers and Richard Lindleys' View

This chapter highlights another problem with Gillon's argument. With great panache, Chalmers and Lindley argue that too much of the discussion about the ethics of medical research has overly emphasised its risks at the expense of playing down the risks of standard therapy. They demonstrate that such therapy is often without a rigorous scientific base and that it may well pose greater risks. Further, they marshall convincing evidence to show that participation in trials may reduce risks and provides more benefit than relying on standard, unassessed therapies. Consequently, a more balanced ethical analysis of informed consent in medical research would make these points. I completely concur with this view and hope that it will have the significant impact on future debates that it deserves to. I will take the authors' arguments more into account in my own writing on the subject in the future.

A practical guide to informed consent to treatment

Andrew D Oxman, Iain Chalmers, David L Sackett

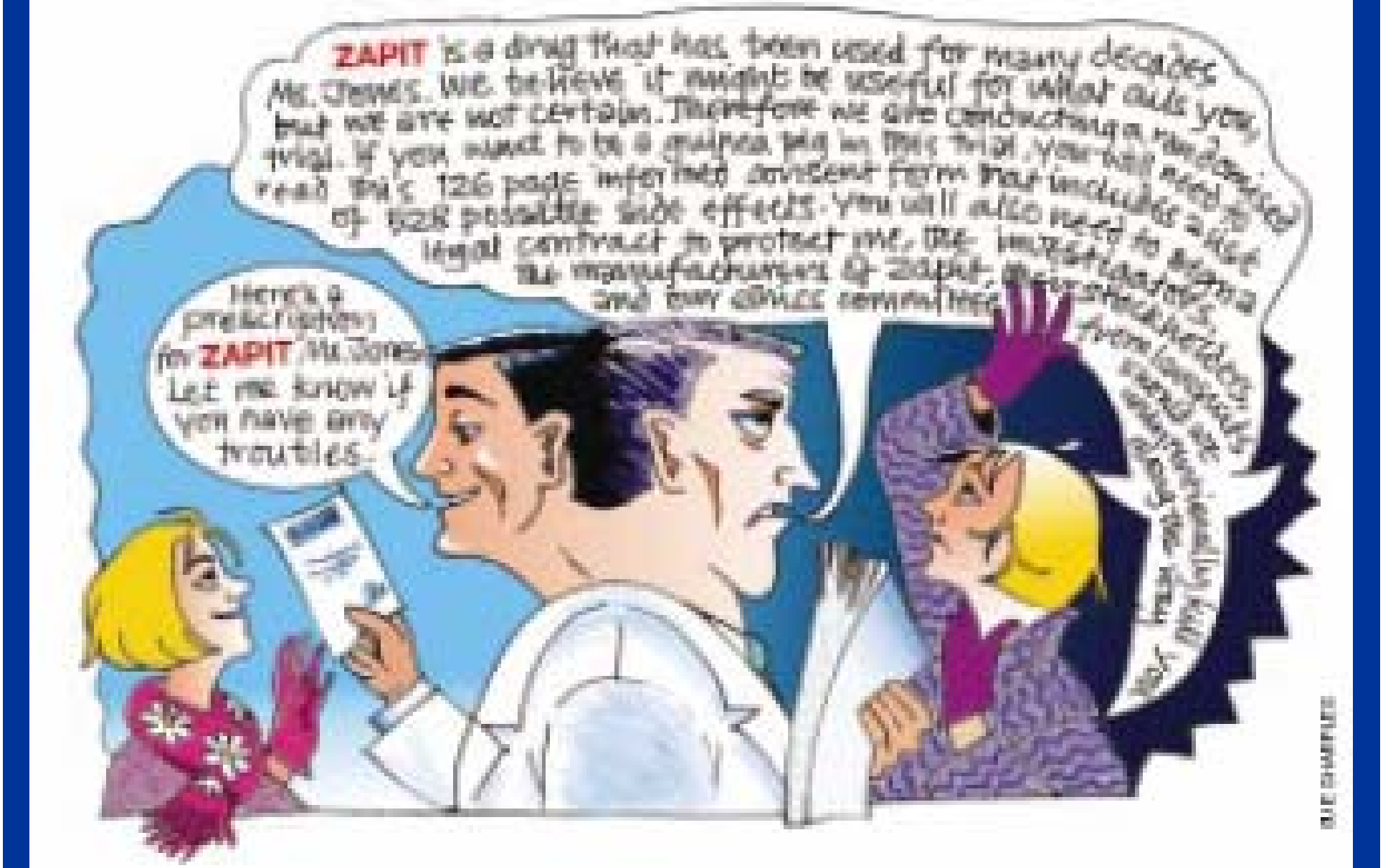
BMJ VOLUME 323 22–29 DECEMBER 2001 bmj.com

