

Individual vs. Community Rights in Clinical Research

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Every community consists of a group of individuals who agree to comply with a set of shared compromises between the rights of the community and the rights of its members. These compromises accumulate as the community builds a productive and civil society. If the community always sacrifices the interests of individuals to the collective interest ("the greater good"), the advantages of community membership become questionable and enforcement of rules becomes difficult. On the other hand, if the community always puts the interests of the individuals first, there is no shared community, just a free-for-all. Communities must thus balance the rights of the community vs. the rights of the individual. For example, traffic laws enable members of the community to travel safely through intersections. Members of the U.S. community pay taxes to support shared benefits, such as education, national defense, and parks.

In certain areas, the balance of rights may tend towards the community; in others, towards the individual. Prior to the Nazi war crimes trials and formulation of the Nuremberg Code in 1946, clinical research subjects had few rights, with the physician/investigator taking paternalistic responsibility for balancing individual vs. community rights. Current clinical research ethical principles and regulations strongly favor the rights of the individual. It is now considered highly unethical to exploit an individual for the benefit of the community. However, without participation of individuals as clinical research subjects, there is no testing of new medical treatments, medical progress grinds to a halt, and the entire community suffers. Have we struck the right balance between individual and community rights in clinical research? This article offers the opposing arguments for the reader to weigh.¹

The Argument in Favor of Individual Rights

A founding principle of the United States was freedom of religion – each individual can practice his personal religion without interference by the state, i.e., the community. Another principle was, "no taxation without representation," a fierce objection to the imposition of taxes without giving a voice to the individuals taxed. The U.S. political and justice systems, albeit imperfect, are designed to protect the individual from government oppression.

The Declaration of Independence of the United States, which established the modern world's first democracy, declares life, liberty and the pursuit of happiness to be fundamental, "inalienable" rights of the individual. The document does not qualify these rights with any consideration of community rights. The primacy of individual rights is based on a well-established tradition in Western philosophy. The British philosopher John Lock (1632-1704) promoted these "natural" rights as inherent to the substance of a human being. The German Enlightenment philosopher Immanuel Kant (1724-1804) extended the argument, emphasizing that a moral community necessarily consists of moral individuals, each with the right to make his or her own moral decisions. Their implication is that no individual should bear an unreasonable burden in clinical research, no matter what the benefit to the community.^{2,3}

The course of history is littered with examples of the greater good resulting in disaster for both individuals and the community as a whole. The dominant totalitarian regimes of the twentieth century in Nazi Germany and Communist Russia demonstrate how a dedication to the greater good inevitably corrupts and destroys the community, wreaking havoc on millions of individuals in the process.

The inhuman Nazi “medical experiments” on helpless prisoners show what can happen when the concept of the greater good invades clinical research. The Nazi experiments were an extreme example, but hardly unique. During World War II, extensive unethical medical experiments were conducted in Japan, the United Kingdom, and the United States in support of the war effort. Even after the end of the war and publication of the Nuremberg Code, the United States saw ghastly clinical research experiments – conducted for the greater good – in places such as Willowbrook State School, Holmesburg Prison, and Tuskegee, Alabama.^{4,5} The greater good argument is a slippery slope that time and time again has harmed many people.

The primacy of individual rights protects every member of the community from abuse by clinical investigators who may have the best intentions to advance public health. In 1965, Henry Beecher exposed dozens of unethical clinical trials conducted by respected physicians across the country. The patients of these doctors trusted them to look out for the patients’ best interests, and were betrayed by the doctors’ reliance on physician paternalism. Physicians play a special role in society. Medical science is so complex and rapidly evolving that patients must rely on their physicians for objective advice to protect their most basic human rights: life and health. The entire system of medical care breaks down if patients cannot trust their physicians to place their individual rights first. Human research subject protections must reinforce this relationship by forcing physicians to put the rights of the individual first.

One of the U.S. government’s primary roles is to protect the rights of the individual. Universal voting rights protect individuals from the self-interest, for example, of those who can afford to pay a poll tax. The rule of law protects individuals from abuse by government officials and other powerful people. Anti-discrimination laws protect minorities from majorities. The U.S. Supreme Court recently ruled that the Second Amendment to the Constitution protects the rights of individuals to possess firearms, even though family members are the mostly likely targets.

