

Guinea pigs or good citizens?

Ethical issues in human participant research

Sarah Chan, deputy director of the Institute for Science, Ethics and Innovation, discusses the dilemmas that society must confront when considering the ethical standards governing human participant research



Key words

Biomedical research
Disease
Ethics

Biomedical research promises great advances in our ability to improve human welfare through treating or curing illness and disease. Experiments involving human participants play an important role in the development of new treatments, as well as in basic science. Yet research on humans remains a contentious issue, fraught with ethical questions and concerns.

Lessons from history

The history of human experimentation has been marked by many examples of unethical conduct by researchers, and the abuse of research subjects. Most notorious among these were the experiments carried out by the Nazi regime during the Second World War, in which subjects were forced to undergo tests and treatments that often resulted in suffering, injury or even death. Findings from these experiments have increased knowledge about human physiology and the ability of the human body to survive extreme conditions. However, the horrific abuses and ethical violations perpetrated in pursuit of this knowledge have led some people to suggest that no

matter how useful the information, the moral price of using it is too high. Even if the data could benefit others and save lives today, perhaps we should not use it because of the tainted circumstances in which it was obtained.

Another example of unethical research is the Tuskegee syphilis study, which was carried out in southern USA. From 1932 to 1972, over 600 African-American males were monitored by doctors studying the progression of the disease. The patients were unaware that they were the subjects of research, and some with syphilis were not even told that they had the disease. Including patients in a study without their knowledge or consent may have been ethically questionable, but what followed was worse. At the time the study began, there was no known treatment for the disease. But when an effective treatment was discovered in the 1950s, the patients were not told and were never offered it. Instead, the researchers gave a list of participants' names to local doctors to ensure that they would not receive treatment elsewhere, as this would have affected the study results.

Another example was research in Guatemala during the 1940s, in which prison inmates and psychiatric patients were

deliberately exposed to infection with sexually transmitted diseases. Using prisoners as experimental subjects was common in the mid-twentieth century. These subjects were readily available and easily controlled, and the huge potential for coercion and abuse was overlooked or ignored. It is obvious that these incidents involved serious ethical violations. The question for the scientific community was what could be done to ensure that similar abuses were not repeated.

Ethical principles and guidelines

The focus of modern research ethics is overwhelmingly on protecting research participants from harm that might be inflicted on them in the course of science. The Nuremberg Code of 1948, formulated by the medical profession in the wake of the Nazi experiments, was the first attempt to establish ethical principles governing human participant research. In 1964, the World Medical Association adopted the Declaration of Helsinki — a set of principles and guidelines for medical research involving humans (see Box 1). Many other professional bodies and scientific organisations have issued their own codes or statements on the subject.

These codes of practice share common principles — concern for the welfare of participants, attention to the scientific value of the research, and consideration of possible harm. Central to all is the requirement for **informed consent**. Participation must be voluntary, adequate information about the research must be provided, and participants have the right to refuse to take part or to withdraw at any time. However, we need to be wary of assuming either that the only matter of ethical concern is whether consent is obtained, or that any research without fully informed consent is necessarily unethical.

Power and vulnerability

One reason that codes of research ethics emphasise so much the protection of the research subject is the imbalance of power between the researcher and the participant. Even where participants are fully **competent** and consenting adults, they will be less familiar with the experimental procedures and less knowledgeable about the subject area than the scientist conducting the research.

In addition, some participants may be further disadvantaged by their social or economic status, or by their access to, or capacity for, education. In this case they are classed as **vulnerable**. The Declaration of Helsinki recognises

Box 1 The Declaration of Helsinki

In 1964, the World Medical Association developed the Declaration of Helsinki for the medical community to govern the conduct of medical research involving human participants. It is not legally binding, but it remains highly influential — medical professionals, scientists and policy-makers often refer to its principles in making decisions about ethical issues in research. The Declaration has been regularly updated since its first publication, most recently in 2013. It can be read online at: www.wma.net/en/30publications/10policies/b3



Eva Mozes Kor holding photographs of herself and her twin sister Miriam and Jews being liberated from a concentration camp. Kor and her twin survived Josef Mengele's infamous experiments on twins but her parents and two older sisters died. She is outraged at proposals to study data from Nazi medical records of the experiments and feels 'no one should benefit from brutal crimes'

this and states that 'vulnerable groups and individuals should receive specifically considered protection'.

We cannot assume, however, that simply because research involves participants who are vulnerable, this automatically makes the research unethical. Some studies by their very nature require participation from groups who are in a vulnerable position. Research on terminal disease may involve patients whose desperate hope for a cure colours their judgement. Patients suffering from mental illness or neurological disease that affects mental capacity may lack the ability to understand what is happening to them and make decisions for themselves.

Some infectious diseases are more common and may be more severe in children — for example, chickenpox, measles and whooping cough. For many genetic diseases, such as cystic fibrosis, the major symptoms and pathology develop during childhood years. To study these may require enrolling children in research even when they are unable fully to understand or agree to take part. Yet without this research, finding new therapies is very difficult. Testing drugs for use in children is also important because their bodies often react



Health research carried out in developing countries can be ethically justified if it benefits these countries

differently from those of adults, with the possibility of unexpected and potentially damaging side effects.