Consent to treatment within RCTs

Human sacrifice RCT consent
Commercial RCT for multicentre fun and profit consent
American consent to RCT treatment for the 40 million uninsured
RCT consent for stockholding investigators
Kilgore Trout RCT consent

Consent to treatment in routine clinical practice

Customary consent
Alternative forms of standard consent to treatment
American emergency consent to treatment
Cultural imperialism consent to treatment
Patients' rights consent to treatment
Interactive, personalised approach to informed consent


ZAPIT is a drug that has been used for many decades Mr. Jones. We believe it might be useful for what ails you but we are not certain. Therefore we are conducting a randomized trial. If you want to be a guinea pig in this trial you will need to read this 126 page informed consent form that includes a list of 528 possible side effects. You will also need to sign a legal contract to protect me, the inventor, the manufacturers of ZAPIT, and any other connected
Here's a prescription for ZAPIT Mr. Jones. Let me know if you have any troubles.

A single standard for informed consent to treatment would require all patients to be told the rationale for selecting the treatments offered to them.

“The more of these operations I do, the more I earn”

“I have stock in the company that makes this drug”

“My institution has a massive grant from the company that makes this equipment”

“This drug was highly recommended at a sponsored symposium in Tenerife last month”

“I was told at medical school thirty years ago that this treatment was the best available”

“A systematic review of the evidence leaves me uncertain which of the possible alternative treatments is going to be best for you”

"Try this—I just bought a hundred shares."

What do I want, as a patient?

[Chalmers I. BMJ 1995;310:1315-18.]

Wish No. 1

"...systematic reviews of carefully controlled research to produce the kind of evidence that I am likely to believe, and that I would wish those offering me care to take into account."

The human costs of failing to cumulate evidence in systematic reviews

"Advice on some life-saving therapies has been delayed for more than a decade, while other treatments have been recommended long after controlled research has shown them to be harmful."

Antman et al. JAMA, 1992

Wish No. 2

"When the relative merits of alternative forms of care are uncertain, I want to be offered **the opportunity to participate in properly controlled research** – and the emergency medical card that I carry makes this explicit."

MEDICAL EMERGENCY CARD

supplied by

VOLUNTARY EUTHANASIA SOCIETY

13 Prince of Wales Terrace London W8 5PG 0171 937 7770

My Full name is

IAIN GEOFFREY CHALMERS

If there is no reasonable prospect of recovery I do NOT wish to be resuscitated or my life to be artificially prolonged
My Advance Directive is lodged with

DR. ANDY CHIVERS
01865 – 558861

1. Medical Information eg. blood group

Invite me to participate in all randomized controlled trials for which I am potentially eligible

2. After my death my organs may be used for medical purposes

YES

3. Next of Kin

JAN CHALMERS
01865 – 554949

Signature **Date**

Iain Chalmers 7/12/98

Is this altruism or self-interest?

My wish to be entered into randomised controlled trials when the relative merits of alternative forms of care are uncertain is purely selfish. Patients receiving treatment as participants in such trials seem to fare better than apparently comparable patients receiving the same treatments outside trials. Furthermore, new technologies seem as likely to be inferior as they are to be superior to existing alternatives, so randomisation provides an efficient hedging strategy in the face of these evenly balanced odds. Thirdly, randomised controlled trials help to generate reliable information on which to base future decisions about my health care.

“The clinician who is convinced that a certain treatment works will almost never find an ethicist in his path, whereas his colleague who wonders and doubts and wants to learn will stumble over piles of them.”

