Article

Ethics review boards in South Africa and the need for patient advocacy

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The development of new therapies is a major undertaking with the potential for huge profits. Consequently a large industry associated with running of clinical trials has arisen. Many clinical trials are undertaken in the developing world. This creates some unique ethical dilemmas of which ethicists in developing countries need to take cognisance. Some of the regulations for research in developing countries are less stringent than in First-World countries and infrastructure to police such work is often lacking. Developing-world patients are often less informed about their rights and are less likely to have access to legal support in the event that they feel aggrieved. In many ways the situation in the world of knowledge reflects the situation as seen in that of trade, with the developing world being rich in natural resources but poor in infrastructure. Managing research in the developing world is a delicate balancing act in which the rights of vulnerable communities need to be protected while facilitating research that may provide meaningful knowledge and therapies. In South Africa ethics review boards need to be advocates of patient rights and not mere overseers of research.

The large sums of money invested by drug companies in clinical research have resulted in a veritable research industry. A great deal of this research is undertaken in the developing world, because these countries have a large burden of 'treatment-naïve' patients with chronic diseases who are willing to participate in human trials. However some of the regulations for research in developing countries are less stringent than in First-World countries. Furthermore the infrastructure to police such work is often lacking in the developing world. Developing-world patients are often less informed about their rights and are less likely to have access to legal support in the event that they feel aggrieved. These unspoken issues have resulted in there being a negative perception about clinical drug trials among certain stakeholders in the developing world. Another issue of concern has been political. In many ways the situation in the world of knowledge reflects the situation as seen in that of trade, with the developing world being rich in natural resources but poor in infrastructure. Consequently the relationship is one of extraction. First-World researchers are perceived as moving in and strip-mining the developing world, without benefiting patients or acknowledging the contribution of local scientists. Managing research in the developing world is a delicate balancing act in which the rights of vulnerable communities need to be protected while facilitating valuable research that may provide meaningful knowledge and therapies.

Historical overview

Although human research has always been part of medicine, Nazi doctors created an outcry when their cruel and inhuman experiments became public knowledge.[1-3] In response the court at Nuremberg issued a 10-point declaration about human research that included the absolute need for voluntary consent, a tangible potential benefit, the avoidance of harm or suffering to the participants and the presence of trained and scientifically qualified individuals to supervise the experiment. In 1954 the World Medical Association (WMA) adopted a code for research and in 1964 published the Helsinki Declaration. These declarations and the growing concern for human rights resulted in legislation in many countries which mandated strategies designed to ensure ethical human research. Most of these strategies involved the creation of institutional review boards to oversee the ethics of clinical research. The thalidomide disaster prompted public concern and added impetus to the empowerment of statutory medicine control and regulatory bodies. Drugs could not be marketed without the approval of these bodies. The rise to prominence of the double-blind randomised controlled trial for the testing of new drugs prior to regulatory body approval has meant that a great deal of pressure is placed on institutional ethics boards to make sure that research is approved expeditiously. Drug companies spend huge amounts of money on researching new therapeutic drugs. The potential profits are great. There is a direct conflict of interests in this as drug companies bring tremendous pressure to bear to get their trials approved, but the review boards need to remain true to their mandate which is to protect the participants in trials. This conflict may be particularly acute in developing-world settings.

Ethical research

Numerous academic and non-governmental bodies have attempted to provide guidelines for human research in the modern world. Good clinical practice guidelines are designed to enhance and foster human rights within clinical trials while ensuring that there is safety and efficacy in the proposed new therapy. There are several criteria which are generally regarded as 'making research ethical'.[4] The research must enhance health or knowledge and must be scientifically valid. Subject

selection must be fair and there must be a favourable risk-benefit ratio. All research must be independently reviewed and informed consent is essential for all enrolled subjects. However, in research there remains a direct conflict between the pillars of modern medical ethics. The physician is asking a patient to take part in an experiment which may not directly benefit the individual concerned in the hope that a broader benefit may accrue to society as a whole.[1-3] Furthermore the double-blind randomised placebo control trial involves deception. If we enrol patients in a study we must be particularly vigilant to protect them and their interests. The institutional ethics review board has to protect the rights and look after the interests of research participants under the board's jurisdiction. At the same time the boards do not want to become obstacles to meaningful research. This involves the risk-benefit ratio. Research is essential to generate new knowledge which may hold potential benefit for society. However, it is unacceptable that new knowledge is generated at the expense of the human subjects that participate in it. With the amount of money invested in research, particularly by large pharmaceutical companies, pressure is bought to bear on review boards.[5]

Doing research in the developing world

There are significant inequalities in the modern world and many people in the world today are particularly vulnerable to exploitation. Whether it is peasants selling kidneys, poor women working as prostitutes or children picking fruit, the relationships between people in the developed world and the developing world are not equal. Why should this interest the pharmaceutical companies? The huge populations in the developing world mean that enrolling patients with a particular disease process is much easier than in the developed world. Furthermore there is a greater chance that these patients may actually be treatment-naïve. This may allow for an improved power in the research design as there may be no pre-existing drugs that cloud the response to the new drug being tested. These are legitimate reasons for doing research in the developing world. However, there are other unmentioned features which may make doing research in the developing world more attractive for companies. One of these is the lack of governance in the developing world. Simply put, there are not enough trained and qualified officials to adequately supervise a clinical trial. This means that there will be less regulation to control research and there will be fewer officials capable of enforcing whatever regulations are in place. It is in the nature of all corporations to drive out costs and maximise profits. If this is not accompanied by a firm commitment to ethical behaviour then this may well result in abuse. With regard to pharmaceutical companies in developing countries in particular, the lack of adequate governance and oversight of research means that ethics review boards are in a particularly difficult situation. On the one hand there are huge financial benefits that a region or institution can accrue by taking part in drug-company-sponsored research, but at the same time extremely vulnerable groups will be expected to participate in these trials.