Refusing to carry out research with any participants who might be considered vulnerable is, therefore, not an ethical solution. To do so would ignore significant health needs — needs that are often specific to those same disadvantaged populations. To deal with this issue, the Declaration of Helsinki states:

Medical research with a vulnerable group is only justified if the research is responsive to the health needs or priorities of this group and the research cannot be carried out in a non-vulnerable group. In addition, this group should stand to benefit from the knowledge, practices or interventions that result from the research.

Research ethics and global justice

One situation to which the above statement applies is research on people in developing countries. Here, populations are often at a disadvantage in terms of socio-economic status and education, have little access to healthcare, and may be poorly protected by laws and social welfare systems. The majority of research, meanwhile, is driven by the priorities of the developed world. The '10/90 gap' is a phrase used to describe the gross inequities of global health research. 90% of global disease affects the developing world, while only 10% of worldwide research funding goes towards addressing this. If research is carried out on developing world populations for the benefit of the wealthy 10%, the situation is made even worse.

Terms explained

Autonomy An individual's ability to make decisions for themselves about their life and what should happen within it. It is also described as 'self-determination'.

Competent A competent individual must have the necessary capacity to make a decision about consent.

De-identified Enough personal data is removed so that a tissue sample is no longer easily identifiable as coming from a particular patient.

Informed consent Participants should understand what the research involves and voluntarily agree to take part.

Vulnerable People who lack power or are more likely than other people to be exploited or abused.

However, this does not mean that all research carried out in the developing world is unethical. Diseases such as tuberculosis, cholera and malaria are more common in the developing world. Therefore, to address the health needs of these people, it may be necessary to carry out research in these populations. But for this research to be ethically justified, we must ensure that the benefits resulting from the research, such as new therapies, are made widely and fairly available to these populations.

Consent revisited

The requirement for informed consent is supposedly based on the ethical principle of respect for **autonomy**. People should be able to make their own decisions about their lives and what happens to them, including whether or not to participate in research.

A requirement for consent makes sense when participants are being subjected to a medical procedure or intervention solely for the purpose of the research — which may not turn out to be of direct benefit to them. They should be able to decide for themselves whether they want to accept the treatment and any associated risks. We might also argue that seeking consent to include patients in observational studies — where the research involves no additional treatment but merely the collection of data — respects their right to decide what is done with their personal information.

There is a danger, however, that complex and time-consuming consent procedures can delay the delivery of effective medical treatment. For example, in the 'CRASH' trial studies for head injury management, treatment of some seriously injured patients was delayed while consent was sought, whereas under normal emergency procedures they would have received exactly the same treatment immediately (see Box 2). Especially where existing treatments are inadequate, new methods will have to be tried. Adding extra red tape to permit doctors to assess the effectiveness of these methods seems counter-productive for science and medicine.

What about studies that make use of data, or of tissue samples, that have already been collected? The use of stored samples and data may have tremendous value for health research. For example, much of our current understanding of the genetic factors involved in cancer was developed through research on archived tissue samples from patients. Should people retain rights over 'their' samples and information indefinitely, even when these have been **de-identified**? It seems a stretch to say that one's autonomy can extend to something so far removed that it has little or no direct effect on one's life. One might argue that requiring consent in this case gives people a choice about whether they wish to support the research by allowing their samples and data to be included. But if there is no direct risk of harm, if the research in question has truly beneficial potential, if the health and lives of others are at stake, is that a choice we should be allowing them to make?

Human participant research: good or bad?

The advances in medical treatment and biological understanding that have been achieved through biomedical

Box 2 The 'CRASH' trial

The 'CRASH' trial tested the effect of different emergency treatment procedures for head injury. At the time, patients with head injury were often treated with steroids to reduce brain swelling, although there was no evidence to support this treatment. The study eventually showed that steroids had no beneficial effect and the group that received steroid treatment had a higher risk of death than untreated patients. The lengthy ethical approval and consent process that took place to permit a formal study of treatments that would have been carried out in any case meant that these valuable results were delayed, potentially costing lives.

For a more detailed explanation, read Ben Goldacre's post on this subject at:

www.badscience.net/2011/03/when-ethics-committees-kill/

time for a new approach to research ethics. Perhaps we ought to think of humans taking part in research as good citizens contributing to advances in medicine and global scientific development, rather than as guinea pigs.

Further reading/things to do

■ Would you volunteer to take part in research to find out more about a disease if:

- 1 You were suffering from it yourself?
- 2 Someone in your family had the disease?
- 3 Your friend or your neighbour had the disease?

Is it fair that patients, their friends and family should be the ones to volunteer, or should we all take our turn? Maybe taking part in medical research should be like doing jury duty or paying tax. Discuss with your classmates.

■ The new NHS Care data initiative aims to make anonymised health data available for use in research. As with the use of stored tissues, this research could have great public health benefits. Should we be concerned about the use of our health information in this way? Patients will have the choice to opt out of the scheme — what would you do? Read more about it and make up your own mind: www.bbc.co.uk/news/health-25919399

research, including research on humans, have been of great value to humans.

The history of human experimentation has rightly led to concerns for participant safety. However, it has perhaps also produced the mistaken view that research is inherently harmful. While the welfare of participants will always be an important ethical concern, we should also consider the benefits that can be achieved. Protecting us from the possible harms of research may itself be harmful, if it delays or prevents the development of new treatments. Perhaps it is

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