Lancet Editorial 1990

I believe the bioethics community has jeopardized my interests as a patient by

acquiescing in

- research which has not been based on systematic reviews of existing evidence;
- biased under-reporting of research; and

encouraging

- double standards on informed consent to treatment

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

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.

Underreporting Research Is Scientific Misconduct

Iain Chalmers, FRCOG

JAMA, March 9, 1990—Vol 263, No. 10

Selected for republication in:

Ethical and Regulatory Aspects of Clinical Research: Readings and Commentary
Ezekiel J. Emanuel (Editor), Robert A. Crouch (Editor), John D. Arras (Editor)
The Johns Hopkins University Press 2004

Just as I resent the arrogance of health professionals who assume without reliable empirical evidence that they are doing right by their patients, so do I resent the arrogance of bioethicists who, confident that they occupy higher moral ground than ordinary mortals, do not assess the consequences, in practice, of their prescriptions and proscriptions for other people.

Iain Chalmers

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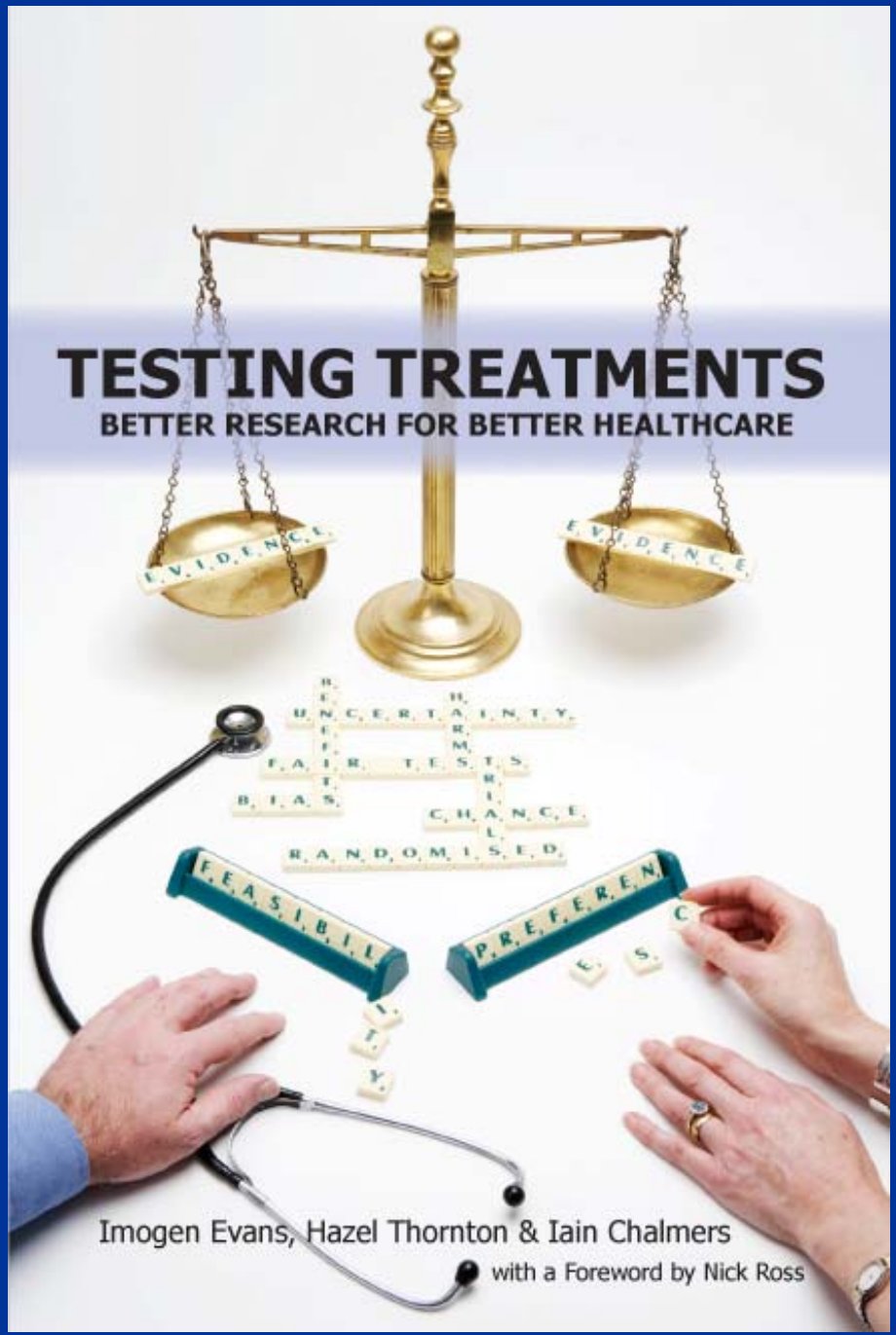
Summertown Pavilion, Oxford OX2 7LG, UK
(e-mail: ichalmers@jameslindlibrary.org)

