Ethical issues in international medical research

Danielle Bromwich
Department of Philosophy
University of Massachusetts, Boston
danielle.bromwich@umb.edu

Overview

The ethical issues that arise when research is conducted in resource poor settings and for the benefit of resource poor populations

Brief introduction

Hello! I'm Danielle

- Philosopher
  - PhD from the University of Toronto
- Bioethicist
  - Post-doc in the Clinical Center at the National Institutes of Health
  - Visiting researcher at the Brocher Foundation in Geneva
- Assistant Professor of Philosophy at UMB
  - Phil 222 (Moral Issues in Medicine) and Phil 337 (The Ethics of Human Subjects Research)

Medical research ethics

Medical research ethics

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  - It is not designed to benefit individual research participants
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Ethics of study design

1.
   - Equipoise exists when there is genuine uncertainty among the scientific community about the superior treatment

2.
   - Members of the control group ought to be given the current standard of care for the condition being studied

Ideal vs. non-ideal conditions

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   - For example, the standard of care issue

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   is permissible?
   - Does reinterpreting our ethical requirements add to the injustice?
   - Or is it ethically appropriate given the well-meaning goals of the research?

Data from UNAIDS

HIV infections and AIDs-related deaths in sub-Saharan Africa

HIV and AIDs in sub-Saharan Africa

- Most heavily affected region of the global epidemic
   - People living with HIV (2011)
      -
      -
   - Pregnant women with HIV (2011)
      -
   - Children who acquire HIV (2011)
      - 90% reside in sub-Saharan Africa

HIV infections & AIDs-related deaths

- HIV infection in sub-Saharan Africa
   - 1.8 million in 2011
   - 25 % decline since 2001 (2.4 million)
- AIDs-related deaths in sub-Saharan Africa
   - 1.2 million in 2011
   - 32% decline since 2005 (1.8. million)
- The results of the medical research and coverage

Perinatal HIV transmission

- Coverage in sub-Saharan Africa
   - 59% coverage of perinatal transmission prevention services
- 6 countries achieved coverage of more than 75%
   - Botswana, Ghana, Namibia, South Africa, Swaziland and Zambia
- 7 countries reported coverage of less than 25%
   - Congo, Eritrea, Ethiopia, Nigeria and South Sudan

History

Perinatal HIV transmission and trials in South Africa

Perinatal HIV transmission

- Mid-1990s
  - Approximately 1,000 HIV-infected babies were born every day in Africa
- 1998
  - Women in sub-Saharan Africa "infected through heterosexual sex, are the fastest growing group with HIV infection, and infected women are the principle source of infected children" Grady, "Science in the Service of Healing" *Hasting Center Report* 1998: 35

Breakthrough HIV research (1994)

- AZT regime (076 regime) shown to reduce perinatal HIV transmission by 70% (from a baseline rate of 25% to 8%)
- U.S. Public Health Service recommended that the 076 regime be recognized as the standard care treatment for HIV-infected pregnant women

Can you anticipate the problems with using the AZT regime in sub-Saharan Africa?

Problem 1: cost

- The 076 regime was expensive
  - In 1994, $1,000 per person
- Most HIV-infected pregnant women live in sub-Saharan Africa
  - Countries with annual budgets of approx $10 per person
  - AZT was unaffordable for those who desperately needed it

Problem 2: complexity

- Treatment started in the second trimester
  - Necessary to receive the drug for a minimum of 12 weeks
- Taken orally 5 times a day
- Administered intravenously during labor
- Taken orally 4 times a day, after birth for 6 weeks
- No breastfeeding
- Not practically possible in sub-Saharan Africa
  - Pregnant women often start prenatal care too late for the regime to work
  - Most are home births
  - Most women have no choice but to breastfeed

The WHO's controversial solution

A regime for *these* women

- In 1994, the WHO met to discuss developing an effective and *affordable* regime for these women.
- They proposed conducting randomized controlled trials (RCTs) of shorter and simpler regimes of AZT against placebo controls

The trials

- 16 trials were developed for 11 countries
- 15 were conducted with placebo controls
- 6 of the 15 were sponsored by NIH and the CDC
- 5 were funded by non US governments
- 1 was funded by the Joint United Nations Programme on HIV/ AIDS (UNAIDS)

The controversy

- Public Citizen's Health Research Group researchers wrote letters to the US secretary for DHHS and a commentary in the NEJM
- They were supported by the NEJM editor, Marcia Angell
- The Director of NIH and Director of CDC wrote a reply defending the research

Discussion

The ethics of the WHO solution

Discussion questions

1. treatment for HIV-infected pregnant women?
2. Is there genuine uncertainty among the scientific community about whether AZT is superior to placebo?
3. Given your answers to (1) and (2) what concerns might you have about the WHO's solution?
4. If you're concerned, do you think that these trials should have been stopped?
5. What argument could be made in favor of these trials?
   - to clinical equipoise or standard of care?
6. Do you think that these trials exploited the participants (women in sub-Saharan Africa) or benefitted them?
7. What else would you want built in to the study design to ensure against exploitation?

Ethical points to consider

Additional considerations for ethics review committees who oversee international research

Framework for non-ideal conditions

- Research ethics committees should assume a default of requiring "the worlds best methods"
- But exceptions should be granted for research that satisfies four conditions

1. Scientific necessity
2. Relevance for host community
3. Sufficient host community benefit
4. Subject and host community nonmaleficence

1. Scientific necessity

- There must be a scientific reason for using less than best methods or treatments.
  - What are the chances the trial will answer an important question *for this community*?
  - What are the chances that using the best methods or treatments will provide an answer?

2. Host community relevance

- The interests of the host community must play a role in the ethical review process
- Sometimes research using less than the best methods is the best hope the community has to address serious health needs

3. Sufficient host community benefit

- Research ethics committees should be attentive whether the balance of burdens to benefits is fair
- If the burdens are greater than the benefit, the host community should receive additional benefits
  - For example, developing of clinics or training or health care professionals

4. Subject and host community nonmaleficence

- Research ethics committees should assess whether the research is likely to make
  - The research subjects worse off
    - For example, by offering them something riskier than what is available to them outside the trial
  - The host community worse off
    - For example, by monopolizing healthcare resources needed by the host community more generally

Thank you!