8-2006

Revisiting the Ethics of HIV Prevention Research in Developing Countries

Charles Weijer
The University of Western Ontario, cweijer@uwo.ca

Guy LeBlanc
McMaster University

Revisiting the ethics of HIV prevention research in developing countries

Charles Weijer
University of Western Ontario

Guy LeBlanc
McMaster University

Weijer C, LeBlanc G. Revisiting the ethics of HIV prevention research in developing countries. A background paper prepared for UNAIDS, Geneva. 2005.

Weijer C, LeBlanc GJ. Balm of Gilead: Is the provision of treatment to those who seroconvert in HIV prevention trials a matter of moral obligation or moral negotiation? *Journal of Law, Medicine & Ethics* 2006; Winter: in press.

For reprints: cweijer@uwo.ca

Tenofovir HIV prevention study

- Groups at high-risk of contracting HIV
- Tenofovir versus “placebo”
- HIV risk-reduction counseling, male condoms, treatment for other sexually transmitted infections
- Gilead Sciences, Inc. agrees to provide drug at cost to developing countries
- Controversy erupted over several issues, including the failure of researchers and sponsors to provide life-long ART to research subjects who contract HIV
- Trials in Cambodia, Cameroon, Malawi, Nigeria stopped

Question

In an HIV prevention trial, do researchers and sponsors in fact have a moral obligation to provide life-long ART to research subjects who contract HIV?

Putative bases for a moral obligation

1. Contracting HIV is a research-related injury and compensation must be provided

2. The ethical principle of beneficence requires that we maximize benefits to research subjects

3. Infected research subjects contribute uniquely and reciprocity requires that they receive something in return

4. Equality requires that HIV-infected subjects be treated regardless of their geographical location

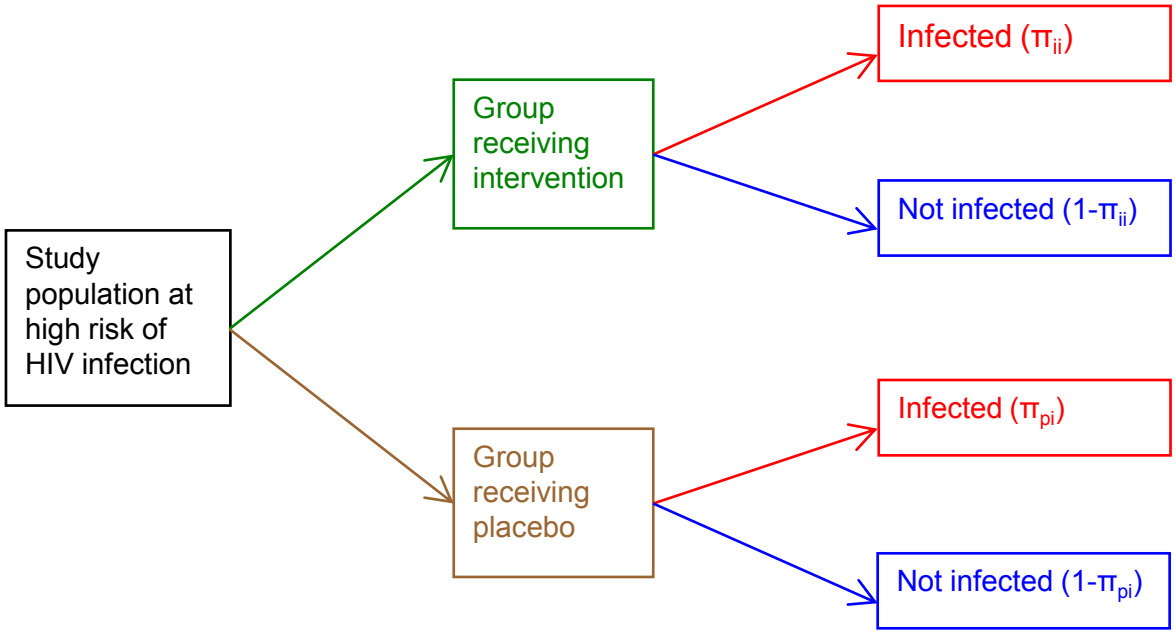
Argument 3: Reciprocity

- The argument from reciprocity
- UNAIDS (2004):
  - “With respect to the principle of *reciprocity*, subjects who become infected contribute importantly to the trial. Without such data, an efficacy trial could draw no conclusions about the intervention studied. People who contribute to this effort deserve something in return.”
- Presumably, this “something in return” is life-long ART

Argument 3: Reciprocity

- Research subjects contribute equally
- Rewarding only those who contract HIV fails to reward all who “contribute to this effort”

- Macklin (2005):
  - “It is certainly true that all research subjects contribute to the success of a trial. However, those who become infected contribute in a unique way. They are the only subjects whose contribution makes it *possible to draw any precise conclusions about the efficacy (or lack thereof) of a preventive vaccine* trial.”



Logic of efficacy

A. Intervention effective *if and only if* $\pi_{pi} > \pi_{ii}$

B. Intervention effective *if and only if* $(1-\pi_{ii}) > (1-\pi_{pi})$

A *is logically equivalent to* B

Argument 3: Reciprocity

- The determination of the efficacy of an intervention rests no more on those who become HIV infected than those who do not
- The *contribution to the determination of efficacy* of those who do and those who do not become infected is equal
- According to the principle of reciprocity, either no group is deserving of reward, or both groups are

- Undermines that claim based on reciprocity that those who contract HIV in the study should receive life-long ART

Question

If the moral basis for the provision of life-long ART to persons who contract HIV in a prevention trial is not moral obligation, then what is it?