Provision of consent. Lancet 2003;362:663-664.


TESTING TREATMENTS
BETTER RESEARCH FOR BETTER HEALTHCARE
EVIDENCE
EVIDENCE
UNCERTAINTY
FAIR TESTS
BIAS
CHANCE
RANDOMISED
FEASIBILITY
PREFERENCES
Imogen Evans, Hazel Thornton & Iain Chalmers
with a Foreword by Nick Ross

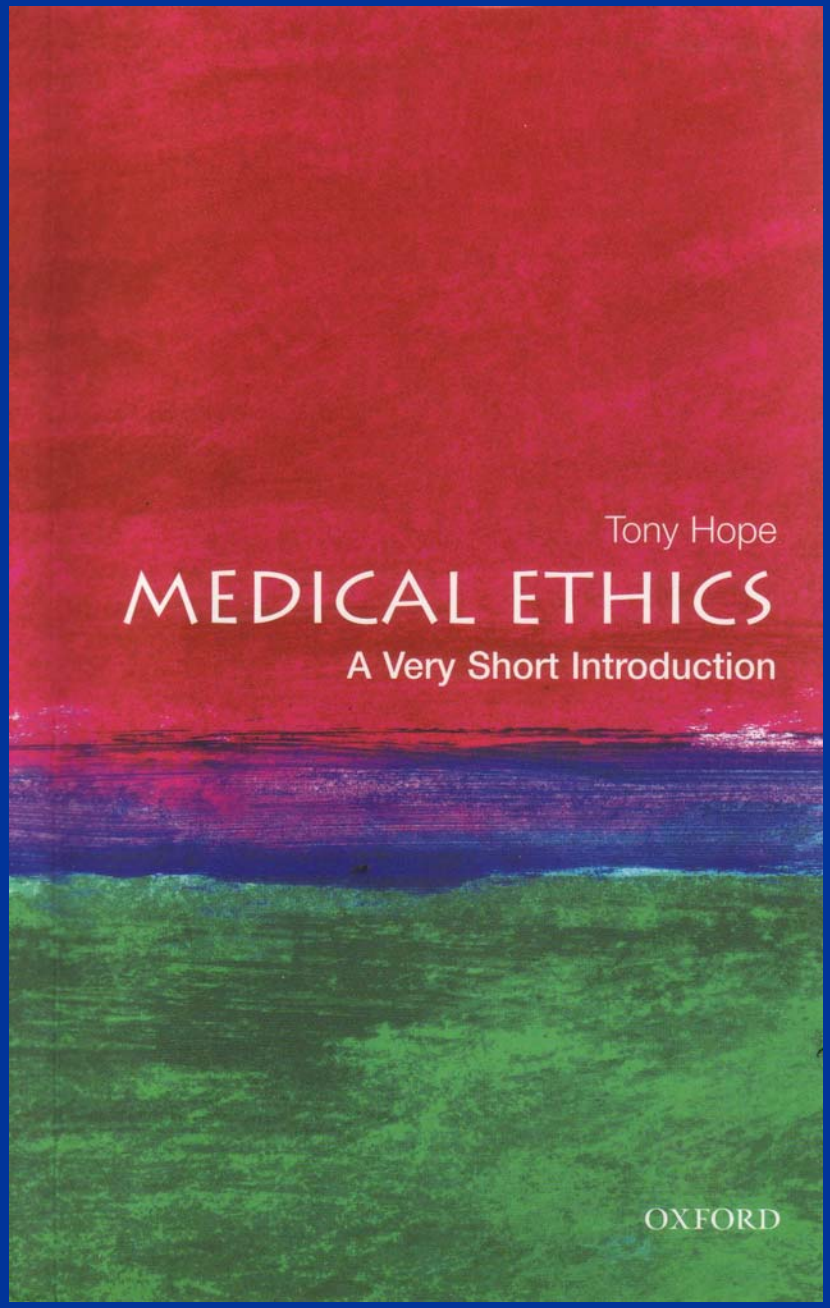
Caveat donor!

