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"Exploitation and Developing Countries: The Ethics of Clinical Research"

Jennifer S. Hawkins and Ezekiel J. Emanuel, editors, 2008, 327 pages, Princeton University Press, $24.95

Review by Norman M. Goldfarb

"Exploitation and Developing Countries: The Ethics of Clinical Research" lays the foundation for a sound ethical framework for conducting clinical trials in the developing world. Given the globalization of clinical research, the importance of this book cannot be overstated.

The book consists of nine chapters:

- Research Ethics, Developing Countries, and Exploitation: A Primer
- Case Studies: The Harvix Trial and the Surfaxin Trial
- Exploitation in Clinical Research
- Testing Our Drugs on the Poor Abroad
- Broadly Utilitarian Theories of Exploitation and Multinational Clinical Research
- Exploitation and the Enterprise of Medical Research
- Exploitation and Placebo Controls
- Addressing Exploitation: Reasonable Availability versus Fair Benefits

The first chapter provides a clear introduction to the topic. The second chapter sets forth two real-world examples, which are employed by the following chapters. The last seven chapters present seven different perspectives on the topic of exploitation in clinical research in developing countries.

Coercing or deceiving people to become study subjects is clearly unethical. The interesting case occurs when the subjects and their community are fully informed, uncoerced and willing to participate. Under these circumstances, does exploitation exist and, if so, is it ethical? In most transactions, each party is exploiting the other party for its own ends, so exploitation, *per se*, is not unethical. What makes certain clinical trials unethical?

For example, imagine you are the benevolent ruler of Ruritania, a very small and very poor country in the developing world. Acme Pharmaceuticals comes to you with the following proposition:

> The company will conduct a trial in your country with 400 neonatal infants. Because the trial is placebo-controlled, 100 Ruritanian infants will die. The alternative is that the trial will be conducted elsewhere, in which case 200 Ruritanian infants will die. Medications currently on the market can save all the infants' lives, but they are too expensive for your country. The trial could employ an active control, but the company, if forced to use an active control, would conduct it in the U.S. for legitimate reasons. If the trial is successful, the new medication will be far too expensive for Ruritanian citizens to afford.

As the benevolent ruler of your country, should you approve this trial? The country of Bolivia had the option to accept a similar trial, for a lung surfactant, and did not approve the

trial. Did it make the right decision? Would it have been ethical for the company to conduct such a trial in Bolivia? Bioethicists wrestle with such questions.

This book provides seven different well-reasoned approaches to answer such questions, about six more than the world would seem to need. However, the book lays the foundation for a synthesis that would be far more nuanced that the Declaration of Helsinki, which is revised every few years in a vain attempt to find a simple black-and-white prescription for a very complex world. The CIOMS International Ethical Guidelines suffer similar limitations. For example, the question for Acme Pharmaceuticals is not whether it is ethical to conduct the trial in Ruritania, but, if it is ethical to conduct a placebo-controlled trial at all, in which country should it conduct the trial? One of the chapters in the book points out that if a worthwhile trial absolutely, positively must be conducted in a developing country, all else being equal, it should be conducted in the country that will be able to afford the new medication the soonest. Numerous other considerations are relevant and specific to each trial.

A fundamental question for Acme Pharmaceuticals is what, if any, obligation it has to the infants in the trial, their parents, and the community — in this case, the other citizens of Ruritania. A persuasive case can be made that it has none whatsoever. Under this reasoning, Acme is ethically free to conduct the trial in Ruritania with no obligations, such as making the drug available to future children of the parents of the dead infants. If Ruritania does not want the trial, Acme can look elsewhere until it finds a country that wants to save the lives of 100 infants. Although this reasoning is logical, at least in a capitalist country, it seems somehow wrong.

At the opposite end of the spectrum, a persuasive case can also be made that Acme has deep obligations to the infants, their parents, and other citizens of Ruritania. Under this reasoning, Acme must conduct an active-control trial in Ruritania with the best treatment available anywhere in the world. Such a trial cannot be conducted in Ruritania, so this reasoning costs the lives of 100 Ruritanian infants. Certainly, there are 100 mothers in Ruritania who would gladly agree to a clinical trial that offers their infants a better chance of survival. Although this reasoning is logical, at least in a socialist country, it seems somehow wrong.

Clearly, a middle way is required, and the book comes to the rescue with two theories. Under the public health theory, when Acme proposes to conduct the trial in Ruritania, it takes on responsibilities for public health that go beyond profit maximization. Under this theory, one question that arises is whether Ruritania is the relevant community, or just an arbitrary geographical entity. When we talk about public health, we need to decide who we mean by “the public.”

Under the Good Samaritan theory, Acme assumes the responsibilities of a Good Samaritan when it conducts the trial in Ruritania. Before the trial, it has no responsibilities to Ruritania, but once it starts the trial, it must make a decent effort to help the infants, their parents, and the other citizens of Ruritania. The Good Samaritan obligation is reinforced because Acme is not just a passer-by, but a beneficiary of the trial. Acme may not be obligated to take measures that double the cost of the trial and jeopardize the survival of the company, but spending, say, an extra 10% does not seem unreasonable under the Good Samaritan theory.

Both of these theories have the advantage (and disadvantage) of requiring in-depth analysis of a given clinical trial in a given location. The resulting ethical answer is thus much more refined than a simple rule can produce. Although extra work is required, both theories certainly support the effort. This book thus lays the groundwork for an ethical framework that is far more sophisticated than the Declaration of Helsinki or CIOMS International Ethical Guidelines.

The book is available in bookstores.

Reviewer

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