The politics of research

Nothing exists in isolation and we cannot separate the creation of knowledge from the current system of commerce and politics that exists in the world today. A rich and powerful developed world coexists with a poor and disenfranchised developing world. Developing countries remain sources of raw natural resources and cheap labour while the developed countries remain as centres for production and manufacturing. This situation of inequality is often replicated in clinical research. Researchers from well-funded and prestigious institutions will descend on a country, use its local people as research subjects, use its local scientists and administrative staff for support and extract the raw data. These raw data are then exported to the developed country for processing where it is turned into the finished product of a scientific publication or a higher degree. Often the country where the research was conducted receives little in return. The local scientists are not adequately acknowledged, and the funds and profits that result from the successful piece of research remain in the foreign institution. There are cases where First-World researchers exploit local researchers as well, underpaying them for their work while frequently not even giving them part of the intellectual credit. Once approved for general use the high cost of new therapies may mean that trial participants and the indigent population of the developing country where the trial took place are denied future access to any new therapies. Ethics committees and review boards in the developing world need to be sensitive to these concerns.

Money and scientific integrity

Huge amounts of money are involved in modern pharmaceutical research.[6] For this research to be credible it must be done in conjunction with trained and qualified scientists and doctors. This creates a conflict of interests. A doctor is supposed to be committed to the care of the patient and to the development of knowledge. A pharmaceutical company is however not dedicated to the creation of knowledge, but to the pursuit of profit. Over the last two decades there has been an increasing tendency for money to influence the outcome of scientific work. There are many ways in which research may be skewed and data manipulated.[6] These would include direct falsification or fabrication of data, the deliberate faulty design of an experiment, trimming data and leaving out data which do not support a hypothesis.[7-9] Ethics committees need to be vigilant when it comes to these conflicts of interest. Almost all the major conflicts of interest that have arisen over the last 15 years have involved quite significant financial interests. The inherent inequalities in the developing world tend to exacerbate these potential conflicts of interest.

The research agenda

Choosing a field of research is a conscious decision and, once made, it means that resources which could have been used to research another field will be diverted to this new field. It is however important for society, and hence for ethics committees, to help decide where their priorities are in deciding on research. The choice is seldom based on a simple utilitarian calculus of deciding which field of research will promote the most general happiness and well-being. This is because the major motivating factor behind a company choosing a disease of interest is in potential profits. Globally, infective diseases such as tuberculosis and malaria kill more people on a daily basis than any of the so-called diseases of affluence like cancer or cardiovascular disease. Yet very few drug companies are heavily involved in research about malaria or tuberculosis. It would seem that there is not much profit to be made in treating developing world infective diseases. Diseases that affect westerners are much

more likely to be the subject of major research. Once again ethics committees in the developing world must raise this as an issue. Their responsibility is to protect the subjects who will participate and to facilitate research while doing so, but they must be vocal on the issue of what is selected as a suitable topic for research. In some ways ethics boards in the developing world need to adopt an activist role in trying to ensure that the research agenda is not simply reflective of the existing power relationships in the modern world.

The current South African response

South Africa is a developing country and ethicists in South Africa need to be advocates rather than mere overseers of patient rights. In light of these concerns there has been a comprehensive legislative and policy response. In 2001 the National Department of Health (NDOH) published the Health Research Policy document.[10] The Policy provides enabling guidelines for health research in South Africa while protecting the interests of the most vulnerable groups in society. Within the NDOH, The National Directorate: Health Research is responsible for the co-ordination of research and has mandated the establishment of Provincial Health Research Committees (PHRCs). Each PHRC must oversee research at provincial level. The National Health Act of 2003[11] provides a legislative framework for the establishment of a National Ethics Research Council (NERC). The Act states that the NERC must ensure that health research agendas and resources focus on priority health problems. These must be informed by the burden of disease, cost effectiveness of the proposed therapy and capacity to implement the interventions. The health needs of vulnerable groups and communities must be prioritised. At the end of 2005 the NDOH issued a notice that all new clinical trials need to be registered in the South African National Clinical Trials Register.[12] The National Health Research Ethics Council (NHREC) was established in October 2006.[13] This is a central body which advises the NDOH on research ethics and which oversees and accredits local ethics committees. The NHREC is tasked with setting norms, adjudicating disputes and instituting disciplinary measures where appropriate. In 2006 updated Good Clinical Practice Guidelines were published.[14] However despite this strong and progressive policy and legislative response, lack of capacity may bedevil effective implementation. The NDOH has identified several barriers to the establishment and functioning of provincial ethics committees, which need to be addressed. These include financial constraints, lack of political will, lack of expertise and lack of human resources.

Conclusion

Ethics committees and institutional review boards in South Africa have a number of important roles to play. They must ensure that the research being done in their jurisdiction is scientifically valid and respects the principles of Nuremberg and Helsinki. It is important to remember that the participants in the study are often doubly jeopardised by their poverty and by their disease process. As such the responsibilities of an ethics review board are much broader in the South African context than in the developed world. The board must keep in mind the social implications of the proposed research and seek always to prevent and reduce exploitative behaviour. South African ethics boards need to insist that funding and profits derived from research find their way back into the community in which the research was done. They need to be advocates for the most disadvantaged in the study, namely the participants. In South Africa ethics review boards need to play an activist role in human rights advocacy and the promotion of the interests of patients. Although there has been a strong legislative and policy response to these issues in South Africa, resource limitations may serve to hinder implementation.

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