Agree to participate in a clinical trial only on condition (i) that the study protocol has been registered publicly on www.controlled-trials.com; (ii) that the protocol refers to the systematic reviews of existing evidence showing that the trial is justified; and (iii) that you receive a written assurance that the full study results will be published, and sent to all participants who indicate that they wish to receive them.

I thank very sincerely:

Mary Dixon-Woods, Richard Ashcroft and the few medical ethicists who have drawn attention to the “confused ethical analysis” reflected in double standards on informed consent to treatment...

...and to them and to others who have called for more thoughtful ethical analyses, informed by empirical research to assess the consequences of ‘ethics interventions’ in the lives of others.



Why should risk of harm be more carefully controlled, and more restrictive, in the context of medical research, than it is in other areas of our lives? We do not prevent the sale or purchase of skis, motorbikes, or hang-gliders, although these expose purchasers to moderate risks. Why should the control of medical research be different?

Double standards

This is only one example where the regulation of medical research imposes standards that seem out of keeping with other areas of life. Another example is with regard to the amount of information provided to patients who are being asked to take part in a clinical trial.

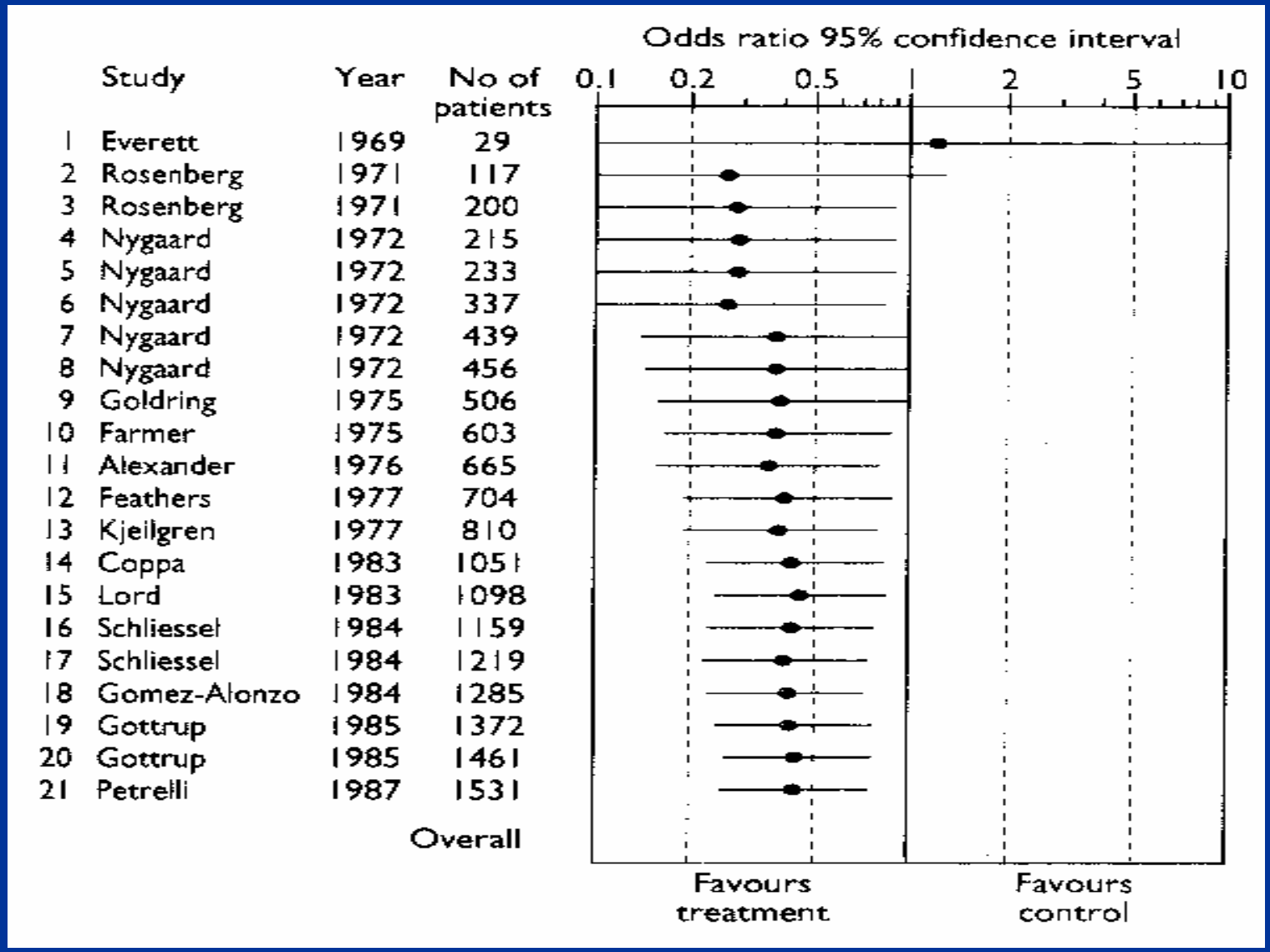
A clinical case and a research case

In the research case the guidelines and research ethics committees (also called institutional review boards) require Dr A to inform B about both drugs, and about the method of choosing which to prescribe. In the clinical case this standard of informing is not the norm. Is this difference justified? If it is, then the standards are simply different. If it is not then we are operating 'double standards' – i.e. standards that are different and where the difference is not justifiable. Double standards are an example of inconsistency. They tell us that at least one of the standards needs to be changed.

Systematic reviews are needed to identify useful treatments efficiently

Would any of you have agreed to participate in a placebo controlled trial of prophylactic antibiotics for colorectal surgery after 1975?

Reduction of perioperative deaths by antibiotic prophylaxis for colorectal surgery