Restrictions on subject compensation illustrate how we protect individual rights in clinical research. Although there are no explicit regulatory requirements for subject compensation in clinical trials, we set limits to protect the subject’s right of autonomy. If set too high, compensation constitutes exploitation. It would be a grim society indeed if wealthy pharmaceutical companies could buy clinical research subjects in the marketplace of human commerce. Consistent levels of compensation across subjects prevent inequities. However, investigators can use their judgment to adjust subject compensation at their sites.⁶⁻⁸

Equipoise is another good example of how human subject protections have evolved to protect individual rights. Equipoise is the fourth cornerstone of ethical clinical research, along with autonomy, beneficence and justice. Equipoise exists when there is genuine uncertainty as to which treatment arm is better for the subjects. In the absence of equipoise, the preferred treatment should always be used. Conducting a trial in the absence of equipoise thus unjustly jeopardizes the health and welfare of some of the subjects. Equipoise is not just a theoretical concept. It exists in a robust, five-step process to protect each individual subject: First, the study sponsor develops what it believes to be a compliant protocol. Next, one or more ethics committees review the protocol for compliance. Each investigator then evaluates the protocol in general, and then for each subject. Finally, the subject decides if the protocol is acceptable.⁹

The magnificent progress we have made in developing both new medical treatments and human subject protections demonstrates that there is no need to sacrifice individual rights on the altar of community rights.

The Argument in Favor of Community Rights

The English philosopher Thomas Hobbes (1588-1679) advanced the notion of a social contract, whereby the members of a community mutually benefit by meeting their obligations to the community. The French philosopher Jean-Jacques Rousseau (1712-1778) further developed the concept and helped inspire the French revolution. Based on social contract theory,³ the Republic of France improved on the U.S. fundamental rights by adopting, as its motto, the phrase, "liberté, égalité and fraternité." This phrase recognizes the individual's right of liberté (liberty), but in the context of a community. The right of "égalité" (equality) applies to each individual, but is meaningless in the absence of a community. Similarly, the right of fraternité (brotherhood) speaks to the rights of the community: each member has the right to rely on the cooperation of other members. The implication is that the community can expect reasonable cooperation from community members in clinical research.

The United States was founded, not by individuals, but by communities who banded together for their very survival. Freedom of religion was exercised by communities, with scant regard for disbelievers. For example, the Pilgrims classified adherents to their particular form of religion as "saints" and non-believers as "strangers."

The founders of the United States did not object to taxation for the benefit of the community, only to taxation by a distant power that did not share the proceeds equitably with the colonies, each a self-defined community. Today, there is certainly no shortage of taxes in the United States.

While the U.S. justice system includes admirable protections for the individual, it also protects the community with harsh sanctions against criminal and civil actions that harm the community. For example, the United States is one of the few countries in the world with the death penalty, the ultimate expression of community over individual rights. We recognize that the government of every nation, including the United States, may harm the interests of some members of the community to advance the interests of others.

When weighing individual vs. community rights, it is easy to forget that the community consists of individuals. The correct comparison is thus the rights of one individual vs. the rights of many individuals. The false choice of individual vs. community rights misses this essential perspective.

Barbaric medical experiments are a shameful part of our history, but they are history. Modern human subject protections prevent such abominations. Unethical trials are now much less common and usually caused by error and self-delusion, not deliberate intention. The tragic deaths of Jesse Gelsinger (1999) and Ellen Roche (2001) are seared on our consciousness because they are so exceptional. Admittedly, many clinical trials feature less than perfect ethical design and conduct, which serves only to prove the imperfectability of man and the impossibility of perfecting it with laws and regulations. Any significant improvements are likely to come from further impositions of community over individual rights – in this case, limitations on the rights of investigators to conduct trials without adequate expertise or oversight.

The concept that patients place absolute trust in their physicians is obsolete. Respect for authority went out in the 1960s. The age of medical paternalism is long gone. Good riddance to it, because it corrupted the patients' sense of responsibility for their own health. Most people now know that physicians are fallible. Most insurance plans cover second opinions. The media continuously pound the medical profession's reputation. Patients now have the capacity to look out for their own medical interests. Exhaustive medical information is available on the Internet. Patients often arrive at medical appointments with recent medical findings that overworked physicians have not yet discovered. Most patients

trust their physicians but that trust is seasoned with a grain of salt. They also trust their lives to bus drivers and airplane mechanics. The pendulum has clearly swung too far in favor of protecting individual rights. People are dying every day because new treatments are delayed by our obsession with individual rights. The entire system of medical research breaks down if excessive protections for the individual obstruct clinical investigators from conducting life-saving research.