Moral negotiation

- Ethical principal of respect for communities (Weijer C, Emanuel EJ. *Science* 2000)
- Community-researcher partnership
- Community should
  - Have input on study question
  - Influence on study design
  - Share in study benefits
- Health priorities and values vary from one community to the next
- Study design and benefit sharing is a matter of *moral negotiation* between community and researcher/sponsor

Moral negotiation

- Community values and health priorities drive what constitutes appropriate benefits
  - Community A: Clean well and a medical clinic to meet the basic health needs of members
  - Community B: Enhanced access to basic HIV treatment for all members
  - Community C: Advanced ART
- To impose a predetermined research question, study design, or benefits package seems paternalistic

Moral negotiation

"[O]nly the host population can determine the value of the benefits for itself. Outsiders are likely to be poorly informed about the health, social, and economic context in which the research is being conducted, and they are unlikely to fully appreciate the importance of the proposed benefits to the population."

Participants in the Conference on Ethical Aspects of Research in Developing Countries (2001)

Learning from tenofovir

- Claims of moral obligation are unsupported currently by sound moral argument

- Moral negotiation
  - Reduces the chance of polarization of positions
  - Allows for middle-ground solutions
  - Allows others to be present at the table
  - Allows for solutions that fit the particular circumstances of the community in question

- Protect and empower communities in research
- Allow much needed research with communities at risk to develop more effective HIV prevention strategies

For reprints: cweijer@uwo.ca

Argument 1: Injury

- Argument from research-related injury
- Contracting HIV in an HIV prevention study is a research related injury and thus compensation, including medical treatment, must be provided
- Research subjects have done their share by participating in research
- When there is serious harm caused by the research it would be unjust for them to shoulder the burden of such harms
- Rather society has an obligation to compensate such individuals and provide them with needed medical care

Argument 1: Injury

- Childress (1976):
  - “(1) The injured party accepts or is compelled to accept a position of risk (‘positional risk’). Objective risks that the injured party would not have otherwise encountered emerge from the position accepted.
  - (2) The activity is for the benefit of society, although any particular individual’s motives may not be to benefit the society...
  - (3) Society, through the government or its agencies, conducts, sponsors, or mandates the practice in question.”

Argument 1: Injury

- *HEW Secretary's Task Force on the Compensation of Injured Research Subjects* (1977):
  - "Harm, disability or death suffered by a subject at risk of biomedical and behavioral research…where such injury is (1) proximately caused by such research, and (2) on balance exceeds that reasonably associated with such illness from which the subject may be suffering, as well as with treatment usually associated with such illness at the time the subject began participation in the research."

Argument 1: Injury

- If a research subject becomes infected due to administration of a vaccine contaminated with HIV or via contaminated needles, then the harm of HIV infection is proximately caused by study participation
- However, in most cases subjects in prevention trials will become infected because of their membership in a high-risk group and not because of trial participation.
- Since trial participation in these cases is not the proximate cause of the harm, there is no research-related injury and no basis for a claim of compensation.

Argument 2: Benefit

- Argument from beneficence
- UNAIDS (2004):
  - "*Beneficence* proposes to maximize benefits and minimize harm to subjects. The obligation to maximize benefits goes beyond the design of a trial and the conduct of a trial itself."
- Providing treatment for HIV maximizes benefit
- Therefore there is a moral obligation to provide it for those who develop the infection during the trial.

Argument 2: Benefit

- An unrestricted moral obligation to “maximize benefits” leads to an unstoppable chain of demands upon researchers:
  - Treating HIV for free is good
  - Building hospitals and staffing them in perpetuity with free doctors and medical supplies is better
  - Making everyone not merely healthy but rich and happy is best of all.
- Right action, according to this view, comes with a hefty price tag.

Argument 2: Benefit

- Macklin (2005):
  - “A principle of health maximization is not intended to lead to an unstoppable chain of claims. Every principle requires interpretation and specifying criteria for its correct—and often limited—application. A full account of what is owed to research subjects and to others in the community or country would have to spell out such criteria and limits.”
- We agree and await just such a specification
- Until that point the argument must be rejected.

Argument 4: Equality

- Argument from equality
- UNAIDS (2004):
  - "*Justice*, as a basis for ethical obligation to provide high standard treatment and care, can be interpreted in a number of ways. Justice as *equality* is based on the notion that subjects in resource-poor countries who become infected are similar in relevant aspects to subjects in industrialized countries and therefore an obligation exists to provide equal treatment to all participants in trials, regardless of their geographical location."

Argument 4: Equality

- One might grant the interpretation as plausible yet deny that researchers or their sponsors have any obligation to provide HIV treatment in developing countries.
- In developed countries, people who become infected during participation in an HIV prevention trial do receive treatment, but that treatment is provided through state or private insurance and not by researchers or sponsors.
- The claim made above is unhelpfully free-floating.

Argument 4: Equality

- Equality does not merely hold across international boundaries; it also holds within states.
- If HIV treatment is generally not available in an undeveloped country, but it is provided to those who become infected in an HIV prevention trial, is this not a violation of equality?
- Slack (2005):
  - “It could be argued that inequalities in access to treatment within a community are as unjust as inequities ‘across the waters’ or between collaborating nations, or at least that it is logically inconsistent to use justice-based arguments to introduce further local inequalities.”