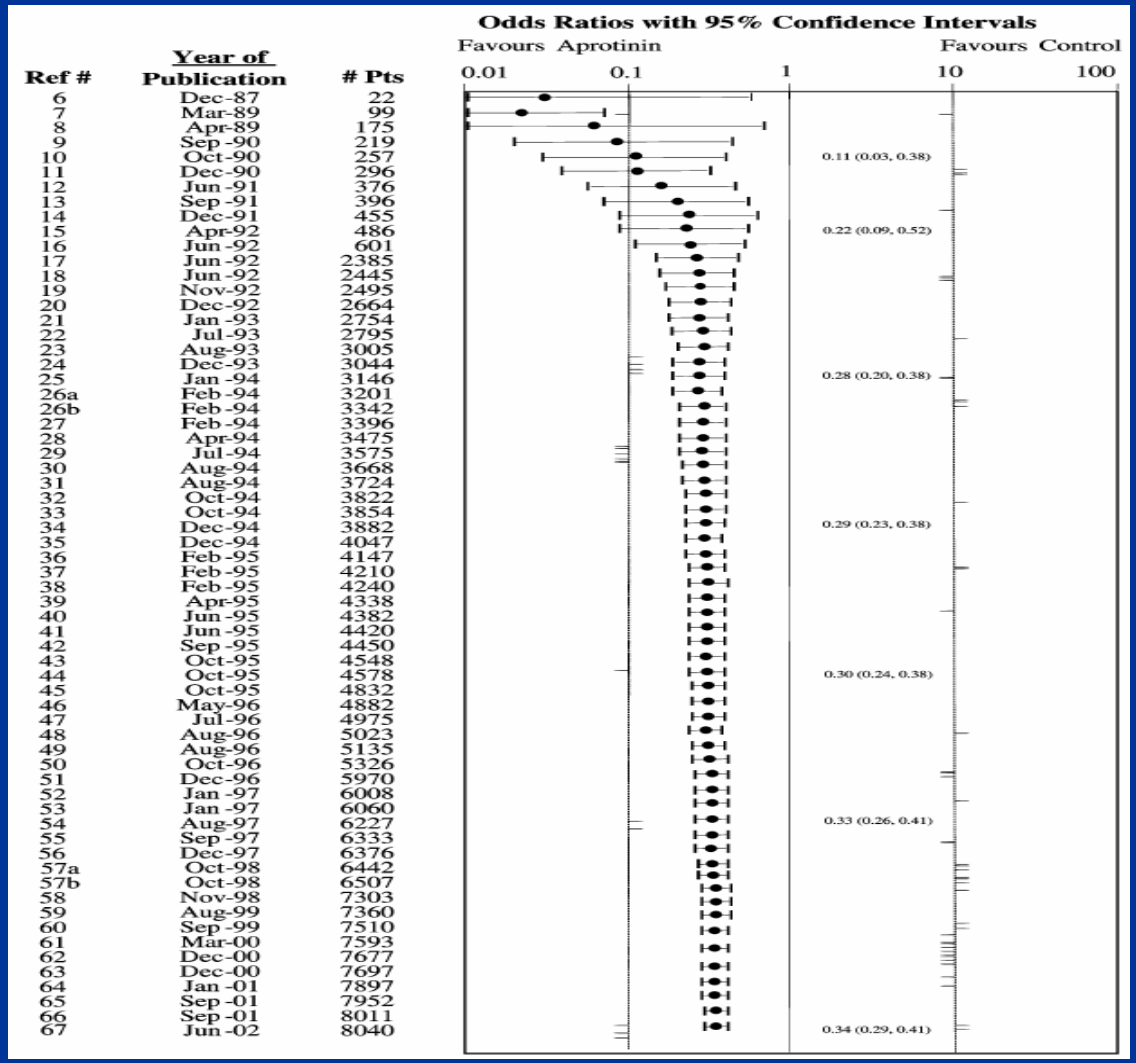
	Study	Year	No of patients
1	Everett	1969	29
2	Rosenberg	1971	117
3	Rosenberg	1971	200
4	Nygaard	1972	215
5	Nygaard	1972	233
6	Nygaard	1972	337
7	Nygaard	1972	439
8	Nygaard	1972	456
9	Goldring	1975	506
10	Farmer	1975	603
11	Alexander	1976	665
12	Feathers	1977	704
13	Kjellgren	1977	810
14	Coppa	1983	1051
15	Lord	1983	1098
16	Schliessel	1984	1159
17	Schliessel	1984	1219
18	Gomez-Alonzo	1984	1285
19	Gottrup	1985	1372
20	Gottrup	1985	1461
21	Petrelli	1987	1531
	Overall		

Randomized controlled trials of aprotinin in cardiac surgery: could clinical equipoise have stopped the bleeding?

Dean Fergusson[a,b], Kathleen Cranley Glass[b,c], Brian Hutton[a] and Stan Shapiro[b,c,d]

Clinical Trials 2005; **2**: 218–232

Cumulative estimate of the effect of aprotinin on perioperative blood transfusion, 1987-2002.



ASTHMA

WHAT THEY WERE TESTING The effects of a chemical irritant to understand why some people get asthma

WHOM THEY TRIED IT ON Three healthy volunteers with normal respiratory systems

WHAT WENT WRONG Two days after inhaling the chemical, Ellen Roche, 24, a technician at the Johns Hopkins Asthma and Allergy Center, developed a cough, fever and muscle pain. She quickly developed respiratory distress. Within a month she was dead. The chemical turned out to be far more toxic than the researchers realized. The lead investigator's literature search of the most common databases (which date back only to 1960) did not turn up earlier studies hinting at the chemical's potential dangers.

Cowley, Skene, Taylor & Hampton 1993

"... When we carried out our study in 1980 we thought that the increased death rate that occurred in the (anti-arrhythmic drug) group was an effect of chance...The development of (the drug) was abandoned for commercial reasons, and this study was therefore never published; it is now a good example of 'publication bias'. The results described here ... might have provided an early warning of trouble ahead."

At the peak of their use in the late 1980s, it has been estimated that anti-arrhythmic drugs were causing – every year - comparable numbers of deaths to the *total* number of Americans who died in the Vietnam war.

Moore 1995.