Proliferation of laws and guidelines

Data access/confidentiality:
- 1998 Data Protection Act
- GMC guidance on confidentiality
- Health & Social Care Act/PIAG

Clinical trial conduct:
- ICH Guideline for GCP
- EU Clinical Trials Directive
- National Research Governance

Ethics & consent:
- Helsinki Declaration

Aspects of RCTs that have become complex.

- Protocols (3-4 fold): visits, tests, data,
- Consent forms (5 -10 fold).
- SAE/AE reporting (>100 fold).
- Contracts (5 to 10 fold).
- No. of approvals(REB, regulatory).
- Indemnification.
- Drug importation & release.
- Violation of the independence of DSMB.
- Complex quality assurance processes .

Consequences of complexities

- Substantial cost escalation and delays.
- Inability to do large trials, or worse many trials are not being done.
- Difficulties in conducting non-industry studies.
- Spillover of regulatory rules onto other human research.

HAS THIS IMPROVED HUMAN RESEARCH AND HEALTH? OR HAS THIS DAMAGED HEALTH?

Evidence to AMS Working Group on Personal Data for Public Good

"Much of my research on the effects of ionising radiation and the use of oral contraceptives, leave alone smoking, would have been impossible without the facility of obtaining unbiased access to medical records."

Professor Sir Richard Doll

Evidence to AMS Working Group on Personal Data for Public Good

“Lives could be threatened, far less protected, by excessive data protection and bureaucracy so complex as to discourage researchers.”

Royal College of Obstetricians and Gynaecologists

Stated aim of the EU Directive on Clinical Trials

Article 1: *"This Directive establishes specific provisions regarding the conduct of clinical trials.... Compliance with this good practice provides assurance that the rights, safety and well-being of trial subjects are protected, and that the results of the clinical trials are credible."*

But is this what the impact of the rules have been?

MRC review: Potential for EU Clinical Trials Directive (2001) to be a major obstacle to important trials

- **Increased bureaucracy** due to requirement for single sponsor (possibly the funding source)
- **Burdensome drug authorisation** and supply (GMP & labelling) processes
- **Threat to trials** of emergency treatments for patients unable to give consent
- **Rigid approach** to pharmacovigilance and site monitoring (through over-interpretation)
- ***Substantial increases in costs*** could result in ***fewer important trials*** being conducted

Objectives of quality assurance in randomised clinical trials

- Protecting the safety, rights and well being of study participants
- Ensuring the reliability and robustness of study results

Need cost-effective strategies

Put greater reliance on design strengths inherent in randomized-controlled trials

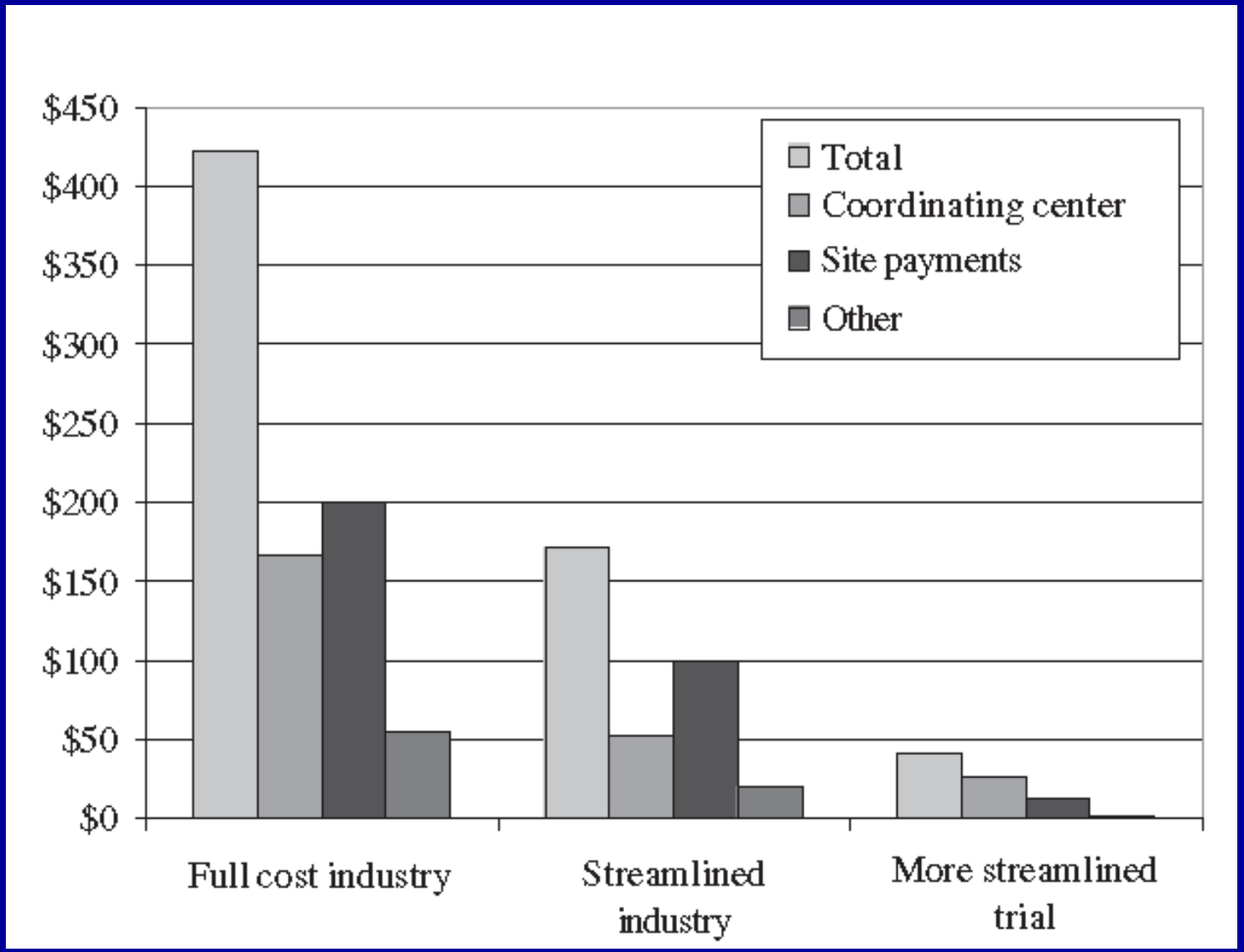
- Randomization: unbiased comparison of patient groups that differ randomly

- Control group: unbiased ascertainment of outcomes in study treatment groups

Yields unbiased assessment of treatment (which will only be reliable if large enough)

Cost comparison (US$M): About half of cost differential due to site monitoring strategy

(based on 20,000 patients treated for 4 years)



THE ENDANGERED SPECIES

"The very research method, the RCT, that has been at the heart of evidence based medicine and has contributed substantially to saving millions of lives every year is in danger of being crushed under the burden a plethora of well intentioned guidelines, regulations & process (or their implementation) for which there is scant evidence of their value, but much evidence of their harm."

How do we come up with sensible and efficient approaches?

- To protect the rights of participants?
- To ensure the reliability and validity of the trial results(not individual data points)?

Using an approach that does not stifle clinical research (both non-commercial and commercial)?

Should we have a risk based approach?