Today's onerous regulations protecting the individual have the negative effect of encouraging clinical investigators to mechanically follow the rules and assume that any behavior not specifically prohibited must be allowed, without consideration of the ethics. The thicket of regulations thus diminishes the investigator's sense of responsibility. For example, when the subject signs the informed consent form, the investigator can say: "You've been warned."

While the rights of the individual cannot be ignored, the U.S. government's primary role is to protect the rights of the community. For example, universal voting rights enable all citizens to vote as a community and share ownership of our government. Given the inevitable flaws of government, that sense of shared ownership is all that stands between us and chaos. The rule of law applies to everyone; it protects the community from individual miscreants, even powerful captains of industry. Class action lawsuits are the embodiment of community rights in our legal system. Anti-discrimination laws are not written for individuals; they protect "classes" (i.e., communities) of people such as minorities. Most U.S. citizens support the government's spending of many billions of taxpayer dollars every year on medical research to promote the public's health. We support government-funded vaccination programs. FDA inspections are an imposition on individual clinical investigators, but we agree on their necessity.

The greater good argument may be a slippery slope, but an infatuation with individual rights is a sticky slope that often mires legitimate clinical research in time-consuming and ultimately self-defeating rules. For example, 15-page informed consent forms may meet the letter of the law, but they are almost useless in practice. In fact, they defeat the objective of informing subjects.

If individual protections haven't delivered yet, there must be a different problem. Today, the real problem is that idealism about individual rights ends up exploiting the subjects. The rules for subject compensation provide a good example. In the same study, some investigators offer compensation of hundreds of dollars while other investigators offer no compensation at all. Such unjust compensation cannot possibly be ethical. Because every subject is different, any one level of payment is wrong for most of them. By treating subjects consistently, we deny their individuality. We pay firefighters, police officers, etc. for the public good, so why not admit to the subjects that clinical research incurs risks for which they deserve fair compensation.

The concept of equipoise is another good example of individual rights gone awry. The first problem with equipoise is that it is, by definition, impossible to meaningfully evaluate the risks and benefits of a drug in development. Only a small fraction of drugs that enter clinical research emerge as marketed products because the risks and benefits are unknown; that is why clinical trials are conducted. The second problem with equipoise is that each subject is a unique individual with unique and unknowable risks and benefits. The third problem is that equipoise is a rationalization that corrupts the integrity of physicians who know very well that equipoise is a myth constructed out of ignorance to discount the real risks borne by the study subjects. By definition, using ignorance to pretend that the risks and benefits are balanced misleads and exploits the subjects.

The fourth problem is that every step in the "robust" equipoise process is flawed: Study sponsors have biased interests and no knowledge of specific subjects. Ethics committees

have limited knowledge of the medical risks and benefits and no knowledge of specific subjects. Most investigators have limited knowledge of the medical risks and benefits, as well as self-serving reasons to enroll a subject that may conflict with the subject's welfare. Study subjects have very little useful knowledge about anything, including their own medical condition.

The most damning problem with equipoise is that it prevents the conduct of legitimate research. Firefighters, police officers, coal miners, and oil field roustabouts all take risks that benefit the community. There is no reason why clinical research subjects, properly informed, cannot accept unbalanced risks as well. The absurdity of equipoise becomes clear when offered the following choice: Would you rather participate in a clinical trial with significant and balanced risks, or a trial with insignificant and unbalanced risks? More attention to community rights and less to individual rights protects us from such absurdities.

Most clinical trials compromise individual rights to some extent. Using ideology-driven rationalizations to deceive and exploit the subjects cannot change that reality. The overgrowth of human subject protections demonstrates that we have gone too far down the road of individual rights. The tighter we squeeze the individual rights Jell-O, the fewer rights to life, liberty and the pursuit of happiness end up in our grasp. The downward trend in FDA drug approvals is no coincidence. It is time to recognize that more attention to the community's rights in clinical research is best for both the community and the individual.

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