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Science at the heart of medicine

The Future of the Declaration of Helsinki

Maintaining a leadership role in global health research ethics

Ruth Macklin, PhD

What will the future be?

- No crystal ball to guide predictions

- Ethics deals with what *should* be, not what *will* be the case

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What *should* the DoH be?

- DoH has stood the test of time since its first skeletal version in 1964 through many revisions and amendments in almost 50 years
- DoH should remain relevant to changing social circumstances and scientific advances
- DoH should be leading the way toward global justice in health research

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DoH 2008 and “standards”

- “Medical research is subject to ethical standards that promote respect for all human subjects and protect their health and rights” (Paragraph 9)
  - Noble statement but does not give specific guidance
  - If the statement were amended to read **equal** respect for all human subjects, it could be interpreted to endorse a single global ethical standard

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DoH 2008 and “standards”

- Physicians should consider the ethical, legal and regulatory norms and standards for research involving human subjects in their own countries as well as applicable international norms and standards (Paragraph 10)
  - What follows from exhorting physicians to “consider” the norms and standards?
    - Anyone may “consider,” then reject norms
  - Insufficient clarity to determine whether the Declaration calls for a single international standard or can permit “double” standards

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"Our standards are very high. We even have high double standards."

International standard: CIOMS guideline

- In externally sponsored research "…the ethical standards applied should be no less stringent than they would be for research carried out in [the sponsoring] country"
  - Guideline 3, Ethical Review of Externally Sponsored Research
  - > Still not enough clarity on what constitutes "standards"
  - > But requires standards in developing countries to be equal or equivalent to those in industrialized countries

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Recent revisions of the DoH

- Weakened in some respects

- Strengthened in other respects

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2000-2002 statement on post-trial obligations

- At the conclusion of the study, every patient entered into the study should be assured of access to the best proven prophylactic, diagnostic and therapeutic methods identified by the study.

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Weakening the DoH: 2008

- At the conclusion of the study, patients entered into the study are entitled to be informed about the outcome of the study and to share any benefits that result from it, for example, access to interventions identified as beneficial in the study or to other appropriate care or benefits (Para. 33)
  - No clear obligation to provide beneficial interventions
  - What other care is appropriate?
  - What other benefits are appropriate?
  - Who is under an obligation to share the benefits?
  - Who should decide?

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2002 paragraph on control groups

- A placebo-controlled trial may be ethically acceptable, even if proven therapy is available, under the following circumstances:
  - Where for compelling and scientifically sound methodological reasons its use is necessary to determine the efficacy or safety of a prophylactic, diagnostic or therapeutic method; **OR**
  - Where a prophylactic, diagnostic or therapeutic method is being investigated for a minor condition and the patients who receive placebo will not be subject to any additional risk of serious or irreversible harm.

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Strengthening the DoH: 2008

- The benefits, risks, burdens and effectiveness of a new intervention must be tested against those of the best current proven intervention, except in the following circumstances:
  - The use of placebo, or no treatment, is acceptable in studies where no current proven intervention exists; or
  - Where for compelling and scientifically sound methodological reasons the use of placebo is necessary to determine the efficacy or safety of an intervention **and** the patients who receive placebo or no treatment will not be subject to any risk of serious or irreversible harm. Extreme care must be taken to avoid abuse of this option

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The way forward

- What's missing from the current DoH?
  - A paragraph addressing women in biomedical research
    - Other leading international ethical guidance address women
      - CIOMS International Ethical Guidelines
      - UNAIDS/WHO Guidance Document
  - Community participation
    - Community engagement before, during, and after research concludes
      - UNAIDS/WHO Guidance Document

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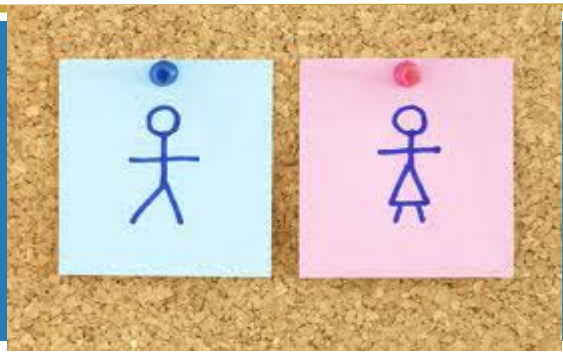
Women in research



- Long history of excluding women from biomedical research
- Current restrictions still exclude pregnant women from most research not directed at pregnancy
- Potentially relevant paragraph in DoH
  - Paragraph 5: Medical progress is based on research that ultimately must include studies involving human subjects. Populations that are under-represented in medical research should be provided appropriate access to participation in research

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Example: CIOMS Guidelines 16 & 17

- Guideline 16 Women as research subjects
  - Investigators, sponsors or ethical review committees should not exclude women of reproductive age from biomedical research. The potential for becoming pregnant during a study should not, in itself, be used as a reason for precluding or limiting participation….
- Guideline 17 Pregnant women
  - Pregnant women should be presumed to be eligible for participation in biomedical research….

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Community engagement

- Current paragraph addressing communities
  - 18. Every medical research study involving human subjects must be preceded by careful assessment of predictable risks and burdens to the individuals and communities involved in the research in comparison with foreseeable benefits to them and to other individuals or communities affected by the condition under investigation.
- What more is needed?

Example: UNAIDS/WHO Guidance document

- Community Participation: Guidance Point 2
  - To ensure the ethical and scientific quality and outcome of proposed research, its relevance to the affected community, and its acceptance by the affected community, researchers and trial sponsors should consult communities through a transparent and meaningful participatory process which involves them in an early and sustained manner in the design, development, implementation, monitoring, and distribution of results of biomedical HIV prevention trials
    - This provision need not apply only to HIV prevention trials

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Conclusion

- The US FDA abandoned adherence to the DoH for foreign studies
  - The rest of the world still looks to the DoH as the leading ethical guidance for research
- The World Health Organization's Ethics Review Committee is guided in its work by the Declaration of Helsinki
- To remain timely and relevant, the Declaration of Helsinki should remain at the forefront of international ethical guidance for research involving human beings

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Global Justice in Health Research

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