Thoughts on informed consent.

Prof Marc Blockman
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Country income groups (World Bank classification)

2012:

LIC = 12.1% of the global population

LIC and LMIC = in excess of 40% of the global population

http://www.worldbank.org/
“Over 80% of the global disease burden occurs in developing countries. Yet the proportion of research conducted in these countries is less than 10% of the global research activity”

Prof. Salim Yusuf
McMaster University; Hamilton; Ontario; Canada

Benefits of clinical studies for the participants?

✓ Access to more effective treatment than local treatments.
✓ Chance for a cure or prolonging life when other methods have failed.
✓ Contribution to medical research that may help someone else in future.
✓ Access to methods of relieving symptoms not otherwise available.
✓ Access to closer and more frequent follow-up.
✓ Financial benefits (cost of treatment and transport cost)

BUT BEWARE the Therapeutic Misconception
Why studies are needed in low resource countries

- Over 80 per cent of the global burden of all diseases occurs in developing countries
- Differences in patterns of diseases in developed and developing countries
- Differences in environmental factors can affect outcome in certain diseases
- Genetic or ethnic differences between individuals may affect outcome of treatment
- Cost: affordable treatments in developed countries are often unaffordable in developing countries.

Pesce et al NDT 2010
Okpechi et al NDT 2011
Appel et al. JASN 2009; 20: 1103–1112
Opie et al. In Drugs for the Heart. 4th edn, Opie LH (ed.)
Hurdles to clinical studies

1. Lack of social infrastructure
Hurdles to clinical studies

2. Lack of medical infrastructure
Hurdles to clinical studies

3. Lack of medical infrastructure

Hurdles to clinical studies

4. Socio-demographic issues
5. Inadequate numbers of healthcare workers

The sizes of circles reflect the percentage share of the total global health workforce of doctors and nurses.

Hurdles to clinical studies

6. Therefore the vulnerable patient

The vulnerable patient:

- Diminished Capacity
- Economically disadvantaged
- Socially disadvantaged
- Minority groups
- Refugees
Hurdles to clinical studies

7. AND the Burden of disease / disease epidemiology

HIV Prevalence

http://www.worldmapper.org/display.php?selected=227
8. Distrust of the pharmaceutical industry

“Pressure to increase profits has forced the industry to adopt a shameless “profit-over-people” strategy, has deepened distrust in the industry”

Miran Epstein
Lancet 2007, 369: 1859

Pfizer accused of testing new drug without ethical approval

Jacqui Wise London

An official inquiry has been set up into allegations that the drug manufacturer Pfizer did not obtain official approval before investigating the trial and alleges that at least one child was not taken off the experimental drug

Pfizer settles with victims of Nigerian drug trial

Jeanne Lenzer

BMJ 2001; 322: 194
BMJ 2008; 336: 11
BMJ 2011; 343:d5268
Hurdles to clinical studies

9. Ethical challenges

- Institutional review board:
  - (Un)availability
  - Capacity
  - Prolonged peer-review process
- Conflict of interest (for the physician – there for the money)

- Post trial / study care of the patients
  - Further medications
  - Access to the health care worker
  - Access to services provided by the health care worker

- The informed consent process – ability of the patient to understand the informed consent
Quick history of research ethics

- Nuremberg Code
- Declaration of Helsinki
- Public becomes more aware of potential research ethics problems.
  - Jewish Chronic Disease Hospital (liver Ca cells)
  - Henry Beecher 1966 NEJM article
  - Tuskegee study
- Tuskegee Ad Hoc panel convened 1972
The National Commission and *The Belmont Report*

- 1974-1978: National Commission for the Protection of Human Subjects in Behavioral and Biomedical Research
  - produced *Belmont Report*, which defined principles for ethical research
    - Beneficence
    - Respect for persons
    - Justice
Three principles of bioethics (from *The Belmont Report*)

- **Beneficence:**
  - duty to protect the welfare of participants

- **Respect for persons**
  - duty to respect autonomy
  - duty to protect those less than fully autonomous

- **Justice**
  - Duty to distribute benefits and burdens fairly
What is informed consent?

- The process whereby **explicit** information is provided to enable a participant to decide whether or not to have a particular treatment, or to take part in a particular trial
- Must be fully ‘informed’, voluntary, competent and freely given
Informed consent

- Respect for autonomy is vital
- No coercion.
- Consent based on adequate information
Informed consent 2

• Full information re risks and benefits of the trial and all the procedures (including discomfort and injury to be expected)

• Verbal discussion only is problematic:

  – A document can be reviewed by the research ethics committee
Informed consent 3

- Comprehension is as important as the information provided – lay terms & patients’ understanding must be assessed along the way
- Official consent gained when the document is signed, with the researcher & participant retaining a copy
Informed consent 4

- Researchers are obligated to keep the participant updated & answer any questions they might have.
- Participant has the right to drop out at any time during the study.
Evidence and consent forms

Some USA data

- Average reading level > 8th grade (numerous studies)
- 65 approved forms: avg. 15th grade (Hammerschmidt and Keane 1992)
  - Ann Landers column avg 7.7 grade
  - Reader’s Digest avg 9.95 grade readability
- RECs’ own boilerplate often > 8th grade (Paasche-Orlow et al 2003)
Participant Understanding: US data

• Appelbaum: “therapeutic misconception”
  – 69% didn’t know how random assignment had been made
  – 32% thought they were in group best for therapeutic needs
  – 44% did not know some patients who wanted treatment would not get it
  – 39% did not understand MD would not know which treatment they received

• Riecken and Ravich
  – 28% didn’t know they were in study, despite having just signed consent form
Interventions to consent forms can improve understanding

- **Shortening form** (Epstein 1969)
  - Overall comprehension: 67% vs. 35%

- **Lowering readability level** (Young 1990)
  - Purpose: 77% vs. 44%; Side effects: 72% vs. 58%

- **More sections, headings, lay language** (Bjorn 1999)

- **Corrected feedback or verbalization**
  - Quiz and correct wrong answers (Taub 1984)
  - Verbalization of surgical risks (Wadey 1997)
Elements of informed consent

• Disclosure
• Understanding
• Voluntariness
• Capacity (competence)
Thank you